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DESCRIPTION

FIELD OF THE INVENTION

[0001] The present invention relates to antibodies, and antigen-binding fragments thereof, which are specific for protease-activated receptor-2 (PAR-2).

BACKGROUND

[0002] Protease-activated receptors ("PARs") are a family of seven-transmembrane G-protein-coupled receptors. Among seven-transmembrane G-protein-coupled receptors PARs have a unique mode of activation; that is, PARs are activated by proteolytic cleavage at the amino terminus to generate a new N-terminal domain which serves as a "tethered ligand." The tethered ligand interacts with the extracellular loop-2 of the receptor thereby resulting in receptor activation. Currently, there are four known members of the PAR family, designated PAR-1, PAR-2, PAR-3 and PAR-4.

[0003] PAR-2 has also been referred to as "C140." (US 5,874,400). Both human and murine PAR-2 share the protease cleavage domain SKGRSLIG (residues 6-13 of SEQ ID NO:852, and residues 8-15 of SEQ ID NO:856). This sequence is cleaved between the R and S residues by a variety of proteases such as trypsin, as well as by mast cell tryptase, tissue factor/factor VIIa complex and factor Xa, neutrophil proteinase 3 (PR-3), human leukocyte elastase, and proteases originating from pathogenic organisms.

[0004] PAR-2 activity has been implicated in or associated with several diseases and conditions including inflammatory diseases, pain, gastrointestinal conditions, neurological diseases, and cardiovascular disorders (see, e.g., Linder et al., 2000, J. Immunol. 165:6504-6510; Vergnolle et al., 2001, Nature Medicine 7:821-826; Cenac et al., 2007, J. Clin. Investigation 117:636-647; Vergnolle, 2004, British J. Pharmacol. 141:1264-1274; Knight et al., 2001, J. Allergy Clin. Immunol. 108:797-803; Schmidlin et al., 2002, J. Immunol. 169:5315-5321). Antibodies that bind to PAR-2 have the potential to antagonize the activity of PAR-2 *in vivo*. Anti-PAR-2 antibodies are therefore potentially useful for treating and/or ameliorating a variety of disease conditions.

[0005] Antibodies that bind to PAR-2, and certain therapeutic uses thereof, are mentioned in US 5,874,400, US 2007/0237759, WO 2009/005726, and US 2010/0119506. Nonetheless, there remains a need in the art for novel PAR-2 modulating agents, including anti-PAR-2 antibodies, that can be used to treat PAR-2-mediated diseases and conditions.

BRIEF SUMMARY OF THE INVENTION

[0006] The present invention provides human antibodies as defined in the claims that bind to human PAR-2. The antibodies of the invention are useful, *inter alia*, for inhibiting PAR-2-mediated signaling and for treating diseases and disorders caused by or related to PAR-2 activation.

[0007] The present invention includes antibodies which interact with the N-terminal region of PAR-2 and block proteolytic cleavage at the activating PAR-2 protease cleavage site (as defined herein) but do not block proteolytic cleavage at one or more non-activating protease cleavage sites. According to certain embodiments, anti-PAR-2 antibodies which exhibit such proteolytic cleavage blocking properties interact with specific amino acids in the vicinity of the activating PAR-2 protease cleavage site. For example, the present invention provides anti-PAR-2 antibodies with protease cleavage blocking activity and which interact with Val-42 and Asp-43 of human PAR-2 (SEQ ID NO:851), and may further interact with one or more human PAR-2 residues selected from the group consisting of Ser-37, Leu-38, Ile-39, Gly-40, and Gly-44.

[0008] According to some embodiments, the anti-PAR-2 antibodies of the present invention specifically bind to human PAR-2 and monkey PAR-2 but do not bind to at least one member selected from the group consisting of mouse, rat, rabbit, dog and pig PAR-2. The present invention also includes antibodies that are capable of inhibiting or attenuating proteolytic activation of PAR-2 but do not block proteolytic cleavage of PAR-2. Exemplary methods for measuring/assessing an antibody's ability to block PAR-2 cleavage or proteolytic activation are described herein.

[0009] The antibodies of the invention can be full-length (for example, an IgG1 or IgG4 antibody) or may comprise only an antigen-binding portion (for example, a Fab, F(ab')₂ or scFv fragment), and may be modified to affect functionality, e.g., to

eliminate residual effector functions (Reddy et al., 2000, J. Immunol. 164:1925-1933).

[0010] Described herein is an antibody or antigen-binding fragment of an antibody comprising a heavy chain variable region (HCVR) having an amino acid sequence 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, 742, 746, 762, 766, 770, 786, 790, 794, 810, 814, 818, 834, and 838, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. The antibody or antigen-binding portion of an antibody may comprise a HCVR having an amino acid sequence selected from the group consisting of SEQ ID NO: 98, 146, 338, and 714.

[0011] Also described herein is an antibody or antigen-binding fragment of an antibody comprising a light chain variable region (LCVR) having an amino acid sequence selected from the group consisting of SEQ ID NO: 10, 20, 24, 34, 44, 48, 58, 68, 72, 82, 92, 96, 106, 116, 120, 130, 140, 144, 154, 164, 168, 178, 188, 192, 202, 212, 216, 226, 236, 240, 250, 260, 264, 274, 284, 288, 298, 308, 312, 322, 332, 336, 346, 356, 360, 370, 380, 384, 394, 404, 408, 418, 428, 432, 442, 452, 456, 466, 476, 480, 490, 500, 504, 514, 524, 528, 538, 548, 552, 562, 572, 576, 586, 596, 600, 610, 620, 624, 634, 644, 648, 658, 668, 672, 682, 692, 696, 706, 716, 720, 730, 740, 744, 754, 764, 768, 778, 788, 792, 802, 812, 816, 826, 836, and 840, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity. The antibody or antigen-binding portion of an antibody may comprise a LCVR having an amino acid sequence selected from the group consisting of SEQ ID NO: 106, 154, 346, and 692.

[0012] Also described herein is an antibody or antigen-binding fragment thereof comprising a HCVR and LCVR (HCVR/LCVR) sequence pair selected from the group consisting of SEQ ID NO: 2/10, 18/20, 22/24, 26/34, 42/44, 46/48, 50/58, 66/68, 70/72, 74/82, 90/92, 94/96, 98/106, 114/116, 118/120, 122/130, 138/140, 142/144, 146/154, 162/164, 166/168, 170/178, 186/188, 190/192, 194/202, 210/212, 214/216, 218/226, 234/236, 238/240, 242/250, 258/260, 262/264, 266/274, 282/284, 286/288, 290/298, 306/308, 310/312, 314/322, 330/332, 334/336, 338/346, 354/356, 358/360, 362/370, 378/380, 382/384, 386/394, 402/404, 406/408, 410/418, 426/428, 430/432, 434/442, 450/452, 454/456, 458/466, 474/476, 478/480, 482/490, 498/500, 502/504, 506/514, 522/524, 526/528, 530/538, 546/548, 550/552, 554/562, 570/572, 574/576, 578/586, 594/596, 598/600, 602/610, 618/620, 622/624, 626/634, 642/644, 646/648, 650/658, 666/668, 670/672, 674/682, 690/692, 694/696, 698/706, 714/716, 714/692, 718/720, 722/730, 738/740, 742/744, 746/754, 762/764, 766/768, 770/778, 786/788, 790/792, 794/802, 810/812, 814/816, 818/826, 834/836, and 838/840. The antibody or fragment thereof may comprise a HCVR and LCVR selected from the amino acid sequence pairs of SEQ ID NO: 98/106, 146/154, 338/346, and 714/692.

[0013] Also described herein is an antibody or antigen-binding fragment of an antibody comprising a heavy chain CDR3 (HCDR3) domain having an amino acid sequence 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, 728, 752, 776, 800, and 824, 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 having an amino acid sequence selected from the group consisting of SEQ ID NO: 16, 40, 64, 88, 112, 136, 160, 184, 208, 232, 256, 280, 304, 328, 352, 376, 400, 424, 448, 472, 496, 520, 544, 568, 592, 616, 640, 664, 688, 712, 736, 760, 784, 808, and 832, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0014] The antibody or antigen-binding portion of an antibody may comprise a HCDR3/LCDR3 amino acid sequence pair selected from the group consisting of SEQ ID NO: 8/16, 32/40, 56/64, 80/88, 104/112, 128/136, 152/160, 176/184, 200/208, 224/232, 248/256, 272/280, 296/304, 320/328, 344/352, 368/376, 392/400, 416/424, 440/448, 464/472, 488/496, 512/520, 536/544, 560/568, 584/592, 608/616, 632/640, 656/664, 680/688, 704/712, 728/736, 752/760, 776/784, 800/808, and 824/832. The antibody or antigen-binding portion of an antibody may comprise a HCDR3/LCDR3 amino acid sequence pair selected from the group consisting of SEQ ID NO: 104/112, 152/160, 344/352 and 704/712. Non-limiting examples of anti-PAR-2 antibodies having these HCDR3/LCDR3 pairs are the antibodies designated H4H588N, H4H591 N, H4H618N, and H4H581 P, respectively.

[0015] Also described herein is an antibody or fragment thereof further comprising a heavy chain CDR1 (HCDR1) domain having an amino acid sequence 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, 724, 748, 772, 796, and 820, 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 having an amino acid sequence 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, 726, 750, 774, 798, and 822, 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 having an amino acid sequence 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, 732, 756, 780, 804, and 828, 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 having an amino acid sequence 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, 734, 758, 782, 806, and 830, or a substantially similar sequence thereof having at least 90%, at least 95%, at least 98% or at least 99% sequence identity.

[0016] Certain non-limiting, exemplary antibodies and antigen-binding fragments comprise HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 domains, respectively, selected from the group consisting of: (i) SEQ ID NO: 100, 102, 104, 108, 110 and 112 (e.g., H4H588N); (ii) SEQ ID NO: 148, 150, 152, 156, 158 and 160 (e.g., H4H591 N); (iii) SEQ ID NO: 340, 342, 344, 348, 350 and 352 (e.g., H4H618N); and (iv) SEQ ID NO: 700, 702, 704, 708, 710 and 712 (e.g., H4H581 P). The amino acid sequences of these exemplary CDRs are depicted in Figs. 2 and 3.

[0017] Also described herein is an antibody or antigen-binding fragment of an antibody which specifically binds PAR-2, wherein the antibody or fragment comprises the heavy and light chain CDR domains contained within heavy and light chain sequences 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, 714/692, 718/720, 722/730, 738/740, 742/744, 746/754, 762/764, 766/768, 770/778, 786/788, 790/792, 794/802, 810/812, 814/816, 818/826, 834/836, and 838/840. The antibody or fragment may comprise the CDR sequences contained within HCVRs and LCVRs selected from the amino acid sequence pairs of SEQ ID NO: 98/106, 146/154, 338/346, and 714/692. Methods and techniques for identifying CDRs within HCVR and LCVR amino acid sequences are well known in the art and can be used to identify CDRs within the specified HCVR and/or LCVR amino acid sequences disclosed herein. Exemplary conventions that can be used to identify the boundaries of CDRs include, e.g., the Kabat definition, the Chothia definition, and the AbM definition. In general terms, the Kabat definition is based on sequence variability, the Chothia definition is based on the location of the structural loop regions, and the AbM definition is a compromise between the Kabat and Chothia approaches. See, e.g., Kabat, "Sequences of Proteins of Immunological Interest," National Institutes of Health, Bethesda, Md. (1991); Al-Lazikani et al., J. Mol. Biol. 273:927-948 (1997); and Martin et al., Proc. Natl. Acad. Sci. USA 86:9268-9272 (1989). Public databases are also available for identifying CDR sequences within an antibody.

[0018] In another aspect, the invention provides nucleic acid molecules encoding the anti-PAR-2 antibodies or fragments thereof of the invention. Recombinant expression vectors carrying the nucleic acids of the invention, and host cells into which such vectors have been introduced, are also encompassed by the invention, as are methods of producing the antibodies by culturing the host cells under conditions permitting production of the antibodies, and recovering the antibodies produced.

[0019] Described herein is an antibody or fragment thereof comprising a HCVR encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, 17, 21, 25, 41, 45, 49, 65, 69, 73, 89, 93, 97, 113, 117, 121, 137, 141, 145, 161, 165, 169, 185, 189, 193, 209, 213, 217, 233, 237, 241, 257, 261, 265, 281, 285, 289, 305, 309, 313, 329, 333, 337, 353, 357, 361, 377, 381, 385, 401, 405, 409, 425, 429, 433, 449, 453, 457, 473, 477, 481, 497, 501, 505, 521, 525, 529, 545, 549, 553, 569, 573, 577, 593, 597, 601, 617, 621, 625, 641, 645, 649, 665, 669, 673, 689, 693, 697, 713, 717, 721, 737, 741, 745, 761, 765, 769, 785, 789, 793, 809, 813, 817, 833, and 837, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof. The antibody or fragment thereof may comprise a HCVR encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 97, 145, 337, and 713.

[0020] Also described herein is an antibody or fragment thereof comprising a LCVR encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 9, 19, 23, 33, 43, 47, 57, 67, 71, 81, 91, 95, 105, 115, 119, 129, 139, 143, 153, 163, 167, 177, 187, 191, 201, 211, 215, 225, 235, 239, 249, 259, 263, 273, 283, 287, 297, 307, 311, 321, 331, 335, 345, 355, 359, 369, 379, 383, 393, 403, 407, 417, 427, 431, 441, 451, 455, 465, 475, 479, 489, 499, 503, 513, 523, 527, 537, 547, 551, 561, 571, 575, 585, 595, 599, 609, 619, 623, 633, 643, 647, 657, 667, 671, 681, 691, 695, 705, 715, 719, 729, 739, 743, 753, 763, 767, 777, 787, 791, 801, 811, 815, 825, 835, and 839, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof. The antibody or fragment thereof may comprise a LCVR encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 105, 153, 345, and 715.

[0021] Also described herein is an antibody or antigen-binding fragment of an antibody comprising a HCDR3 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 7, 31, 55, 79, 103, 127, 151, 175, 199, 223, 247, 271, 295, 319, 343, 367, 391, 415, 439, 463, 487, 511, 535, 559, 583, 607, 631, 655, 679, 703, 727, 751, 775, 799, and 823, 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, 735, 759, 783, 807, and 831, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof. The antibody or fragment thereof may comprise HCDR3 and LCDR3 sequences encoded by the nucleic acid sequence pairs selected from the group consisting of SEQ ID NO: 103/111, 151/159, 343/351, and 703/711.

[0022] Also described herein is an antibody or fragment thereof which 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, 723, 747, 771, 795, and 819, 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, 725, 749, 773, 797, and 821, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof; a LCDR1 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 11, 35, 59, 83, 107, 131, 155, 179, 203, 227, 251, 275, 299, 323, 347, 371, 395, 419, 443, 467, 491, 515, 539, 563, 587, 611, 635, 659, 683, 707, 731, 755, 779, 803, and 827, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof; and a LCDR2 domain encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 13, 37, 61, 85, 109, 133, 157, 181, 205, 229, 253, 277, 301, 325, 349, 373, 397, 421, 445, 469, 493, 517, 541, 565, 589, 613, 637, 661, 685, 709, 733, 757, 781, 805, 829, or a substantially identical sequence having at least 90%, at least 95%, at least 98%, or at least 99% homology thereof.

[0023] The antibody or fragment thereof may comprise the heavy and light chain CDR sequences encoded by the nucleic acid sequences of SEQ ID NO: 97 and 105; SEQ ID NO: 145 and 153; SEQ ID NO: 337 and 345; or SEQ ID NO: 713 and 715.

[0024] Also described herein is an isolated antibody or antigen-binding fragment of an antibody that specifically binds PAR-2, comprising a HCDR3 and a LCDR3, wherein the HCDR3 comprises an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 - X^9 - X^{10} - X^{11} - X^{12}$ (SEQ ID NO:843) wherein X^1 is Ala or Val, X^2 is Lys, X^3 is Gly or Glu, X^4 is Asp or Gly, X^5 is Phe or Asp, X^6 is Trp or Ser, X^7 is Ser or Gly, X^8 is Gly or Tyr, X^9 is Tyr or Asp, X^{10} is Phe or Leu, X^{11} is Asp or Ala, and X^{12} is Tyr; and the LCDR3 comprises an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 - X^9$ (SEQ ID NO:846) wherein X^1 is Met or Gln, X^2 is Gln, X^3 is Ala or Tyr, X^4 is Thr or Lys, X^5 is Gln, Ser or Ile, X^6 is Phe or Ser, X^7 is Pro, X^8 is Thr or Leu, and X^9 is Thr or absent.

[0025] A more specific isolated antibody or fragment thereof that specifically binds PAR-2 may comprise a HCDR1 sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8$ (SEQ ID NO:841), wherein X^1 is Gly, X^2 is Phe, X^3 is Thr, X^4 is Phe, X^5 is Ser or Arg, X^6 is Ser or Arg, X^7 is Tyr, and X^8 is Gly, Ala or Thr; a HCDR2 sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8$ (SEQ ID NO:842), wherein X^1 is Ile, X^2 is Ser, Gly or Thr, X^3 is Tyr, Gly or Asp, X^4 is Asp, Gly or Ser, X^5 is Gly or Arg, X^6 is Ile, Gly or Ala, X^7 is Asn, Ser, Arg or Gly, and X^8 is Lys, Ala or Thr; a HCDR3 sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 - X^9 - X^{10} - X^{11} - X^{12}$ (SEQ ID NO:843) wherein X^1 is Ala or Val, X^2 is Lys, X^3 is Gly or Glu, X^4 is Asp or Gly, X^5 is Phe or Asp, X^6 is Trp or Ser, X^7 is Ser or Gly, X^8 is Gly or Tyr, X^9 is Tyr or Asp, X^{10} is Phe or Leu, X^{11} is Asp or Ala, and X^{12} is Tyr; a LCDR1 sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 - X^9 - X^{10} - X^{11}$ (SEQ ID NO:844) wherein X^1 is Gln, X^2 is Ser or Gly, X^3 is Leu or Ile, X^4 is Val or Ser, X^5 is His, Asn or Thr, X^6 is Ser, Asn or Tyr, X^7 is Asp or absent; X^8 is Gly or absent, X^9 is Asn or absent, X^{10} is Thr or absent, and X^{11} is Tyr or absent; a LCDR2 sequence of the formula $X^1 - X^2 - X^3$ (SEQ ID NO:845) wherein X^1 is Lys or Ala, X^2 is Ile, Ala or Thr, and X^3 is Ser; and a LCDR3 comprises an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 - X^9$ (SEQ ID NO:846) wherein X^1 is Met or Gln, X^2 is Gln, X^3 is Ala or Tyr, X^4 is Thr or Lys, X^5 is Gln, Ser or Ile, X^6 is Phe or Ser, X^7 is Pro, X^8 is Thr or Leu, and X^9 is Thr or absent.

[0026] The invention encompasses anti-PAR-2 antibodies having a modified glycosylation pattern. In some applications, modification to remove undesirable glycosylation sites may be useful, or an antibody lacking a fucose moiety present on the

oligosaccharide chain, for example, 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).

[0027] In another aspect, the invention provides a pharmaceutical composition as defined in the claims comprising a recombinant human antibody or fragment thereof which specifically binds PAR-2 and a pharmaceutically acceptable carrier. Also described herein is a composition which is a combination of a PAR-2 inhibitor and a second therapeutic agent. The PAR-2 inhibitor may be an antibody or fragment thereof. The second therapeutic agent may be any agent that is advantageously combined with a PAR-2 inhibitor. Exemplary agents that may be advantageously combined with a PAR-2 inhibitor include, without limitation, other agents that inhibit PAR-2 activity (including other antibodies or antigen-binding fragments thereof, peptide inhibitors, small molecule antagonists, etc) and/or agents which interfere with PAR-2 upstream or downstream signaling.

[0028] Also described herein are methods for inhibiting PAR-2 activity using the anti-PAR-2 antibody or antigen-binding portion of an 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 invention provides the isolated human antibody or antigen-binding fragment or the pharmaceutical composition of the invention for use in a method of treating a patient, wherein the patient exhibits one or more symptoms or indicia of a disease or disorder caused by PAR-2 activity, wherein the disease or disorder caused by PAR-2 activity is a disease or disorder selected from the group consisting of pain, pruritus, asthma, rheumatoid arthritis, fibrosis, atopic dermatitis, inflammatory bowel disease, ulcerative colitis, pancreatitis, ulcer, Crohn's disease, cancer, and Netherton's disease. The anti-PAR-2 antibody or antibody fragment of the invention may function to block the interaction between PAR-2 and a protease (*e.g.*, trypsin or trypsin-like serine proteases) or otherwise inhibit protease-mediated activation of PAR-2. Alternatively, or additionally, the anti-PAR-2 antibodies of the invention may interfere with the interaction between the PAR-2 tethered ligand and one or more of the PAR-2 extracellular loops (*see, e.g.*, MacFarlane et al., 2001, Pharmacological Reviews 53:245-282 for a general discussion of PAR-2 proteolytic cleavage and activation). The antibody or antibody fragment may be used alone or in combination with one or more additional therapeutic agents.

[0029] The present invention also includes the use of an anti-PAR-2 antibody or antigen binding portion of an antibody of the invention in the manufacture of a medicament for the treatment of a disease or disorder related to or caused by PAR-2 activity in a patient, as defined in the claims.

[0030] Other embodiments will become apparent from a review of the ensuing detailed description.

BRIEF DESCRIPTION OF THE FIGURES

[0031]

Fig. 1. Sequence comparison table of heavy chain variable regions and CDRs of antibodies H4H581P, H4H588N, H4H591N and H4H618N.

Fig. 2. Sequence comparison table of light chain variable regions and CDRs of antibodies H4H581P, H4H588N, H4H591N and H4H618N.

Fig. 3. The top panel (A) shows C- and N-terminal biotin labeled peptides corresponding to the sequence surrounding the activating PAR-2 protease cleavage site (GTNRSSKGRSLIGKVDGT; SEQ ID NO:852). The protease cleavage sites are designated by number 1 (an upstream, non-activating protease cleavage site) and number 2 (the activating PAR-2 protease cleavage site). The expected sizes of the uncleaved and cleaved fragments are indicated in the top table. The bottom panel (B) shows the fragment sizes that were observed following 0, 5, and 15 minutes of trypsin treatment in the presence of anti-PAR-2 antibodies or negative control.

Fig. 4. The top panel (A) shows the mouse, rat and human peptides corresponding to the sequence surrounding the activating PAR-2 protease cleavage sites (SEQ ID NOs:883, 858 and 852, respectively). The protease cleavage sites are designated by numbers 1 and 2 (upstream, non-activating protease cleavage sites) and number 3 (the activating PAR-2 protease cleavage site). The expected sizes of the uncleaved and cleaved fragments are indicated in the top table. The bottom panel (B) shows the fragment sizes that were observed following 0 and 5 minutes of trypsin treatment in the presence of anti-PAR-2 antibodies or negative control.

Fig. 5. Depiction of alanine scanning epitope mapping results for antibody binding to the sequence surrounding the PAR-2

activating protease cleavage site (SEQ ID NO:852). Open triangles represent protease cleavage sites located upstream from the activating PAR-2 protease cleavage site. The activating PAR-2 protease cleavage site is designated by a closed triangle. The numbers in parentheses indicate the amino acid numbering in the full-length human PAR-2 sequence (SEQ ID NO:851). Numbers in circles under the amino acid residues indicate the percent of T_{1/2} of antibody binding to alanine-scan mutant peptide relative to the T_{1/2} of antibody binding to wild-type peptide, as shown in Tables 24-26 and 28. If duplicate experiments were conducted, the average T_{1/2} percentage is shown in the circle. Black circles with white numbers indicate amino acids that, when changed to alanine, reduce the T_{1/2} of antibody binding to 30% or less of the T_{1/2} of antibody binding to wild-type peptide. Such amino acids are defined herein as residues with which the antibody interacts.

DETAILED DESCRIPTION

[0032] Before the present invention is 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.

[0033] 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. As used herein, the term "about," when used in reference to a particular recited numerical value, means that the value may vary from the recited value by no more than 1%. For example, as used herein, the expression "about 100" includes 99 and 101 and all values in between (e.g., 99.1, 99.2, 99.3, 99.4, etc.).

[0034] Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are now described.

Definitions

[0035] As used herein, the terms "proteinase-activated receptor-2," "protease-activated receptor-2," and "PAR-2," refer to full-length PAR-2 protein. Human PAR-2 is encoded by the nucleic acid sequence shown in SEQ ID NO:850 and has the amino acid sequence of SEQ ID NO:851. Amino acid sequences of PAR-2 molecules from non-human species (e.g., mouse, monkey, rabbit, dog, pig, etc.) are available from public sources.

[0036] The term "PAR-2 fragment," as used herein, means a peptide or polypeptide comprising 4, 5, 6, 7, 8, 9, 10 or more contiguous amino acids located upstream from (*i.e.*, N-terminal to) the activating PAR-2 protease cleavage site (as defined herein below) and/or 4, 5, 6, 7, 8, 9, 10 or more contiguous amino acids located downstream from (*i.e.*, C-terminal to) the activating PAR-2 protease cleavage site. Exemplary PAR-2 fragments are illustrated in Example 2, Table 2 (designated Peptides "A" through "J"; *i.e.*, SEQ ID NOs:852 through 861, respectively).

[0037] The expressions "PAR-2" and "PAR-2 fragment," as used herein refer to the human PAR-2 protein or fragment unless specified as being from a non-human species (e.g., "mouse PAR-2," "mouse PAR-2 fragment," "monkey PAR-2," "monkey PAR-2 fragment," etc.).

[0038] As used in the context of the present disclosure, the expression "activating PAR-2 protease cleavage site" means the junction of residues Arg-36 and Ser-37 of human PAR-2 (SEQ ID NO:851). The activating PAR-2 protease cleavage site is the site which, when cleaved, results in the formation of the PAR-2 tethered ligand in the naturally occurring protein.

[0039] The term "PAR-2 protease," as used herein, means an enzyme which is capable of cleaving a PAR-2 or PAR-2 fragment at the activating PAR-2 protease cleavage site. Exemplary PAR-2 proteases include trypsin, cathepsin G, acrosin, tissue factor VIIa, tissue factor Xa, human airway trypsin-like protease, tryptase, membrane-type serine protease-1 (MT-SP1), TMPRSS2, protease-3, elastase, kallikrein-5, kallikrein-6, kallikrein-14, activated protein C, duodenase, gingipains-R, Der p1, Der p3, Der p9, thermolysin, serravalysin, and *T. dentica* protease.

[0040] The term "antibody," as used herein, is intended to refer to immunoglobulin molecules comprising four polypeptide chains, two heavy (H) chains and two light (L) chains interconnected by disulfide bonds, as well as multimers thereof (e.g., IgM). Each

heavy chain comprises a heavy chain variable region (abbreviated herein as HCVR or V_H) and a heavy chain constant region. The heavy chain constant region comprises three domains, C_H1 , C_H2 and C_H3 . Each light chain comprises a light chain variable region (abbreviated herein as LCVR or V_L) and a light chain constant region. The light chain constant region comprises one domain (C_L1). The V_H and V_L regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDRs), interspersed with regions that are more conserved, termed framework regions (FR). Each V_H and V_L 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. In different embodiments of the invention, the FRs of the anti-Ang-2 antibody (or antigen-binding portion thereof) may be identical to the human germline sequences, or may be naturally or artificially modified. An amino acid consensus sequence may be defined based on a side-by-side analysis of two or more CDRs.

[0041] The term "antibody," as used herein, also includes antigen-binding fragments of full antibody molecules. The terms "antigen-binding portion" of an antibody, "antigen-binding fragment" of an antibody, and the like, as used herein, include any naturally occurring, enzymatically obtainable, synthetic, or genetically engineered polypeptide or glycoprotein that specifically binds an antigen to form a complex. Antigen-binding fragments of an antibody may be derived, e.g., from full antibody molecules using any suitable standard techniques such as proteolytic digestion or recombinant genetic engineering techniques involving the manipulation and expression of DNA encoding antibody variable and optionally constant domains. Such DNA is known and/or is readily available from, e.g., commercial sources, DNA libraries (including, e.g., phage-antibody libraries), or can be synthesized. The DNA may be sequenced and manipulated chemically or by using molecular biology techniques, for example, to arrange one or more variable and/or constant domains into a suitable configuration, or to introduce codons, create cysteine residues, modify, add or delete amino acids, etc.

[0042] Non-limiting examples of antigen-binding fragments include: (i) Fab fragments; (ii) $F(ab')_2$ fragments; (iii) Fd fragments; (iv) Fv fragments; (v) single-chain Fv (scFv) molecules; (vi) dAb fragments; and (vii) minimal recognition units consisting of the amino acid residues that mimic the hypervariable region of an antibody (e.g., an isolated complementarity determining region (CDR)). Other engineered molecules, such as diabodies, triabodies, tetrabodies and minibodies, are also encompassed within the expression "antigen-binding fragment," as used herein.

[0043] An antigen-binding fragment of an antibody will typically comprise at least one variable domain. The variable domain may be of any size or amino acid composition and will generally comprise at least one CDR which is adjacent to or in frame with one or more framework sequences. In antigen-binding fragments having a V_H domain associated with a V_L domain, the V_H and V_L domains may be situated relative to one another in any suitable arrangement. For example, the variable region may be dimeric and contain V_H - V_H , V_H - V_L or V_L - V_L dimers. Alternatively, the antigen-binding fragment of an antibody may contain a monomeric V_H or V_L domain.

[0044] In certain embodiments, an antigen-binding fragment of an antibody may contain at least one variable domain covalently linked to at least one constant domain. Non-limiting, exemplary configurations of variable and constant domains that may be found within an antigen-binding fragment of an antibody of the present invention include: (i) V_H - C_H1 ; (ii) V_H - C_H2 ; (iii) V_H - C_H3 ; (iv) V_H - C_H1 - C_H2 ; (v) V_H - C_H1 - C_H2 - C_H3 ; (vi) V_H - C_H2 - C_H3 ; (vii) V_H - C_L ; (viii) V_L - C_H1 ; (ix) V_L - C_H2 ; (x) V_L - C_H3 ; (xi) V_L - C_H1 - C_H2 ; (xii) V_L - C_H1 - C_H2 - C_H3 ; (xiii) V_L - C_H2 - C_H3 ; and (xiv) V_L - C_L . In any configuration of variable and constant domains, including any of the exemplary configurations listed above, the variable and constant domains may be either directly linked to one another or may be linked by a full or partial hinge or linker region. A hinge region may consist of at least 2 (e.g., 5, 10, 15, 20, 40, 60 or more) amino acids which result in a flexible or semi-flexible linkage between adjacent variable and/or constant domains in a single polypeptide molecule. Moreover, an antigen-binding fragment of an antibody of the present invention may comprise a homo-dimer or hetero-dimer (or other multimer) of any of the variable and constant domain configurations listed above in non-covalent association with one another and/or with one or more monomeric V_H or V_L domain (e.g., by disulfide bond(s)).

[0045] As with full antibody molecules, antigen-binding fragments may be monospecific or multispecific (e.g., bispecific). A multispecific antigen-binding fragment of an antibody will typically comprise at least two different variable domains, wherein each variable domain is capable of specifically binding to a separate antigen or to a different epitope on the same antigen. Any multispecific antibody format, including the exemplary bispecific antibody formats disclosed herein, may be adapted for use in the context of an antigen-binding fragment of an antibody of the present invention using routine techniques available in the art.

[0046] The constant region of an antibody is 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.

[0047] 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 antibodies 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 antibodies in which CDR sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences.

[0048] The term "recombinant human antibody", as used herein, is intended to include all human antibodies that are prepared, expressed, created or isolated by recombinant means, such as antibodies expressed using a recombinant expression vector transfected into a host cell (described further below), antibodies isolated from a recombinant, combinatorial human antibody library (described further below), antibodies isolated from an animal (e.g., a mouse) that is transgenic for human immunoglobulin genes (see e.g., Taylor et al. (1992) Nucl. Acids Res. 20:6287-6295) or antibodies prepared, expressed, created or isolated by any other means that involves splicing of human immunoglobulin gene sequences to other DNA sequences. Such recombinant human antibodies have variable and constant regions derived from human germline immunoglobulin sequences. In certain embodiments, however, such recombinant human antibodies are subjected to *in vitro* mutagenesis (or, when an animal transgenic for human Ig sequences is used, *in vivo* somatic mutagenesis) and thus the amino acid sequences of the VH and VL regions of the recombinant antibodies are sequences that, while derived from and related to human germline VH and VL sequences, may not naturally exist within the human antibody germline repertoire *in vivo*.

[0049] Human antibodies can exist in two forms that are associated with hinge heterogeneity. In one form, an immunoglobulin 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.

[0050] The frequency of appearance of the second form in various intact IgG isotypes is due to, but not limited to, structural differences associated with the hinge region isotype of the antibody. A single amino acid substitution in the hinge region of the human IgG4 hinge can significantly reduce the appearance of the second form (Angal et al. (1993) Molecular Immunology 30:105) to levels typically observed using a human IgG1 hinge. The instant invention encompasses antibodies having one or more mutations in the hinge, CH2 or CH3 region which may be desirable, for example, in production, to improve the yield of the desired antibody form.

[0051] An "isolated antibody," as used herein, means an antibody that has been identified and separated and/or recovered from at least one component of its natural environment. For example, an antibody that has been separated or removed from at least one component of an organism, tissue or cell in which the antibody naturally exists or is naturally produced is an "isolated antibody" for purposes of the present invention. An isolated antibody also includes an antibody *in situ* within a recombinant cell, as well as an antibody that has been subjected to at least one purification or isolation step. According to certain embodiments, an isolated antibody may be substantially free of other cellular material and/or chemicals.

[0052] 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 a dissociation constant of 1×10^{-6} M or less. Methods for determining whether two molecules specifically bind are well known in the art and include, for example, equilibrium dialysis, surface plasmon resonance, and the like. For example, an antibody that "specifically binds" human PAR-2, as used in the context of the present invention, includes antibodies that bind human PAR-2 or portion thereof (e.g., a PAR-2 fragment comprising the activating protease cleavage site) with a K_D of less than about 1000 nM, less than about 500 nM, less than about 300 nM, less than about 200 nM, less than about 100 nM, less than about 90 nM, less than about 80 nM, less than about 70 nM, less than about 60 nM, less than about 50 nM, less than about 40 nM, less than about 30 nM, less than about 20 nM, less than about 10 nM, less than about 5 nM, less than about 4 nM, less than about 3 nM, less than about 2 nM, less than about 1 nM or less than about 0.5 nM, as measured in a surface plasmon resonance assay. (See, e.g., Example 4, herein). An isolated antibody that specifically binds human PAR-2 may, however, have cross-reactivity to other antigens, such as PAR-2 molecules from other species.

[0053] A "neutralizing" or "blocking" antibody, as used herein, is intended to refer to an antibody whose binding to PAR-2: (i) interferes with the interaction between PAR-2 or a PAR-2 fragment and one or more proteases, (ii) prevents cleavage of PAR-2 or a PAR-2 fragment by a PAR-2 protease, (iii) inhibits the interaction between the PAR-2 tethered ligand and a PAR-2 extracellular loop, and/or (iv) results in inhibition of at least one biological function of PAR-2. The inhibition caused by a PAR-2 neutralizing or blocking antibody need not be complete so long as it is detectable using an appropriate assay. Exemplary assays for detecting

PAR-2 inhibition are described herein.

[0054] The fully-human anti-PAR-2 antibodies disclosed herein may comprise one or more amino acid substitutions, insertions and/or deletions in the framework and/or CDR regions of the heavy and light chain variable domains as compared to the corresponding germline sequences. Such mutations can be readily ascertained by comparing the amino acid sequences disclosed herein to germline sequences available from, for example, public antibody sequence databases. The present invention includes antibodies, and antigen-binding fragments thereof, which are derived from any of the amino acid sequences disclosed herein, wherein one or more amino acids within one or more framework and/or CDR regions are back-mutated to the corresponding germline residue(s) or to a conservative amino acid substitution (natural or non-natural) of the corresponding germline residue(s) (such sequence changes are referred to herein as "germline back-mutations"). A person of ordinary skill in the art, starting with the heavy and light chain variable region sequences disclosed herein, can easily produce numerous antibodies and antigen-binding fragments which comprise one or more individual germline back-mutations or combinations thereof. In certain embodiments, all of the framework and/or CDR residues within the V_H and/or V_L domains are mutated back to the germline sequence. In other embodiments, only certain residues are mutated back to the germline sequence, *e.g.*, only the mutated residues found within the first 8 amino acids of FR1 or within the last 8 amino acids of FR4, or only the mutated residues found within CDR1, CDR2 or CDR3. Furthermore, the antibodies of the present invention may contain any combination of two or more germline back-mutations within the framework and/or CDR regions, *i.e.*, wherein certain individual residues are mutated back to the germline sequence while certain other residues that differ from the germline sequence are maintained. Once obtained, antibodies and antigen-binding fragments that contain one or more germline back-mutations can be easily tested for one or more desired property such as, improved binding specificity, increased binding affinity, improved or enhanced antagonistic or agonistic biological properties (as the case may be), reduced immunogenicity, etc. Antibodies and antigen-binding fragments obtained in this general manner are encompassed within the present invention.

[0055] Also described herein are anti-PAR-2 antibodies comprising variants of any of the HCVR, LCVR, and/or CDR amino acid sequences disclosed herein having one or more conservative substitutions. For example, included are anti-PAR-2 antibodies having HCVR, LCVR, and/or CDR amino acid sequences with, *e.g.*, 10 or fewer, 8 or fewer, 6 or fewer, 4 or fewer, etc. conservative amino acid substitutions relative to any of the HCVR, LCVR, and/or CDR amino acid sequences disclosed herein. The antibody may comprise an HCVR having the amino acid sequence of SEQ ID NO:698 with 8 or fewer conservative amino acid substitutions. The antibody may comprise an HCVR having the amino acid sequence of SEQ ID NO:698 with 6 or fewer conservative amino acid substitutions. The antibody may comprise an HCVR having the amino acid sequence of SEQ ID NO:698 with 4 or fewer conservative amino acid substitutions. The antibody may comprise an HCVR having the amino acid sequence of SEQ ID NO:698 with 2 or fewer conservative amino acid substitutions. The antibody may comprise an LCVR having the amino acid sequence of SEQ ID NO:706 with 8 or fewer conservative amino acid substitutions. The antibody may comprise an LCVR having the amino acid sequence of SEQ ID NO:706 with 6 or fewer conservative amino acid substitutions. The antibody may comprise an LCVR having the amino acid sequence of SEQ ID NO:706 with 4 or fewer conservative amino acid substitutions. The antibody may comprise an LCVR having the amino acid sequence of SEQ ID NO:706 with 2 or fewer conservative amino acid substitutions.

[0056] The term "surface plasmon resonance", as used herein, refers to an optical phenomenon that allows for the analysis of real-time interactions by detection of alterations in protein concentrations within a biosensor matrix, for example using the BIAcore™ system (Biacore Life Sciences division of GE Healthcare, Piscataway, NJ).

[0057] The term " K_D ", as used herein, is intended to refer to the equilibrium dissociation constant of a particular antibody-antigen interaction.

[0058] The term "epitope" refers to an antigenic determinant that interacts with a specific antigen binding site in the variable region of an antibody molecule known as a paratope. A single antigen may have more than one epitope. Thus, different antibodies may bind to different areas on an antigen and may have different biological effects. Epitopes may be either conformational or linear. A conformational epitope is produced by spatially juxtaposed amino acids from different segments of the linear polypeptide chain. A linear epitope is one produced by adjacent amino acid residues in a polypeptide chain. In certain circumstance, an epitope may include moieties of saccharides, phosphoryl groups, or sulfonyl groups on the antigen.

[0059] 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 95%, and more preferably at least about 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. A nucleic acid molecule having substantial identity to a reference nucleic acid molecule may, in certain

instances, encode a polypeptide having the same or substantially similar amino acid sequence as the polypeptide encoded by the reference nucleic acid molecule.

[0060] 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 95% sequence identity, even more preferably at least 98% or 99% sequence identity. Preferably, residue positions which are not identical differ by conservative amino acid substitutions. A "conservative amino acid substitution" is one in which an amino acid residue is substituted by another amino acid residue having a side chain (R group) with similar chemical properties (e.g., charge or hydrophobicity). In general, a conservative amino acid substitution will not substantially change the functional properties of a protein. In cases where two or more amino acid sequences differ from each other by conservative substitutions, the percent sequence identity or degree of similarity may be adjusted upwards to correct for the conservative nature of the substitution. Means for making this adjustment are well-known to those of skill in the art. See, e.g., Pearson (1994) *Methods Mol. Biol.* 24: 307-331. 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 chains are cysteine and methionine. Preferred conservative amino acids substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine, glutamate-aspartate, and asparagine-glutamine. Alternatively, a conservative replacement is any change having a positive value in the PAM250 log-likelihood matrix disclosed in Gonnet et al. (1992) *Science* 256: 1443-1445. A "moderately conservative" replacement is any change having a nonnegative value in the PAM250 log-likelihood matrix.

[0061] Sequence similarity for polypeptides, which is also referred to as sequence identity, is typically measured using sequence analysis software. Protein analysis software matches similar sequences using measures of similarity assigned to various substitutions, deletions and other modifications, including conservative amino acid substitutions. For instance, GCG software contains programs such as Gap and Bestfit which can be used with default parameters to determine sequence homology or sequence identity between closely related polypeptides, such as homologous polypeptides from different species of organisms or between a wild type protein and a mutein thereof. See, e.g., GCG Version 6.1. Polypeptide sequences also can be compared using FASTA using default or recommended parameters, a program in GCG Version 6.1. FASTA (e.g., FASTA2 and FASTA3) provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences (Pearson (2000) *supra*). Another preferred algorithm when comparing a sequence of the invention to a database containing a large number of sequences from different organisms is the computer program BLAST, especially BLASTP or TBLASTN, using default parameters. See, e.g., Altschul et al. (1990) *J. Mol. Biol.* 215:403-410 and Altschul et al. (1997) *Nucleic Acids Res.* 25:3389-402.

Preparation of Human Antibodies

[0062] Methods for generating monoclonal antibodies, including fully human monoclonal antibodies are known in the art. Any such known methods can be used in the context of the present invention to make human antibodies that specifically bind to human PAR-2.

[0063] Using VELOCIMUNE™ technology or any other known method for generating monoclonal antibodies, high affinity chimeric antibodies to PAR-2 are initially isolated having a human variable region and a mouse constant region. As in the experimental section below, the antibodies are characterized and selected for desirable characteristics, including affinity, selectivity, epitope, etc. The mouse constant regions are replaced with a desired human constant region to generate the fully human antibody of the invention, for example wild-type or modified IgG1 or IgG4. While the constant region selected may vary according to specific use, high affinity antigen-binding and target specificity characteristics reside in the variable region.

Bioequivalents

[0064] The anti-PAR-2 antibodies and antibody fragments of the present invention encompass proteins having amino acid sequences that vary from those of the described antibodies, but that retain the ability to bind human PAR-2. Such variant antibodies and antibody fragments comprise one or more additions, deletions, or substitutions of amino acids when compared to parent sequence, but exhibit biological activity that is essentially equivalent to that of the described antibodies. Likewise, the anti-PAR-2 antibody-encoding DNA sequences of the present invention encompass sequences that comprise one or more additions, deletions, or substitutions of nucleotides when compared to the disclosed sequence, but that encode an anti-PAR-2 antibody or

antibody fragment that is essentially bioequivalent to an anti-PAR-2 antibody or antibody fragment of the invention. Examples of such variant amino acid and DNA sequences are discussed above.

[0065] Two antigen-binding proteins, or antibodies, are considered bioequivalent if, for example, they are pharmaceutical equivalents or pharmaceutical alternatives whose rate and extent of absorption do not show a significant difference when administered at the same molar dose under similar experimental conditions, either single dose or multiple dose. Some antibodies will be considered equivalents or pharmaceutical alternatives if they are equivalent in the extent of their absorption but not in their rate of absorption and yet may be considered bioequivalent because such differences in the rate of absorption are intentional and are reflected in the labeling, are not essential to the attainment of effective body drug concentrations on, e.g., chronic use, and are considered medically insignificant for the particular drug product studied.

[0066] In one embodiment, two antigen-binding proteins are bioequivalent if there are no clinically meaningful differences in their safety, purity, and potency.

[0067] In one embodiment, two antigen-binding proteins are bioequivalent if a patient can be switched one or more times between the reference product and the biological product without an expected increase in the risk of adverse effects, including a clinically significant change in immunogenicity, or diminished effectiveness, as compared to continued therapy without such switching.

[0068] 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.

[0069] Bioequivalence may be demonstrated by in vivo and in vitro methods. Bioequivalence measures include, e.g., (a) an in vivo test in humans or other mammals, in which the concentration of the antibody or its metabolites is measured in blood, plasma, serum, or other biological fluid as a function of time; (b) an in vitro test that has been correlated with and is reasonably predictive of human in vivo bioavailability data; (c) an in vivo test in humans or other mammals in which the appropriate acute pharmacological effect of the antibody (or its target) is measured as a function of time; and (d) in a well-controlled clinical trial that establishes safety, efficacy, or bioavailability or bioequivalence of an antibody.

[0070] Bioequivalent variants of anti-PAR-2 antibodies of the invention may be constructed by, for example, making various substitutions of residues or sequences or deleting terminal or internal residues or sequences not needed for biological activity. For example, cysteine residues not essential for biological activity can be deleted or replaced with other amino acids to prevent formation of unnecessary or incorrect intramolecular disulfide bridges upon renaturation. In other contexts, bioequivalent antibodies may include anti-PAR-2 antibody variants comprising amino acid changes which modify the glycosylation characteristics of the antibodies, e.g., mutations which eliminate or remove glycosylation.

Biological Characteristics of the Antibodies

[0071] The antibodies of the present invention may function through complement-dependent cytotoxicity (CDC) or antibody-dependent cell-mediated cytotoxicity (ADCC). "Complement-dependent cytotoxicity" (CDC) refers to lysis of antigen-expressing cells by an antibody of the invention in the presence of complement. "Antibody-dependent cell-mediated cytotoxicity" (ADCC) refers to a cell-mediated reaction in which nonspecific cytotoxic cells that express Fc receptors (FcRs) (e.g., Natural Killer (NK) cells, neutrophils, and macrophages) recognize bound antibody on a target cell and thereby lead to lysis of the target cell. CDC and ADCC can be measured using assays that are well known and available in the art. (See, e.g., U.S. 5,500,362 and 5,821,337, and Clynes et al. (1998) Proc. Natl. Acad. Sci. (USA) 95:652-656).

[0072] Alternatively, or additionally, the antibodies of the invention may be therapeutically useful in blocking a PAR-2 interaction or inhibiting receptor component interaction. In the case of the PAR-2 antibodies of the present invention, the antibodies may function by, *inter alia*, blocking or obscuring the activating PAR-2 protease cleavage site. Alternatively, the antibodies of the invention may function by interfering with the interaction between the tethered ligand and one or more extracellular loops (e.g., loop-1, loop-2 and/or loop-3).

[0073] More specifically, the anti-PAR-2 antibodies of the invention may exhibit one or more of the following characteristics: (1) ability to bind to a human PAR-2 or human PAR-2 fragment and to a non-human (e.g., mouse, monkey, rat, rabbit, dog, pig, etc.) PAR-2 or PAR-2 fragment; (2) ability to bind to a human PAR-2 or human PAR-2 fragment but not to a non-human (e.g., mouse, monkey, rat, rabbit, dog, pig, etc.) PAR-2 or PAR-2 fragment; (3) ability to bind to a human PAR-2 or human PAR-2 fragment and

to a monkey PAR-2 or monkey PAR-2 fragment, but not to a mouse, rat, rabbit, dog or pig PAR-2 or PAR-2 fragment; (4) ability to bind to a human PAR-2 or human PAR-2 fragment and to a human PAR-1, PAR-3 or PAR-4 or fragment thereof; (5) ability to bind to a human PAR-2 or human PAR-2 fragment but not to a human PAR-1, PAR-3, or PAR-4 or fragment thereof; (6) ability to bind to a human PAR-2 or human PAR-2 fragment and to a non-human (e.g., mouse, monkey, rat, rabbit, dog, pig, etc.) PAR-1, PAR-3 or PAR-4 or fragment thereof; (7) ability to bind to a human PAR-2 or human PAR-2 fragment but not to a non-human (e.g., mouse, monkey, rat, rabbit, dog, pig, etc.) PAR-1, PAR-3 or PAR-4 or fragment thereof; (8) ability to block proteolytic cleavage of a PAR-2 or a PAR-2 fragment; (9) ability to block proteolytic cleavage of a human PAR-2 or human PAR-2 fragment and a non-human (e.g., mouse, monkey, rat, rabbit, dog, pig, etc.) PAR-2 or PAR-2 fragment; (10) ability to block proteolytic cleavage of a human PAR-2 or human PAR-2 fragment but not a non-human (e.g., mouse, monkey, rat, rabbit, dog, pig, etc.) PAR-2 or PAR-2 fragment; (11) ability to block proteolytic cleavage of a human PAR-2 or human PAR-2 fragment and a human PAR-1, PAR-3 or PAR-4 or fragment thereof; (12) ability to block proteolytic cleavage of a human PAR-2 or human PAR-2 fragment but not a human PAR-1, PAR-3 or PAR-4 or fragment thereof; (13) ability to block proteolytic cleavage of a human PAR-2 or human PAR-2 fragment and a non-human (e.g., mouse, monkey, rat, rabbit, dog, pig, etc.) PAR-1, PAR-3 or PAR-4 or fragment thereof; and/or (14) ability to block proteolytic cleavage of a human PAR-2 or human PAR-2 fragment but not a non-human (e.g., mouse, monkey, rat, rabbit, dog, pig, etc.) PAR-1, PAR-3 or PAR-4 or fragment thereof.

[0074] As used in items (8) - (14) above, the term "proteolytic cleavage" means cleavage of a PAR molecule (PAR-1, PAR-2, PAR-3 or PAR-4) or fragment thereof by a PAR-2 protease or other enzyme that is capable of cleaving PAR-2 at the activating PAR-2 protease cleavage site.

[0075] The N-terminal region of human PAR-2 has at least two "non-activating" protease cleavage sites, *i.e.*, sites that are capable of being cleaved by trypsin but do not result in activation of the receptor. The N-terminal non-activating protease cleavage sites are located: (a) at the junction of residues Arg-31 and Ser-32 of human PAR-2 (SEQ ID NO:851); and (b) at the junction of residues Lys-34 and Gly-35 of human PAR-2 (SEQ ID NO:851). The activating and non-activating cleavage sites at the N-terminus of PAR-2 are illustrated in Fig. 5 (white triangles indicate the non-activating protease cleavage sites and the black triangle indicates the activating PAR-2 protease cleavage site); see also Fig. 4. The present invention includes anti-PAR-2 antibodies that block the activating PAR-2 protease cleavage site but do not block one or both of the non-activating protease cleavage sites. Whether a candidate antibody blocks or does not block a particular protease cleavage site can be determined by a person of ordinary skill in the art using any suitable assay such as the exemplary *in vitro* blocking assays set forth in Example 8 herein. As illustrated in Example 8, the exemplary antibody H4H581 P was shown to block trypsin cleavage at the activating PAR-2 protease cleavage site and at the non-activating protease cleavage site located at the junction of residues Lys-34 and Gly-35 of human PAR-2 (SEQ ID NO:851), but did not block cleavage at the non-activating protease cleavage site located at the junction of residues Arg-31 and Ser-32 of human PAR-2 (SEQ ID NO:851). By contrast, the comparator antibody used in Example 8 blocked cleavage at the activating PAR-2 protease cleavage site and at both non-activating sites. The differential blocking capabilities of these exemplary anti-PAR-2 antibodies most likely reflects differences in the particular regions of the PAR-2 molecule with which these antibodies bind (see, e.g., Example 9 herein).

[0076] As used herein, an antibody "does not bind" to a specified target molecule (e.g., mouse PAR-2, rat PAR-2, rabbit PAR-2, dog PAR-2, pig PAR-2, or fragment thereof) if the antibody, when tested for binding to the target molecule at 25°C in a surface plasmon resonance assay, exhibits a K_D of greater than 500 nM, or if tested for binding to the target molecule at 25°C in an enzyme-linked immunosorbent assay (ELISA) exhibits an EC_{50} of greater than 50 nM, or fails to exhibit any binding in either type of assay or equivalent thereof.

[0077] Certain anti-PAR-2 antibodies of the present invention are able to inhibit or attenuate PAR-2 activation in an *in vitro* cellular assay. A non-limiting, exemplary *in vitro* cellular assay for PAR-2 activation is illustrated in Example 6, herein. In this Example, cells are used which express PAR-2 and harbor a construct comprising NF- κ B fused to a reporter molecule (e.g., luciferase). Briefly, such cells are combined with an anti-PAR-2 antibody, followed by treatment with a PAR-2 protease. Cells that are treated with the protease in the presence of an inhibitory anti-PAR-2 antibody will exhibit significantly less or no reporter signal as compared to cells treated with the protease in the absence of an inhibitory anti-PAR-2 antibody. The concentration of antibody necessary to achieve half-maximal inhibition of reporter signal (IC_{50}) can be calculated using such an assay. The present invention includes inhibitory anti-PAR-2 antibodies that exhibit an IC_{50} of less than 300 nM when tested in an *in vitro* cellular assay for PAR-2 activation as described above. For example, the invention includes anti-PAR-2 antibodies with an IC_{50} of less than 300, 290, 280, 270, 260, 250, 240, 230, 220, 210, 200, 190, 180, 170, 160, 150, 140, 130, 120, 110, 100, 90, 80, 70, 60, 50, 40, 30, 20, 10, 18, 16, 14, 12, 10, 9, 8, 7, 6, 5, 4, 3, 2, or 1 nM when tested in an *in vitro* cellular assay for PAR-2 activation as described above in which the cells are incubated with the antibody for 1 h at 37°C followed by treatment with 20 nM trypsin (or other PAR-2 protease) for 5 h at 37°C.

[0078] The present invention includes anti-PAR-2 antibodies and antigen binding fragments thereof which bind to one or more of the following peptides: Peptide A (GTNRSSKGRSLIGKVDGT, SEQ ID NO:852); Peptide B (SLIGKVDGTSHVTG, SEQ ID NO:853); Peptide C (SLIGKV, SEQ ID NO:854); Peptide D (N-terminal domain of human PAR-2 - mouse IgG, SEQ ID NO:855); Peptide E (LAPGRNNSKGRSLIGRLETQ, SEQ ID NO:856); Peptide F (GTNRSSKGRSLIGRVDGT, SEQ ID NO:857); Peptide G (GPNKGRSLIGRLDTP, SEQ ID NO:858); Peptide H (GTNKTSGRSLIGRNTGS, SEQ ID NO:859); Peptide I (GTNRTSKGRSLIGKTDS, SEQ ID NO:860); Peptide J (GTSRPSKGRSLIGKADNT, SEQ ID NO:861); Peptide K (ATNATLDPRSFLLRNPND, SEQ ID NO:862); Peptide L (DTNNLAKPTLPIKTRGA, SEQ ID NO:863); or Peptide M (ESGSTGGDDSTPSILPAP, SEQ ID NO:864). Additional information regarding these peptides can be found in Example 3 herein. These peptides may contain no additional labels or moieties, or they may contain an N-terminal or C-terminal label or moiety. In one embodiment, the label or moiety is biotin. In a binding assay, the location of a label (if any) may determine the orientation of the peptide relative to the surface upon which the peptide is bound. For example, if a surface is coated with avidin, a peptide containing an N-terminal biotin will be oriented such that the C-terminal portion of the peptide will be distal to the surface.

[0079] With regard to the aforementioned Peptides, the present invention includes anti-PAR-2 antibodies with one or more of the following binding profiles: (1) binding to Peptides A and B, but not binding to Peptide C; (2) binding to Peptides A, B and D, but not binding to Peptide C; (3) binding to Peptides A, B, D and F, but not binding to Peptide C; (4) binding to Peptides A, B, D and F, but not binding to either of Peptides C or E; (5) binding to Peptides A, B and D, but not binding to any of Peptides K, L or M; (6) binding to Peptides A, B and F, but not binding to any of Peptides K, L or M; (7) binding to Peptides A, B, D and F, but not binding to any of Peptides K, L or M; and/or (8) binding to at least three of Peptides A, B, C, D, E, F, G, I and J, but not binding to Peptide H. Other binding profiles of the antibodies of the invention will be evident from the examples herein.

Epitope Mapping and Related Technologies

[0080] To screen for antibodies that bind to a particular epitope (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., NY) can be performed. Other methods include alanine scanning mutants, peptide blots (Reineke, 2004, Methods Mol Biol 248:443-463), or peptide cleavage analysis. In addition, methods such as epitope excision, epitope extraction and chemical modification of antigens can be employed (Tomer, 2000, Protein Science 9:487-496).

[0081] The term "epitope" refers to a site on an antigen to which B and/or T cells respond. B-cell epitopes can be formed both from contiguous amino acids or noncontiguous amino acids juxtaposed by tertiary folding of a protein. Epitopes formed from contiguous amino acids are typically retained on exposure to denaturing solvents, whereas epitopes formed by tertiary folding are typically lost on treatment with denaturing solvents. An epitope typically includes at least 3, and more usually, at least 5 or 8-10 amino acids in a unique spatial conformation.

[0082] 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). Each category may reflect a unique epitope either distinctly different from or partially overlapping with epitope represented by another category. This technology allows rapid filtering of genetically identical antibodies, such that characterization can be focused on genetically distinct antibodies. 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-PAR-2 antibodies of the invention into groups of antibodies binding different epitopes.

[0083] The present invention includes anti-PAR-2 antibodies which bind to an epitope at or near (e.g., within 5, 10, 15 or 20 amino acids of) the activating PAR-2 protease cleavage site. In certain embodiments, the anti-PAR-2 antibodies bind to an epitope located upstream from (i.e., N-terminal to) the activating PAR-2 protease cleavage site. In certain other embodiments of the invention, the anti-PAR-2 antibodies bind to an epitope located downstream from (i.e., C-terminal to) the activating PAR-2 protease cleavage site. In yet other embodiments, the anti-PAR-2 antibodies of the invention may bind an epitope that includes both amino acid sequences located upstream from the activating PAR-2 protease cleavage site and amino acid sequences located downstream from the activating PAR-2 protease cleavage site.

[0084] Alternatively, the anti-PAR-2 antibodies of the invention may, in certain embodiments, bind to an epitope located on one or more extracellular loops of the PAR-2 protein (e.g., extracellular loop 1, extracellular loop 2 and/or extracellular loop 3).

[0085] The present invention includes isolated human antibodies or antigen-binding fragments thereof that interact with certain

amino acid residues located downstream from the activating PAR-2 protease cleavage site. For example, the present invention includes isolated human antibodies or antigen-binding fragments thereof that interact with Val-42 and Asp-43 of human PAR-2 (SEQ ID NO:851). In addition to these two residues, the isolated human antibodies or antigen-binding fragments thereof may also interact with one or more of the following residues located downstream from the activating PAR-2 protease cleavage site: Ser-37, Leu-38, Ile-39, Gly-40 or Gly-44 of human PAR-2 (SEQ ID NO:851). In certain embodiments, the isolated human antibody or antigen binding fragment thereof does not interact with Lys-41 of human PAR-2 (SEQ ID NO:851). For example, the present invention includes isolated human antibodies or antigen-binding fragments thereof that interact with Ser-37, Leu-38, Ile-39, Gly-40, Val-42 and Asp-43 of human PAR-2 (SEQ ID NO:851), and do not interact with Lys-41 of human PAR-2 (SEQ ID NO:851). The experimental procedures illustrated in Example 9 can be used to determine if a candidate anti-PAR-2 antibody "interacts with" or "does not interact with" a particular amino acid residue of PAR-2. For example, if a candidate antibody is tested for binding to a peptide having SEQ ID NO:879 (corresponding to the N-terminal region of PAR-2 wherein Val-42 of PAR-2 is mutated to alanine, see, e.g., Tables 24-28) using the procedure of Example 9, and the $T_{1/2}$ of the antibody is less than 30% the $T_{1/2}$ observed when the candidate antibody is tested for binding to the wild-type peptide (SEQ ID NO:871), then for purposes of the present disclosure, the candidate antibody is deemed to "interact with" the amino acid that was mutated to alanine (in this case, Val-42); that is, binding of the candidate antibody is substantially reduced when the amino acid corresponding to Val-42 is mutated to alanine (such residues are depicted by black circles in Figure 5). On the other hand, if a candidate antibody is tested for binding to a peptide having SEQ ID NO:878 (corresponding to the N-terminal region of PAR-2 wherein Lys-41 of PAR-2 is mutated to alanine, see, e.g., Tables 24-28) using the procedure of Example 9, and the $T_{1/2}$ of the antibody is greater than or equal to 30% the $T_{1/2}$ observed when the candidate antibody is tested for binding to the wild-type peptide (SEQ ID NO:871), then for purposes of the present disclosure, the candidate antibody is deemed to "not interact with" the amino acid that was mutated to alanine (in this case, Lys-41); that is, binding of the candidate antibody is not substantially reduced when the amino acid corresponding to Lys-41 is mutated to alanine (such residues are depicted by white circles in Figure 5).

[0086] Described herein are anti-PAR-2 antibodies that bind to the same epitope as the specific exemplary antibodies H4H581 P or H4H588N. Also described herein are anti-PAR-2 antibodies that cross-compete for binding to PAR-2 or a PAR-2 fragment with any of the specific exemplary antibodies described herein (e.g., H4H581 P, H4H588N, H4H591 N or H4H618N).

[0087] One can easily determine whether an antibody binds to the same epitope as, or competes for binding with, a reference anti-PAR-2 antibody by using routine methods known in the art. For example, to determine if a test antibody binds to the same epitope as a reference anti-PAR-2 antibody described herein, the reference antibody is allowed to bind to a PAR-2 protein or peptide under saturating conditions. Next, the ability of a test antibody to bind to the PAR-2 molecule is assessed. If the test antibody is able to bind to PAR-2 following saturation binding with the reference anti-PAR-2 antibody, it can be concluded that the test antibody binds to a different epitope than the reference anti-PAR-2 antibody. On the other hand, if the test antibody is not able to bind to the PAR-2 molecule following saturation binding with the reference anti-PAR-2 antibody, then the test antibody may bind to the same epitope as the epitope bound by the reference anti-PAR-2 antibody described herein. 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 antibody or if steric blocking (or another phenomenon) is responsible for the lack of observed binding. Experiments of this sort can be performed using ELISA, RIA, Biacore, flow cytometry or any other quantitative or qualitative antibody-binding assay available in the art. In accordance with certain aspects described herein, two antibodies bind to the same (or overlapping) epitope if, e.g., 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 are deemed to bind to the same epitope if essentially all amino acid mutations in the antigen that reduce or eliminate binding of one antibody reduce or eliminate binding of the other. Two antibodies are deemed to have "overlapping epitopes" if only a subset of the amino acid mutations that reduce or eliminate binding of one antibody reduce or eliminate binding of the other.

[0088] To determine if an antibody competes for binding with a reference anti-PAR-2 antibody, the above-described binding methodology is performed in two orientations: In a first orientation, the reference antibody is allowed to bind to a PAR-2 molecule under saturating conditions followed by assessment of binding of the test antibody to the PAR-2 molecule. In a second orientation, the test antibody is allowed to bind to a PAR-2 molecule under saturating conditions followed by assessment of binding of the reference antibody to the PAR-2 molecule. If, in both orientations, only the first (saturating) antibody is capable of binding to the PAR-2 molecule, then it is concluded that the test antibody and the reference antibody compete for binding to PAR-2. 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 same epitope as the reference antibody, but may sterically block binding of the reference antibody by binding an overlapping or adjacent epitope.

Species Selectivity and Species Cross-Reactivity

[0089] According to certain embodiments of the invention, the anti-PAR-2 antibodies bind to human PAR-2 but not to PAR-2 from other species. Alternatively, the anti-PAR-2 antibodies of the invention, in certain embodiments, bind to human PAR-2 and to PAR-2 from one or more non-human species. For example, the anti-PAR-2 antibodies of the invention may bind to human PAR-2 and may bind or not bind, as the case may be, to one or more of mouse, rat, guinea pig, hamster, gerbil, pig, cat, dog, rabbit, goat, sheep, cow, horse, camel, cynomolgous, marmoset, rhesus or chimpanzee PAR-2.

Immunoconjugates

[0090] The invention encompasses anti-PAR-2 monoclonal antibodies conjugated to a therapeutic moiety ("immunoconjugate"), such as a cytotoxin, a chemotherapeutic drug, an immunosuppressant or a radioisotope. Cytotoxic agents include any agent that is detrimental to cells. Examples of suitable cytotoxic agents and chemotherapeutic agents for forming immunoconjugates are known in the art, see for example, WO 05/103081).

Multispecific Antibodies

[0091] The antibodies of the present invention may be monospecific, bi-specific, or multispecific. Multispecific antibodies 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; Kufer et al., 2004, Trends Biotechnol. 22:238-244. The anti-PAR-2 antibodies of the present invention 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 bi-specific or a multispecific antibody with a second binding specificity. For example, the present invention includes bi-specific antibodies wherein one arm of an immunoglobulin is specific for human PAR-2 or a fragment thereof, and the other arm of the immunoglobulin is specific for a second therapeutic target or is conjugated to a therapeutic moiety such as a trypsin inhibitor.

[0092] 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) C_H3 domain and a second Ig C_H3 domain, wherein the first and second Ig C_H3 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 C_H3 domain binds Protein A and the second Ig C_H3 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 C_H3 may further comprise a Y96F modification (by IMGT; Y436F by EU). Further modifications that may be found within the second C_H3 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.

Therapeutic Formulation and Administration

[0093] The invention provides therapeutic compositions comprising the anti-PAR-2 antibodies or antigen-binding fragments thereof of the present invention. The administration of therapeutic compositions in accordance with the invention will be administered with suitable carriers, excipients, and other agents that are incorporated into formulations to provide improved transfer, delivery, tolerance, and the like. A multitude of appropriate formulations can be found in the formulary known to all pharmaceutical chemists: Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, PA. These formulations include, for example, powders, pastes, ointments, jellies, waxes, oils, lipids, lipid (cationic or anionic) containing vesicles (such as LIPOFECTIN™), DNA conjugates, anhydrous absorption pastes, oil-in-water and water-in-oil emulsions, emulsions carbowax (polyethylene glycols of various molecular weights), semi-solid gels, and semi-solid mixtures containing carbowax. See also Powell et al. "Compendium of excipients for parenteral formulations" PDA (1998) J Pharm Sci Technol 52:238-311.

[0094] The dose of antibody may vary depending upon the age and the size of a subject to be administered, target disease, conditions, route of administration, and the like. The preferred dose is typically calculated according to body weight or body

surface area. When an antibody of the present invention is used for treating a condition or disease associated with PAR-2 activity in an adult patient, it may be 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. Effective dosages and schedules for administering PAR-2 antibodies may be determined empirically; for example, patient progress can be monitored by periodic assessment, and the dose adjusted accordingly. Moreover, interspecies scaling of dosages can be performed using well-known methods in the art (e.g., Mordenti et al., 1991, *Pharmaceut. Res.* 8:1351).

[0095] 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.

[0096] A pharmaceutical composition of the present invention can be delivered subcutaneously or intravenously with a standard needle and syringe. In addition, with respect to subcutaneous delivery, a pen delivery device readily has applications in delivering a pharmaceutical composition of the present invention. Such a pen delivery device can be reusable or disposable. A reusable pen delivery device generally utilizes a replaceable cartridge that contains a pharmaceutical composition. Once all of the pharmaceutical composition within the cartridge has been administered and the cartridge is empty, the empty cartridge can readily be discarded and replaced with a new cartridge that contains the pharmaceutical composition. The pen delivery device can then be reused. In a disposable pen delivery device, there is no replaceable cartridge. Rather, the disposable pen delivery device comes prefilled with the pharmaceutical composition held in a reservoir within the device. Once the reservoir is emptied of the pharmaceutical composition, the entire device is discarded.

[0097] Numerous reusable pen and autoinjector delivery devices have applications in the subcutaneous delivery of a pharmaceutical composition of the present invention. Examples include, but are not limited to AUTOPEN™ (Owen Mumford, Inc., Woodstock, UK), DISETRONIC™ pen (Disetronic Medical Systems, Bergdorf, Switzerland), HUMALOG MIX 75/25™ pen, HUMALOG™ pen, HUMALIN 70/30™ pen (Eli Lilly and Co., Indianapolis, IN), NOVOPEN™ I, II and III (Novo Nordisk, Copenhagen, Denmark), NOVOPEN JUNIOR™ (Novo Nordisk, Copenhagen, Denmark), BD™ pen (Becton Dickinson, Franklin Lakes, NJ), OPTIPEN™, OPTIPEN PRO™, OPTIPEN STARLET™, and OPTICLIK™ (sanofi-aventis, Frankfurt, Germany), to name only a few. Examples of disposable pen delivery devices having applications in subcutaneous delivery of a pharmaceutical composition of the present invention include, but are not limited to the SOLOSTAR™ pen (sanofi-aventis), the FLEXPEN™ (Novo Nordisk), and the KWIKPEN™ (Eli Lilly), the SURECLICK™ Autoinjector (Amgen, Thousand Oaks, CA), the PENLET™ (Haselmeier, Stuttgart, Germany), the EPIPEN (Dey, L.P.), and the HUMIRA™ Pen (Abbott Labs, Abbott Park IL), to name only a few.

[0098] 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.), 1974, CRC Pres., Boca Raton, Florida. 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, 1984, in *Medical Applications of Controlled Release*, supra, vol. 2, pp. 115-138). Other controlled release systems are discussed in the review by Langer, 1990, *Science* 249:1527-1533.

[0099] The injectable preparations may include dosage forms for intravenous, subcutaneous, intracutaneous and intramuscular injections, drip infusions, etc. These injectable preparations may be prepared by methods publicly known. For example, the injectable preparations may be prepared, e.g., by dissolving, suspending or emulsifying the antibody or its salt described above in a sterile aqueous medium or an oily medium conventionally used for injections. As the aqueous medium for injections, there are, for example, physiological saline, an isotonic solution containing glucose and other auxiliary agents, etc., which may be used in combination with an appropriate solubilizing agent such as an alcohol (e.g., ethanol), a polyalcohol (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, 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.

[0100] 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.

Therapeutic Uses of the Antibodies

[0101] The antibodies of the invention are useful, *inter alia*, for the treatment, prevention and/or amelioration of any disease or disorder associated with PAR-2 activity, including diseases or disorders associated with the proteolytic activation of PAR-2. Exemplary diseases and disorders that can be treated with the anti-PAR-2 antibodies of the present invention include pain conditions such as nociceptive pain and visceral pain, as well as pain associated with conditions such as inflammation, post-operative incision, neuropathy, bone fracture, burn, osteoporotic fracture, bone cancer, gout, migraine headache, fibromyalgia, etc. The antibodies of the invention may also be used to treat, prevent and/or ameliorate inflammatory conditions such as joint inflammation, airway inflammation (e.g., asthma), skin inflammation, dermatitis (e.g., atopic dermatitis, allergic contact dermatitis, etc.), inflammatory bowel disease (IBD), glomerulonephritis, interstitial cystitis, bladder inflammation, hyperalgesia, rheumatoid arthritis, osteoarthritis, inflammatory arthritis, multiple sclerosis, anti-phospholipid syndrome, alpha-1-antitrypsin deficiency, etc. The antibodies of the present invention may be used to treat fibrotic conditions, including, e.g., scleroderma, biliary cirrhosis, post-transplant fibrosis, renal fibrosis, lung fibrosis, liver fibrosis, pancreatic fibrosis, testicular fibrosis, hypertrophic scarring and cutaneous keloids. In certain embodiments, the antibodies of the invention are useful for the treatment of gastrointestinal conditions (e.g., celiac disease, Crohn's disease, ulcerative colitis, idiopathic gastroparesis, pancreatitis, irritable bowel syndrome (IBS) and ulcers (including gastric and duodenal ulcers)); acute lung injury; acute renal injury; and sepsis. The anti-PAR-2 antibodies of the present invention are also useful for the treatment of pruritus; e.g., dermal/pruritoceptive, neuropathic, neurogenic, and psychogenic itch, as well as pruritus associated with atopic dermatitis, psoriasis, burn scarring (burn-related itch), hypertrophic scarring, keloids, renal failure and hepatic failure. Other therapeutic uses of the anti-PAR-2 antibodies of the present invention include the treatment, prevention and/or amelioration of Alzheimer's disease, Netherton's disease, pathological angiogenesis, chronic urticaria, angioedema, mastocytosis, endometriosis, infertility (e.g., male infertility associated with testicular fibrosis), mast cell-mediated diseases, *Clostridium difficile* Toxin-A induced enteritis, and cancer (e.g., blood cell cancer, brain cancer, breast cancer, colon cancer, head and neck cancer, liver cancer, lung cancer, ovarian cancer, pancreatic cancer, prostate cancer, skin cancer, stomach cancer, etc.).

Combination Therapies

[0102] The present invention relates to therapeutic administration regimens which comprise administering an anti-PAR-2 antibody of the present invention in combination with at least one additional therapeutically active component. Non-limiting examples of such additional therapeutically active components include other PAR-2 antagonists (e.g., anti-PAR-2 antibody or small molecule inhibitor of PAR-2 (e.g., N1-3-methylbutyryl-N4-6-aminohexanoyl-piperazine; ENMD-1068)), cytokine inhibitors (e.g., an interleukin-1 (IL-1) inhibitor (such as rilonacept or anakinra, a small molecule IL-1 antagonist, or an anti-IL-1 antibody); IL-18 inhibitor (such as a small molecule IL-18 antagonist or an anti-IL-18 antibody); IL-4 inhibitor (such as a small molecule IL-4 antagonist, an anti-IL-4 antibody or an anti-IL-4 receptor antibody); IL-6 inhibitor (such as a small molecule IL-6 antagonist, an anti-IL-6 antibody or an anti-IL-6 receptor antibody); antiepileptic drugs (e.g., gabapentin); nerve growth factor (NGF) inhibitors (e.g., a small molecule NGF antagonist or an anti-NGF antibody); low dose cocaine; aspirin; NSAIDs; steroids (e.g., prednisone, methotrexate, etc.); low dose cyclosporine A; tumor necrosis factor (TNF) or TNF receptor inhibitors (e.g., a small molecule TNF or TNFR antagonist or an anti-TNF or TNFR antibody); uric acid synthesis inhibitors (e.g., allopurinol); uric acid excretion promoters (e.g., probenecid, sulfinpyrazone, benzbromarone, etc.); other inflammatory inhibitors (e.g., inhibitors of caspase-1, p38, IKK1/2, CTLA-4lg, etc.); and/or corticosteroids. The additional therapeutically active component(s) may be administered prior to, concurrent with, or after the administration of the anti-PAR-2 antibody of the present invention.

Diagnostic Uses of the Antibodies

[0103] The anti-PAR-2 antibodies of the present invention may also be used to detect and/or measure PAR-2 in a sample, e.g., for diagnostic purposes. For example, an anti-PAR-2 antibody, or fragment thereof, may be used to diagnose a condition or disease characterized by aberrant expression (e.g., over-expression, under-expression, lack of expression, etc.) of PAR-2. Exemplary diagnostic assays for PAR-2 may comprise, e.g., contacting a sample, obtained from a patient, with an anti-PAR-2 antibody of the invention, wherein the anti-PAR-2 antibody is labeled with a detectable label or reporter molecule. Alternatively, an unlabeled anti-PAR-2 antibody can be used in diagnostic applications in combination with a secondary antibody which is itself

detectably labeled. The detectable label or reporter molecule can be a radioisotope, such as ^3H , ^{14}C , ^{32}P , ^{35}S , or ^{125}I , a fluorescent or chemiluminescent moiety such as fluorescein isothiocyanate, or rhodamine; or an enzyme such as alkaline phosphatase, β -galactosidase, horseradish peroxidase, or luciferase. Specific exemplary assays that can be used to detect or measure PAR-2 in a sample include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence-activated cell sorting (FACS).

[0104] Samples that can be used in PAR-2 diagnostic assays include any tissue or fluid sample obtainable from a patient which contains detectable quantities of PAR-2 protein, or fragments thereof, under normal or pathological conditions. Generally, levels of PAR-2 in a particular sample obtained from a healthy patient (*e.g.*, a patient not afflicted with a disease or condition associated with abnormal PAR-2 levels or activity) will be measured to initially establish a baseline, or standard, level of PAR-2. This baseline level of PAR-2 can then be compared against the levels of PAR-2 measured in samples obtained from individuals suspected of having a PAR-2 related disease or condition.

EXAMPLES

[0105] 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 (*e.g.*, amounts, temperature, etc.) but some experimental errors and deviations should be accounted for. Unless indicated otherwise, parts are parts by weight, 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 PAR-2

[0106] An immunogen comprising human PAR-2 peptide having the amino acid sequence GTNRSSKGRSLIGKVDGT (SEQ ID NO:852) was administered directly, with an adjuvant to stimulate the immune response, to a VELOCIMMUNE[®] mouse comprising DNA encoding human Immunoglobulin heavy and kappa light chain variable regions. The antibody immune response was monitored by a PAR-2-specific immunoassay. When a desired immune response was achieved splenocytes were harvested and fused with mouse myeloma cells to preserve their viability and form hybridoma cell lines. The hybridoma cell lines were screened and selected to identify cell lines that produce PAR-2-specific antibodies. Using this technique several anti-PAR-2 chimeric antibodies (*i.e.*, antibodies possessing human variable domains and mouse constant domains) were obtained; exemplary antibodies generated in this manner were designated as follows: H2M588, H2M589, H1M590, H2M591, H1M592, H1M595, H2M609, H2M610, H2M611, H1M612, H1M613, H2M614, H1M615, H1M616, H3M617, H2M618, H1M619, and H3M620.

[0107] Anti-PAR-2 antibodies were also isolated directly from antigen-positive B cells without fusion to myeloma cells, as described in U.S. 2007/0280945A1. Using this method, several fully human anti-PAR-2 antibodies (*i.e.*, antibodies possessing human variable domains and human constant domains) were obtained; exemplary antibodies generated in this manner were designated as follows: H1 H571, H1 H572, H1 H573, H1 H574, H1 H575, H1 H576, H1 H577, H1H578, H1H579, H1H580, H1H581, H1H583, H1H584, H1H585, H1H586, and H1H587.

[0108] The biological properties of the exemplary anti-PAR-2 antibodies generated in accordance with the methods of this Example are described in detail in the Examples set forth below.

Example 2. Heavy and Light Chain Variable Region Amino Acid Sequences

[0109] Table 1 sets forth the heavy and light chain variable region amino acid sequence pairs of selected anti-PAR-2 antibodies and their corresponding antibody identifiers. The N, P and G designations refer to antibodies having heavy and light chains with identical CDR sequences but with sequence variations in regions that fall outside of the CDR sequences (*i.e.*, in the framework regions). Thus, N, P and G variants of a particular antibody have identical CDR sequences within their heavy and light chain variable regions but differ from one another within their framework regions.

Table 1

Name	HCVR/LCVR SEQ ID NOs	Name	HCVR/LCVR SEQ ID NOs	Name	HCVR/LCVR SEQ ID NOs
H1H571N	458/466	H1H571P	474/476	H1H571G	478/480
H1H572N	482/490	H1H572P	498/500	H1H572G	502/504
H1H573N	506/514	H1H573P	522/524	H1H573G	526/528
H1H574N	530/538	H1H574P	546/548	H1H574G	550/552
H1H575N	554/562	H1H575P	570/572	H1H575G	574/576
H1H576N	578/586	H1H576P	594/596	H1H576G	598/600
H1H577N	602/610	H1H577P	618/620	H1H577G	622/624
H1H578N	626/634	H1H578P	642/644	H1H578G	646/648
H1H579N	650/658	H1H579P	666/668	H1H579G	670/672
H1H580N	674/682	H1H580P	690/692	H1H580G	694/696
H1H581N	698/706	H1H581P	714/692	H1H581G	718/720
H1H583N	722/730	H1H583P	738/740	H1H583G	742/744
H1H584N	746/754	H1H584P	762/764	H1H584G	766/768
H1H585N	770/778	H1H585P	786/788	H1H585G	790/792
H1H586N	794/802	H1H586P	810/812	H1H586G	814/816
H1H587N	818/826	H1H587P	834/836	H1H587G	838/840
H2M588N	98/106	H2M588P	114/116	H2M588G	118/120
H2M589N	122/130	H2M589P	138/140	H2M589G	142/144
H1M590N	218/226	H1M590P	234/236	H1M590G	238/240
H2M591N	146/154	H2M591P	162/164	H2M591G	166/168
H1M592N	242/250	H1M592P	258/260	H1M592G	262/264
H1M595N	266/274	H1M595P	282/284	H1M595G	286/288
H2M609N	170/178	H2M609P	186/188	H2M609G	190/192
H2M610N	194/202	H2M610P	210/212	H2M610G	214/216
H2M611N	290/298	H2M611P	306/308	H2M611G	310/312
H1M612N	2/10	H1M612P	18/20	H1M612G	22/24
H1M613N	410/418	H1M613P	426/428	H1M613G	430/432
H2M614N	314/322	H2M614P	330/332	H2M614G	334/336
H1M615N	26/34	H1M615P	42/44	H1M615G	46/48
H1M616N	50/58	H1M616P	66/68	H1M616G	70/72
H3M617N	362/370	H3M617P	378/380	H3M617G	382/384
H2M618N	338/346	H2M618P	354/356	H2M618G	358/360
H1M619N	74/82	H1M619P	90/92	H1M619G	94/96
H3M620N	386/394	H3M620P	402/404	H3M620G	406/408
FP3B12F6N	434/442	FP3B12F6P	450/452	FP3B12F6G	454/456

Example 3. Antibody Binding to PAR-2 Peptides

[0110] Synthetic peptides (Celtek Bioscience, Nashville, TN) of PAR-2 and PAR-2 related sequences were generated to characterize the binding profiles of anti-PAR-2 antibodies. Both biotinylated and unbiotinylated forms for the various peptides were generated for the examples set forth below. For biotinylated forms, biotin moieties were covalently attached to the peptide at either the C-terminus or the N-terminus via a G₄S linker. Table 2 sets forth the sequence and derivation of these peptides.

Table 2

Designation	Species	Gene	Sequence	SEQ ID NO:
Peptide A	Human	PAR-2	GTNRSSKGRSLIGKVDGT	852
Peptide B	Human	PAR-2	SLIGKVDGTSHVTG	853
Peptide C	Human	PAR-2	SLIGKV	854
Peptide D	Human	PAR-2	SLIGKVDGTSHVTGKGVTVE TVFSVDEFSASVLTGKLTTFV LP - mouse IgG2a	855
Peptide E	Mouse (<i>Mus musculus</i>)	PAR-2	LAPGRNNSKGRSLIGRLETQ	856
Peptide F	Monkey (<i>Macaca mulatta</i>)	PAR-2	GTNRSSKGRSLIGRVDGT	857
Peptide G	Rat (<i>Rattus norvegicus</i>)	PAR-2	GPNSKGRSLIGRLDTP	858
Peptide H	Rabbit (<i>Oryctolagus cuniculus</i>)	PAR-2	GTNKTSGRSLIGRNTGS	859
Peptide I	Dog (<i>Canis familiaris</i>)	PAR-2	GTNRTSKGRSLIGKTDSS	860
Peptide J	Pig (<i>Sus scrofa</i>)	PAR-2	GTSRPSKGRSLIGKADNT	861
Peptide K	Human	PAR-1	ATNATLDPRSFLLRNPND	862
Peptide L	Human	PAR-3	DTNNLAKPTLPIKTFRGA	863
Peptide M	Human	PAR-4	ESGSTGGGDDSTPSILPAP	864

[0111] Anti-PAR-2 antibodies were tested for their ability to bind to the PAR-2 peptides. Various PAR-2 Peptides (Table 3) were coated onto 96-well plates at a concentration of 2 µg/ml and incubated overnight followed by blocking in a suitable blocking agent for one hour. In a similar fashion, for biotinylated peptides (N-Term: N-terminal biotinylated; C-Term: C-terminal biotinylated), avidin was coated on plates at 2 µg/ml followed by incubation with biotinylated PAR-2 peptides at a concentration of 0.2 µg/ml and incubated for one hour. Purified anti-PAR-2 antibodies were added to the plate coated with PAR-2 peptides to a final concentration ranging from 0.2 to 2.0 µg/ml and incubated for one hour at room temperature. Detection of bound antibodies was determined with Horse-Radish Peroxidase (HRP) conjugated anti-mouse or human IgG (Jackson Immuno Research Lab, West Grove, PA) and developed by standard colorimetric response using tetramethylbenzidine (TMB) substrate. Absorbance was read at OD₄₅₀ for 0.1 second.

[0112] Relative binding (+++, ++, +) to unbiotinylated (No Biotin) or biotinylated Peptides A, B and C as compared to no binding (-) for each anti-PAR-2 antibody tested according to the observed OD₄₅₀ value (1.0 - 4.0, 0.50 - 0.99, 0.1 - 0.49, 0.0 - 0.09, respectively) is shown in Table 3. Control: "Sam11," a commercially available mouse monoclonal antibody that binds human PAR-2 (Santa Cruz Biotechnology, Santa Cruz, CA).

Table 3

Antibody	Peptide A			Peptide B			Peptide C	
	No Biotin	N-Term	C-Term	No Biotin	N-Term	C-Term	N-Term	C-Term
H2M588N	+++	+++	+++	+++	+++	+++	-	-
H2M589N	+++	+++	+++	+++	+++	+++	-	-
H1M590N	+++	+++	+++	-	-	-	-	-
H2M591N	+++	+++	+++	+++	+++	+++	-	-
H1M592N	+++	+++	+++	-	++	+++	+++	+++
H1M595N	+++	+++	+++	-	-	-	++	-
H2M609N	+++	+++	+++	-	-	-	-	-
H2M610N	+++	+++	+++	-	-	-	-	-
H2M611N	+++	+++	+++	+++	+++	+++	-	-

Antibody	Peptide A			Peptide B			Peptide C	
	No Biotin	N-Term	C-Term	No Biotin	N-Term	C-Term	N-Term	C-Term
H1M612N	+++	+++	+++	-	-	-	-	-
H1M613N	+++	+++	+++	-	++	+++	+++	+++
H2M614N	++	+++	+++	-	-	-	-	-
H1M615N	+++	+++	+++	-	-	-	-	-
H1M616N	+++	+++	+++	-	-	-	-	-
H2M618N	+++	+++	+++	+++	+++	+++	-	-
H1M619N	+++	+++	+++	-	-	-	-	-
H3M620N	+++	++	+++	-	-	-	-	-
Control	-	-	-	+++	+++	+++	-	-

[0113] In a similar experiment, selected anti-PAR-2 antibodies cloned onto a mutant human IgG4 (SEQ ID NO:849) were tested for their ability to bind unbiotinylated and biotinylated forms of human PAR-2 peptides (as described above). Results are shown in Table 4.

Table 4

Antibody	Peptide A			Peptide B			Peptide C	
	No Biotin	N-Term	C-Term	No Biotin	N-Term	C-Term	N-Term	C-Term
H4H572P	-	-	-	-	-	-	-	-
H4H573P	+++	+++	+++	-	-	-	-	-
H4H576P	+	-	-	-	-	-	-	-
H4H578P	+++	+++	+++	-	-	-	-	-
H4H579P	+++	+++	+++	+++	+++	+++	-	-
H4H580P	+++	+++	+++	+++	+++	+++	-	-
H4H581P	+++	+++	+++	+++	+++	+++	++	+
H4H583P	+++	+++	+++	-	-	-	-	-
H4H584P	+++	+++	+++	+++	+++	+++	-	-
H4H585P	+++	+++	+++	+++	+++	+++	+	+
H4H587P	-	-	-	-	-	-	-	+
H4H588N	+++	+++	+++	+++	+++	+++	-	-
H4H591N	+++	+++	+++	+++	+++	+++	-	-
H4H618N	+++	+++	+++	+++	+++	+++	-	-
Control	-	-	-	+++	+++	+++	-	-

[0114] In another experiment, selected anti-PAR-2 antibodies were tested for binding to unbiotinylated Peptides D, K, L and M (as described above). Results for chimeric antibodies (e.g. H2M588N) and fully human antibodies (e.g. H4H572P) are shown in Tables 5 and 6, respectively. For Peptide D, detection of bound antibodies was determined with Horse-Radish Peroxidase (HRP) conjugated anti-mouse κ (Southern Biotech, Birmingham, AL).

Table 5

Antibody	Peptide D	Peptide K	Peptide L	Peptide M
H2M588N	+++	-	-	-
H2M589N	+++	-	-	-
H1M590N	-	-	-	-
H2M591 N	+++	-	-	-

Antibody	Peptide D	Peptide K	Peptide L	Peptide M
H1M592N	+	-	-	-
H1M595N	-	-	-	-
H2M609N	+	-	-	-
H2M610N	-	-	-	-
H2M611 N	+	-	-	-
H1M612N	-	-	-	-
H1M613N	+	-	-	-
H2M614N	-	-	-	-
H1M615N	-	-	-	-
H1M616N	-	-	-	-
H2M618N	+++	-	-	-
H1M619N	-	-	-	-
H3M620N	-	-	-	-
Control	+++	-	-	-

Table 6

Antibody	Peptide D	Peptide K	Peptide L	Peptide M
H4H572P	+	-	-	-
H4H573P	+	-	-	-
H4H576P	+	-	-	-
H4H578P	+	-	-	-
H4H579P	+++	-	-	-
H4H580P	+++	-	-	-
H4H581P	+++	+	+	+
H4H583P	++	-	-	-
H4H584P	+++	-	-	-
H4H585P	+++	+	+	+
H4H587P	+	-	-	-
H4H588N	+++	-	-	-
H4H591N	+++	+	+	+
H4H618N	+++	-	-	-
Control	+++	-	-	-

[0115] In another experiment, selected anti-PAR-2 antibodies were tested for binding to N-terminal biotinylated mouse (Peptide E N-Term) and monkey (Peptide F N-Term) PAR-2 peptides (as described above).

Table 7

Antibody	Peptide E N-Term	Peptide F N-Term
H2M588N	-	+++
H2M589N	-	+++
H1M590N	+++	+++
H2M591N	-	+++
H1M592N	-	-
H1M595N	+++	+++
H2M609N	+++	+++
H2M610N	+++	+++

Antibody	Peptide E N-Term	Peptide F N-Term
H2M611N	-	+++
H1M612N	+++	+++
H1M613N	-	-
H2M614N	+++	+++
H1M615N	+++	+++
H1M616N	+++	+++
H2M618N	-	+++
H1M619N	+++	+++
H3M620N	+++	++
Control	-	-

[0116] In another experiment, selected anti-PAR-2 antibodies cloned onto human IgG4 were tested for binding to unbiotinylated and biotinylated forms of Peptides E through J (as described above). Results are shown in Table 8.

Table 8

Antibody	Peptide E		Peptide F N-Term	Peptide G			Peptide H	Peptide I	Peptide J
	No Biotin	N-Term		No Biotin	N-Term	C-Term			
H4H572P	+	-	-	-	-	+	-	-	-
H4H573P	+++	+++	+++	+++	+++	++	+++	+++	+++
H4H576P	+	-	-	-	-	+	-	-	-
H4H578P	+++	+++	+++	+++	+++	+	+++	+++	+++
H4H579P	+++	+++	+++	+++	+++	+++	+	+++	+
H4H580P	+++	+++	+++	+++	+++	+++	-	+++	+
H4H581P	+++	+++	+++	+++	+++	+++	-	+++	+++
H4H583P	+++	+++	+++	+++	+++	+++	+++	+++	+++
H4H584P	+++	+++	+++	+++	+++	+++	-	+++	++
H4H585P	+++	+++	+++	+++	+++	+++	+	+++	+++
H4H587P	-	-	-	-	+	-	-	-	+
H4H588N	-	-	+++	-	+	-	-	-	-
H4H591N	+	+	+++	+	+	+	+	-	+
H4H618N	-	-	+++	-	-	-	-	-	-
Control	-	-	-	-	-	-	-	-	-

[0117] In another experiment, selected anti-PAR-2 antibodies cloned onto human IgG4 were tested for binding to unbiotinylated and biotinylated forms of PAR-2 peptides (Peptides A, E, F and G; as described above). In this experiment, anti-PAR-2 antibodies, serially diluted threefold from 13.3 nM to 0.22 pM, were incubated on the peptide-coated plates for one hour at room temperature. Absorbance values at 450 nm were analyzed using a sigmoidal dose-response model in GraphPad Prism (GraphPad Software, Inc., La Jolla, CA) and EC₅₀ values were reported (Table 9). EC₅₀ values are defined as the antibody concentration required to achieve 50% maximal binding to PAR-2 peptide.

Table 9

Antibody	EC ₅₀ (nM)								
	Peptide A			Peptide E		Peptide F N-Term	Peptide G		
	No Biotin	C-Term	N-Term	No Biotin	N-Term		No Biotin	C-Term	N-Term
H4H572P	>50	>50	>50	>50	>50	>50	>50	>50	>50

Antibody	EC ₅₀ (nM)								
	Peptide A			Peptide E		Peptide F N-Term	Peptide G		
	No Biotin	C-Term	N-Term	No Biotin	N-Term		No Biotin	C-Term	N-Term
H4H573P	0.093	0.022	0.093	0.355	0.016	0.018	0.014	10.130	0.017
H4H576P	>50	>50	>50	>50	>50	>50	>50	>50	>50
H4H578P	0.034	0.040	0.062	2.778	0.090	0.036	0.046	>50	0.081
H4H579P	0.038	0.076	0.077	0.713	0.540	0.061	0.055	0.044	0.059
H4H580P	0.090	0.202	0.160	2.533	0.932	0.148	0.139	0.100	0.142
H4H581P	0.012	0.028	0.020	0.029	0.032	0.020	0.020	0.013	0.019
H4H583P	0.008	0.018	0.015	0.019	0.014	0.013	0.012	0.630	0.015
H4H584P	0.012	0.015	0.019	2.152	0.511	0.012	0.013	0.015	0.012
H4H585P	0.017	0.021	0.026	0.308	0.189	0.017	0.018	0.021	0.017
H4H587P	>50	>50	>50	>50	>50	>50	>50	>50	>50
H4H588N	0.010	0.016	0.019	>50	>50	0.012	>50	>50	>50
H4H591N	0.010	0.016	0.022	>50	>50	0.011	>50	>50	>50
H4H618N	0.009	0.016	0.021	>50	>50	0.011	>50	>50	>50
Control	>50	>50	>50	>50	>50	>50	>50	>50	>50

[0118] As indicated by the foregoing experiments, antibodies H4H581 P, H4H588N, H4H591 N or H4H618N all show substantial binding to human Peptides A, B and D, which comprise the sequence SLIGKVDGT (amino acids 10-18 of SEQ ID NO:852), as well as to monkey Peptide F, which comprises the sequence SLIGRVDGT (amino acids 10-18 of SEQ ID NO:857). For antibodies H4H588N, H4H591 N and H4H618N, the sequence VDG, located downstream from the activating PAR-2 protease cleavage site, appears to be particularly important for binding since changes to this sequence resulted in substantially reduced or no binding by these antibodies (see, e.g., binding data for Peptides E (mouse), G (rat), H (rabbit), I (dog) and J (pig)).

Example 4. Antigen Binding Affinity Determination

[0119] Equilibrium dissociation constants (K_D values) for antigen binding to selected purified PAR-2 antibodies were determined by surface kinetics using a real-time surface plasmon resonance biosensor assay. Antibody was captured on either a rabbit anti-mouse IgG polyclonal antibody (GE Healthcare, Piscataway, NJ) surface or a goat anti-human IgG polyclonal antibody (Jackson Immuno Research Lab, West Grove, PA) surface created through direct amine chemical coupling to a BIACORE™ CM5 sensor chip to form a captured antibody surface. Various concentrations (ranging from 15.6 to 250 nM) of monomeric human PAR-2 peptides (Peptides A and B) were injected at a rate of 100 μ l/min over the captured antibody surface for 90 seconds. Antigen-antibody binding and dissociation were monitored in real time at room temperature. Kinetic analysis was performed to calculate K_D and half-life of antigen/antibody complex dissociation (Table 10). For those antibodies where no $T_{1/2}$ value is shown, steady state analysis was used to calculate the K_D value. NB: no binding observed under current experimental conditions. ND: not determined.

Table 10

Antibody	Peptide A		Peptide B	
	K_D (nM)	$T_{1/2}$ (min)	K_D (nM)	$T_{1/2}$ (min)
H4H572P	NB	-	ND	-
H4H573P	749	-	ND	-
H4H576P	NB	-	ND	-
H4H578P	245	0.17	ND	-
H4H579P	15	4	>500	-
H4H580P	103	0.88	ND	-

Antibody	Peptide A		Peptide B	
	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)
H4H581P	9.44	1.4	>500	-
H4H583P	37.1	0.37	NB	-
H4H584P	22	0.73	>500	-
H4H585P	8.78	3.7	>500	-
H4H587P	NB	-	ND	-
H1M590N	173	-	ND	-
H1M592N	2100	-	ND	-
H1M595N	510	-	ND	-
H1M612N	180	-	ND	-
H1M613N	2100	-	ND	-
H1M615N	162	-	ND	-
H1M616N	144	-	ND	-
H1M619N	164	-	ND	-
H2M588N	4.47	60.8	61.7	7.7
H2M589N	3.75	51.3	128	7.3
H2M591N	4.22	42.7	151	8.1
H2M610N	71.3	-	360	0.8
H2M611N	72.8	4.1	1090	1.2
H2M614N	470	-	ND	-
H2M618N	9.62	6.7	126	3.5
Control	NB	-	149	0.1

[0120] In a similar experiment, K_D values for binding to unbiotinylated monomeric mouse (Peptide E) and N-terminal biotinylated monkey (Peptide F N-Term) PAR-2 peptides of selected antibodies cloned onto human IgG4 were determined (as described above) (Table 11). Antibodies H4H588N, H4H591 N, and H4H618N did not bind Peptide E, while the Control antibody did not bind to either Peptide E or F.

Table 11

Antibody	Peptide F N-Term	
	K _D (nM)	T _{1/2} (min)
H4H588N	7.10	24
H4H591N	8.54	21
H4H618N	13.8	5

[0121] In another series of experiments, equilibrium dissociation constants (K_D values) for purified antibody binding to selected biotinylated and unbiotinylated forms of PAR-2 peptides were determined by surface kinetics using a real-time surface plasmon resonance biosensor assay. Neutravidin (Pierce, Rockford, IL) was covalently coupled to the surface of a Biacore™ C1 chip or CM5 chip using amine coupling chemistry. Biotinylated (N-Term or C-Term) PAR-2 peptides (Peptides A and B) were immobilized on the surface via the high affinity binding interaction between biotin and the amine coupled Neutravidin.

[0122] In a first experiment using this format, varying concentrations (ranging from 5 to 100 µg/ml) of purified antibody were injected at a rate of 50 µl/min over a surface coated with immobilized peptide at low-density (<1 RU) for 300 seconds. Antibody-peptide binding and dissociation was monitored in real time 25°C (Table 12).

Table 12

Antibody	Peptide A C-Term		Peptide B C-Term	
	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)
H2M588N	0.826	169	1.49	140
H1M590N	1.27	13	NB	-
H2M591N	0.545	209	1.82	94
H2M618N	1.8	79	2.32	60
Control	NB	-	0.99	19

[0123] In another similar experiment, K_D values for binding to a low-density surface (<1 RU) of biotinylated forms of Peptides A, B, C, E, F and G of selected antibodies cloned onto human IgG4 were determined (as described above). Results for binding to C-terminal and N-terminal biotinylated PAR-2 peptides are shown in Tables 13-14, respectively. In this experiment, only antibody H4H581 P demonstrated affinity for N-terminal biotinylated Peptide C (K_D of >100 nM), while all other antibodies tested, including the control, showed no binding to this peptide.

Table 13

Antibody	Peptide A C-Term		Peptide B C-Term	
	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)
H4H579P	0.143	479	0.453	96
H4H581P	0.237	134	0.346	49
H4H583P	0.898	34	NB	-
H4H584P	0.688	55	1.66	15
H4H585P	0.151	493	0.376	123
H4H588N	0.517	141	1.03	70
H4H590N	3.56	3	NB	-
Control	NB	-	0.935	14

Table 14

Antibody	Peptide A N-Term		Peptide B N-Term		Peptide E N-Term		Peptide F N-Term		Peptide G N-Term	
	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)
H4H579P	1.61	46	5.44	55	3.40	20	0.796	70	1.16	38
H4H581P	0.498	41	2.72	38	1.13	21	0.272	78	0.354	62
H4H583P	0.412	46	NB	-	1.68	11	0.291	73	1.49	13
H4H584P	0.525	43	3.20	30	>100	-	0.565	40	1.39	15
H4H585P	1.69	48	5.41	63	>100	-	0.899	66	1.36	35
H4H588N	1.05	189	0.0272	>1155	NB	-	1.81	94	NB	-
H4H590N	1.52	3	NB	-	1.28	7	1.84	2	2.94	2
Control	NB	-	0.279	32	NB	-	NB	-	NB	-

[0124] In a similar experiment, K_D values for binding to monomeric biotinylated and unbiotinylated forms of PAR-2 peptides (Peptides A, B, E - M) for selected antibodies cloned onto human IgG4 were determined (as described above for the captured antibody surface). Results are shown in Tables 15-16. None of the antibodies tested showed binding to Peptides K, L or M.

Table 15

Antibody	Peptide A		Peptide B		Peptide E	
	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)
H4H579P	15	4.1	>500	-	>500	-

Antibody	Peptide A		Peptide B		Peptide E	
	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)
H4H581P	9.44	1.4	>500	-	>500	-
H4H583P	37.1	0.37	NB	-	>500	-
H4H584P	22	0.73	NB	-	NB	-
H4H585P	8.78	3.7	>500	-	>500	-
H4H588N	4.95	25.1	84	9	NB	-
H4H590N	>500	-	NB	-	>500	-
Control	ND	-	149	0.1	ND	-

Table 16

Antibody	Peptide F N-Term		Peptide G		Peptide H		Peptide I		Peptide J	
	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)	K _D (nM)	T _{1/2} (min)
H4H579P	49.4	2	134	0.45	NB	-	311	0.26	NB	-
H4H581P	36.6	0.53	40.2	0.63	NB	-	143	0.07	NB	-
H4H583P	112	0.47	530	0.07	189	0.17	320	0.16	190	0.16
H4H584P	93.3	0.23	246	0.13	NB	-	>500	-	NB	-
H4H585P	46.2	2	162	0.33	NB	-	372	0.19	NB	-
H4H588N	10.8	20	NB	-	NB	-	NB	-	NB	-
H4H590N	>500	-	>500	-	>500	-	>500	-	>500	-

Example 5. Antibody Binding to Cells Engineered to Express PAR-2

[0125] To further characterize anti-PAR-2 antibodies, cells of the human embryonic kidney 293 cell line (HEK293) were genetically engineered to overexpress either full length human (SEQ ID NO:851) or mouse (SEQ ID NO:866) PAR-2.

[0126] HEK293 cells were transfected with an NF-κB-luciferase-IRES-eGFP reporter plasmid. Stability of transfected cells was demonstrated by response to IL-1β as detected by eGFP expression through flow cytometry and luciferase activity. A clonal cell line, named D9, having low background levels of luciferase activity and high levels of eGFP when induced with IL-1β was made by a series of successive sorts of cell populations using flow cytometry. The 293/D9 cell line was then separately transfected with human PAR-2 or mouse PAR-2 to create the stable cell lines 293/D9/hPAR-2rec and 293/D9/mPAR-2rec, respectively.

[0127] Binding of anti-PAR-2 antibodies to 293/D9/hPAR-2rec cells was determined by ELISA. 293/D9 and 293/D9/hPAR-2rec cells were plated at a density of 5×10^4 cells/well in media and incubated overnight at 37°C and 5% CO₂. Purified antibody was added to the cells to a final concentration of 10 μg/ml and incubated at room temperature for one hour. Cells were then fixed and washed before detection of bound antibodies with HRP conjugated anti-mouse IgG and developed by standard colorimetric response using TMB substrate. Absorbance was read at OD₄₅₀ for 0.1 second. The A₄₅₀ ratio of antibody binding to 293/D9/hPAR-2rec cells compared to 293/D9 cells is shown in Table 17.

Table 17

Antibody	A ₄₅₀ ratio
H2M588N	2.50
H2M589N	2.03
H1M590N	1.81
H2M591N	2.25
H1M592N	1.25
H1M595N	1.80

Antibody	A ₄₅₀ ratio
H2M609N	1.54
H2M610N	1.66
H2M611N	1.76
H1M612N	1.90
H1M613N	1.27
H2M614N	1.17
H1M615N	2.18
H1M616N	2.78
H2M618N	2.44
H1M619N	1.51
H3M620N	1.24
Control	1.49

[0128] In a similar experiment, anti-PAR-2 antibodies were tested for binding to 293/D9, 293/D9/hPAR-2rec and 293/D9/mPAR-2rec cells using electro-chemiluminescence technology (Meso Scale Discovery, MSD, Gaithersburg, MD). Cells were plated on MSD high-bind 96 well plates at a density of 4×10^4 cells/well in PBS and incubated for one hour at room temperature. Cells were then blocked in PBS with 2% BSA and incubated at room temperature for one hour. Anti-PAR-2 antibodies (ranging from 100 nM to 0.098 nM) were serially diluted two-fold in PBS with 0.5% BSA and incubated with the cells for one hour at room temperature followed by washing in PBS with 0.5% BSA. Sulfo-tagged anti-human IgG antibody (MSD) at a concentration of 0.1 µg/ml was then added to the cell/antibody mixture and incubated at room temperature for an additional hour. After another wash, a 1 X non-surfactant containing read buffer was added and electro-chemiluminescent signal was read on the MSD Sector Imager. Signal of antibody binding to 293/D9 cells was subtracted from signal to 293/D9/hPAR-2rec or 293/D9/mPAR-2rec cells. Subtracted data were analyzed using a sigmoidal dose-response model in GraphPad Prism and EC₅₀ and B_{max} values were reported (Table 18). EC₅₀ values are defined as the antibody concentration required to achieve 50% maximal binding (B_{max}) to cells.

Table 18

Antibody	293/D9/hPAR-2rec		293/D9/mPAR-2rec	
	EC ₅₀ (nM)	B _{max} (MSD Unit)	EC ₅₀ (nM)	B _{max} (MSD Unit)
H4H579P	1.86	25049	NB	-
H4H580P	8.69	30177	NB	-
H4H581P	0.652	28224	NB	-
H4H583P	2.12	13252	9.28	7219
H4H584P	1.45	26044	NB	-
H4H585P	1.95	22540	NB	-
H4H588N	5.95	27549	NB	-
H4H590N	9.72	6554	5.76	13255

Example 6. *In vitro* Blocking of Human PAR-2 Activation By Anti-PAR-2 Antibodies

[0129] Blocking of PAR-2 activation (signaling) was determined by binding of selected purified anti-PAR-2 antibodies to 293/D9/hPAR-2rec cells (see Example 5) by a luciferase assay. 293/D9/hPAR-2rec cells were plated at a concentration ranging from 5×10^4 to 10^5 cells/well in a 96 well plate in low serum media and incubated overnight at 37°C with 5% CO₂. The media was removed and purified anti-PAR-2 antibodies were added to the cells at various concentrations (ranging from 51 pM to 1 µM) and incubated for one hour at 37°C with 5% CO₂. Various concentrations of different serine proteases (Trypsin, Human Trypsin 1, Factor Xa and Lung Tryptase) were then added separately to the cell/antibody mixture and incubated for five hours at 37°C with 5% CO₂. Proteolytic cleavage of PAR-2 in this assay leads to expression of the NF-κB-luciferase reporter construct, whereas a

reduced or attenuated level of luciferase signal indicates inhibition of PAR-2 cleavage. IC₅₀ values are shown in Table 19. ND: not determined.

Table 19

Antibody	IC ₅₀ (nM)							
	Trypsin					10 nM Human Trypsin 1	200 nM Factor Xa	750 nM Lung Trypsin
	250 nM	75 nM	30 nM	20 nM	10 nM			
H2M588N	2.3	5.7	33.0	26.8	10.4	164.9	45.3	1.0
H2M589N	6.3	3.7	ND	ND	ND	ND	ND	ND
H1M591N	4.5	ND	ND	121.8	24.2	149.6	51.5	88.1
H2M618N	6.6	7.8	ND	70	12.4	153.5	54.2	7.0

[0130] As shown in Table 20, antibodies H4H581 P, H4H588N, H4H591 N and H4H618N were able to significantly block protease activation of PAR-2 in reporter cells. By contrast, anti-PAR-2 antibodies H4H592N, H4H595N, H4H611 N, H4H613N, H4H614N, H4H615N, H4H616N, H4H617N and H4H619N did not demonstrate any measurable blocking of PAR-2 cleavage/activation in this assay (data not shown).

Table 20

Antibody	20 nM Trypsin IC ₅₀ (nM)
H4H579P	4.1
H4H580P	3.5
H4H581P	1.1
H4H583P	14
H4H584P	5.6
H4H585P	8.9
H4H588N	16.9
H4H591N	204.1
H4H618N	50.2

[0131] Under the experimental conditions used in this Example, no blocking of PAR-2 signaling was observed for antibodies H4H572P, H4H573P, H4H576P, H4H578P or H4H587P, whereas significant blockage (to varying degrees) was observed with antibodies H4H579P, H4H580P, H4H581 P, H4H583P, H4H584P, H4H585P, H4H588N, H4H591 N and H4H618N.

[0132] In another similar experiment, antibody blocking of PAR-2 signaling mediated by human Trypsin 1, Factor Xa and Lung Trypsin was determined for selected purified anti-PAR-2 antibodies cloned onto human IgG4 (as described above). Results are shown in Table 21.

Table 21. IC₅₀ (nM)

Antibody	10 nM Human Trypsin 1	200 nM Factor Xa	750 nM Lung Trypsin
H4H581P	7.4	5.3	1.1
H4H588N	42.7	17.1	1.6
H4H591N	104.7	74.6	62.9
H4H618N	92.2	47.2	8.5

[0133] HEK293/NFκB-luciferase cells expressing human, monkey, mouse or rat PAR-2 were treated with various proteases after preincubation with increasing amounts of anti-PAR-2 antibody H4H581 P, and the IC₅₀ was determined. Results are summarized in Table 22.

Table 22

Activator (6h)	PAR-2 Species	EC ₅₀ (nM)	H4H581P IC ₅₀ (nM)
Human Pancreatic Trypsin	Human	0.8	1.9
	mouse	1.4	491.0
	monkey	2.4	5.4
	rat	6.0	700.0
Human Kallikrein 5	Human	28.0	0.9
	mouse	ND	ND
	monkey	16.8	11
Human Kallikrein 14	Human	5.0	1.2
	mouse	8.0	256.0
	monkey	6.3	11.6
Bovine Factor Xa	Human	27.2	2.5
	mouse	46.3	340.4
	monkey	58.2	0.9
Human Factor Xa	Human	46.3	1.1
	mouse	78.7	109
	monkey	ND	ND
Trypsin	Human	61.1	3.5
	mouse	ND	ND
	monkey	ND	ND

[0134] Under the particular experimental conditions used, the H4H581 P antibody effectively inhibited protease-activation of human and monkey PAR-2, but not mouse or rat PAR-2.

Example 7. *In vitro* Antibody Blocking of Human PAR-2 Dependent Calcium Mobilization

[0135] Blocking of trypsin-stimulated PAR-2 activation (signaling) was determined by treating HEK293 cells with selected purified anti-PAR-2 antibodies cloned onto human IgG4 in a calcium mobilization FLIPR assay (Molecular Devices, Sunnyvale, CA). Also tested in this assay was a non-PAR-2 specific control antibody.

[0136] Briefly, 8×10^4 HEK293 cells were plated on Poly-D-Lysine plates (BD Biosciences, San Jose, CA) in low serum media (DME with 0.5% FBS) and incubated overnight at 37°C with 5% CO₂. The following day cells were incubated with various concentrations (ranging from 0 to 1 μ M) of selected anti-PAR-2 antibodies, or a control antibody, followed by the addition of trypsin. Trypsin-mediated activation of PAR-2 is indicated by calcium mobilization. In-cell measurement of calcium signaling was measured using a Fluo-4 NW Calcium Assay Kit (Invitrogen, Carlsbad, CA) on a FlexStation 3 (Molecular Devices, Sunnyvale, CA). The antibody concentration necessary to cause half-maximal inhibition of trypsin-mediated calcium signaling (IC₅₀) was measured for each experimental and control antibody. Results are shown in Table 23 as IC₅₀ (nM).

Table 23

Antibody	100 nM Trypsin
H4H581P	54.96
H4H588N	29.47
Non-Specific Control	> 1000

[0137] As shown in this Example, antibodies H4H581P and H4H588N each inhibited trypsin-stimulated calcium signaling to a significant extent as compared to the control antibody.

Example 8. *In vitro* Blocking of Trypsin-mediated Cleavage of PAR-2 Peptides

[0138] A Matrix Assisted Laser Desorption Ionization - Time of Flight (MALDI-TOF) assay was developed to determine the ability of selected purified anti-PAR-2 antibodies to block Trypsin-mediated cleavage of human PAR-2 peptide (Peptide A, SEQ ID NO:852). Biotinylated versions of Peptide A (containing C-terminal or N-terminal biotin) were mixed with anti-PAR-2 antibody to achieve a 3:1 molar ratio of antibody to peptide, and then trypsin was added to the peptide-antibody mixture. Biotinylated peptides were recovered by immuno-precipitation (IP) via mono-avidin and analyzed by MALDI-TOF.

[0139] In a typical experiment, selected purified anti-PAR-2 antibodies cloned onto human IgG4 (H4H581 P and H4H588N) were tested for their ability to block Trypsin-mediated cleavage of the biotinylated PAR-2 peptides. A non-PAR-2-specific antibody of the same isotype was used as a negative control ("Neg Ctrl" in Fig. 3). For H4H581 P and the negative control antibody, biotinylated peptides were used at a final concentration of 4.75 μ M and antibodies were used at 14.25 μ M. For H4H588N, biotinylated peptides were used at a final concentration of 2.45 μ M and the antibody at 7.35 μ M. Peptide and antibody were mixed in PBS and allowed to come to equilibrium for 1 hr at room temperature. Trypsin (96 ng) was then added and the mixture incubated at 37°C for 0, 5, 10 and 15 minutes. At each time point an aliquot equaling 100 ng of biotinylated peptide was removed and mixed with 10 μ l of monomeric avidin resin (Pierce) for 1 minute. The bound peptides were rinsed 3x with 200 μ l of PBS and then eluted with 20 μ l of 100 mM glycine pH 2.5. Salt was removed from the eluted peptide mixture using ZipTips (Millipore). The molecular weights of the major biotinylated PAR-2 peptides produced after trypsin cleavage, as revealed by MALDI-TOF analysis, are summarized in Fig. 3.

[0140] The PAR-2 peptides used in these experiments contain two R/S protease cleavage sites. The first site (designated site "(1)" in Fig. 3) is an "upstream" cleavage site located N-terminal to the activating PAR-2 protease cleavage site. The activating PAR-2 protease cleavage site (designated site "(2)" in Fig. 3) is the site which, when cleaved, results in the formation of the PAR-2 tethered ligand in the naturally occurring protein. The sizes of the peptides detected following cleavage at the different sites are shown in the top portion of Fig. 3 (panel A).

[0141] As indicated in Fig. 3 (panel B), the C-terminal biotin PAR-2 peptide, when treated with the isotype-matched control antibody, followed by trypsin incubation, produced a cleavage fragment of 1558 Da (containing residues 10-18 of SEQ ID NO:852). The 1558 Da fragment is the result of cleavage at the activating PAR-2 protease cleavage site (2). This cleavage pattern was also observed in the experiment using the H4H588N anti-PAR-2 antibody. Thus, according to this assay, neither the control antibody nor the H4H588N antibody inhibit trypsin cleavage at the activating PAR-2 protease cleavage site (2).

[0142] By contrast, the C-terminal biotin PAR-2 peptide, when treated with the H4H581 P antibody, followed by trypsin incubation, produced a cleavage fragment of 2073 Da (containing residues 5-18 of SEQ ID NO:852). The 2073 Da fragment is the fragment produced by cleavage at the upstream cleavage site (1) only. Thus, cleavage at the activating PAR-2 protease cleavage site (2) was apparently blocked by the H4H581 P antibody.

[0143] Experiments with the N-terminal biotin PAR-2 peptide showed trypsin cleavage at the upstream cleavage site (1) and thus produced a 988 Da N-biotinylated fragment (containing residues 1-4 of SEQ ID NO:852) in the presence of all antibodies tested. Therefore, none of the antibodies tested blocked cleavage at the upstream cleavage site (1) under these experimental conditions.

[0144] As shown in Examples 6 and 7 above, both H4H581 P and H4H588N blocked PAR-2 activation by trypsin in cell-based assays. In the present Example, however, only H4H581 P blocked trypsin cleavage at the activating PAR-2 protease cleavage site. Without being bound by any mechanistic theory, it therefore appears that H4H588N may exert its inhibitory effect(s) by interfering with the interaction between the tethered ligand and one or more extracellular loops (e.g., loop 1, loop 2 and/or loop 3) of PAR-2. On the other hand, H4H581 P may inhibit PAR-2 activity primarily by blocking protease cleavage but may also interfere with tethered ligand interactions as well.

[0145] To further investigate the protease cleavage-blocking properties of anti-PAR-2 antibodies, additional MALDI-TOF experiments were conducted using C-terminal biotinylated mouse, rat and human PAR-2 peptides. (See Fig. 4). The antibodies tested in these experiments were H4H581 P, H4H588N, a comparator antibody having the heavy and light chain variable regions of the antibody referred to as "1A1" in WO 2009/005726 (referred to in Fig. 5 as "Comp. Ab"), and a negative control antibody (referred to in Fig. 4 as "Neg Ctrl"). The same experimental procedures that were used in the previous MALDI-TOF experiment (described above) were used in this experiment as well.

[0146] The peptides used in these experiments each possess multiple sites capable of being cleaved by trypsin (designated "

(1)," "(2)," and "(3)" in Fig. 5.) Site (3) for each peptide is the activating protease cleavage site. The sizes of the peptides produced following cleavage at the different sites are shown in the top portion (panel A) of Fig. 4.

[0147] As summarized in Fig. 4, the biotinylated human PAR-2 peptide, after being treated with H4H581 P, and following trypsin incubation, produced a 2074 kDa peptide which corresponds to cleavage at site (1) only. Thus, H4H581 P blocks cleavage at both site (2) and at site (3). By contrast, the human PAR-2 peptide, after being treated with the comparator antibody, and following trypsin incubation, remained at 2502 kDa which signifies no cleavage. Thus, the comparator antibody blocks all three protease cleavage sites in this assay, including the N-terminal-most site (1). When pre-treated with antibody H4H588N, the human PAR-2 peptide produces both a 1772 kDa and a 1558 kDa fragment following trypsin cleavage. This cleavage pattern suggests that H4H588N partially blocks cleavage at the activating site (3) but completely blocks the middle site (2).

[0148] This experiment was also conducted using a comparator antibody having the heavy and light chain variable regions of the antibody referred to as Sam-11 (Molino et al., *Arterioscler. Thromb. Vasc. Biol.* 18:825-832 (1998)). As expected, this particular comparator antibody did not block cleavage at any of the protease cleavage sites (data not shown).

Example 9. Epitope Mapping by Alanine Scanning Mutagenesis of PAR-2 Peptide

[0149] In order to more particularly identify the amino acids of PAR-2 with which the PAR-2 antibodies interact, an alanine scanning study was carried out using peptides comprising the activating PAR-2 protease cleavage site. For these experiments, 11 separate C-terminal biotinylated peptides were synthesized in which each amino acid from position 35 through 45 of human PAR-2 (SEQ ID NO:851) was individually replaced with an alanine (SEQ ID NOs: 871-882). An additional set of C-terminal biotinylated peptides was also used which comprise the 14 amino acids located immediately C-terminal to the activating PAR-2 protease cleavage site, with Val-42 and/or Asp-43 changed to alanine (SEQ ID NOs: 884-887).

[0150] The ability of each peptide mutant to bind to PAR-2 antibodies was measured using biolayer interferometry (Octet Red; ForteBio). Each peptide (2.5µg/ml) was captured on streptavidin coated biosensor tips (Octet SA sensor) for 10 seconds. To measure binding and dissociation between each peptide and PAR-2 antibody, the peptide-coated biosensors were contacted with 200nM solutions of PAR-2 antibodies for 5 minutes (binding) followed by transfer to buffer with no antibody for 10 min (dissociation). The binding of PAR-2 antibody to each peptide was expressed as percent native signal after dividing individual antibody binding signals by the original peptide loading signal observed for that peptide, to correct for slight variations in peptide loading on the individual biosensors. Dissociation half-lives ($T_{1/2}$) were calculated from the dissociation curves using the Scrubber version 2.0a curve-fitting software, and relative half-lives were calculated by dividing observed half-lives for an individual peptide by the half-life of the native peptide. The results are expressed as percent binding and percent $T_{1/2}$ relative to WT peptide (Tables 24-28). [Comparator 1 = an antibody having the heavy and light chain variable regions of the antibody referred to as "1A1" in WO 2009/005726; Comparator 2 = an antibody having the heavy and light chain variable regions of the antibody referred to as Sam-11 (Molino et al., *Arterioscler. Thromb. Vasc. Biol.* 18:825-832 (1998)); and Comparator 3 = an antibody having the heavy and light chain variable regions of the antibody referred to as "PAR-B" in US 2010/0119506]. In certain cases, the binding experiments were repeated (indicated under the column headings Exp1 and Exp2). NB = no binding observed.

Table 24: H4H581P

SEQ ID NO:	SEQUENCE	% Rel Binding		% Rel $T_{1/2}$	
		Exp1	Exp2	Exp1	Exp2
871	GTNRSSKGRSLIGKVDGT-----GGGGSK-B	100	100	100	100
872	GTNRSSK <u>A</u> RSLLIGKVDGT-----GGGGSK-B	78	97	118	117
873	GTNRSSK <u>G</u> ASLLIGKVDGT-----GGGGSK-B	87	105	122	90

SEQ ID NO:	SEQUENCE	% Rel Binding		% Rel T _{1/2}	
		Exp1	Exp2	Exp1	Exp2
874	GTNRSSKGR <u>A</u> LIGKVDGT-----GGGGSK-B	45	56	7	3
875	GTNRSSKGR <u>S</u> LIGKVDGT-----GGGGSK-B	9	19	0.4	0
876	GTNRSSKGRSL <u>A</u> GKVDGT-----GGGGSK-B	8	14	0.2	0
877	GTNRSSKGRSLI <u>A</u> KVDGT-----GGGGSK-B	101	92	33	15
878	GTNRSSKGRSLIG <u>A</u> VDGT-----GGGGSK-B	113	109	63	49
879	GTNRSSKGRSLIGK <u>A</u> DGT-----GGGGSK-B	36	46	1	1
880	GTNRSSKGRSLIGKV <u>A</u> GT-----GGGGSK-B	18	5	36	4
881	GTNRSSKGRSLIGKVD <u>A</u> T-----GGGGSK-B	67	102	117	124
882	GTNRSSKGRSLIGKVDG <u>A</u> -----GGGGSK-B	65	91	129	94
884	SLIGKVDGTSHVTG-GGGGSK-B	—	100	—	100
885	SLIGKADGTSHVTG-GGGGSK-B	—	19	—	0
886	SLIGKV <u>A</u> GTSHVTG-GGGGSK-B	—	NB	—	NB
887	SLIGK <u>AA</u> GTSHVTG-GGGGSK-B	—	NB	—	NB

Table 25: H4H588N

SEQ ID NO:	SEQUENCE	% Rel Binding		% Rel T _{1/2}	
		Exp1	Exp2	Exp1	Exp2
871	GTNRSSKGRSLIGKVDGT-----GGGGSK-B	100	100	100	100
872	GTNRSSK <u>A</u> RSKIGKVDGT-----GGGGSK-B	122	99	100	253
873	GTNRSSK <u>G</u> SLIGKVDGT-----GGGGSK-B	208	115	100	180

SEQ ID NO:	SEQUENCE	% Rel Binding		% Rel T _{1/2}	
		Exp1	Exp2	Exp1	Exp2
874	GTNRSSKGR <u>A</u> LIGKVDGT-----GGGGSK-B	119	93	100	70
875	GTNRSSKGR <u>S</u> LIGKVDGT-----GGGGSK-B	127	105	100	42
876	GTNRSSKGRSL <u>A</u> GKVDGT-----GGGGSK-B	92	85	36	8
877	GTNRSSKGRSLI <u>A</u> KVDGT-----GGGGSK-B	30	30	1	0
878	GTNRSSKGRSLIG <u>A</u> VDGT-----GGGGSK-B	217	121	108	60
879	GTNRSSKGRSLIGK <u>A</u> DGT-----GGGGSK-B	74	52	1	0
880	GTNRSSKGRSLIGKV <u>A</u> GT-----GGGGSK-B	35	8	4	5
881	GTNRSSKGRSLIGKVD <u>A</u> T-----GGGGSK-B	81	67	1	1
882	GTNRSSKGRSLIGKVDG <u>A</u> -----GGGGSK-B	125	121	94	33
884	SLIGKVDGTSHVTG-GGGGSK-B	-	100	-	100
885	SLIGK <u>A</u> DGTSHVTG-GGGGSK-B	-	83	-	0
886	SLIGKV <u>A</u> GTSHVTG-GGGGSK-B	-	NB	-	NB
887	SLIGK <u>A</u> AGTSHVTG-GGGGSK-B	-	NB	-	NB

Table 26: Comparator 1

SEQ ID NO:	SEQUENCE	% Rel Binding		% Rel T _{1/2}	
		Exp1	Exp2	Exp1	Exp2
871	GTNRSSKGRSLIGKVDGT-----GGGGSK-B	100	100	100	100
872	GTNRSSK <u>A</u> RS L IGKVDGT-----GGGGSK-B	111	111	29	27
873	GTNRSSK <u>G</u> AS L IGKVDGT-----GGGGSK-B	135	87	0.2	0

SEQ ID NO:	SEQUENCE	% Rel Binding		% Rel T _{1/2}	
		Exp1	Exp2	Exp1	Exp2
874	GTNRSSKGR <u>A</u> LIGKVDGT-----GGGGSK-B	126	102	223	148
875	GTNRSSKGRS <u>A</u> LIGKVDGT-----GGGGSK-	147	105	2	1
	B				
876	GTNRSSKGRSL <u>A</u> GKVDGT-----GGGGSK-B	156	108	47	41
877	GTNRSSKGRSLI <u>A</u> KVDGT-----GGGGSK-B	139	108	31	24
878	GTNRSSKGRSLIG <u>A</u> VDGT-----GGGGSK-B	118	84	3	2
879	GTNRSSKGRSLIGK <u>A</u> DGT-----GGGGSK-B	148	104	173	100
880	GTNRSSKGRSLIGKV <u>A</u> GT-----GGGGSK-B	124	102	192	111
881	GTNRSSKGRSLIGKVD <u>A</u> T-----GGGGSK-B	119	97	130	121
882	GTNRSSKGRSLIGKVDG <u>A</u> -----GGGGSK-B	132	119	154	116
884	SLIGKVDGTSHVTG-GGGGSK-B	—	NB	—	NB
885	SLIGK <u>A</u> DGTSHVTG-GGGGSK-B	—	NB	—	NB
886	SLIGKV <u>A</u> GTSHVTG-GGGGSK-B	—	NB	—	NB
887	SLIGK <u>AA</u> GTSHVTG-GGGGSK-B	—	NB	—	NB

Table 27: Comparator 2

SEQ ID NO:	SEQUENCE	% Rel Binding		% Rel T _{1/2}	
		Exp1	Exp2	Exp1	Exp2
871	GTNRSSKGRSLIGKVDGT-----GGGGSK-B	—	NB	—	NB
872	GTNRSSK <u>A</u> RS L IGKVDGT-----GGGGSK-B	—	NB	—	NB

SEQ ID NO:	SEQUENCE	% Rel Binding		% Rel T _{1/2}	
		Exp1	Exp2	Exp1	Exp2
873	GTNRSSKGR <u>A</u> SLICKVDGT-----GGGGSK-B	—	NB	—	NB
874	GTNRSSKGR <u>A</u> SLICKVDGT-----GGGGSK-B	—	NB	—	NB
875	GTNRSSKGR <u>A</u> SLICKVDGT-----GGGGSK-B	—	NB	—	NB
876	GTNRSSKGRSL <u>A</u> CKVDGT-----GGGGSK-B	—	NB	—	NB
877	GTNRSSKGRSLI <u>A</u> KVDGT-----GGGGSK-B	—	NB	—	NB
878	GTNRSSKGRSLI <u>A</u> VDGT-----GGGGSK-B	—	NB	—	NB
879	GTNRSSKGRSLICK <u>A</u> DGT-----GGGGSK-B	—	NB	—	NB
880	GTNRSSKGRSLICKV <u>A</u> GT-----GGGGSK-B	—	NB	—	NB
881	GTNRSSKGRSLICKVD <u>A</u> T-----GGGGSK-B	—	NB	—	NB
882	GTNRSSKGRSLICKVDG <u>A</u> -----GGGGSK-B	—	NB	—	NB
884	SLIGKVDGTSHVTG-GGGGSK-B	—	100	—	100
885	SLIGK <u>A</u> DGTSHVTG-GGGGSK-B	—	120	—	159
886	SLIGK <u>V</u> AGTSHVTG-GGGGSK-B	—	88	—	27
887	SLIGK <u>AA</u> GTSHVTG-GGGGSK-B	—	87	—	27

Table 28: Comparator 3

SEQ ID NO:	SEQUENCE	% Rel Binding		% Rel T _{1/2}	
		Exp1	Exp2	Exp1	Exp2
871	GTNRSSKGRSLIGKVDGT-----GGGGSK-B	—	100	—	100
872	GTNRSSK <u>A</u> RLIGKVDGT-----GGGGSK-B	—	101	—	109

SEQ ID NO:	SEQUENCE	% Rel Binding		% Rel T _{1/2}	
		Exp1	Exp2	Exp1	Exp2
873	GTNRSSKGR <u>A</u> SLIGKVDGT-----GGGGSK-B	—	98	—	7
874	GTNRSSKGR <u>A</u> SLIGKVDGT-----GGGGSK-B	—	106	—	21
875	GTNRSSKGRS <u>A</u> LIGKVDGT-----GGGGSK-B	—	115	—	79
876	GTNRSSKGRSL <u>A</u> GKVDGT-----GGGGSK-B	—	92	—	7
877	GTNRSSKGRSLI <u>A</u> KVDGT-----GGGGSK-B	—	101	—	8
878	GTNRSSKGRSLIG <u>A</u> VDGT-----GGGGSK-B	—	109	—	95
879	GTNRSSKGRSLIGK <u>A</u> DGT-----GGGGSK-B	—	96	—	98
880	GTNRSSKGRSLIGKV <u>A</u> GT-----GGGGSK-B	—	99	—	120
881	GTNRSSKGRSLIGKVD <u>A</u> T-----GGGGSK-B	—	93	—	128
882	GTNRSSKGRSLIGKVDG <u>A</u> -----GGGGSK-B	—	117	—	118
884	SLIGKVDGTSHVTG-GGGGSK-B	—	NB	—	NB
885	SLIGK <u>A</u> DGTSHVTG-GGGGSK-B	—	NB	—	NB
886	SLIGKV <u>A</u> GTSHVTG-GGGGSK-B	—	NB	—	NB
887	SLIGK <u>A</u> AGTSHVTG-GGGGSK-B	—	NB	—	NB

[0151] The results from the alanine scanning experiments are summarized in Fig. 5, where the black circles indicate amino acids of PAR-2 which, when changed to alanine, substantially reduce binding by the corresponding antibody (*i.e.*, the T_{1/2} of antibody binding to the mutated peptide is less than 30% of the T_{1/2} of antibody binding to the wild-type peptide). (Open triangles in Fig. 5 indicate non-activating upstream protease cleavage sites, and the black triangle indicates the activating protease cleavage site). As illustrated in Fig. 5, Comparators 1 and 3 were sensitive to mutations at residues on both sides of the activating protease cleavage site. By contrast, antibodies H4H581 P and H4H588N are only sensitive to mutations at residues which are found C-terminal to the activating protease cleavage site. Thus, the H4H581 P binding site on PAR-2 appears to be shifted by about 2-4 amino acids in the C-terminal direction relative to binding site of the Comparator 1 and 3 antibodies, and the H4H588N binding site is shifted by about 2-4 amino acids in the C-terminal direction from the H4H581 P binding site. The Comparator 2 antibody only bound to the peptides comprising the 14 amino acids downstream from the activating PAR-2 protease cleavage site, *i.e.*, SLIGKVDGTSHVTG (residues 1-14 of SEQ ID NO:884), and was sensitive to mutations at the aspartic acid residue (Asp-43 of

SEQ ID NO:851), but not to mutations at the valine residue (Val-42 of SEQ ID NO:851).

[0152] Significantly, this experiment indicates that antibodies H4H581 P and H4H588N both interact with the first V and D residues located C-terminal to the activating PAR-2 protease cleavage site (*i.e.*, Val-42 and Asp-43 of SEQ ID NO:851), whereas the Comparator 1 and 3 antibodies do not interact with either of these residues, and the Comparator 2 antibody interacts with Asp-43 but not Val-42. The shifted binding of H4H581 P on PAR-2 as compared to the comparator antibodies may explain the functional superiority of H4H581 P over the comparator as demonstrated in the following *in vivo* examples.

Example 10. Dose Response of Anti-PAR-2 Antibody in Pruritus Models

[0153] In this Example, the ability of the anti-PAR-2 antibody H4H581 P to attenuate itch in two different protease-induced pruritus models was assessed. Transgenic mice expressing human PAR-2 (hPAR2 ^{+/+}) were used for all cohorts in these experiments. Separate cohorts of mice received 150 mg/kg (s.c.) of an isotype control mAb or 10, 25, 50, 75, 100, and 150 mg/kg (s.c.) of H4H581 P. Twenty-four hours after antibody dosing all cohorts received 150 µg of porcine trypsin, or 10 µg recombinant human beta tryptase, (s.c., interscapular), which produced bouts of scratching behavior for 30 to 60 minutes. A dose-response relationship was observed in mice receiving H4H581 P prior to trypsin injection, with an estimated ED₅₀ of 25 mg/kg. The results of these experiments, expressed in terms of the percent change in the total number of scratching bouts recorded over a 30 minute period following trypsin administration, or over a 60 minute period following tryptase administration, are shown in Table 29 (all data are represented as mean ± SEM; ND = not determined; * = p<0.05 compared to the isotype control group).

Table 29

Dose of mAb H4H581P (mg/kg)	Percent Change in Scratching Bouts Relative to Control	
	Trypsin	Tryptase
10	9.9 ± 23.1	-40.7 ± 23.4
25	-26.6 ± 11.3	-38.5 ± 11.1
50	-31.3 ± 13.5	-47.7 ± 8.0*
75	-34.9 ± 4.7*	ND
100	-55.2 ± 8.0*	-39.6 ± 6.9*
150	-42.9 ± 9.7*	ND

[0154] As shown in this Example, mAb H4H581 P was able to block protease-induced pruritus behaviors in a dose dependent manner using two different protease-induced itch models.

Example 11. Reduction of Pruritus Behaviors by Administration of an Anti-PAR-2 Antibody in a Hapten-Induced Chronic Dermatitis Model

[0155] To further assess the ability of the anti-PAR-2 antibody H4H581P to reduce pruritus behaviors in a physiologically relevant disease state, a mouse model of chronic dermatitis was used. In this model, mice received repeated cutaneous applications of the haptenizing agent, oxazolone. This chronic oxazolone-induced dermatitis model has been shown to recapitulate many of the clinical, histological, and immunological hallmarks of atopic dermatitis in humans (Man et al., 2008, J. Invest. Dermatol. 128(1):79-86).

[0156] Mice were sensitized with a single cutaneous application of 1% oxazolone on the left ear or vehicle (100 mg/kg, s.c.). The mice then received nine total cutaneous applications (challenges) of 0.6% oxazolone between the scapulae beginning seven days after the sensitization application. Weekly dosing (3 total) of the H4H581 P anti-PAR2 antibody was initiated 24 hours prior to the first oxazolone challenge (100 mg/kg, s.c.). This dosing paradigm significantly reduced pruritus behaviors as measured by reduced numbers of scratching bouts elicited by the final oxazolone challenge. All data are represented as mean number of scratching bouts ± SEM for n=6 mice/group; * = p<0.05 by Tukey post-hoc test as compared to the Oxazolone + IgG control group; # = p<0.05 by Tukey post-hoc test compared to the Vehicle + IgG control group).

Table 30

Treatment	Time (minutes)						Total
	0-10	10-20	20-30	30-40	40-50	50-60	
Vehicle + IgG control	0.0±0.0	0.8±0.6	2.2±1.4	3.4±1.3	4.8±2.0	2.4±1.0	13.6±4.2
Oxazolone + IgG control	0.5±0.5	11.3±3.9	24.8±9.7	28.0±7.3	21.0±7.9	21.3±7.3	#106.8±33.2
Oxazolone + H4H581 P	0.2±0.2	1.6±1.2	*6.0±2.4	16.6±5.1	18.2±4.8	18.0±5.5	60.6±11.6

[0157] Histological analysis showed a significant increase in epidermal hyperplasia and immune cell infiltrate in the oxazolone-challenged animals. (Data not shown). No significant differences were observed in any of these parameters between the H4H581 P anti-PAR2 antibody and the isotype control.

Example 12. Comparison of Pruritus Inhibiting Activities of mAb H4H581P

[0158] In this Example, the ability of mAb H4H581P to attenuate itching bouts in a mouse pruritus model was compared to that of a comparator anti-PAR-2 mAb (Comparator "1A1" described in WO 2009/005726).

[0159] Transgenic mice expressing human PAR-2 (hPAR2^{+/+}) were divided into 3 cohorts. Cohort A received 50 mg/kg (s.c.) of an isotype control mAb, cohort B received 50 mg/kg (s.c.) of H4H581 P, and Cohort C received 50 mg/kg (s.c.) of the comparator anti-PAR-2 antibody. Twenty-four hours after antibody dosing all cohorts received 150 µg of trypsin (s.c., interscapular), which produced bouts of scratching behavior for 30 minutes. The percent change in the number of scratching bouts observed for the treated mice as compared to control-treated mice is shown in Table 29 (all data are represented as mean ± SEM).

Table 31

Antibody Treatment (50 mg/kg)	(% change in scratching bouts from control)
mAb H4H581 P	- 41.1 ± 13.5
Comparator mAb	- 13.9 ± 9.9

[0160] As shown in this Example, mAb H4H581P was substantially more effective than the comparator mAb in reducing pruritus behaviors in the trypsin-induced itch model used herein.

[0161] The present invention is not to be limited in scope by the specific embodiments describe herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and the accompanying figures.

SEQUENCE LISTING

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<120> High Affinity Human Antibodies to Human Protease Activated Receptor-2

<130> 6110A-WO

<140> To be assigned

<141> Filed herewith

<150> 61/240,783

<151> 2009-09-09

<150> 61/242,821

<151> 2009-09-16

<150> 61/317,839

<151> 2010-03-26

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35     40     45
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50     55     60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr

65      70      75      80
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<213> Artificial Sequence

<220>

<223> Synthetic

<400> 6

Ile Thr Trp Asn Ser Gly Asn Met
1 5

<210> 7

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 7

gcaaaagaaa actgggcctt tgactac 27

<210> 8

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 8

Ala Lys Glu Asn Trp Ala Phe Asp Tyr

1 5

<210> 9

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 9

gatatgtgta tgaaccagac tccactctcc tcacctgtca cccttggaac gccggcctcc 60
atctcctgca ggtctagtca cagcctccta cacagtgatg gaaacacctt cttgagttgg 120
cttcagcaga ggcacagcca gctccaaga ctctaatctt ataagatttc taaccgggttc 180
tctgggggtc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggttg aagctgagga tgtcgggggt tattctctga tgcaagctac acaatttcgg 300
tacacttttg gccaggcgac caagctggag atcaaaa 336

<210> 10

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 10

```

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

```

<210> 11

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 11

cacagcctcg tacacagtga tggaacacc tac 33

<210> 12

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 12

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

```

<210> 13

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 13

aagattct 9

<210> 14

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 14

Lys Ile Ser

1

<210> 15

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 15

atgcaagcta cacaatttcc gtacact 27

<210> 16

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 16

Met Gln Ala Thr Gln Phe Pro Tyr Thr
1 5

<210> 17

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 17

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gaagtgcagc tgggtggagtc tggggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tctgtgtcag cctctggatt cacttttgat gattatgcca tgcactgggt ccggcaagct 120
ccagggaagg gcctagagtg ggtctcaggt attacttggc atagtggtaa catggcctat 180
gcggactctg tgaaggcccg attcaccato tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttat attactgtgc aaaagaaaac 300
tgggcctttg actactgggg ccagggaacc ctggtcaccg tctctcca 348

```

<210> 18

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 18

```

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

```

<210> 19

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 19

```

gatattgtga tgaccacagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctcctgca ggtctagtca cagcctcgta cacagtgatg gaaacacctt cttgagttgg 120
cttcacgaga gccacagcca gcctccaaga ctctcaattt ataagatttc taaccgggttc 180
tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggttg aagctgagga tgtcgggggt tattctgca tgcaagctac acaatttccg 300
tacacttttg gccaggcgac caagctggag atcaaa 336

```

<210> 20

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 20

```

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

```

<210> 21

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 21

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gaagtgacgc tgggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatgcc a tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attacttgga atagtggtaa catgggctat 180
gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagctctgag agctgaggac acggccttgt attactgtgc aaaagaaaac 300
tgggcctttg actactgggg ccagggaacc ctggtcaccg tctctcca 348

```

<210> 22

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 22

```

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

```

<210> 23

<211> 337

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 23

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gatattgtga tgacccagac tccactotcc tcacctgtca cccttgagca gccggcctcc 60
atctctctga ggtctactca cagctctgta cacagtgatg gaaacacctt cttgagttgg 120
cttcagcaga ggccagccca gctccaaga ctctaatatt ataagatttc taaccgggtc 180
tctgggggtc cagacaçatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggtgg aagctgagga tgcgggggtt tattactgca tgcaagctac acaatttcog 300
tacacttttg gccaggcgac caagctggag atcaaac 337

```

<210> 24

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 24

```

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

```

<210> 25

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 25

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gaagtgcagc tgggtggagtc tgggggaggc gtggtccagc ctggcaggtc cctgagactc 60
tctgtgcag cctctgcatc cacctttgat gattatacca tgcactgggt ccggcaagtt 120
ccagggaagg acctgaagtg ggtctcaggt attacttgga atggtggtag aaaagcctat 180
gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctcttt 240
ctgcaaatga acagctctgag agctgaggac acggccttct attactgtgc aaaagaagat 300
gaggcttttg actactgggg ccagggaacc ctggtcaccg tctctctca 348

```

<210> 26

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 26

```

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

```

<210> 27

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 27

ggattcacct ttgatgatta tacc 24

<210> 28

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 28

```

Gly Phe Thr Phe Asp Asp Tyr Thr
 1          5

```

<210> 29

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 29

attacttgga atggtgtag aaaa 24

<210> 30

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 30

```

Ile Thr Trp Asn Gly Gly Arg Lys
 1          5

```

<210> 31

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 31

gcaaaagaag atgaggcttt tgactac 27

<210> 32

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 32

Ala Lys Glu Asp Glu Ala Phe Asp Tyr
1 5

<210> 33

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 33

gatattgtga tgaccagagac tccactctcc tcacctgcca cctttggaca gccggcctcc 60
atctcctgca ggtctagta aagcctcgta cacagtgatc gcaacaccta cttgagttgg 120cttcagcaga ggccaggcca gcctccaaga ctccctaattt ataagatttc taaccggttt 180
tttggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaato 240
agcagggtgg aggcagagga tgtcggcggt tattaccgca tgcaagcaac acaatttccg 300
tacacttttg gccaggggac caagctggag atcaaaa 336

<210> 34

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 34

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

<210> 35

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 35

caaagcctcg tacacagtga tggcaacacc tac 33

<210> 36

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 36

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

<210> 37

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 37

aagatttct 9

<210> 38

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 38

Lys Ile Ser

1

<210> 39

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 39

atgcaagcaa cacaatttc gtacact 27

<210> 40

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 40

Met Gln Ala Thr Gln Phe Pro Tyr Thr
1 5

<210> 41

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 41

```

gaagtgcagc tgggtggagtc tggggggaggc gtggtccagc ctggcaggtc cctgagactc 60
tctgtgtag cctctggatt cacttttgat gattatacca tgcactgggt ccggcaagtt 120
ccagggaagg acctgaagtg ggtctcaggt attacttggc atggtggtag aaaagcctat 180
gcggactctg tgaaggcccg attcaccctc tccagagaca acgccaagaa ctccctcttt 240
ctgcaaatga acagctcagc agctgaggac acggccttct attactgtgc aaaagaagat 300
gaggcttttg actactgggg ccagggaacc ctggtcaccg tctctcca 348

```

<210> 42

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 42

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

```

<210> 43

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 43

```

gatattgtga tgacccagac tccactctcc tcacctgtca cccttgagca gccggcctcc 60
atctcttgca ggtctactca aagcctcgta cacagtgatg gcaacacctc cttgagttgg 120
cttcagcaga gggcaggcca gcctccaaga ctctaatatt ataagatttc taaccgggtt 180
tttgggggtc cagacacatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggttg aggcaggga tgcggcggtt tattactgca tgcaagcaac acaatttcgg 300
tacacttttg gccaggcgac caagctggag atcaaa 336

```

<210> 44

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 44

```

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

```

100

105

110

<210> 45

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 45

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gaagtgcagc tgggtggagtc tggggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgat gattatacca tgcactgggt ccggcaagct 120
ccagggaagg gcttgagtg ggtctcaggt attacttga atgggtgtag aaaaggctat 180
gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagctgag agctgaggac acggccttgt attactgtgc aaaagaagat 300
gaggcttttg actactgggg ccagggaacc ctggtcaccg tctctcca 348

```

<210> 46

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 46

```

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

```

<210> 47

<211> 337

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 47

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gatattgtga tgaccagac tccactctcc tcacctgtca cccttgaca gccggcctcc 60
atctctctga ggtctactca aagcctcgta cacagtgtat gcaacaccta cttgagttgg 120
cttcagcaga ggccaagcca gctccaaga ctctaatat ataagatttc taaccgggtc 180
tctgggggtc cagacaatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggttg aagctgagga tgcgggggtt tattactgca tgcaagcaac acaatttccg 300
tacacttttg gccaggggac caagctggag atcaaac 337

```

<210> 48

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 48

```

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

```

<210> 49

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 49

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gaagtgcagt tgggtggagtc tggggggaggc ttggcacagc ctggcaggtc cctgagagtc 60
tctgtttcag cctctgcatt caattttgat gattatgcc tgcactgggt ccggcaagct 120
ccggggaagg gcctggagtg ggtctcaggt attagtggga atagtggtag cagaggctat 180
gggactctg tgaaggccg cttcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccctgt attactgtgt aaaagagaac 300
tgggcctttg aatactgggg ccagggaacc ctggtcaccg tctctcca 348

```

<210> 50

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 50

```

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

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
 85           90           95
Val Lys Glu Asn Trp Ala Phe Glu Tyr Trp Gly Gln Gly Thr Leu Val
 100          105          110
Thr Val Ser Ser
 115

```

<210> 51

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 51

```

ggattcaatt ttgatgatta tgcc          24

```

<210> 52

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 52

Gly Phe Asn Phe Asp Asp Tyr Ala
1 5

<210> 53

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 53

atagttgga atagtggtag caga 24

<210> 54

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 54

Ile Ser Trp Asn Ser Gly Ser Arg
1 5

<210> 55

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 55

gtaaaagaga actgggcctt tgaatac 27

<210> 56

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 56

Val Lys Glu Asn Trp Ala Phe Glu Tyr
1 5

<210> 57

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 57

gatattgtga tgaaccagac tccactotcc tcacctgtca cccttggaac gccggcctcc 60
atctcctgca ggtcactca tagcctcgta cacagtgatg gaagcaccta cttgagttgg 120
cttcagcaga ggccaggcca gctccaaga ctccataatt ataaaatttc taaccgattc 180
lclggggctc cagacagall caglggcagl ggggcaggga cagalllcc acgaaaaac 240
agcagggtgg aagcagga tgcgggctt tattactgca tgcaggctac acaatttccg 300
tacacttttg gccaggcgac caagctggag atcaaa 336

<210> 58
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 58
 Asp Ile Val Met Thr Gln Thr Pro Leu Ser Ser Pro Val Thr Leu Gly
 1 5 10 15
 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser His Ser Leu Val His Ser
 20 25 30
 Asp Gly Ser Thr Tyr Leu Ser Trp Leu Gln Gln Arg Pro Gly Gln Pro
 35 40 45
 Pro Arg Leu Leu Ile Tyr Lys Ile Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ala Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Arg Val Glu Ala Glu Asp Val Gly Leu Tyr Tyr Cys Met Gln Ala
 85 90 95
 Thr Gln Phe Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 59
 <211> 33
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 59
 catagcctcg tacacagtga tggaagcacc tac 33

<210> 60
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 60
 His Ser Leu Val His Ser Asp Gly Ser Thr Tyr
 1 5 10

<210> 61
 <211> 9
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 61
 aaaattct 9

<210> 62
 <211> 3
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 62
 Lys Ile Ser
 1

<210> 63
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 63
 atgcaggcta cacaatttcc gtacact 27

<210> 64
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 64
 Met Gln Ala Thr Gln Phe Pro Tyr Thr
 1 5

<210> 65
 <211> 348
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 65
 gaagtgcagc tggtaggagtc tgggggaggc ttggcacagc ctggcaggtc cctgagagtc 60
 tcctgttccag cctotggatt caattttgat gattatgccca tgcactgggt ccggcaagct 120
 ccggggaagg gccctggagtg ggtctcaggt attagttgga atagtggtag cagaggctat 180
 gcggactctg tgaagggecg ctccaccatc tccagagaca acgccaagaa ctccctgtat 240
 ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgt aaaagagaac 300
 tgggcctttg aatactgggg ccagggaacc ctggtcaccg tctctctca 348

<210> 66
 <211> 116
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 66
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ala Gln Pro Gly Arg
 1 5 10 15
 Ser Leu Arg Val Ser Cys Ser Ala Ser Gly Phe Asn Phe Asp Asp Tyr
 20 25 30
 Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Gly Ile Ser Trp Asn Ser Gly Ser Arg Gly Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
 85 90 95
 Val Lys Glu Asn Trp Ala Phe Glu Tyr Trp Gly Gln Gly Thr Leu Val
 100 105 110
 Thr Val Ser Ser
 115

<210> 67
 <211> 336
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic

<400> 67

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gataattgtga tgaaccagac tccactctcc tcaactgtca cccctggaca gccggccctcc 60
atctctctgca ggtctactca tagcctcgtc cacagtgatg gaagcaccta cttgagttgg 120
cttcagcaga gccacagcca gcctccaaga ctccataatt ataaaatttc taaccgatto 180
tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaato 240
agcagggttg aagctgagga tgcggggctt tattactgca tgcaggctac acaatttcgg 300
tacacttttg gccaggggac caagctggag atcaaaa 336

```

<210> 68

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 68

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

```

<210> 69

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 69

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gaagtgcagc tgggtggagtc tggggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tctgtgtcag cctctggatt caattttgat gattatgcca tgcactgggt ccggccaagct 120
ccagggaagg gccctggagt ggtctcaggt attagtgtga atagtggtag cagaggctat 180
gcggactctg tgaaggcccg attcaccato tccagagaca acgccaaaga ctccctgtat 240
ctgcaaatga acagctctgag agctgaggac acggccttgt attactgtgt aaaagagaac 300
tgggcctttg aatactgggg ccagggaacc ctggtcaccg tctctcca 348

```

<210> 70

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 70

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

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

```

<210> 71
 <211> 337
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 71
 gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
 atctctctga ggtctagtca tagcctcgta cacagtgatg gaagcaccta cttgagttgg 120
 cttcagcaga gccacgcca gccccaaga ctccataatt ataaaatttc taaccggttc 180
 tctgggggtc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
 agcagggtgg aagctgagga tgtcgggggt tattactgca tgcaggctac acaatttcgg 300
 tacacttttg gccaggggac caagctggag atcaaac 337

<210> 72
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 72
 Asp Ile Val Met Thr Gln Thr Pro Leu Ser Ser Pro Val Thr Leu Gly
 1 5 10 15
 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser His Ser Leu Val His Ser
 20 25 30
 Asp Gly Ser Thr Tyr Leu Ser Trp Leu Gln Gln Arg Pro Gly Gln Pro
 35 40 45
 Pro Arg Leu Leu Ile Tyr Lys Ile Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ala Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
 85 90 95
 Thr Gln Phe Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 73
 <211> 348
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 73
 gaagtgcagc tgggtggagtc tgggggaggc ttggtacagg ctggcaggcc cctgcgactc 60
 tctctgtcag cctctggatt cacccttgat gattatgccg tgcactgggt ccggcaagct 120
 ccagggaagg gccctggagt ggtctcaggt attagtggga atagtggtag cagaggctat 180
 gccgactctg tgaaggggcg attcaccatc tccagagaca acgcaaaaaa ctccctgcat 240
 ctgcaaatgt acagtctgag agctgaggac acggccttgt attactgtgc aaaagagAAC 300
 tggtcctttg actactgggg ccagggaacc ctggtcacgc tctcctca 348

<210> 74
 <211> 116
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 74

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

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<210> 75

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 75

ggattcacct ttgatgatta tgcc 24

<210> 76

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 76

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Gly Phe Thr Phe Asp Asp Tyr Ala
 1           5

```

<210> 77

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 77

attagttgga atagtggtag caga 24

<210> 78

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 78

```

Ile Ser Trp Asn Ser Gly Ser Arg
 1           5

```

<210> 79

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 79

gcaaaagaga actggtcctt tgactac 27

<210> 80

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 80

Ala Lys Glu Asn Trp Ser Phe Asp Tyr
1 5

<210> 81

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 81

gatattgtga tgacccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctcctgca ggtctagtca aagcctcgta cacagtgatg gaaacaccta cttgagttgg 120
cttcagcaga ggccaggcca gcctccaaga ctctaatatt ataagatttc ttaccggttc 180tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaato 240
agcagggtgg caactgagga tgtcggggtt tattacgca tgcaagctac acaattgccg 300
tacacttttg gccaggggac caagctggag atcaaaa 336

<210> 82

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 82

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

<210> 83

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 83

caaagcctcg tacacagtga tggaaacacc tac 33

<210> 84

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 84

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

<210> 85

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 85

aagatttct 9

<210> 86

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 86

Lys Ile Ser
1

<210> 87

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 87

atgcaagcta cacaattgcc gtacact 27

<210> 88

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 88

Met Gln Ala Thr Gln Leu Pro Tyr Thr
1 5

<210> 89

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 89

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gaagtgcagc tgggtggagtc tggggggagcg ttggtacagg ctggcaggtc cctgcgactc 60
tcctgtgcag cctctgggatt cacctttgat gattatgccg tgcaactgggt cgggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag cagaggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccccaaa ctccctgcat 240
ctgcaaatgt acagtctgag agctgaggac acggccttgt attactgtgc aaaagagaaac 300
tggtcctttg actactgggg ccagggaacc ctggtcacgc tctctctca 348

```

<210> 90

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 90

```

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

```

<210> 91

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 91

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gatattgtga tgaccagagc tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctctctga ggctcactca aagcctcgta cacagtgatg gaaacacctc cttgagttgg 120
cttcagcaga gccacggcca gcctccaaga ctctaatatt ataagatttc ttaccgggtc 180
tctggggctc cagacacatt cagtggcagt ggggcaggga cagatttcac actgaaaato 240
agcagggttg caactgagga tgtcgggggt tattactgca tgcaagctac acaattgcog 300
tacacttttg gccaggcgac caagctggag atcaaaa 336

```

<210> 92

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 92

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

```

<210> 93

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 93

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gaagtgcagc tgggtggagt tgggggaggo ttggtacago ctggcaggto cctgagacto 60
tctgtgcag cctctggatt cacccttgat gattatgcca tgcactgggt ccggcaagct 120
ccaggggaagg gctctggagt ggtctcaggt attagttgga atagtggtag cagaggctat 180
gcggaactctg tgaaggcccg attcaccato tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccctgt attactgtgc aaaagagaac 300
tggtcctttg actactgggg ccaggggaacc ctggtcaccg tctctca 348

```

<210> 94

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 94

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

```

<210> 95

<211> 337

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 95

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gatattgtga tgaccagac tccactotcc tcacctgtca cccctggaca gccggcctcc 60
atctcttga ggtctagta aagccttgta cacagtgatg gaaacacctt cttgagttgg 120
cttcagcaga ggccagccca gcctccaaga ctctaatatt ataagatttc taaccggttc 180
tctggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaato 240
agcagggtgg aagctgagga tgtcggggtt tattactgca tgcaagctac acaattgccg 300
tacacttttg gccaggcgac caagctggag atcaaac 337

```

<210> 96

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 96

```

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

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<210> 97
 <211> 357
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 97
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 tcctgtgcag cctctggatt cactcttagc agctatgccg tgacctgggt ccgccaggct 120
 ccggggaagg ggcctgattg ggtctcagct attagtgggt gtcgtggtag cgcatactac 180
 gcagactcgg tgaaggcccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240
 ctgcaaatga acagcctgcg agccgaggac acggccgtat attactgtgc gaaagagggg 300
 gatagtggct acgatttggc ctactggggc cggggaaccc tggtcaccgt ctcgtca 357

<210> 98
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 98
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30
 Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Tyr Trp Val
 35 40 45
 Ser Ala Ile Ser Gly Gly Arg Gly Ser Ala Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Lys Glu Gly Asp Ser Gly Tyr Asp Leu Ala Tyr Trp Gly Arg Gly
 100 105 110
 Thr Leu Val Thr Val Ser Ser
 115

<210> 99
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 99
 ggattcacct ttacagcta tgcc 24

<210> 100
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 100
 Gly Phe Thr Phe Ser Ser Tyr Ala
 1 5

<210> 101
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic

<400> 101

attagtgggt gtcgtgtag cgca 24

<210> 102

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 102

Ile Ser Gly Gly Arg Gly Ser Ala
1 5

<210> 103

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 103

gcgaaagagg gggatagtgg ctacgatttg gcctac 36

<210> 104

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 104

Ala Lys Glu Gly Asp Ser Gly Tyr Asp Leu Ala Tyr
1 5 10

<210> 105

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 105

gacatccaga tgaccagtc tccatcctca ctgtccgcat ctgtaggaga cagagtcacc 60
atcacttgct gggcgaggca gggcattagt aataatttag cctggcttca gcagaaacca 120
gggaaagccc ctaagtccct gatctatgct gcatccagtt tgcaaagtgg gatcccatca 180
aagttcagcg gcagtggatc tgggacatat ttcactctca ccacagcag cctgcagcct 240
gaagattttg cgacttatta ctgccaaaca tataaaagtt ccccgctcac ttccggcgga 300
gggaccaagg tggagatcaa a 321

<210> 106

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 106

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

```

<210> 107

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 107

cagggcatta gtaataat 18

<210> 108

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 108

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Gln Gly Ile Ser Asn Asn
 1           5

```

<210> 109

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 109

gctgcatcc 9

<210> 110

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 110

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Ala Ala Ser
 1

```

<210> 111

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 111
caacaatata aaagttcccc gctcact 27

<210> 112

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 112
Gln Gln Tyr Lys Ser Ser Pro Leu Thr
1 5

<210> 113

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 113
gaggtgcagc tgttgagtc tgggggaggc ttggtacagc cggggggggt cctgagactc 60
tcctgtgcag cctctggatt caccttttagc agctatgccg tgacctgggt ccgccaggct 120
ccggggaagg ggcctgtattg ggtctcagct attagtgggt gtcgtggtag cgcatactac 180
gcagactccg tgaaggcccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgcg agccgaggac acggccgtat attactgtgc gaaagagggg 300
gatatgggt acgatttggc ctactggggc cggggaaccc tggtcaccgt ctcctca 357

<210> 114

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 114
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Tyr Trp Val
35 40 45
Ser Ala Ile Ser Gly Gly Arg Gly Ser Ala Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Lys Glu Gly Asp Ser Gly Tyr Asp Leu Ala Tyr Trp Gly Arg Gly
100 105 110
Thr Leu Val Thr Val Ser Ser
115

<210> 115

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 115
gacatccaga tgaccagtc tccatcctca ctgtccgcct ctgtaggaga cagagtcacc 60
atcacttgct gggcgagcca gggcattagt aataatttag cctggcttca gcagaaacca 120
gggaaagccc ctgaagcccc gactctatgct gcacccagtt tgcaaaagtg galcccatca 180
aagttcagcg gcagtgcatc tgggacatat ttcactctca ccatcagcag cctgcagcct 240
gaagattttg cgacttatta ctgccaacaa tataaaagtt ccccgctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 116
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 116
 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Arg Val Thr Ile Thr Cys Arg Ala Arg Gln Gly Ile Ser Asn Asn
 20 25 30
 Leu Ala Trp Leu Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile
 35 40 45
 Tyr Ala Ala Ser Ser Leu Gln Ser Gly Ile Pro Ser Lys Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Tyr Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80
 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Lys Ser Ser Pro Leu
 85 90 95
 Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 117
 <211> 357
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 117
 gaggtgcagc tgttgagtc tgggggaggc ttggtacagc ctgggggggct cctgagactc 60
 tcctgtgcag cctcgcatt cactcttagc agctatgccca tgagctgggt ccgccaggct 120
 ccaggggaagg ggcctggagt ggtctcagct attagtgggt gtcgtggtag cgcatactac 180
 gcagactcgc tgaaggcccg gttcaccatc tccagagaca attccaagaa cagctgtgat 240
 ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagagggg 300
 gatagtggct acgatttggc ctactggggc cagqqaacco tggtcaccgt ctcctca 357

<210> 118
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 118
 Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30
 Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Ala Ile Ser Gly Gly Arg Gly Ser Ala Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Lys Glu Gly Asp Ser Gly Tyr Asp Leu Ala Tyr Trp Gly Gln Gly
 100 105 110
 Thr Leu Val Thr Val Ser Ser
 115

<210> 119
 <211> 322
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 119

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gacatccaga tgacccagtc tccatccctca ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgtc gggcgagtc gggcattagt aataatttag cctgggtttca gcagaaacca 120
gggaaagccc ctaagtcocct gatctatgct gcatccagtt tgcaaaagtgg ggtcccatca 180
aggttcagsg gcagtgagtc tgggacagat ttcactctca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgccaacaa tataaaagt tccccgtcac tttcggcgga 300
gggaccaagg tggagatcaa ac 322

```

<210> 120

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 120

```

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

```

<210> 121

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 121

```

gaggtgcagc tgttgagtc ggggggaggc ttggtacagc ctggggggtc cctgagactc 60
tcctgtgcaa cctctgcat cactcttagc agatatacca tgacctgggt ccgccaggct 120
ccagggaagg ggcgtgtttg ggtctcaggt attggtggta gtggtggtcg cgcatactac 180
gcagactccg tgaaggcccg gttcaccctc tccagagaca attccaagaa cactgtgtat 240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagagggg 300
gatagtggct acgatttga ctactggggc cggggaaccc tggtcaccgt ctctgca 357

```

<210> 122

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 122

```

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

```

<210> 123

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 123

ggattcacct ttagcagata tacc 24

<210> 124

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 124

Gly Phe Thr Phe Ser Arg Tyr Thr
1 5

<210> 125

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 125

attggtgga gtggtggtcg cgca 24

<210> 126

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 126

Ile Gly Gly Ser Gly Gly Arg Ala
1 5

<210> 127

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 127

gcgaaagagg gggatagtg ctacgatttg gactac 36

<210> 128

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 128

Ala Lys Glu Gly Asp Ser Gly Tyr Asp Leu Asp Tyr
1 5 10

<210> 129
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 129
 gacatccaga tgacccagta tccatccotca ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgto qggcgacgca qggcataagt aattatttaq cctggcttca qcagaaacca 120
 gggaaagccc ctaagtcctt gatctatgct gcatccagtt tgcaaagggg ggtcccatca 180
 aagttcagcg gcaggggato tgggacagat ttcactctca ccatcagcag cctgcagcct 240

 gaagattctg caacttatta ctgccaacaa tataaaattt ccccgctcac tttcggcgga 300
 gggaccaagg tggagatcaa g 321

<210> 130
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 130
 Asp Ile Gln Met Thr Gln Tyr Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Arg Val Thr Ile Thr Cys Arg Ala Arg Gln Gly Ile Ser Asn Tyr
 20 25 30
 Leu Ala Trp Leu Gln Gln Lys Pro Gly Lys Ala Pro Lys Ser Leu Ile
 35 40 45
 Tyr Ala Ala Ser Ser Leu Gln Arg Gly Val Pro Ser Lys Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80
 Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Tyr Lys Ile Ser Pro Leu
 85 90 95
 Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 131
 <211> 18
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 131
 cagggcataa gtaattat 18

<210> 132
 <211> 6
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 132
 Gln Gly Ile Ser Asn Tyr
 1 5

<210> 133
 <211> 9
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic

<400> 133

gctgcatcc 9

<210> 134

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 134

Ala Ala Ser

1

<210> 135

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 135

caacaatata aaatttcccc gctcact 27

<210> 136

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 136

Gln Gln Tyr Lys Ile Ser Pro Leu Thr

1 5

<210> 137

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 137

```
gaggtgcagc tgttgagtc tgggggagc ttggtacagc ctgggggggc cctgagactc 60
tcctgtgcaa cctctggatt cacttttagc agatatacca tgacctgggt ccgccaggct 120
ccagggaagg ggcgtttttg ggtctcaggt attggtggta gtggtggteg cgcatactac 180
gcagactccg tgaagggccg gttcaccctc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagagggg 300
gatagtggct acgatttggc ctactggggc cggggaaccc tggtcaccgt ctectca 357
```

<210> 138

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 138

```

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

```

<210> 139

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 139

```

gacatccaga tgacccagtc tccatcctca ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgic gggcgaggca gggcataagt aattatttag cctggettca gcagaaacca 120
gggaaagccc ctaagtccct gatctatgct gcatccagtt tgcaaaaggg ggtcccatca 180
aagttcagcg gcagtggatc tgggacagat ttcactetca ccatcagcag cctgcagcct 240
gaagattctg caacttatta ctgccacaa tataaaattt ccccgctcac tttagggcga 300
gggaccaagg tggagatcaa a                               321

```

<210> 140

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 140

```

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

```

<210> 141

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 141

```

gaggtgcagc tgttgagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
tctgtgacag cctctggatt cactcttagc agatatacca tgagctgggt ccgccaggct 120
ccaggaagg ggctggagtg ggtctcagct attggtggta gtggtggtcg cgcatactac 180
gcagactccg tgaaggcccg gtteaccato tccagagaca attccaagaa cacgtgtgat 240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagagggg 300
gatagtggct acgatttga ctactggggc cagggaaccc tggtcacctt ctcctca 357

```

<210> 142

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 142

```

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

```

<210> 143

<211> 322

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 143

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gacatccaga tgacccagtc tccatcctca ctgtctgcat ctgtaggaga cagagtcacc 60
atcaattgtc gggcgagtc gggcataagt aattatttag cctggtttca gcagaaacca 120
gggaaagccc ctaagtccct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
aggttcagcg gcagtggtac tgggacagat ttcactctca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgccaacaa tataaaattt ccccgctcac ttctggcgga 300
gggaccaagg tggagatcaa ac                                     322

```

<210> 144

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 144

```

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

```

<210> 145

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 145

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gaggtgcagc tgttgagtc ggggggagc ttggtacagc ctggggggtc cctgagactc 60
tcctgtgcaa cctctgcatt caccttttagc agatatacca tgacctgggt ccgccaggct 120
ccagggaagg ggcgtgttttg ggtctcaggt attggttgta gtggtggtcg cgcatactac 180
gcagactccg tgaaggcccg gttcacctc tccagagaca attccaagaa cacgtgttat 240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagagggg 300
gatagtggct acgatttga ctactggggc cggggaacco tggtcaccgt ctcgtca 357

```

<210> 146

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 146

```

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

Ala Lys Glu Gly Asp Ser Gly Tyr Asp Leu Asp Tyr Trp Gly Arg Gly
100    105    110
Thr Leu Val Thr Val Ser Ser
115

```

<210> 147

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 147

```

ggattcacct ttacagata tacc      24

```

<210> 148

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 148

```

Gly Phe Thr Phe Ser Arg Tyr Thr
1      5

```

<210> 149

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 149

```

attggtggta gtggtggtcg cgca      24

```

<210> 150

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 150

Ile Gly Gly Ser Gly Gly Arg Ala
1 5

<210> 151

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 151

gcgaaagagg gggatagtg ctacgattg gactac 36

<210> 152

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 152

Ala Lys Glu Gly Asp Ser Gly Tyr Asp Leu Asp Tyr
1 5 10

<210> 153

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 153

gacatccaga tgaccagta tccatcctca ctgtctgcat ctgtaggaga cagagtcacc 60
atcaattgtc gggcgaggca gggcataagt aattatttag cctggcttca gcagaaacca 120
gggaaagccc ctaagtccct gatctatgct gcatccagtt tgcaaaagggg ggtcccatca 180
aagttcagcg gcagtggtgc tgggacagat ttcactctca ccacagcag cctgcagcct 240
gaagattctg caactatta cggccaacaa tataaaattt ccccgctcac tttcggcgga 300
gggaccaagg tgcagatcaa g 321

<210> 154

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 154

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

<210> 155
 <211> 18
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 155
 cagggcataa gtaattat 18

<210> 156
 <211> 6
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 156
 Gln Gly Ile Ser Asn Tyr
 1 5

<210> 157
 <211> 9
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 157
 gctgcatcc 9

<210> 158
 <211> 3
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 158
 Ala Ala Ser
 1

<210> 159
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 159
 caacaatata aaattccccc gctcact 27

<210> 160
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 160

Gln Gln Tyr Lys Ile Ser Pro Leu Thr
1 5

<210> 161

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 161

gaggtgcagc tgttgagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
tcctgtgcaa cctctggatt cacccttagc agatatacca tgacctgggt ccgcccaggct 120
ccagggaagg ggctgttttg ggtctcaggt attggtggta gtggtggctc cgcatactac 180
gcagactccg tgaaggcccg gttcaccctc tccagagaca attccaagaa caccgtgtat 240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagagggg 300
gatagtggct acgatttga ctactggggc cggggaaccc tggtcaccgt ctctca 357

<210> 162

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 162

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

<210> 163

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 163

gacatccaga tgaccagtc tcatctctca ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgct gggcgagcca gggcataagt aattatttag cctggcttca gcagaaacca 120
gggaaagccc ctaagtccct gatctatgct gcatccagtt tgcaaagggg ggtcccatca 180
aagttcagcg gcagtggatc tgggacagat ttactctcca ccacagcag cctgcagcct 240
gaagattctg caacttatta ctgccaaaca tataaaattt ccccgctcac ttccggcgga 300
gggaccaagg tggagatcaa a 321

<210> 164

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 164

```

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

```

<210> 165

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 165

```

gaggtgcagc tgttgagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
tcctgtgcag cctctggatt caccttttagc agatatacca tgagctgggt ccgccaggct 120
ccagggaagg ggtctggagt ggtctcagct attggtggtg gtggtggtcg cgcatactac 180
gcagactccg tgaaggggcg gttcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagagggg 300
gatagtggct acgatttga ctactggggc cagggaaccc tggtcacogt ctctca 357

```

<210> 166

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 166

```

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 Arg Tyr
20           25           30
Thr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

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

```

<210> 167

<211> 322

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 167

```

gacatccaga tgacccagtc tccatccotca ctgtctgcat ctgtaggaga cagagtcacc 60
atcaacttgc gggcgactca gggcataagt aattatttag cctggtttca gcagaaacca 120
gggaaagccc ctaagtccct gatctatgct gcattccagt tgcaaatggt ggtcccatca 180
aggttcagcg gcagtgcatc tgggacagat ttccactctca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgccaacaa tataaaattt ccccgctcac ttctggcgga 300
gggaccaagg tggagatcaa ac
322

```

<210> 168

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 168

```

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

```

<210> 169

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

```

<400> 169
gaagtgcagt tgggtggagtc tggggggagtc ttagtacagc ctggcaggtc cctgagactc 60
tccgtgacag cctctggcatt caccctttagt gattatgccg tgcactgggt ccggccaagct 120
ccaggggaagg gcctggaatg ggtctcaggt attagttgga atagcggtag caaaggcttt 180
gcggaactctg tgaaggcccg gtaccacatc tccagagaca acgccaagaa ctccctctat 240
ctgcaaatga acagctctgag agttgaagac acggccttgt attactgtgc aaaagagaac 300
tggtcctttg tactactggg ccaggggaacc ctggtcaccg tctctctca 348

```

<210> 170

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 170

```

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

```

<210> 171

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 171

```

ggattcacct ttgatgatta tgcc          24

```

<210> 172

<211> 8

<212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 172
 Gly Phe Thr Phe Asp Asp Tyr Ala
 1 5

<210> 173
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 173
 attagttgga atagcggtag caaa 24

<210> 174
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 174
 Ile Ser Trp Asn Ser Gly Ser Lys
 1 5

<210> 175
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 175
 gcaaaagaga actggtcctt tgactac 27

<210> 176
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 176
 Ala Lys Glu Asn Trp Ser Phe Asp Tyr
 1 5

<210> 177
 <211> 336
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 177

```

gatattgtga tgacccagac tccactctcc tcgectgtca cccctggaca gccggcctcc 60
atctctctga ggctctaçtca aagcctcgta cacagtgatg gaaatatcta cttgagttgg 120
cttcagcaga gccacagcca gccctccaga ctcttaattt ataagatttc taaccgggttc 180
tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggttg aagctgaaga tgcgggaatt tattattgca tgcaagcttc gcattttccg 300
tacacttttg gccaggggac caagctggag atcaaa 336

```

<210> 178

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 178

```

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

```

<210> 179

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 179

```

caaagcctcg tacacagtga tggaaataic tac 33

```

<210> 180

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 180

```

Gln Ser Leu Val His Ser Asp Gly Asn Ile Tyr
 1             5             10

```

<210> 181

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 181

```

aagatttct 9

```

<210> 182

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 182

Lys Ile Ser
1

<210> 183

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 183

atgcaagctt cgcattttcc gtacact 27

<210> 184

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 184

Met Gln Ala Ser His Phe Pro Tyr Thr
1 5

<210> 185

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 185

```

gaagtgcagc tgggtggagtc tggggggaggc ttagtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctgcatt cacctttgat gattatgcc a tgcactgggt ccggcaagct 120
ccagggaagg gctctgaatg ggtctcaggt attagttgga atagcggtag caaaggcctt 180
ggggactctg tgaaggcccg gttcaccatc tccagagaca acgccaagaa ctcctcttat 240
ctgcaaatga acagtctgag agttgaagac acggccttgt attactgtgc aaaagagaa 300
tggctccttg actactgggg ccagggaacc ctggctacug tctctctc 348

```

<210> 186

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 186

```

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

```

<210> 187
 <211> 336
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 187
 gatattgtga tgacccagac tccactctcc tcgectgtca cccttggaca gccggcctcc 60
 atctctctga ggtctagtca aagcctcgta cacagtgatg gaaatatcta cttgagttgg 120
 cttcagcaga gccacagcca gccccaaga ctccataattt ataagatttc taaccgggtc 180
 tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
 agcagggtgg aagctgaaga tgtcggaatt tattattgca tgcaagcttc gcattttccg 300
 tacacttttg gccaggggac caagctggag atcaaaa 336

<210> 188
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 188
 Asp Ile Val Met Thr Gln Thr Pro Leu Ser Ser Pro Val Thr Leu Gly
 1 5 10 15
 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
 20 25 30
 Asp Gly Asn Ile Tyr Leu Ser Trp Leu Gln Gln Arg Pro Gly Gln Pro
 35 40 45
 Pro Arg Leu Leu Ile Tyr Lys Ile Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ala Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Ala
 85 90 95
 Ser His Phe Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 189
 <211> 348
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 189
 gaagtgcagc tgggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
 tctgtgtcag cctctggatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120
 ccagggaagg gcttgaggtc ggtctcaggt attagttgga atagcggtag caaaggctat 180
 gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
 ctgcaaatga acagctctgag agctgaggac acggccttgt attactgtgc aaaagagaa 300
 tggctctttg actactgggg ccagggaacc ctggtcaccg tctctctc 348

<210> 190
 <211> 116
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 190

```

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

```

<210> 191

<211> 337

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 191

```

gatattgtga tgaccacagac tccactctcc tcacctgtca cccttgagca gccggcctcc 60
atctcctgca ggtctactca aagcctcgta cacagtgatg gaaatatcta cttgagttgg 120
cttcagcaga ggcacagcca gccccaaga ctcctaatll alaagallc laaccggllc 180
tctgggggtcc cagacacatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggtgg aagctgagga tgtcgggggtt tattactgca tgcaagcttc gcattttccg 300
tacacttttg gccaggggac caagctggag atcaaac 337

```

<210> 192

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 192

```

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

```

<210> 193

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 193

```

gaagtgaat tggtagagtc tgggggaaac ttggtacagc ctggcaggtc cctgagactc 60
tctgtgcag cctctgcatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120
ccaggaaggg gccctggagt ggtctcaggt atcagtgga atagtggtag tagaggctat 180
gggactctg tgaaggcccg attcaccatt tccagagaca acgcaaaaaa ctccctgtat 240
ctgcaaatga acagctgag aactgaggac acggcctttt attattgtac aaaagaagac 300
gaggcttttg actactgggg ccagggaacc ctggtaacgg tctctca 348

```

<210> 194

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 194

```

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

```

100 105 110
Thr Val Ser Ser
115

<210> 195

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 195

```

ggattcacct ttgatgatta tgcc      24

```

<210> 196

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 196

```

Gly Phe Thr Phe Asp Asp Tyr Ala
 1           5

```

<210> 197

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 197

```

atcagttgga atagtggtag taga      24

```

<210> 198

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 198

```

Ile Ser Trp Asn Ser Gly Ser Arg
 1           5

```

<210> 199

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 199

acaaaagaag acgaggcttt tgactac 27

<210> 200

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 200

Thr Lys Glu Asp Glu Ala Phe Asp Tyr
1 5

<210> 201

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 201

```

gatattgtga tgacccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctctctga ggctcagtc aagcctcgta cacagtgate gaaacacctt cttgagttgg 120
cttcagcaga gccagggcca gccccaaga ctcttatttt ataagatttc taaccgggtc 180
ctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttoac actgaaaato 240
agcagggttg aagctgagga tgcggggttt tattactgca tgcaggccac acaatttcog 300
tacacttttg gccaggcgac caaactgcag atcaat 336

```

<210> 202

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 202

```

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

```

<210> 203

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 203

caaagcctcg tacacagtga tcgaaacacc tac 33

<210> 204

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 204

Gln Ser Leu Val His Ser Asp Arg Asn Thr Tyr
1 5 10

<210> 205

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 205

aagatttct 9

<210> 206

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 206

Lys Ile Ser
1

<210> 207

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 207

atgcaggcca cacaatttc gtacact 27

<210> 208

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 208

Met Gln Ala Thr Gln Phe Pro Tyr Thr
1 5

<210> 209

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 209

```

gaagtgcagc tggtaggagc tgggggaaac ttggtacagc ctggcaggtc cctgagagtc 60
tcctgtgcag cctcgcgatt cacctttgat gattatgcc a tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt atcagttgga atagtggtag tagaggctat 180
gcggactctg tgaaggcccg attcaccatt tccagagaca acgccccaaa ctccctgtat 240
ctgcaaatga acagctcgag aactgaggac acggcctttt attattgtac aaaagaagac 300
gaggcttttg actactgggg ccagggaacc ctggtcaccc tctcctca 348

```

<210> 210

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 210

```

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

```

<210> 211

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 211

```

gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctctctga ggtctactca aagccctcga cacagtgate gaaacaccta cttgagttgg 120

cttcagcaga ggccaggcca gcctccaaga ctcttatttt ataagatttc taaccgggtc 180
tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggtgg aagctgagga tgtcgggttt tattactgca tgcaggccac acaatttcgg 300
tacacttttg gccaggggac caagcgggag atcaaaa 336

```

<210> 212

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 212

```

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

```

<210> 213

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 213

```

gaagtgcagc tgggtggagtc tggggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tctgtgtcag cctctgcatt cacctttgat gattatgcc a tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt atcagttgga atagtggtag tagaggctat 180
gaggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtac aaaagaagac 300
gaggcttttg actactgggg ccagggaacc ctggtcaccg tctctcca 348

```

<210> 214

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 214

```

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1             5             10             15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
 20             25             30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35             40             45

```

```

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

```

<210> 215

<211> 337

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 215

```

gatattgtga tgaccacagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctcttgca ggctcactca aagcctcgta cacagtgate gaaacacct a cttgagttgg 120
cttcagcaga gccagagcca gcctccaaga ctctaatit ataagattc taaccggttc 180
tctgggggtc cagacacatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggtgg aagctgagga tgtcgggggt tattactgca tgcaggccac acaatttccg 300
tacacttttg gccaggcgac caagctggag atcaaac 337

```

<210> 216

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 216

```

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

```

<210> 217

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 217

```

gaagtgcagc tgggtggagtc tggggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggcctt cacctttgat gattatgcc a tgcactgggt ccggcaagct 120
ccggggaagg gcctagagtg ggtctcaggt attacttga atagtggtag catggcctat 180
gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagctctgag agctgaggac acggccttat attactgtgc aaaagaaaac 300
tgggcctttg actactgggg ccagggaacc ctggtcaccg tctcctca 348

```

<210> 218

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 218

```

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

```

<210> 219

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 219

ggcttcacct ttgatgatta tgcc 24

<210> 220

<211> 8
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 220
 Gly Phe Thr Phe Asp Asp Tyr Ala
 1 5

 <210> 221
 <211> 24
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 221
 attactgga atagtgtac catg 24

 <210> 222
 <211> 8
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 222
 Ile Thr Trp Asn Ser Gly Thr Met
 1 5

 <210> 223
 <211> 27
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 223
 gcaaaagaaa actgggcctt tgactac 27

 <210> 224
 <211> 9
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 224
 Ala Lys Glu Asn Trp Ala Phe Asp Tyr
 1 5

 <210> 225
 <211> 336
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 225

```

gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctctctgca ggtctagtca cagccctcgta cacagtgatg gaaacaccta cttgagttgg 120
cttcagcaga gccacagcca gccctcaaga ctcttaattt ataagatttc taaccgggttc 180
tctgggggtcc cagacaçatt cagtggcagt ggggcagggg cagatttcac actgaaaatc 240
agcagggtgg aagctgagga tgtcgggggt tatttctgca tgcaagctac acaatttcg 300
tacacttttg gccaggggac caagctggag atcaaa 336

```

<210> 226

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 226

```

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

```

<210> 227

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 227

cacagcctcg tacacagtga tggaacacc tac 33

<210> 228

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 228

```

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

```

<210> 229

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 229

aagatttct 9

<210> 230

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 230

Lys Ile Ser
1

<210> 231

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 231

atgcaagcta cacaatttcc gtacact 27

<210> 232

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 232

Met Gln Ala Thr Gln Phe Pro Tyr Thr
1 5

<210> 233

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 233

```

gaagtgcagc tgggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctgcctt cacctttgat gattatgcc a tgcactgggt ccggcaagct 120
ccggggaagg gcctagagtg ggtctcaggt attacttga atagtggta c atggcctat 180
gggactctg tgaaggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccctat attactgtgc aaaagaaaac 300
tgggccttly actactggg ccagggaacc ctggcaccg tctcttca 348

```

<210> 234

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 234

```

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

```

<210> 235
 <211> 336
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 235
 gatattgtga tgaaccagac tccactctcc tcacctgtca cccttgagca gccggcctcc 60
 atctctctga ggtctagtca cagcctcgta cacagtgatg gaaacacctt cttgagttgg 120
 cttcagcaga ggccaggcca gctccaaga ctctaatat ataagatttc taaccgggtc 180
 tctgggggtc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
 agcagggtgg aagctgagga tgtcgggggt tatttcgca tgcaagctac acaatttcg 300
 tacacttttg gccaggggac caagctggag atcaaa 336

<210> 236
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 236
 Asp Ile Val Met Thr Gln Thr Pro Leu Ser Ser Pro Val Thr Leu Gly
 1 5 10 15
 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser His Ser Leu Val His Ser
 20 25 30
 Asp Gly Asn Thr Tyr Leu Ser Trp Leu Gln Gln Arg Pro Gly Gln Pro
 35 40 45
 Pro Arg Leu Leu Ile Tyr Lys Ile Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ala Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Met Gln Ala
 85 90 95
 Thr Gln Phe Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 237
 <211> 348
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 237
 gaagtgcagc tggtagagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
 tctgtgcagc cctctgctt cactcttgat gattatgcca tgcactgggt ccggcaagct 120
 ccagggaagg gcttgagtg ggtctcaggt attacttga atagtggtao catgggctat 180
 gccgactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
 ctgcaaatga acagctgag agctgaggac acggccttgt attactgtgc aaaagaaaac 300
 tgggcctttg actactgggg ccagggaacc ctggtcacag tctctcca 348

<210> 238
 <211> 116
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 238

```

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

```

<210> 239

<211> 337

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 239

```

gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctcctgca ggtctagctc cagccctcgt cacagtgatg gaaacacctc cttgagttgg 120
cttcagcaga ggccagccca gcctccaaga ctctaatatt ataagatttc taaccggttc 180
tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggtgg aagcagagga tctcggggtt tattactgca tgcaagctac acaatttccg 300
tacacttttg gccaggggac caagctggag atcaaac 337

```

<210> 240

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 240

```

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

```

<210> 241

<211> 384

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 241

```

gaagtgcagc tgggtggagtc tggggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tctctgtcag cctctggatt cactcttgat gattatgccg tgcactgggt ccggcaagcc 120
ccagggaagg gcctggagtg ggtctcaggt attagtggga atagtggtag cataggctat 180
ggggactctg tgaaggggcg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagataga 300
ttccctccgt ataatataaa cagtggcggt ttttctgatg cttttgaaat ctggggccaa 360
gggacaatgg tcaccgtctc ttca 384

```

<210> 242

<211> 128

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 242

```

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

          100          105          110
Asp Ala Phe Glu Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
      115          120          125

```

<210> 243

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 243

ggattcacct ttgatgatta tgcc 24

<210> 244

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 244

```

Gly Phe Thr Phe Asp Asp Tyr Ala
 1             5

```

<210> 245

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 245

attagttgga atagtggtag cata 24

<210> 246

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 246

```

Ile Ser Trp Asn Ser Gly Ser Ile
 1             5

```

<210> 247

<211> 63

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 247

```

gcaaaagata gattccctcc gtataagtat aacagtgggtg gttttttctga tgcttttgaa 60
atc                                         63

```

<210> 248

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 248

```

Ala Lys Asp Arg Phe Pro Pro Tyr Lys Tyr Asn Ser Gly Gly Phe Ser
 1             5             10            15
Asp Ala Phe Glu Ile
                20

```

<210> 249

<211> 324

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 249

```

gaaatttgtt tgaacgagtc tccaggcacc ctgtcttttgt ctccaggggga aagagccacc 60
ctctctctgca gggccagtica gatttttagc agcagctact tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatctat ggtgcateca gcagggccac tggcatccca 180
gacaggttca gtggcagtggt gtctggggaca gacttcaact tcaccatcag cagactggag 240
cctgaagatt ttgcagtgta ttactgtcag cagtatggta gttcaccgat caccttcggc 300
caagggacac gactggagat tgaa                                     324

```

<210> 250

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 250

```

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

```

<210> 251

<211> 21

<212> DNA

<213> Artificial Sequence

<220>
 <223> Synthetic

<400> 251
 cagagtttta gcagcagcta c 21

<210> 252
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 252
 Gln Ser Phe Ser Ser Ser Tyr
 1 5

<210> 253
 <211> 9
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 253
 ggtgcatcc 9

<210> 254
 <211> 3
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 254
 Gly Ala Ser
 1

<210> 255
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 255
 cagcagtatg gtagttcacc gatcacc 27

<210> 256
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 256
 Gln Gln Tyr Gly Ser Ser Pro Ile Thr
 1 5

<210> 257

<211> 384

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 257

```

gaagtgcagc  tggtaggagtc  tgggggagggc  ttggtacagc  ctggcaggtc  cctgagactc  60
tccctgtgcag  cctctgggatt  cacccttggat  gantatgcca  tgcactgggt  cgggcaagct  120
ccagggaagg  gctctggagtg  ggtctcaggt  attacttggg  atagtggtag  cataggctat  180
gcggaactctg  tgaaggggcgg  attcaccatc  tccagagaca  acgccaagaa  ctccctgtat  240
ctgcaaatga  acagtctgag  agctgaggac  acggccttgt  attactgtgc  aaaagataga  300
ttccctccgt  ataagtataa  cagtgggtgt  ttctctgatg  cttttgaaat  ctggggccaa  360
gggacaatgg  tcaccgtctc  ttca

```

<210> 258

<211> 128

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 258

```

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

```

<210> 259

<211> 324

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 259

```

gaaattgtgt  tgaagcagtc  tccaggccacc  ctgtctttgt  ctccagggga  aagagccacc  60
ctctcctgca  gggccactca  gagtttttagc  agcagcact  tagcctggta  ccagcagaaa  120
cctggccagg  ctcccaggct  cctcatctat  ggtgcaccca  gcagggccac  tggcatccca  180
gacaggttca  gtggcactgg  gtctgggaca  gacttcactc  tcaccatcag  cagactggag  240
cctgaagatt  ttgcagtgt  ttactgtcag  cagtatggta  gttcaccgat  caccctcggc  300
caagggacac  gactggagat  taaa

```

<210> 260

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 260

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

<210> 261

<211> 384

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 261

gaagtgcagc tgggtggagtc tggggggagc ttggtacagc ctggcaggtc cctgagactc 60
 tctgtgcag cctctgcatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120
 ccagggaagg gcctggagtg ggtctcaggt attagtggga atagtggtag cataggctat 180
 gcggaactct tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
 ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagataga 300
 ttccctccgt ataagtataa cagtgtgtgt ttttctgatg cttttgaaat ctggggccaa 360
 gggacaatgg tcaccgtctc tcca 384

<210> 262

<211> 128

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 262

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

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

<210> 263

<211> 325

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 263

gaaattgtgt tgacgcagtc tccaggccacc ctgtctttgt ctccagggga aagagccacc 60
 ctctcctgca gggccactca gagttttagc agcagctact tagcctggta ccagcagaaa 120
 cctggccagg ctcccaggct cctcatctat ggtgcaccca gcagggccac tggcatccca 180
 gacagggtca gtggcactgg gtctgggaca gaattcactc tcaccatcag cagactggag 240
 cctgaagatt ttgactgtga ttactgtcag cagtatggta gttcacccat caccttcggc 300
 caagggacac gactggagat taaac 325

<210> 264

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 264

```

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

```

<210> 265

<211> 366

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 265

```

gaggtgcagc tgggtggagtc tgggggagcgc ttggtacagc ctgggggggc cctgagactc 60
tcctgtgcag cctctgcatt caccctcagc agctacgaca tgcactgggt ccgccaagtt 120
acaggaaaag gtcctgaatg ggtctcagtc attggtactg ttggtgacac atactatcca 180
ggctccctga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt 240
caaatgaaca ccctgacagc cggggacacg gctgttttatt actgtgcaag aactggagca 300
gcagcccaact cgtactacta cgggtatggac gtctggggcc aagggaacct ggteaccgtc 360
tcctca                                     366

```

<210> 266

<211> 122

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 266

```

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

```

<210> 267

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 267

ggattcacct tcagtagcta cgac 24

<210> 268

<211> 8
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 268
 Gly Phe Thr Phe Ser Ser Tyr Asp
 1 5

 <210> 269
 <211> 21
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 269
 attggtactg ttggtgacac a 21

 <210> 270
 <211> 7
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 270
 Ile Gly Thr Val Gly Asp Thr
 1 5

 <210> 271
 <211> 48
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 271
 gcaagaactg gagcagcagc ccactcgtac tactacggta tggacgtc 48

 <210> 272
 <211> 16
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 272
 Ala Arg Thr Gly Ala Ala Ala His Ser Tyr Tyr Tyr Gly Met Asp Val
 1 5 10 15

 <210> 273
 <211> 336
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 273

```

gatattgtga tgactcagtc tccactctcc ctgcccgta cccctggaga gccggcctcc 60
atctctctgca ggctctagtca gagcctcctg tatagtaatg gatacaacta tttggattgg 120
tacctacaga agccagggca gtctccacag ctctcgatct atttgggttc taatcgggccc 180
tccgggggtcc ctgacacggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagagtgg aggcagagga tgttgaatt tattactgca tgcaagctct acaaactccg 300
tgacggttcg gccaaaggac caaggtggaa atcaaa 336

```

<210> 274

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 274

```

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

```

<210> 275

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 275

```

cagagcctcc tgtatagtaa tggatacaac tat      33

```

<210> 276

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 276

```

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

```

<210> 277

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 277

```

ttgggttct      9

```

<210> 278

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 278

Leu Gly Ser
1

<210> 279

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 279

atgcaagctc tacaaactcc gtggacg 27

<210> 280

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 280

Met Gln Ala Leu Gln Thr Pro Trp Thr
1 5

<210> 281

<211> 363

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 281

```

gaggtgcagc tggtagagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
tcctgtgcag cctctggatt cacttcagtc agctacgaca tgcactgggt ccgccaagtt 120
acaggaaaag gtctggaatg ggtctcagtc attggtactg ttggtgacac atactatcca 180
ggctccctga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt 240
caaatgaaca cctgacagc cggggacacg gctgtttatt actgtgcaag aactggagca 300
gcagcccaact cgtactacta cgggtatggac gtctggggcc aaggggaccac ggteaccgtc 360
tcc 363

```

<210> 282

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 282

```

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

```

<210> 283
 <211> 336
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 283
 gatattgtga tgaactcagtc tccactctcc ctgcccgta cccctggaga gccggcctcc 60
 atctctctga ggtctactca gagctctctg tataqtaatg gatacaacta tttggattgg 120
 tacctacaga agccaggcca gtctccacag ctctgatct atttgggttc taatcgggcc 180
 tccgggggtcc ctgacaggtt cagtggcagt ggatcaggca cagatittac actgaaaatc 240
 agcagagtgg aggtcgagga tgttggatt tattactgca tgcaagctct acaaaactcc 300
 tggacgttcg gccaaaggac caaggtggaa atcaaa 336

<210> 284
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 284
 Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Tyr Ser
 20 25 30
 Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Ala
 85 90 95
 Leu Gln Thr Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> 285
 <211> 364
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 285
 gaggtgcagc tgggtggagtc tgggggagcc ttggtacagc ctgggggggc cctgagactc 60
 tctgtgcag cctctggatt caccttcagt agctacgaca tgcactgggt ccgccaagct 120
 acaggaaaag gtctggagtg ggtctcagct attggtactg ttggtgacac atactatcca 180
 ggctccgtga agggccgatt caccatctcc agagaaaatg ccaagaacte cttgtatctt 240
 caaatgaaca gcctgacagc cggggacacg gctgtgtatt actgtgcaag aactggagca 300
 gcagcccact cgtactacta cggtatggac gtctggggcc aagggaccac gggtcacgct 360
 tctt 364

<210> 286
 <211> 121
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 286

```

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

```

<210> 287

<211> 337

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 287

```

gatattgtga tgactcagtc tccactctcc ctgcccgta cccctggaga gccggcctcc 60
atctcccgca ggtctactca gagcctccctg tataagtaatg gatacaacta tttggattgg 120

```

```

tacctgcaga agccagggca gtctccacag ctctgatct atttgggttc taatcgggcc 180
tccgggggtcc ctgacagggt cagtggcagt ggatcaggca cagattttac actgaaaatc 240
agcagaqgtg aggtgaqqa ttttgggttt tattacttca tqcaagctct acaaaactccg 300
tggacgttcc gccaaaggac caaggtggaa atcaaac 337

```

<210> 288

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 288

```

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

```

<210> 289

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 289

```

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60
tctgtgtcag cctctggatt caccttttagc agctatgccg tgacctgggt cgcagggt 120
ccagggaagg ggcgtgattg ggtctcagct attagtggta gtggtggtag cgcatactac 180
gcagactccg tgaaggcccg gtccaccatc tccagagaca attccaagaa cagcgtgtat 240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagagggg 300
gatagtggct acgatttggc ctactggggc cggggaaccc tggtcaccgt ctogtca 357

```

<210> 290

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 290

```

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1           5           10           15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20           25           30
Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Tyr Trp Val
 35           40           45

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

```

<210> 291

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 291

ggattcacct ttagcagcta tgcc 24

<210> 292

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 292

```

Gly Phe Thr Phe Ser Ser Tyr Ala
 1           5

```

<210> 293

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 293

attagtggta gtggtgtag cgca 24

<210> 294

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 294

```

Ile Ser Gly Ser Gly Gly Ser Ala
 1           5

```

<210> 295

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 295

gcgaaagagg gggatagtgg ctacgatttg gactac 36

<210> 296

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 296

Ala Lys Glu Gly Asp Ser Gly Tyr Asp Leu Asp Tyr
1 5 10

<210> 297

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 297

```

gacatccaga tgacccagtc tccatcccca ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgtc gggcgaggca gggcattagt aattatttag cctggcttca gcagaaacca 120
gggaaagccc ctaagtcctt gatctatgct gcattccagtt tgcaaagtgg ggtcccatca 180
aagttcagcg gcagtggatc tgggacagat tteactotca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgccaaaca tataaaagtt ccccgctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

```

<210> 298

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 298

```

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

```

100

105

<210> 299

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 299

cagggcatta gtaattat 18

<210> 300

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 300

Gln Gly Ile Ser Asn Tyr
1 5

<210> 301

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 301

gctgcatcc 9

<210> 302

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 302

Ala Ala Ser
1

<210> 303

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 303

caacaatata aaagtcccc gctcact 27

<210> 304

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 304

Gln Gln Tyr Lys Ser Ser Pro Leu Thr
1 5

<210> 305

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 305

```

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
tcctgtgcag cctcgggatt caccttttagc agctatgccg tgacctgggt ccgccaggct 120
ccagggaagg ggcgtgtattg ggtctcagct attagtggta gtggtggtag cgcatactac 180
gcagactccg tgaaggcccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagagggg 300
gatagtggct acgatttggc ctactggggc cggggaaccc tggtcaccgt ctcctca 357

```

<210> 306

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 306

```

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

```

<210> 307

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 307

```

gacatccaga tgaccagtc tccatcctca ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgtc gggcgaggca gggcattagt aattatttag cctggcttca gcagaaacca 120
gggaaagccc ctaagtcctc gatctatgct gcatccagtt tgcaaatggg ggtcccatca 180
aagttcagcg gcagtgcatc tgggacagat ttactctcca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgccaacaa tataaaagt tccccctcac tttcggcgga 300
gggaccaagg tggagatcaa a
321

```

<210> 308

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 308

```

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

```

<210> 309

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 309

```

gaggtgcagc tgttgagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
tcctgtgcag cctcgcatt caccttttagc agctatgccg tgagctgggt ccgccaggct 120
ccagggaagg ggcctggagt ggtctcagct attagtggta gtggtgtag cgatactac 180
gcagactcgc tgaaggcccg gttcaccatc tccagagaca attccaagaa cagcctgtat 240
ctqcaaatga acaqccctga agccgaqqac acqccqctat attactgtc qaaagaqqq 300
gatagtggct acgatttga ctactggggc cagggaacco tggtcaccgt ctctca 357

```

<210> 310

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 310

```

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

```

<210> 311

<211> 322

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 311

```

gacatccaga tgacccagtc tccatcctca ctgtctgcat ctgaggaga cagagtcacc 60
atcaactgtc gggcgagtc gggcattagt aattatttag cctggtttca gcagaaacca 120
gggaaagccc ctaagtccct gatctatgct gcattccagt tgcaaaagtgg ggtcccatca 180
aggttcagcg gcagtggtgc tgggacagat ttcactctca ccaacagcag cctgcagcct 240
gaagattttg caactatta ctgccaaaca tataaaagtt ccccgctcac ttctggcgga 300
gggaccaagg tggagatcaa ac
322

```

<210> 312

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 312

```

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

```

<210> 313

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 313

```

gaagtgcagt tgggtggagtc tggggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctcgcgatt cacccttgat gattatgccca tgcactgggt ccggcaagtt 120
ccaggggaagg gctcggagtg ggtctcaggt attacttgga atagtggtag catagactat 180
gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagctctgag agctgaggac acggccttct attattgtgt aaaagaagat 300
gaggcttttg actactgggg ccaggggaacc ctggtcaccg tctctctca 348

```

<210> 314

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 314

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

```

<210> 315

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 315

ggattcacct ttgatgatta tgcc 24

<210> 316

<211> 8
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 316
 Gly Phe Thr Phe Asp Asp Tyr Ala
 1 5

 <210> 317
 <211> 24
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 317
 attacttgga atagtggtag cata 24

 <210> 318
 <211> 8
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 318
 Ile Thr Trp Asn Ser Gly Ser Ile
 1 5

 <210> 319
 <211> 27
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 319
 gtaaaagaag atgaggcttt tgactac 27

 <210> 320
 <211> 9
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 320
 Val Lys Glu Asp Glu Ala Phe Asp Tyr
 1 5

 <210> 321
 <211> 336
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 321

```

gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctctctgta ggctctactca aagcctcgta cacagtgatg gaaacacctt tttgagttgg 120
cttcagcaga gccacagcca gcctccaaga ctcttaattt ataagatttc taaccgggttc 180
tctgggggtcc cagacaçaat cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggtgg aggtcgagga tgtcggcggt tattattgca tgcaagctac acaatttccg 300
tacacttttg gccaggggac caagctggag atcaaa 336

```

<210> 322

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 322

```

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

```

<210> 323

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 323

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caaagcctcg tacacagtga tggaaacacc tat 33

```

<210> 324

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 324

```

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

```

<210> 325

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 325

```

aagatttct 9

```

<210> 326

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 326

Lys Ile Ser
1

<210> 327

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 327

atgcaagcta cacaatttcc gtacact 27

<210> 328

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 328

Met Gln Ala Thr Gln Phe Pro Tyr Thr
1 5

<210> 329

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 329

```

gaagtgcagc tgggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctgcatt cacctttgat gattatgcc tgcactgggt ccggcaagtt 120
ccagggaagg gctctggagtg ggtctcaggt attacttga atagtggtag catagactat 180
gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttct attattgtgt aaaagaagat 300
gaggccttctg actactgggg ccagggaacc ctgggcacug tctctctca 348

```

<210> 330

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 330

```

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

```

<210> 331
 <211> 336
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 331
 gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaac gccggcctcc 60
 atctctgtga ggtctactca aagcctcgtc cacaqtgatq gaaacacctt tttaggttgg 120
 cttcagcaga gccagcgcca gccctcaaga ctcttaattt ataagatttc taaccgggtc 180
 tctgggggtcc cagacaçaat cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
 agcagggtgg aggtcgagga tgtcggcggt tattattgca tgcaagctac acaatttcgg 300
 tacacttttg gccaggcgac caagctggag atcaaaa 336

<210> 332
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 332
 Asp Ile Val Met Thr Gln Thr Pro Leu Ser Ser Pro Val Thr Leu Gly
 1 5 10 15
 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
 20 25 30
 Asp Gly Asn Thr Tyr Leu Ser Trp Leu Gln Gln Arg Pro Gly Gln Pro
 35 40 45
 Pro Arg Leu Leu Ile Tyr Lys Ile Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60
 Asp Arg Ile Ser Gly Ser Gly Ala Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
 85 90 95
 Thr Gln Phe Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 333
 <211> 348
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 333
 gaagtgcagc tgggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
 tctgtgcag cctctgcatc cacctttgat gattatgcca tgcactgggt ccggcaagct 120
 ccagggaagg gcttgagtg ggtctcaggt attacttga atagtggtag cataggctat 180
 gccgactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
 ctgcaaatga acagctcgag agctgaggac acggccttgt attactgtgt aaaagaagat 300
 gaggcctttg actactgggg ccagggaacc ctggtcaccg tctcctca 348

<210> 334
 <211> 116
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 334

```

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

```

<210> 335

<211> 337

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 335

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gatattgtga tgaccagac tccactotcc tcacctgtca cccttggaca gccggcotcc 60
atctcctgca ggtctactca aagcctcgta cacagtgatg gaaacaccta tttagattgg 120
cttcagcaga ggccagccca gcctccaaga ctctaatatt ataagatttc taaccgggttc 180

```

```

tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaaac 240
agcagqqtgq aagctgaqqa tqtcqqqqt ttactactca tqcaagctac acaatttccq 300
tacacttttg gccaggggac caagctggag atcaaac 337

```

<210> 336

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 336

```

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

```

<210> 337

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 337

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gaggtgcaac tgttggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
tcctgtgcag cctctggatt cacctttaga agttatacca tgacctgggt ccgccaggct 120
ccaggaagg gactggattg ggtctcaggt attactgata gtggtgctgg cacatactac 180
ggagactccg tgaagggccg gttcaccato tccagagaca attccaagaa cagcgtgtat 240
ctgcaaalga acagcccgag agccgaggac acggccglgl allactglgl gaaagagggg 300
gatagtggct acgatttggc ctactggggc cagggaaccc tggtcaccgt ctctca 357

```

<210> 338

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 338

```

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

```

<210> 339

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 339

ggattcacct ttagaagtta tacc 24

<210> 340

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 340

```

Gly Phe Thr Phe Arg Ser Tyr Thr
 1           5

```

<210> 341

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 341

attactgata gtggtgctgg caca 24

<210> 342

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 342

```

Ile Thr Asp Ser Gly Ala Gly Thr
 1           5

```

<210> 343

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 343

gtgaaagagg gggatagtg ctacgatttg gactac 36

<210> 344

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 344

Val Lys Glu Gly Asp Ser Gly Tyr Asp Leu Asp Tyr
1 5 10

<210> 345

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 345

gacatccaga tgaccagtc tccatcctca ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgtc gggcgactca gggcattagt acttatctag cctggcttca gcagaaaacca 120
gggaaagccc ctaagtcctt gatctatgct acatccagtt tgcaaagtgg ggtcccatca 180
aagttcagcg gcagtagatc tgggacagat ttcactctca ccacagcag cctgcagcct 240
gaagattttg caacttatta ctgccaacaa tataagagtt ccccgctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321

<210> 346

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 346

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

<210> 347

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 347
 cagggcatta gtacttat 18

 <210> 348
 <211> 6
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 348
 Gln Gly Ile Ser Thr Tyr
 1 5

 <210> 349
 <211> 9
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 349
 gctacatcc 9

 <210> 350
 <211> 3
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 350
 Ala Thr Ser
 1

 <210> 351
 <211> 27
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 351
 caacaatata agagttcccc gctcact 27

 <210> 352
 <211> 9
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 352
 Gln Gln Tyr Lys Ser Ser Pro Leu Thr
 1 5

 <210> 353
 <211> 357
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic

<400> 353

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gagggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
tcctgtgcag cctctggatt caactttaga agttatacca tgacctgggt ccgccaggct 120
ccagggaagg gactggattg ggtctcaggt attactgata gtggtgctgg cacatactac 180
ggagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgtgtgat 240
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgt gaaagagggg 300
gatagtggct acgatttgga ctactggggc cagggaacco tggtcaccgt ctctca 357

```

<210> 354

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 354

```

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

```

<210> 355

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 355

```

gacatccaga tgaccagtc tccatcctca ctgtctgcat ctgtaggaga cagagtcacc 60
atcaattgtc gggcgactca gggcattagt acttatctag cctggcttca gcagaaaacca 120
gggaaagccc ctaagtccct gatctatgct acatccagtt tgcaaagtgg ggtcccatca 180
aagttcagcg gcagtagatc tgggacagat ttcactctca ccatcagcag cctgcagcct 240
gaagattttg caactatta ctgccaacaa tataagagtt ccccgctcac ttctggcgga 300
gggaccaagg tggagatcaa a
321

```

<210> 356

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 356

```

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

```

<210> 357
 <211> 357
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 357
 gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
 tcctgtgcag cctctggatt cacctttaga agttatacca tgagctgggt ccgccaggcc 120
 ccagggaagc ggctggagtg ggtctcagct attactgata gtggtgctgg cacatactac 180
 gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cagctgtatc 240
 ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgt gaaagagggg 300
 gatagtggct acgatttggc ctactggggc cagggaaccc tggtcaccgt ctctca 357

<210> 358
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 358
 Glu Val Gln Leu Leu 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 Arg Ser Tyr
 20 25 30
 Thr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Ala Ile Thr Asp Ser Gly Ala Gly Thr Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Val Lys Glu Gly Asp Ser Gly Tyr Asp Leu Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Leu Val Thr Val Ser Ser
 115

<210> 359
 <211> 322
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 359
 gacatccaga tgacccagtc tccatcctca ctgtctgcat ctgtaggaga cagagtcacc 60
 atcaattgtc gggcgagtc gggcattagt acttatttag cctggtttca gcagaaacca 120
 gggaaagccc ctaagtcctt gatctatgct acatccagtt tgcaaaagtgg ggtcccatca 180
 aggttcagcg gcagtgagtc tggcacagat ttcactotca ccatcagcag cctgcagcct 240
 gaagattttg caacttatta ctgccaaaca tataagagtt ccccgctcac tttcggcgga 300
 gggaccaagg tggagatcaa ac 322

<210> 360
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 360

```

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

```

<210> 361

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 361

```

gaagtgcac tggtggagtc tgggggagac ttggtacagc ctggcaggtc cctgagactc 60
tctgtgcag cctcggcatt cacctttgat gattatgcc a tgcactgggt ccggcaagct 120
ccaggaggag gcctagagtg ggtctcaggt attacttga atagtggta c atggcctat 180
gcggaactct tggaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctacaaatga acagtctgag agctgaggac acggccttat attactgtgc aagagaaaac 300
tgggcctttg actactgggg ccagggaacc ctggtcaccg tctctcctc 348

```

<210> 362

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 362

```

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

```

<210> 363

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 363

```

ggattcacct ttgatgatta tgcc          24

```

<210> 364

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 364
Gly Phe Thr Phe Asp Asp Tyr Ala
1 5

<210> 365

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 365

attacttgga atagtgttac catg 24

<210> 366

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 366

Ile Thr Trp Asn Ser Gly Thr Met
1 5

<210> 367

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 367

gcaagagaaa actgggcctt tgactac 27

<210> 368

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 368

Ala Arg Glu Asn Trp Ala Phe Asp Tyr
1 5

<210> 369

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 369

gatattgtga tgaaccagac tccactctcc tcacctgtca cccttgagaca gccggcctcc 60
atctcctgca ggctcactca cagcctcgta cacagtgatg gaaacacctt cttgagttgg 120
cttcagcaga ggcacagcca gcctccaaga ctctaatatt ataagatttc taaccoggttc 180
tctggggctc cagacagatt cagtggcagt gggccaggga cagatttcac actgaaaatc 240
agcagggtgg aagctgagga tgcgggggtt tatttcgca tgcaagctac acaatttcgg 300
tacacttttg gccaggcgac caagctggag atcaaaa 336

<210> 370

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 370

```

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

```

<210> 371

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 371

```

cacagcctcg tacacagtga tggaacacc tac          33

```

<210> 372

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 372

```

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

```

<210> 373

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 373

```

aagattct          9

```

<210> 374

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 374

```

Lys Ile Ser
 1

```

<210> 375

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 375

atgcaagcta cacaatttcc gtacact 27

<210> 376

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 376

Met Gln Ala Thr Gln Phe Pro Tyr Thr
1 5

<210> 377

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 377

```

gaagtgcagc tgggtggagtc tggggggagac ttggtacagc ctggcaggc cctgagactc 60
tctctgtgcag cctctggatt cacctttgat gattatgcc tgcactgggt ccggcaagct 120
ccagggagggg gcctagagtg ggtctcaggt attacttggc atagtggtag catggcctat 180
gcggactctg tggaggggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctacaaatga acagtctgag agctgaggac acggccttat attactgtgc aagagaaaac 300
tgggcctttg actactgggg ccagggaacc ctggtcaccg tctcctca 348

```

<210> 378

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 378

```

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

```

<210> 379

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 379

```

gatattgtga tgacccagac tccactctcc tcacctgtca cccctggaca gccggcctcc 60
atctcctgca ggtctagtc cagcctcgta cacagtgatg gaaacaccta cttgagttgg 120
cttcagcaga ggccaggcca gcctccaaga ctectaattt ataagatttc taaccgggtc 180
tctgggggtcc cagacagatt cagtggcagt gggccaggga cagatttcac actgaaaatc 240
agcagggtgg aagctgagga tgtcgggggtt taattctgca tgcaagctac acaatttccg 300
tacacttttg gccaggggac caagctggag atcaaaa 336

```

<210> 380

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 380

```

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

```

<210> 381

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 381

```

gaagtgcagc tgggtgagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctgcatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attacttgga atagtggtae catgggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagctctgag agctgaggac acggccttgt attactgtgc aagagaaaac 300
tgggcctttg actactgggg ccagggaacc ctggtcaccg tctctcca 348

```

<210> 382

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 382

```

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

```

<210> 383
 <211> 337
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 383
 gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
 atctctgtca ggtctagtca cagcctcgta cacagtgatg gaaacacctc cttgagttgg 120
 cttcagcaga ggccaggcca gccccaaga ctcttaattt ataagatttc taaccgggtc 180
 tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240

agcaggggtg aagctgagga tgtcgggggt tattactgca tgcaagctac acaatttccg 300
 tacacttttg gccaggggac caagctggag atcaaac 337

<210> 384
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 384
 Asp Ile Val Met Thr Gln Thr Pro Leu Ser Ser Pro Val Thr Leu Gly
 1 5 10 15
 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser His Ser Leu Val His Ser
 20 25 30
 Asp Gly Asn Thr Tyr Leu Ser Trp Leu Gln Gln Arg Pro Gly Gln Pro
 35 40 45
 Pro Arg Leu Leu Ile Tyr Lys Ile Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ala Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
 85 90 95
 Thr Gln Phe Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 385
 <211> 354
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 385
 gaggtgcaac tgggtgagtc tgggggaaac gtggtacggc cggggggggt cctgagactc 60
 tctgtgacag cctctgcatc cacctttgat gattatggca tgacctgggt ccgccaagtt 120
 ccggggaagg ggcctggagt ggtctctggt attaatgga atggtggtag tacagattat 180
 gcagactctg tgaaggcccg attcaccata tctagagaca acgccaagaa ctccctgtat 240
 ctgcaaatga atagctgag agccgaggac acggccttat attactgtgc gagagataag 300
 gggttctacg gtatggaagt ctggggccaa gggaccacgg tcacctgtct ctea 354

<210> 386
 <211> 118
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 386

```

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

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

```

<210> 387

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 387

ggattcacct ttgatgatta tggc 24

<210> 388

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 388

```

Gly Phe Thr Phe Asp Asp Tyr Gly
 1          5

```

<210> 389

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 389

attaattgga atggtgtag taca 24

<210> 390

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 390

```

Ile Asn Trp Asn Gly Gly Ser Thr
 1          5

```

<210> 391

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 391

gcgagagata aggggttcta cggatggac gtc 33

<210> 392

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 392

Ala Arg Asp Lys Gly Phe Tyr Gly Met Asp Val
1 5 10

<210> 393

<211> 339

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 393

gacatcgtga tgacccagtc tccagactcc ctggtgtgtg ctctgggcga gagggccacc 60
atcaactgca agtccagcca gaatccttta tacaactcca acaaaaagaa gtacttagct 120
tggtaccagc agaaaccagg acagcccccct aagctgggta ttactggggc atctaccggg 180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240
atcaccagcc tacaggctga agatgtggca gtctattact gtcaacaata ttatagtact 300
ccgtacactt ttggccaggg gaccaagctg gagatcaaa 339

<210> 394

<211> 113

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 394

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

<210> 395

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 395

cagaatcct tatacaactc caacaaaaag aagtac 36

<210> 396

<211> 12
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 396
 Gln Asn Pro Leu Tyr Asn Ser Asn Lys Lys Lys Tyr
 1 5 10

 <210> 397
 <211> 9
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 397
 tgggcatct 9

 <210> 398
 <211> 3
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 398
 Trp Ala Ser
 1

 <210> 399
 <211> 27
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 399
 caacaatatt atagtactcc gtacact 27

 <210> 400
 <211> 9
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 400
 Gln Gln Tyr Tyr Ser Thr Pro Tyr Thr
 1 5

 <210> 401
 <211> 351
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 401

```

gaggtgcagc tgggtggagtc tgggggaaac gtggtacggc cggggggggtc cctgagactc 60
tctgtgacag cctctggatt cactcttgat gattatggca tgacctgggt ccgccaagtt 120
ccggggaagg ggcctggagtg ggtctctggt attaatgga atgggtgtag tacagattat 180
gcagactctg tgaaggcccg attcaccata tctagagaca acgccaagaa ctccctgtat 240
ctgcaaatga atagctgag agcogaggac acggccctat attactgtgc gagagataag 300
gggttctacg gtaaggacgt ctggggccaa gggaccacgg tcaccgtctc c 351

```

<210> 402

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 402

```

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

```

<210> 403

<211> 339

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 403

```

gacatctgta tgaccacagtc tccagactcc ctggctgtgt ctctggggga gagggccacc 60
atcaactgca agtcacagca gaatccttta tacaactcca acaaaaaagaa gtacttagct 120
tgggtaccagc agaaaccagg acagcccctc aagctgggca tttactgggc atctaccgg 180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240
atcaccagcc tacaggctga agatgtggca gtttattact gtcaacaaa ttatagtact 300
ccgtacactt ttggccaggg gaccaagctg gagatcaaa 339

```

<210> 404

<211> 113

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 404

```

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

```

<210> 405

<211> 352

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 405

```
gaggtgcagc tgggtggagtc tggggggaggt gtggtacggc ctgggggggtc cctgagactc 60
tctgtgacag cctctggatt cacctttgat gattatggca tgagctgggt ccgccaagct 120
ccaggggaagg ggcctggagtg ggtctctggt attaatgga atgggtgtag tacaggttat 180
gcagactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagctgag agccgaggac acggccctgt atcactgtgc gagagataag 300
gggttctaac gtatggacgt ctggggccaa gggaccacgg tcaccgtctc ct 352
```

<210> 406

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 406

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

<210> 407

<211> 340

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 407

```
gacatcgtga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc 60
atcaactgca agtcacgcca gaatccttta tacaactcca acaaaaagaa gtacttagct 120
tgggtaccagc agaaaccagg acagcctcct aagctgtctc tttactgggc atctaccagg 180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt castctcacc 240
atcagcagcc tgcaggctga agatgtggca gtttattact gtcaacaata ttatagtact 300
ccgtacactt ttggccaggg gaccaagctg gagatcaaac 340
```

<210> 408

<211> 113

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 408

```

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

```

<210> 409

<211> 384

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 409

```

gaagtgcagc tgggtggagtc tggggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctgcatt cacccttgat gattatgccg tgcactgggt ccggcaagct 120
ccagggaagg gctcggagtg ggtctcaggt attagtggga atagtggtag cataggctat 180
gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccctgt attactgtgc aaaagataga 300
ttccctccgt ataagtataa cagtgggtgt tttctgatg cttttgaaat ctggggccaa 360
gggacaatgg tcaccgtctc ttca

```

<210> 410

<211> 128

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 410

```

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

```

<210> 411

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 411

ggattcacct ttgatgatta tgcc 24

<210> 412

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 412

Gly Phe Thr Phe Asp Asp Tyr Ala
1 5

<210> 413

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 413

attagttgga atagtgtag cata 24

<210> 414

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 414

Ile Ser Trp Asn Ser Gly Ser Ile
1 5

<210> 415

<211> 63

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 415

gcaaaagata gattccotcc gtataagtat aacagtgggtg gttttttotga tgcttttgaa 60
atc 63

<210> 416

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 416

Ala Lys Asp Arg Phe Pro Pro Tyr Lys Tyr Asn Ser Gly Gly Phe Ser
1 5 10 15
Asp Ala Phe Glu Ile
20

<210> 417

<211> 324

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 417

```

gaaattgtgt tgaocgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
ctctctctgca gggccaçtca gagtttttagc agcagctact tagcctggta ccagcagaaa 120
cctgggccaagg ctcccaggct cctcatctat ggtgcateca gcagggccac tggcaccaca 180
gacaggttca gtggcagtgg gtctgggaca gacttcacto tcaccatcag cagactggag 240
cctgaagatt ttgcagtgtt ttactgtcag cagtatggta gttcaccgat caccttcggc 300
caagggacac gactggagat tgaa 324

```

<210> 418

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 418

```

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

```

<210> 419

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 419

cagagtttta gcagcagcta c 21

<210> 420

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 420

```

Gln Ser Phe Ser Ser Ser Tyr
1      5

```

<210> 421

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 421

ggtgcatcc 9

<210> 422

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 422

Gly Ala Ser
1

<210> 423

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 423

cagcagtatg gtagtcacc gatcacc 27

<210> 424

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 424

Gln Gln Tyr Gly Ser Ser Pro Ile Thr
1 5

<210> 425

<211> 384

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 425

```
gaagtgcagc tgggtggagtc tggggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggcatt cacccttgat gattatgcc a tgcactgggt ccggcaagct 120
ccaggggaagg gctctggagtg ggtctcaggt attagttgga atagtggtag cataggctat 180
gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagataga 300
ttccctccgt ataagtataa cagtgggtgt ttttctgatg cttttgaaat ctggggccaa 360
gggacaatgg tcaccgtctc ttca 384
```

<210> 426

<211> 128

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 426

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

<210> 427
 <211> 324
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 427
 gaaattgtgt tgacgcagtc tccaggaacc ctgtctttgt ctccaggga aagagccacc 60
 ctctcctgca gggccagtc gagtttttagc agcagctact tagcctggta ccagcagaaa 120
 cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180
 gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240
 cctgaagatt ttgcagtgtt ttactgtcag cagtatggta gtteaccgat caccttcggc 300
 caagggacac gactggagat taaa 324

<210> 428
 <211> 108
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 428
 Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Phe Ser Ser Ser
 20 25 30
 Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
 35 40 45
 Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
 50 55 60
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
 65 70 75 80
 Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
 85 90 95
 Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
 100 105

<210> 429
 <211> 384
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 429
 gaagtgcagc tgggtggagt tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
 tectgtgcag cctctggatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120
 ccagggaagg gctctggagt ggtctcaggt attagtggga atagtggtag cataggctat 180
 gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
 ctgcaaatga acagctgag agctgaggac acggccttgt attactgtgc aaaagataga 300
 ttccctccgt ataagtataa cagtgggtgt ttttctgatg cttttgaaat ctggggccaa 360
 gggacaatgg tcaccgtctc ttca 384

<210> 430
 <211> 128
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 430
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
 20 25 30
 Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
 85 90 95
 Ala Lys Asp Arg Phe Pro Pro Tyr Lys Tyr Asn Ser Gly Gly Phe Ser
 100 105 110
 Asp Ala Phe Glu Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120 125

<210> 431

<211> 325

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 431

gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccaac 60
 ctctcctgca gggccagtc gagttttgag agcagctact tagcctggta ccagcagaaa 120
 cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatocca 180
 gacaggttca gtggcagtggt gtctgggaca gacttcaact tcaccatcag cagactggag 240
 cctgaagatt ttgcagtgtt ttactgtcag cagtatggta gttcaccgat caccttcggc 300
 caagggacac gactggagat taaac 325

<210> 432

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 432

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

<210> 433

<211> 366

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 433

gaggtgcagc tgggtggagtc tgggggaagc ttggtacagc ctgggggggc cctgagactc 60
 tctgtgagc cctctggatt caccttcagt agctacgaca tgcactgggt ccgccaagtt 120
 acaggaagag gtctggaatg ggtctcagtc attggtactg ttggtgacac atactatcca 180
 ggctccctga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt 240
 caaatgaaca cctgagagc cggggacacg gctgtttatt actgtgcaag aactggagca 300
 qcaqcccact cgtactacta cgttatggac gtctggggcc aagggacat ggtcaccgtc 360
 tctca 366

<210> 434

<211> 122

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 434

```

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

```

<210> 435

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 435

ggattcacct ttagtagcta cgac 24

<210> 436

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 436

```

Gly Phe Thr Phe Ser Ser Tyr Asp
 1           5

```

<210> 437

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 437

attggtactg ttggtgacac a 21

<210> 438

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 438

```

Ile Gly Thr Val Gly Asp Thr
 1           5

```

<210> 439

<211> 48

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 439

gcaagaactg gacgacgagc ccactcgtac tactacggta tggacgtc 48

<210> 440

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 440

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

<210> 441

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 441

```

gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccacggga aagagccacc 60
ctctcctgca gggccagtcg gactgtttagc agcagctact tagcctggta ccagcagaaa 120
cctggccagg ctccacgggt cctcatctat ggtgcataca gcaggggcac tggcatocca 180
gacaggtlca glggcagtggt gctcgggaca gacttcaalc tcaccalcag cagactggag 240
cctgaagatt ttgcagtgtt ttactgtcag cagtatggta gctcaccac tttcggcgga 300
gggaccaagg tggagatcaa a                                     321

```

<210> 442

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 442

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

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

<210> 443

<211> 21

<212> DNA

<213> Artificial Sequence

<220>
 <223> Synthetic

<400> 443
 cagagtgtta gcagcagcta c 21

<210> 444
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 444
 Gln Ser Val Ser Ser Tyr
 1 5

<210> 445
 <211> 9
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 445
 ggtgcatcc 9

<210> 446
 <211> 3
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 446
 Gly Ala Ser
 1

<210> 447
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 447
 cagcagtatg gtagctcacc cact 24

<210> 448
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 448
 Gln Gln Tyr Gly Ser Ser Pro Thr
 1 5

<210> 449

<211> 363
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 449
 gaggtgcagc tgggtggagtc tggggggaggc ttggtacagc ctgggggggtc cctgagactc 60
 tctgtgtcag cctctgggatt caccttcagt agctacgaca tgcactgggt cgcgcaagtt 120
 acaggaaaag gtctggaatg ggtctcagtc attggtactg ttggtgacac atactatcca 180
 ggctccctga agggccgatt caccatctcc agagaaaatg ccaagaactc cttgtatctt 240
 caaatgaaca cctgaagcgc cggggacacg gctgtttatt actgtgcaag aactggagca 300
 gcagcccaact cgtactacta cggtaagcac gtctggggcc aaggggaccac ggtcacccgc 360
 tcc 363

<210> 450
 <211> 121
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 450
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30
 Asp Met His Trp Val Arg Gln Val Thr Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Val Ile Gly Thr Val Gly Asp Thr Tyr Tyr Pro Gly Ser Leu Lys
 50 55 60
 Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Tyr Leu
 65 70 75 80
 Gln Met Asn Thr Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Ala

85 90 95
 Arg Thr Gly Ala Ala Ala His Ser Tyr Tyr Tyr Gly Met Asp Val Trp
 100 105 110
 Gly Gln Gly Thr Thr Val Thr Val Ser
 115 120

<210> 451
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 451
 gaaattgtgt tgaagcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
 ctctcctgca gggccaactca gagtgttagc agcagctact tagcctggta ccagcagaaa 120
 cctggccaagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcctccca 180
 gacaggttca gtggcactgg gtctgggaca gaattcactc tcaccatcag cagactggag 240
 cctgaagatt ttgcagtgtt ttactgtcag cagtattgta gctcaccacc tttcggcgga 300
 gggaccaagg tggagatcaa a 321

<210> 452
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 452

```

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

```

<210> 453

<211> 364

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 453

```

gaggtgcagc tgggtggagtc tggggggaggc ttggtacagc ctgggggggtc cctgagactc 60
tcctgtgcag cctctggcatt caccttcagtc agctacgcaca tgcactgggt ccgccaagct 120
acaggaaaaag gtctggagtg ggtctcagct attggtactg ttggtgacac atactatcca 180
ggctccgtga agggcccgatt caccaactcc agagaaaatg ccaagaactc cttgtatctt 240

```

```

caaatgaaca gctgagagc cggggacacg gctgtgatt actgtgcaag aactggagca 300
gcagcccact cgtactacta cggtatggac gtctggggcc aaggggaccac ggtcacogtc 360
tcct
364

```

<210> 454

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 454

```

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

```

<210> 455

<211> 322

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 455

```

gaaattgtgt tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
ctctcctgca gggccactca gagtgttagc agcagctact tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatctat ggtgcaccca gcaggggccac tggcatocca 180
gacaggttca gtggcactgg gtctgggaca gacttcactc tcaccatcac cagactggag 240
cctgaagatt ttgcagtgtt ttactgtcag cagtatggta gtcaccccac tttcggcgga 300
gggaccaagg tggagatcaa ac
322

```

<210> 456

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 456

```

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

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

```

<210> 457

<211> 345

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic

<400> 457

```

gaggtgcagc tgggtggagt tgggggtcag gtgaagaagc ctggggccctc agtgaaggtc 60
tcctgtaagg cttctggatt cacccttcacc gactacata tgcactgggt gcgacaggcc 120
cctggacaag ggcctggagt gctgggatgg atcaacccta agagtgggtgc gacaaagtat 180
gcacagaggt ttcagggcag ggtoaccatg accaggggaca cgtccatcag cacagcctac 240
atggaactga acggactaag atctgacgac acggccgttt tttactgtgc gcgaactgat 300
gcttttgata tctgggccc aaggacaatg gtcaccgtct cttca 345

```

<210> 458

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 458

```

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

```

<210> 459

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 459

```

ggattcacct tcaccgacta ctat      24

```

<210> 460
 <211> 8
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 460
 Gly Phe Thr Phe Thr Asp Tyr Tyr
 1 5

 <210> 461
 <211> 24
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 461
 atcaacccta agagtggtgc gaca 24

 <210> 462
 <211> 8
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 462
 Ile Asn Pro Lys Ser Gly Ala Thr
 1 5

 <210> 463
 <211> 24
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 463
 gcgcgaactg atgctttga tatc 24

 <210> 464
 <211> 8
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 464
 Ala Arg Thr Asp Ala Phe Asp Ile
 1 5

 <210> 465
 <211> 321
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

<400> 465

```

gacatccagt tgacccagtc tccttccacc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttggc gggccagtc gagtggtagt aactgggtgg cctgggtatca gcagaaacca 120
gggaaagccc ctaaactcct gatctattcg gcgtctactt tagaaagtgg ggtcccatca 180
aggttcagcg gcagtggaatc tgggacagaa ttcactctca ccacagcag cctgcagcct 240
gatgattttg caacttatta ctgccaacac tataatagtt attggacgtt cggccaaggg 300
accaaggtgg aaatcaaacg a                                     321

```

<210> 466

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 466

```

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

```

<210> 467

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 467

cagagtgtta gtaactgg 18

<210> 468

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 468

```

Gln Ser Val Ser Asn Trp
1      5

```

<210> 469

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 469

tcggcgtct 9

<210> 470

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 470

Ser Ala Ser
1

<210> 471

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 471

caacactata atagtattg gacg 24

<210> 472

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 472

Gln His Tyr Asn Ser Tyr Trp Thr
1 5

<210> 473

<211> 345

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 473

```

caggtgcagc tgggtgcagtc tggggctgag gtgaagaagc ctggggccc c agtgaaggtc 60
tcctgtaagg cttctggatt cacotteacc gactactata tgcactgggt gcgacaggcc 120
cctggacaag ggccttgagtg gctgggatgg atcaacccta agagtgggtgc gacaaagtat 180
gcacagaggt ttcagggcag ggtcaccatg accagggaca cgtccatcag cacagcctac 240
atggaactga acggactaag atctgacgac acggccggtt ttactgtgc gcgaactgat 300
gcttttgata tctggggcca agggacaatg gtcaccgtct cttea 345

```

<210> 474

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 474

```

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

```

<210> 475
 <211> 318
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 475
 gacatccaga tgaccagtc tcttccacc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc gggccagtc gagtgtagt aactggttgg cctgggtatca gcagaaacca 120
 gggaaagccc ctaactcct gatctattcg gcgtctactt tagaaagtgg ggtcccatca 180
 aggttcagcg gcagtgaatc tgggacagaa ttcactctca ccatcagcag cctgcagcct 240
 gatgattttg caacttatta ctgccaacac tataatagtt attggacgtt cggccaaggg 300
 accaaggtgg aaatcaaa 318

<210> 476
 <211> 106
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 476
 Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Val Ser Asn Trp
 20 25 30
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45
 Tyr Ser Ala Ser Thr Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 Ser Glu 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 His Tyr Asn Ser Tyr Trp Thr
 85 90 95
 Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 477
 <211> 345
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 477
 caggtgcagc tgggtcagtc tggggctgag gtgaagaagc ctggggccctc agtgaaggtc 60
 tcttgcaagg ctctggatt caccttcacc gactactata tgcactgggt gcgacaggcc 120
 cctggacaag ggcttgagtg gatgggatgg atcaacccta agagtgggtc gacaaactat 180
 gcacagaagt ttcaggccag ggtoaccatg accagggaca cgtccatcag cacagcotac 240
 atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gcgaactgat 300
 gcttttgata tctgggcca agggacaatg gtcaccgtct ctcca 345

<210> 478
 <211> 115
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 478

```

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

```

<210> 479

<211> 319

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 479

```

gacatccaga tgacccagtc tccctccacc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggccaagtc gagtggttagt aactgggttgg cctgggtatca gcagaaacca 120
gggaaaqccc ctaagctcct gatctattcg gcgtctagt ttgaaaagtgg ggtcccatca 180
aggttcagcg gcagtgcatc tgggacagaa ttcaactctca ccatcagcag cctgcagcct 240
gatgattttg caacttatta ctgccaacac tataatagtt attggacgtt cggccaaggg 300
accaaggtgg aaatcaaac
          319

```

<210> 480

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 480

```

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

```

<210> 481

<211> 354

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 481

```

gaggtgcagc tgggtggagtc tggggggaggc gtggtccagc ctggggagtc cctgagactc 60
tctgtgcag cgtctgcatc cactctcagt agctatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggtctggagtg ggtggcagtt atatggtatg atggaagtaa taaatactat 180
gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa cactgtgtat 240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatgga 300
tatagtggct acgatgaeta ctggggccag ggaaccctgg tcaccgtctc ctca
          354

```

<210> 482

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 482

```

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

```

<210> 483

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 483

ggattcacct tcagtagcta tggc 24

<210> 484

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 484

```

Gly Phe Thr Phe Ser Ser Tyr Gly
 1           5

```

<210> 485

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 485

atatggtatg atggaagtaa taaa 24

<210> 486

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 486

```

Ile Trp Tyr Asp Gly Ser Asn Lys
 1           5

```

<210> 487

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 487

gcgagagatg gatatagtgg ctacgatgac tac 33

<210> 488

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 488

Ala Arg Asp Gly Tyr Ser Gly Tyr Asp Asp Tyr
1 5 10

<210> 489

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 489

```

gacatccaga tgacccagtc tccatccctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtcg gggcaataga aatgatttag gctggatatca gcagaaacca 120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tacaaagtgg ggtcccatca 180
aggttcagcg gcagggcgtc tggcacagat ttcaactotca ccacacagag cctgcagcct 240
gaagattttg caacttatta ctgtctacaa gattacaatt accctcggac gttcggccaa 300
gggaccaagg tggaaatcaa a 321

```

<210> 490

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 490

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

<210> 491

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 491
 cagggcatta gaaatgat 18

 <210> 492
 <211> 6
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 492
 Gln Gly Ile Arg Asn Asp
 1 5

 <210> 493
 <211> 9
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 493
 gctgcatcc 9

 <210> 494
 <211> 3
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 494
 Ala Ala Ser
 1

 <210> 495
 <211> 27
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 495
 ctacaagatt acaattaccc tcggacg 27

 <210> 496
 <211> 9
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 496
 Leu Gln Asp Tyr Asn Tyr Pro Arg Thr
 1 5

 <210> 497
 <211> 354
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic

<400> 497

```

caggtgcagc tgggtgagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tctgtgacag cgtctgcatt cactctcagt agctatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggtctgagtg ggtggcagtt atatgggatg atggaagtaa taaatactat 180
gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa caogetgtat 240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatgga 300
tatagtggct acgatgacta ctggggccag ggaacctctg tcaccgtctc ctca 354

```

<210> 498

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 498

```

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

```

<210> 499

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 499

```

gccatccaga tgaccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaactca gggcattaga aatgatctag gctggatatc gcagaaacca 120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tacaaagtgg ggtcccatca 180
aggttcagcg gcagtgcac tggcacagat ttcactctca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacaa gattacaatt accctcggac gttcggccaa 300
gggaccaagg tggaaatcaa a 321

```

<210> 500

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 500

```

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

```

<210> 501
 <211> 354
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 501
 caggtgcagc tgggtggagtc tggggggaggc gtgggtccagc ctggggaggtc cctgagagtc 60
 tcctgtgcag cgtctgggatt caccttcagt agctatggca tgcactgggt ccgccaggcc 120
 ccaggcaagg ggctagagtg ggtggcagtt atatggtatg atggaagtaa taaatactat 180
 gcagactcgc tgaaggggcg attcaccatc tccagagaca attccaagaa cacgtgtat 240

 ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagagatgga 300
 tatagtggct acgatgacta ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 502
 <211> 118
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 502
 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30
 Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Asp Gly Tyr Ser Gly Tyr Asp Asp Tyr Trp Gly Gln Gly Thr
 100 105 110
 Leu Val Thr Val Ser Ser
 115

<210> 503
 <211> 322
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 503
 gccatccaga tgacccagtc tccatcctcc ctgtctgcat ctgaggaga cagagtcacc 60
 atcaattgcc gggcaagtc gggcattaga aatgatttag gctgggtatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctatgct gcattccagtt tacaaagtgg ggtcccatca 180
 aggttcagcg gcagtggatc tggcacagat ttcactctca ccaacagcag cctgcagcct 240
 gaagattttg caacttatta ctgtctacaa gattacaatt accctcggac gttcggccaa 300
 gggaccaagg tggaaatcaa ac 322

<210> 504
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 504

```

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

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

```

<210> 505

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 505

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gaggtgcagc tgggtgcagtc tgggggagggc ttggtacagc ctggcaggtc cctgagactc 60
tctgtgtcag cctctggatt cacctttgat gattatgccca tgcactgggt ccgacaaggt 120
ccagggaagg gccctggagtg ggtctcaggt attagtggga atgggtgtag cgcaggctat 180
ggcgactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaattga acagtctgag agctgaggac acggccttgt attactgtgc aaaagaagac 300
tatgtctttg atatctgggg ccaaggggaca atggtcaccg tctctcca 348

```

<210> 506

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 506

```

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

```

<210> 507

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 507

```

ggattcacct ttgatgatta tgcc          24

```

<210> 508

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 508

Gly Phe Thr Phe Asp Asp Tyr Ala
1 5

<210> 509

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 509

atagttgga atggtgtag cgca 24

<210> 510

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 510

Ile Ser Trp Asn Gly Gly Ser Ala
1 5

<210> 511

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 511

gcaaaagaag actatgctt tgatac 27

<210> 512

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 512

Ala Lys Glu Asp Tyr Ala Phe Asp Ile

1 5

<210> 513

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 513

```

gacatcgtga tgaccagac tccactctcc tcacctgtca ccttggaca gccggcctcc 60
atctcctgca ggtctagtca aagcctccta cacagtgatg gaaacacctt cttgagttgg 120
cttcagcaga gccacagcca gccctcaaga ctcttaattt ataagatttc taaccgggttc 180
ctcgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaato 240
agcagggttg aagctgagga tgcggggctt tattactgca tgcaagctac acaatttccg 300
tacacttttg gccaggcgac caaggtggag atcaaa 336

```

<210> 514

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 514

```

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

```

<210> 515

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 515

```

caaagcctcg tacacagtga tggaaacacc tac 33

```

<210> 516

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 516

```

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

```

<210> 517

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 517

```

aagatttct 9

```

<210> 518

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 518

Lys Ile Ser

1

<210> 519

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 519

atgcaagcta cacaatttcc gtacact 27

<210> 520

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 520

Met Gln Ala Thr Gln Phe Pro Tyr Thr

1

5

<210> 521

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 521

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gaagtgcagc tgggtggagtc tggggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tccctgtgcag cctctggatt cacccttggat gattatgcca tgcactgggt cgcacaaggt 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atggtggtag cgcaggctat 180
gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaattga acagtctgag agctgaggac acggccttgt attactgtgc aaaagaagac 300
tatgcttttg atatctgggg ccaagggaca atggtcaccg tctcttca 348

```

<210> 522

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 522

```

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

```

<210> 523
 <211> 336
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 523
 gatattgtga tgacccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
 atctctctga ggtctagtca aagcctcgta cacagtgatg gaaacacctt cttgagttgg 120
 cttcagcaga ggccagccca gccccaaga ctccataatt ataagatttc taaccgggtc 180
 tctgggggtcc cagacaatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
 agcagggtgg aagctgagga tgtcggggtt tattactgca tgcaagctac acaatttcgg 300
 tacacttttg gccaggggac caagctggag atcaaa 336

<210> 524
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 524
 Asp Ile Val Met Thr Gln Thr Pro Leu Ser Ser Pro Val Thr Leu Gly
 1 5 10 15
 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
 20 25 30
 Asp Gly Asn Thr Tyr Leu Ser Trp Leu Gln Gln Arg Pro Gly Gln Pro
 35 40 45
 Pro Arg Leu Leu Ile Tyr Lys Ile Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ala Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
 85 90 95
 Thr Gln Phe Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 525
 <211> 348
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 525
 gaagtgcagc tgggtggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
 tectgtgcag cctotggatt cacctttgat gattatgcca tgcactgggt ccggcaagct 120
 ccaggggaagg gcttgagtg ggtctcaggt attagttgga atggttgtag cgcaggctat 180
 gcggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
 ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagaagac 300
 tatgcttttg atatctgggg ccaagggaca atggtcaccg tctcttca 348

<210> 526
 <211> 116
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 526

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

<210> 527

<211> 337

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 527

gatattgtga tgaccagac tccactctcc tcacctgtca ccttggaca gccggcctcc 60
 atctcctgca ggtctagta aagcctcgta cacagtgatg gaaacaccta cttgagttgg 120
 cttcagcaga gccacggcca gccccaaga ctctaatit ataagatttc taaccggttc 180
 tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaato 240
 agcagggtgg aagcagagga tgcgggggtt tattactgca tgcaagctac acaatttccg 300
 tacacttttg gccaggggac caagctggag atcaaac 337

<210> 528

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 528

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

<210> 529

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 529

gaggtgcagc tgggtgagtc tgggggaggc ttggtacagc ctggcaggte cctgagactc 60
 tctctgtcag cctctgcatt cacttttgaa gattatgcca tgcactgggt ccggcaagct 120
 ccagggaagg gccctggaatg ggtctcaggt attacttga atagtataa taaaggctat 180
 ggggactctg tgaagggccg attcaccatc tccagagaca acgccaagta ctccctgtat 240
 ctgcaaatga acagtctgag agctgaggac acggccttgt attactgtgc aaaagaggac 300
 tgggcgtttg actactgggg ccagggaacc ctggtcaccg tctctca 348

<210> 530

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 530

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

```

<210> 531

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 531

ggattcacct tgaagatta tgcc 24

<210> 532

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 532

```

Gly Phe Thr Phe Glu Asp Tyr Ala
 1              5

```

<210> 533

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 533

attacttgga atagtataa taaa 24

<210> 534

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 534

```

Ile Thr Trp Asn Ser Asp Asn Lys
 1              5

```

<210> 535

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 535

gcaaaagagg actgggcgtt tgactac 27

<210> 536

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 536

Ala Lys Glu Asp Trp Ala Phe Asp Tyr
1 5

<210> 537

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 537

gacatccaga tgaccagtc tccatcttcc gtgtctgcat ctgtaggaga cagagtcacc 60
atcacttgtc gtgcgactca gggatattaac agttggtag cctgggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctacgct gcatccagtt tgcagagtgg ggtcccatca 180
aggttcagcg gcagtgcatc tgggacagat ttcactctca ccatcagcgg cctccagcct 240
gaagattttg caacttacta ttgtcaacag gctaacagtt tcccgtaac ttttggccag 300
gggaccaagg tggaaatcaa a 321

<210> 538

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 538

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

<210> 539

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 539

caggttatta acagttgg 18

```

<210> 540
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 540
Gln Gly Ile Asn Ser Trp
 1             5

<210> 541
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 541
gctgcatcc      9

<210> 542
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 542
Ala Ala Ser
 1

<210> 543
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 543
caacaggcta acagttccc gtacact      27

<210> 544
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 544
Gln Gln Ala Asn Ser Phe Pro Tyr Thr
 1             5

<210> 545
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

```

<400> 545

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gaagtgcagc tgggtggagtc tggggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tcctgtgcag cctctggatt cacctttgaa gattatgcc tgcactgggt ccggcaagct 120
ccagggaagg gccttgaatg ggtctcaggt attacttggg atagtataaa taaaggctat 180
gcggactctg tgaaggcccg attcaccato tccagagaca acgccaagta ctccctgtat 240
ctgcaaatga acagcttgag agctgaggac acggccttgt attactgtgc aaaagaggac 300
tgggcgtttg actactgggg ccagggaacc ctggtcaccg tctcctca 348

```

<210> 546

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 546

```

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

Ala Lys Glu Asp Trp Ala Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
100    105    110
Thr Val Ser Ser
115

```

<210> 547

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 547

```

gacatccaga tgaccagtc tccatcttcc gtgtctgcat ctgtaggaga cagagtcacc 60
atcacttgtc gtgcgactca gggattatac agttggtag cctgggtatca gcagaaacca 120
gggaaagccc ctaagctctc gatetacgct gcattccagtt tgcagagtgg ggtcccatca 180
aggttcagcg gcagtgcato tgggacagat ttactctca ccatcagcgg cctccagcct 240
gaagattttg caacttacta ttgtcaacag gctaacagtt tcccgtaaac ttttggccag 300
gggaccaagc tggagatcaa a 321

```

<210> 548

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 548

```

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

```

<210> 549

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 549

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gaagtgcagc  tgctggagtc  tgggggaggc  ttggtacagc  ctggcaggtc  cctgagactc  60
tctgtgcag  cctctggatt  cacctttgaa  gattatgcca  tgcactgggt  cgggcaagct  120
ccagggaagc  gcctggagtg  ggtctcaggt  attacttgga  atagtataa  taaaggctat  180
gcggaactctg  tgaagggcg  attcaccatc  tccagagaca  acgccaagaa  ctccctgtat  240
ctgcaaatga  acagtctgag  agctgaggac  acggccttgt  attactgtgc  aaaagaggac  300

```

```

tggggcgtttg  actactgggg  ccagggaacc  ctggtcaccg  tctcctca  348

```

<210> 550

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 550

```

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

```

<210> 551

<211> 322

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 551

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gacatccaga  tgaccagtc  tccatcttct  gtgtctgcat  ctgtaggaga  cagagtcacc  60
atcacttgtc  gggcgagtc  ggggtattaac  agttgggttag  cctgggtatca  gcagaaacca  120
gggaaagccc  ctaagctcct  gatctatgct  gcattccagtt  tgcaaagtgg  ggtcccatca  180
aggttcagcg  gcagtgagtc  tgggacagat  ttcactctca  ctatcagcag  cctgcagcct  240
gaagattttg  caacttacta  ttgtcaacag  gctaacagtt  tcccgtaaac  ttttggccag  300
gggaccaagc  tggagatcaa  ac  322

```

<210> 552

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 552

```

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

```

```

      5C          55          60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65          70          75          80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Tyr
      85          90          95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
      100          105

```

<210> 553

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 553

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gaggtgcagc tgggtgcagtc tgggggaggc ttggtacagc ctggcaggtc cctgagagtc 60
tcctgtgcag cctctgcatt cacotttgat gattatgccg tgactgggt cgggcaagct 120
ccaagggaagq qctctgagtg qgtctcaagt attagttaga atagtggtaq caaaggctat 180
gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagctctgag acgtgaggac acggccttgt attactgtgt aaaagaggac 300
tgggcgtttg actactcggg ccagggaacc ctggtcaccg tctctcca 348

```

<210> 554

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 554

```

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

```

<210> 555

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 555

```

ggattcacct ttgatgatta tgcc          24

```

<210> 556

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 556

```

Gly Phe Thr Phe Asp Asp Tyr Ala
1          5

```

<210> 557
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 557
 attagttgga atagtggtag caaa 24

<210> 558
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 558
 Ile Ser Trp Asn Ser Gly Ser Lys
 1 5

<210> 559
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 559
 gtaaaagagg actgggcgtt tgactac 27

<210> 560
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 560
 Val Lys Glu Asp Trp Ala Phe Asp Tyr
 1 5

<210> 561
 <211> 315
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 561
 gacatccaga tgacceagtc tccatectcc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc agggagctca ggacattagc aactatttaa attggtatca acaaaaaacca 120
 gggaaagccc ctaagttcct gatctacgat gcatccaatt tgggaacagg ggtcccatca 180
 aggttcagtg gaagtggatc tgggacagat tttactttca ccatcagcag cctgcagcct 240
 gaagatattg cgacatatta ctgtcaacag tatgataatc tccctttcgg cggaggggacc 300
 aaggtggaaa tcaaa 315

<210> 562
 <211> 105
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Synthetic

<400> 562
 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Ser Asn Tyr
 20 25 30
 Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Phe Leu Ile
 35 40 45
 Tyr Asp Ala Ser Asn Leu Gly Thr Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80
 Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Asn Leu Pro Phe
 85 90 95
 Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 563

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 563

caggacatta gcaactat 18

<210> 564

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 564

Gln Asp Ile Ser Asn Tyr
 1 5

<210> 565

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 565

gatgcatcc 9

<210> 566

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 566

Asp Ala Ser
 1

<210> 567

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 567

caacagtatg ataattcccc t 21

<210> 568

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 568

Gln Gln Tyr Asp Asn Leu Pro
1 5

<210> 569

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 569

```

gaagtgcagc tggtaggagtc tgggggaggc ttggtacagc ctggcaggtc cctgagactc 60
tctctgtcac cctctggatt cacttttgat gattatgcca tgcactgggt ccggcaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag caaaggctat 180
gcggaactctg tgaagggcgc attcaccatc tccagagaca acgccaagaa ctcctgtgat 240
ctgcaaatga acagtctgag acgtgaggac acggccttgt attactgtgt aaaagaggac 300
tgggcgtttg actactgggg ccagggaacc ctggteaccg tctctcca 348

```

<210> 570

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 570

```

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

```

<210> 571

<211> 315

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 571

```

gacatccaga tgaccagtc tccatccctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcactttgc aggcgaçtca ggacattagc aactatttaa attggtatca acaaaaaacca 120
gggaaagccc ctaagtctcc gatctacgat gcatccaatt tgggaacagg ggtcccatca 180
aggttcagtg gaagtçgato tgggacagat tttactttca ccatcagcag cctgcagcct 240
gaagatatgg cgacatatta ctgtcaacag tatgataatc tccctttcgg cggaggggacc 300
aaggtggaga tcaaa 315

```

<210> 572

<211> 105

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 572

```

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

```

<210> 573

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 573

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gaagtgcagc tgggtggagtc tggggggagcc ttggtacagc ctggcaggtc cctgagagtc 60
tcctgtgcag cctcçggatt cacctttgat gattatgcca tgcactgggt ccggccaagct 120
ccagggaagg gcctggagtg ggtctcaggt attagttgga atagtggtag caaaggctat 180
gcggactctg tgaaggcccg attcaccatc tccagagaca acgccaagaa ctccctgtat 240
ctgcaaatga acagctçtgag agctgaggac acggccttgt attactgtgt aaaagaggac 300
tgggcgtttg actactgggg ccagggaacc ctggtcaccg tctcctca 348

```

<210> 574

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 574

```

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

```

<210> 575

<211> 316

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 575

```

gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc aggcgactca ggacattagc aactatttaa attggtatca gcagaaacca 120
gggaaagccc ctaagctcct gatctacgat gcattccaatt tggaaacagg ggtcccatca 180
aggttcagtg gaag-gcatt tgggacacat ttactttca ccatcagcag cctgcagcct 240
gaagatattg caacatatta ctgtcaacag tatgataatc tccctttcgg cggaggggacc 300
aaggtggaga tcaaac                                     316

```

<210> 576

<211> 105

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 576

```

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

```

<210> 577

<211> 375

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 577

```

caggtgcagc tgggtcagtc aggtccagga ctggtgaagc cctcgcagac cctctcactc 60
acctgtgccca tctccgggga cagtgtctct agcaacagtg ctgcttgga cttggtcagg 120
cagtcccat cgagagccct tgagtggctg ggaaggacat actacaggtc caagtgggat 180
aatgattatg cagtatctgt gaaaagtoga ataaccatca acccagacac atccaagaac 240
cagttctccc tgcagctgaa ctctgtgact cccgaggaca cggctgtgta ttactgtgca 300
agaggggtata gcagcagctg gtacgggggt gcttttgata tctggggcca agggacaatg 360
gtcacctgtct ctcca                                     375

```

<210> 578

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 578

```

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

```

<210> 579
 <211> 30
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 579
 ggggacagtg tctctagcaa cagtgctgct 30

 <210> 580
 <211> 10
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 580
 Gly Asp Ser Val Ser Ser Asn Ser Ala Ala
 1 5 10

 <210> 581
 <211> 27
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 581
 acatactaca ggtccaagtg gtataat 27

 <210> 582
 <211> 9
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 582
 Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn
 1 5

 <210> 583
 <211> 45
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 583
 gcaagagggt atagcagcag ctggtacggg ggtgcttttg atatc 45

 <210> 584
 <211> 15
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

<400> 584

Ala Arg Gly Tyr Ser Ser Ser Trp Tyr Gly Gly Ala Phe Asp Ile
 1 5 10 15

<210> 585

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 585

gacatccaga tgaccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc gggcaagtc gagcattagc agttatttaa gttgggtatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctatgct gcaccagtt tgcaaagtgg ggtcccatca 180
 aggttcagtg gcagtggtgc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
 gaagattttg caacttacta ctgtcaacag agttacagta ccccatcac tttgggcct 300
 gggaccaagg tggaaatcaa a 321

<210> 586

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 586

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

<210> 587

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 587

cagagcatta gcagttat 18

<210> 588

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 588

Gln Ser Ile Ser Ser Tyr
 1 5

<210> 589

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 589

gctgcatcc 9

<210> 590

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 590

Ala Ala Ser
1

<210> 591

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 591

caacagagtt acagtacccc attcact 27

<210> 592

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 592

Gln Gln Ser Tyr Ser Thr Pro Phe Thr
1 5

<210> 593

<211> 375

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 593

```
caggtacagc tgcagcagtc aggtccagga ctggtgaagc cctcgcagac cctctcactc 60
acctgtgcca tctccgggga cagtgtctct agcaacagtg ctgcttggaa ctggatcagg 120
cagtcgccat cgagagccct tgagtggctg ggaaggacat actacaggto caagtgggat 180
aatgattatg cagtatctgt gaaaagtoga ataaccatca acccagacac atccaagaac 240
cagttctccc tgcagctgaa ctctgtgact cccgaggaca cggctgtgta ttactgtgca 300
agaggggtata gcagcacctg gtacggggct gcttttgata tctggggcca agggacaatg 360
gtcacctgtct cttca 375
```

<210> 594

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 594

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

85 90 95
 Tyr Tyr Cys Ala Arg Gly Tyr Ser Ser Ser Trp Tyr Gly Gly Ala Phe
 100 105 110
 Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120 125

<210> 595

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 595

gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcacttgcc gggcaagtc gagcattagc agttatttaa gttggtatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180
 aggttcagtg gcagtgcatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
 gaagattttg caacttacta ctgtcaacag agttacagta ccccatcacc tttcgccct 300
 gggaccacaag tggatatcaa a 321

<210> 596

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 596

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

<210> 597

<211> 375

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 597

caggtacagc tgcagcagtc aggtccagga ctggtgaagc cctgcagac cctctcactc 60
 acctgtgcca tctccgggga cagtgtctct agcaecagtg ctgcttgga cttggtcagg 120
 cagtcccat cgagaggcct tgagtggctg ggaaggacat actacaggtc caagtggat 180
 aatgattatg cagtatctgt gaaaagtoga ataaccatca acccagacac atccaagaac 240

cagtctctcc tgcagctgaa ctctgtgact cccgaggaca cggtctgtga ttactgtgca 300
 agaggggtata gcagcagctg gtacgggggt gcttttgata tctggggcca agggacaatg 360
 gtcaccgtct cttaa 375

<210> 598
 <211> 125
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 598
 Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
 1 5 10 15
 Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
 20 25 30
 Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
 35 40 45
 Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala
 50 55 60
 Val Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn
 65 70 75 80
 Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
 85 90 95
 Tyr Tyr Cys Ala Arg Gly Tyr Ser Ser Ser Trp Tyr Gly Gly Ala Phe
 100 105 110
 Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120 125

<210> 599
 <211> 322
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 599
 gacatccaga tgacccagtc tccatccctcc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcaacttgc gggcaagtc gagcattagc agttatttaa attggtatca gcagaaacca 120
 gggaaagccc ctaagctcct gatctatgct gcattccagtt tgcaaaagtgg ggtcccatca 180
 aggttcagtg cgaatggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240
 gaagattttg caacttacta cgtcaacag agttacagta ccccatcac tttcggcct 300
 gggaccaaaag tggatatcaa ac 322

<210> 600
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 600
 Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
 20 25 30
 Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45
 Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80
 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Phe
 85 90 95
 Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
 100 105

<210> 601
 <211> 357
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 601

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caggtgcagc tgcaggagtc tgggggaggc tcggtacagc ctgggggggc cctgcgactc 60
tcctgtgcaa cctctggatt cacctttacc aactttgcca taagctgggt ccgccaggct 120
ccaagcagtg ggcctggagtg ggtctcatct attactggta gtggtgatta cgcatactac 180
gcagactccg tgaaggcccg gttcaccatc tccagagaca gttccaagaa cagcctctat 240
ctacaaatga acagcctgag agccgacgac acggcccgat atttctgtac gagagaagac 300
tatattaact cgtcctttga ctactggggc cagggaaacca cggtcacccg ctctctca 357

```

<210> 602

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 602

```

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

```

<210> 603

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 603

```

ggattcacct ttaccaactt tgcc          24

```

<210> 604

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 604

```

Gly Phe Thr Phe Thr Asn Phe Ala
 1          5

```

<210> 605

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 605

```

attactggta gtggtgatta cgca          24

```

<210> 606

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 606

Ile Thr Gly Ser Gly Asp Tyr Ala
1 5

<210> 607

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 607

acgagagaag actatatataa ctgcctctt gactac 36

<210> 608

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 608

Thr Arg Glu Asp Tyr Ile Asn Ser Ser Phe Asp Tyr
1 5 10

<210> 609

<211> 333

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 609

gacatccaga tgacccagac tccactctcc tcacctgtca cccctggaca gccggcctcc 60
atctctctga ggtctagtca gagcctcgta cacactgatg gaaatacccta cttgagttgg 120
cttcagcgga ggccaggcca gcctccaaga ctcttaattt ataagatttc taaccgggtc 180
tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaatc 240
agcagggtgg aagctgagga tgtcgggggtt tattaactgca tgcaagctac acaacttcg 300
acgttcggcc aagggaacaa ggtggaaatc aaa 333

<210> 610

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 610

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

<210> 611
 <211> 33
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 611
 cagagcctcg tacacagtga tggaaatacc tac 33

 <210> 612
 <211> 11
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 612
 Gln Ser Leu Val His Ser Asp Gly Asn Thr Tyr
 1 5 10

 <210> 613
 <211> 9
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 613
 aagatttct 9

 <210> 614
 <211> 3
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 614
 Lys Ile Ser
 1

 <210> 615
 <211> 24
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <400> 615
 atgcaagcta cacaacttc gacg 24

 <210> 616
 <211> 8
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

<400> 616

Met Gln Ala Thr Gln Leu Pro Thr
1 5

<210> 617

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 617

```

gaggtgcagc tgttgagtc tgggggaggc tcggtacagc ctgggggggtc cctgcgactc 60
tcctgtgcaa cctctggatt cacccttacc aactttgcca taagctgggt cgcgcaggct 120
ccaggcagtg ggctggagtg ggtctcatct attactggta gtggtgatta cgcatactac 180
gcagactccg tgaaggcccg gtccaccatc tccagagaca gttccaagaa cagctcttat 240
ctacaatatga acagcctgag agccgacgac acggccggtat attctgtac gagagaagac 300
tatattaact cgtcctttga ctactggggc cagggaaacc tggtcaccgt ctctca 357

```

<210> 618

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 618

```

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

```

<210> 619

<211> 333

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 619

```

gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaac gccggcctcc 60
atctcctgta ggtctagtca gagcctcgta cacagtgatg gaaataccta cttgagttgg 120
cttcagcgga ggccaggcca gcctccaaga ctccataatt ataagatttc taaccgggtc 180
ctcgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggtgg aagctgagga tgcgggggtt tattactgca tgcaagctac acaacttcgc 300
acgttcggcc aagggaacca ggtggaaatc aaa 333

```

<210> 620

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 620

```

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

```

<210> 621

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 621

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gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggc cctgagactc 60
tcctgtgcag cctctggatt cacctttacc aactttgcca tgagctgggt ccgccaggct 120
ccagggaagg ggtctggagt ggtctcagct attactggta gtggtgattc cgcatactac 180
gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgtgtgat 240
ctgcaaatga acagcctgag agccgaggac acggccgcat attactgtac gagagaagac 300
tatattaact cgtcctttga ctactggggc cagggaaccc tggtcaccgt ctctctca 357

```

<210> 622

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 622

```

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

```

<210> 623

<211> 334

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 623

```

gatattgtga tgaccagagc tccactctcc tcacctgtca cccctggaca gccggcctcc 60
atctctgcga ggtctagtca gagctctgta cacagtgatg gaaataccta cttagttgg 120
cttcagcaga gccagggcca gctccaaga ctcttaattt ataagatttc taaccgggtc 180
tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggttg aagctgagga tgtcggggtt tattactgca tgcaagctac acaacttcgc 300
acgttcggcc aagggaacca ggtggaatc aaac
 334

```

<210> 624

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 624

```

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

```

<210> 625

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 625

```

caggtgcagc tgggtggagtc tgggggaggc gtggtccagc ctgggatgct cctgagactc 60
tcctgtgcag cgtccgcatt taccttcagg agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggcctggagtg ggtggcagtt atatgggatg atggaagtaa taaatattat 180
gtagattccg tgaaggcccg attcaccatc tccagagaca attccaagaa cagcgtgtat 240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gacgaaaatt 300
acaagtgggg actggttcga cccctggggc cagggaaacc tggtcaccgt ctcctca 357

```

<210> 626

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 626

```

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

```

<210> 627

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 627

ggatttacct tcaggagata tggc 24

<210> 628

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 628

Gly Phe Thr Phe Arg Arg Tyr Gly
 1 5

<210> 629

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 629

atatggtatg atggaagtaa taaa 24

<210> 630

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 630

Ile Trp Tyr Asp Gly Ser Asn Lys
 1 5

<210> 631

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 631

gcgagcgaaa ttacagtgg ggactgggtc gacccc 36

<210> 632

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 632

Ala Ser Glu Ile Thr Val Gly Asp Trp Phe Asp Pro
 1 5 10

<210> 633

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 633

```

gacatccaga tgacccagtc tccatctctc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgtc gggcaagtc gggcattaga aatgatttag gctgggtatca gcagaaacca 120
gggaaagccc ctaaacctct gatctatgct gcatccagtt tacacagtgg ggtcccatca 180
aggttcagcg gcagtgagtc tggcacagat ttcactctca ccacagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag gatttcaatt accctctcac tttcggcgga 300
gggaccaagg tggagatcaa a                               321

```

<210> 634

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 634

```

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

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

```

<210> 635

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 635

```

cagggcatta gaaatgat      18

```

<210> 636

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 636

```

Gln Gly Ile Arg Asn Asp
 1             5

```

<210> 637

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 637

```

gctgcatcc      9

```

<210> 638

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 638

Ala Ala Ser
1

<210> 639

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 639

ctacaggatt tcaattacc tctcact 27

<210> 640

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 640

Leu Gln Asp Phe Asn Tyr Pro Leu Thr
1 5

<210> 641

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 641

```
cagggtgcagc tgggtggagtc tggggggaggc gtgggtccagc ctgggatgtc cctgagactc 60
tcctgtgcag cgctccgatt taccttcagg agatatggca tgcactgggt ccgccaggct 120
ccaggccaagg ggctggagtg ggtggcagtt atatggtatg atggaagtaa taaatattat 180
gtagattccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gaggcaaat 300
acagttgggg actggttcga cccctggggc cagggaacco tggtcaccgt ctctca 357
```

<210> 642

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 642

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

```

      85              90              95
Ala Ser Glu Ile Thr Val Gly Asp Trp Phe Asp Pro Trp Gly Gln Gly
      100              105              110
Thr Leu Val Thr Val Ser Ser
      115

```

<210> 643

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 643

```

gccatccaga tgaccacgac tccatccctc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgct gggcaactca gggcattaga aatgatttag gctggtatca gcagaaacca 120
gggaaagccc ctaaactcct gatctatgct gcattccagt tacacagtgg ggtcccatca 180
aggttcagcg gcagtggatc tggcacagat ttcactotca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtccacag gatttcaatt accctctcac tttcggcgga 300
gggaccaagg tggagatcaa a                               321

```

<210> 644

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 644

```

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

```

<210> 645

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 645

```

caggtgcagc tggctggagtc tgggggaggc gtggtccagc ctgggaagtc cctgagactc 60
tctctgtgcag cgtctggatt taccttcagg agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggcctggagt ggtggcagtt atatggtatg atggaagtaa taaatactat 180
gcagactccg tgaagggccg attcaccatc tccagagaca actccaagaa cacgctgtat 240

```

```

ctgcaaatga acagcctgag agccgaggac acgctgtgtg attactgtgc gagcgaaatt 300
acagttgggg actggttcga cccctgggga cagggaaccc tggtcaccgt ctctctca 357

```

<210> 646

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 646

```

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

```

<210> 647

<211> 322

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 647

```

gccatccaga tgaccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtc gggcattaga aatgatttag gctggatatca gcagaaacca 120
ggqaaaagcc ctaagctcct gatctatgct qcatccaqtt tacaaaqtqq ggtcccatca 180
aggttcagcg gcagtgagtc tggcacagat ttcactctca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag gatttcaatt accctctcac ttteggcgga 300
gggaccaagg tggagatcaa ac                                     322

```

<210> 648

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 648

```

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

```

```

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

```

<210> 649

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 649

```

caggtgcagc tgggtggagtc tgggggaggc gtgggtccagc ctgggaggtc cctgagactc 60
tctgtgtgag cctcgggatt caccctcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggcctggagtg gctgacagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa cacgggtgtat 240
ctgcasaatga acagcctgag agctgaggac acgggagtggt attactgtgc gaaaggggac 300
ttttggagtg gttactttga ctactggggc cagggaaccc tgggtcactgt ctctca 357

```

<210> 650

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 650

```

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

```

<210> 651

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 651

ggattcacct tcagtagata tggc 24

<210> 652

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 652

```

Gly Phe Thr Phe Ser Arg Tyr Gly
 1          5

```

<210> 653

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 653

atatcatatg atggaattaa taaa 24

<210> 654

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 654

```

Ile Ser Tyr Asp Gly Ile Asn Lys
 1          5

```

<210> 655

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 655

gcgaaagggg actttggag tggttactt gactac 36

<210> 656

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 656

Ala Lys Gly Asp Phe Trp Ser Gly Tyr Phe Asp Tyr

1 5 10

<210> 657

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 657

```

gacatcgtga tgaccacagac tocactctcc tcacctgtca cccctggaca gccggcctcc 60
atctcctgca ggctcactca aagcctcgto cacagtgatg gaaacaccta cttgagttgg 120
cttcaccaga ggccagccca gcctccaaga ctctaatatt ataagatttc taaccgggtc 180
tctgggggtcc cagacacatt cagtggcagt ggggcaggga cagattttac actgcaaatc 240
agcagggtgg aagctgagga tgtcgggatt tattactgca tgcaagggtac acaatttccg 300
actttcggcg gagggaccaa ggtggagato aaacga 336

```

<210> 658

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 658

```

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

```

<210> 659

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 659

caaagcctcg tccacagtga tggaaacacc tac 33

<210> 660

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 660

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

<210> 661

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 661

aagatttct 9

<210> 662

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 662

Lys Ile Ser
1

<210> 663

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 663

atgcaaggta cacaatttc gact 24

<210> 664

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 664

Met Gln Gly Thr Gln Phe Pro Thr
1 5

<210> 665

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 665

```
cagggtgcagc tgggtggagtc tggggggaggc gtggtccagc ctggggaggtc cctgagactc 60
tcctgtgtag cctctggatt cacccttcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg gctgatatgt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa cacgggtgtat 240
ctgcaaatga acagcctgag agctgaggac acgggagtggt attactgtgc gaaaggggac 300
ttttggagtg gttactttga ctactggggc cagggaaccc tggtcaccgt ctcctca 357
```

<210> 666

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 666

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

<210> 667

<211> 333

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 667

```
gatattgtga tgaaccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctcctgca ggctactca aagcctcgto cacagtgatg gaaacacctt cttgagttgg 120
cttcaccaga ggccagccca gcctccaaga ctctaatatt ataagatttc taaccgggtc 180
cttgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgcaaato 240
agcagggttg aagctgagga tgtcgggatt tattactgca tgcaaggtag acaatttccg 300
actttcggcg gagggaccac ggtggagato aaa 333
```

<210> 668

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 668

```

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

```

<210> 669

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 669

```

cagggtgcagc tgggtggagtc tggggggaggc gtggtccagc ctgggaggct cctgagactc 60
tccgtgtgcag cctctgcatt caccttcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggcctggagtg ggtggcagtt atatcatatg atggaattaa taaatactat 180
gcagactcgc tgaaggcccg attcaccatc tccagagaca attccaagaa cagcgtgtat 240
ctqcaaatga acaqccctga agctgaqqac acgqctgtgt attactgtgc qaaagqqqac 300
ttttggagtg gttactttga ctactggggc cagggaacco tggtcaccgt ctcctca 357

```

<210> 670

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 670

```

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

```

<210> 671

<211> 334

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 671

```

gatattgtga tgaccagac tccactctcc tcacctgtca cccttgga gcccgcctcc 60
atctcctgca ggtctactca aagcctcgtc cacagtgtat gaaacacctt cttgagttgg 120
cttcagcaga ggcacgcca gcctccaaga ctctaatat ataagatttc taaccgggtc 180
cttgggggtc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggtgg aagctgagga tgtcggggtt tattactgca tgcaaggtae acaatttccg 300
actttcggcg gagggaccaaa ggtggagatc aaac
334

```

<210> 672

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 672

```

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

```

<210> 673

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 673

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caggtgcagc tgggtcagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgtag cctctggatt cacccttcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggcctggagtg ggtggttagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa caccgtgtat 240
ctgcacaaag acagcccgag agcagaggac acggcclgcl alcacclgtc gaaaggggac 300
ttttggagtg gttactttga ctactggggc caggaaccc tggtcacccg ctccctca 357

```

<210> 674

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 674

```

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

```

<210> 675

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 675

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ggattcacct tcagtagata tggc      24

```

<210> 676

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 676

Gly Phe Thr Phe Ser Arg Tyr Gly
1 5

<210> 677

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 677

atatcatatg atggaattaa taaa 24

<210> 678

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 678

Ile Ser Tyr Asp Gly Ile Asn Lys
1 5

<210> 679

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 679

gcgaaagggg actttggag tggttacttt gactac 36

<210> 680

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 680

Ala Lys Gly Asp Phe Trp Ser Gly Tyr Phe Asp Tyr
1 5 10

<210> 681

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 681

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gacatcgtga tgaccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctcctgca ggtctagtca aagcctcgta cacagtgatg gaaacacctt cttgagttgg 120
cttcaccaga gccacaggca gccctcaaga ctcttaattt ataagatttc taaccgggttc 180
tctggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgcaaato 240
agcagggttg aagctgagga tgtcgggatt tattaccgca tgcaagcaac acaatttccg 300
actttcggcg gagggaccac ggtggaaato aaacga 336

```

<210> 682

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 682

```

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

```

```

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

```

<210> 683

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 683

```

caaagcctcg tacacagtga tggaacacc tac 33

```

<210> 684

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 684

```

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

```

<210> 685

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 685

```

aagatttct 9

```

<210> 686

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 686

Lys Ile Ser
1

<210> 687

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 687

atgcaagcaa cacaatttc gact 24

<210> 688

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 688

Met Gln Ala Thr Gln Phe Pro Thr
1 5

<210> 689

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 689

```

caggtgcagc tgggtggagtc tgggggaggc gtggtccagc ctggggagtc cctgagactc 60
tcctgtgtag cctctggatt caccttcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggcctggagtg ggtggtagtt atatcatatg atggaattaa taaatactat 180
gcagactcgg tgaaggcccg attcaccatc tccagagaca attccaagaa cacgggtgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt atcactgtgc gaaaggggac 300
llllggagtg gllactllga clactlgygc cagggaaccc lggllacccg clccclca 357

```

<210> 690

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 690

```

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

Ala Lys Gly Asp Phe Trp Ser Gly Tyr Phe Asp Tyr Trp Gly Gln Gly
100 105 110
Thr Leu Val Thr Val Ser Ser
115

```

<210> 691
 <211> 333
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 691
 gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaaca gccggcctcc 60
 atctctctga ggtctactca aagcctcgtc cacactggtg gaaacacctt cttgagttgg 120
 cttcaccaga ggccagccca gcctccaaga ctcttaattt ataagatttc taaccgggtc 180
 tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgcaaacc 240
 agcagggtgg aagctgagga tgtcgggatt tattactgca tgcaagcaac acaatttcgg 300
 actttcggcg gagggaccaa ggtggagatc aaa 333

<210> 692
 <211> 111
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 692
 Asp Ile Val Met Thr Gln Thr Pro Leu Ser Ser Pro Val Thr Leu Gly
 1 5 10 15
 Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
 20 25 30
 Asp Gly Asn Thr Tyr Leu Ser Trp Leu His Gln Arg Pro Gly Gln Pro
 35 40 45
 Pro Arg Leu Leu Ile Tyr Lys Ile Ser Asn Arg Phe Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ala Gly Thr Asp Phe Thr Leu Gln Ile
 65 70 75 80
 Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Ala
 85 90 95
 Thr Gln Phe Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> 693
 <211> 357
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 693
 caggtgcagc tgggtggagt tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
 tectgtgcag cctctggatt caccttcagt agatatggca tgcactgggt ccgccaggct 120
 ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaattaa taaatactat 180
 gcagactccg tgaaggcccg attcaccato tccagagaca attccaagaa cagcgtgtat 240
 ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300

ttttggagtg gttactttga ctactggggc cagggaaccc tggtcaccgt ctctctca 357

<210> 694
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 694

```

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

```

<210> 695

<211> 334

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 695

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gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctcctgca ggtctagtca aagcctcgtc cacagtgatg gaaacacctc cttgagttgg 120
cttcagcaga gccacagcca gccccaaga ctccataatt ataagatttc taaccggttc 180
tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggtgg aagctgagga tgtcggggtt tattactgca tgcaagcaac acaatttcg 300
actttcggcg gagggaccaa ggtggagatc aaac 334

```

<210> 696

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 696

```

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

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

```

<210> 697

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 697

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caggtgcagc tgggtcagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tctgtgttag cctctggatt caccttcagt agatatggca tacactgggt ccgccaggct 120
ccaggcaagg ggcctggagt ggtgatagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa caccgtatat 240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gaaaggggac 300
ttttggagtg gttactttga ctattggggc cagggaaccc tggtcaccgt ctctca 357

```

<210> 698

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 698

```

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

```

<210> 699

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 699

ggattcacct tcagtagata tggc 24

<210> 700

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 700

```

Gly Phe Thr Phe Ser Arg Tyr Gly
 1           5

```

<210> 701

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 701

atatcatatg atggaattaa taaa 24

<210> 702

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 702

```

Ile Ser Tyr Asp Gly Ile Asn Lys
 1           5

```

<210> 703

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 703

gcgaaagggg actttggag tggttacttt gactat 36

<210> 704

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 704

Ala	Lys	Gly	Asp	Phe	Trp	Ser	Gly	Tyr	Phe	Asp	Tyr
1				5					10		

<210> 705

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 705

```

gaaattgtgc tgactcagac tccactctct tcacctgtca cccttggaca gccggcctcc 60
atctctctgta ggtctaatca aagcctcgtc cacagtgatg gaaacacctt cttgagttgg 120
cttcaccaga ggccaggcca gcctccaaga ctctaatatt ataagatttc taaccgggtc 180
cttgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgcaaatc 240
agcagggtgg aagctgagga tgtcgggtatt tattactgca tgcaagctac acaatttcog 300
actttcggcg gagggaccaa ggtggaaatc aaacga 336

```

<210> 706

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 706

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

<210> 707

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 707

caaagcctcg tacacagtga tggaaacacc tac 33

<210> 708

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 708

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

<210> 709

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 709

aagatttct 9

<210> 710

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 710

Lys Ile Ser
1

<210> 711

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 711

atgcaagcta cacaatttcc gact 24

<210> 712

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 712

Met Gln Ala Thr Gln Phe Pro Thr
1 5

<210> 713

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 713

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caggtgcagc tgggtggagtc tgggggaggc gtggtccagc ctggggagtc cctgagactc 60
tctgtgttag cctctggatt cacttcagtc agatatggca tacactgggt ccgccagggt 120
ccaggcaagg ggcctggagtg ggtgatagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa cagggtatat 240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gaaaggggac 300
tttggagtg gttactttga ctattggggc cagggaaacc tggtcaccgt ctctca 357

```

<210> 714

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 714

```

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

```

<210> 715

<211> 333

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 715

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gatattgtga tgaccagac tccactctct tcacctgtca cccttggaaca gccggcctcc 60
atctcctgta ggtcmaatca aagcctcgtc cacagtgatg gaaacaccta cttgaghttg 120
cttcaccaga gcccaggcca gctccaaga ctctaatat ataagatttc taaccgggtc 180
tctgggggtc cagacaqatt cagtggcagt ggggcaggga cagatttcac actgcaaatc 240
agcagggtgg aagctgagga tgtcgggtatt tattactgca tgcaagctac acaatttcg 300
actttcggcg gagggaccac ggtggagato aaa 333

```

<210> 716

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 716

```

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

```

<210> 717
 <211> 357
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 717
 caggtgcagc tgggtggagtc tggggggaggc gtggtccagc ctggggaggtc cctgagactc 60
 tctgtgtcag cctctgcatt cactctcagt agatatggca tgcactgggt ccgccaggct 120
 ccaggcaagg ggcctggagt ggtggcagtt atatcatatg atggaattaa taaatactat 180
 gcagactcgg tgaaggcccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
 ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300
 ttttgagtg gttactttga ctattggggc cagggaaccc tggtcaccgt ctcctca 357

<210> 718
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 718
 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
 20 25 30
 Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ala Val Ile Ser Tyr Asp Gly Ile Asn Lys Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Lys Gly Asp Phe Trp Ser Gly Tyr Phe Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Leu Val Thr Val Ser Ser
 115

<210> 719
 <211> 334
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 719
 gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaaca gccggcctcc 60
 atctcctgca ggtcctagca aagcctcgta cacagtgatg gaaacaccta cttgagttgg 120
 cttcagcaga ggccaggcca gcctccaaga ctctaatatg ataagatttc taaccgggtc 180
 tctgggggtcc cagacaattt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
 agcagggttg aagctgagga tgtcgggggt tattacgca tgcaagctac acaatttccg 300
 actttcggcg gagggaccaa ggtggagatc aaac 334

<210> 720
 <211> 111
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 720

```

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

```

<210> 721

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 721

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caggtgcagc tgggtggagtc tggggggaggc gtggtccagc ctgggatgtc cctgagactc 60
tctgtacacg cgtccggatt tacgttcagg agatatggca tgcactgggt ccgccagggt 120
ccaggcaagg ggtctggagtg ggtggcagtt atttggtatg atggaagtaa taaatattat 180
gcagactccg tgaaggcagc attcaccata accagagaca attccaagaa cactgtgtat 240
ctgcaaatga acagcctgag agccgaggac acggctatat attttgtgc gagcgaaata 300
acaattgggg actggttcga cccccggggc cagggaaacc tggtcaccgt ctcctca 357

```

<210> 722

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 722

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

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<210> 723

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 723

ggatttacgt tcaggagata tggc 24

<210> 724

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 724

Gly Phe Thr Phe Arg Arg Tyr Gly
1 5

<210> 725

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 725

atttggtatg atggaagtaa taaa 24

<210> 726

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 726

Ile Trp Tyr Asp Gly Ser Asn Lys
1 5

<210> 727

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 727

gcgagcgaaa taacaattgg ggactgggtc gacccc 36

<210> 728

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 728

Ala Ser Glu Ile Thr Ile Gly Asp Trp Phe Asp Pro
1 5 10

<210> 729

<211> 324

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 729

gccatccaga tgaccacagtc tocatcctcc ctgtctgcct ctgttgaggaga cagagtcacc 60
atcacttgct gggcaactca gggcattaga aatgatlttag gctggtttca acagaaacca 120
gggaaagtcc ctaaaactcct gatctatgct gcatccactt tacacagtgg ggtcccatca 180
aggttcagcg gcagtgcat tggcacagat ttcactctca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag gatttcaatt accctctcac tttcggcgga 300
gggaccaagg tggagatcaa acga 324

<210> 730
 <211> 108
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 730
 Ala Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Asp
 20 25 30
 Leu Gly Trp Phe Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
 35 40 45
 Tyr Ala Ala Ser Thr Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 Ser Gly Phe Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80
 Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asp Phe Asn Tyr Pro Leu
 85 90 95
 Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
 100 105

<210> 731
 <211> 18
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 731
 cagggcatta gaaatgat 18

<210> 732
 <211> 6
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 732
 Gln Gly Ile Arg Asn Asp
 1 5

<210> 733
 <211> 9
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 733
 gctgcatcc 9

<210> 734
 <211> 3
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 734

Ala Ala Ser
1

<210> 735

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 735

ctacaggatt tcaattaccc tctcact 27

<210> 736

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 736

Leu Gln Asp Phe Asn Tyr Pro Leu Thr
1 5

<210> 737

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 737

caggtagcagc tggtaggagtc tgggggaggc gtggtccagc ctgggatgto cctgagactc 60
tcctgtacag cgctccgatt tacgttcagg agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcagtt atttggtatg atggaagtaa taaatattat 180
gcagactccg tgaaggcacg attcaccata accagagaca attccaagaa cacgttgtat 240
ctgcaaatga acagcctgag agccgaggac acggtatat atttttgtgc gagcgaaata 300
acaattgggg actggttcga cccccggggc caggggaacc tggtcacctt ctctca 357

<210> 738

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 738

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

<210> 739

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 739

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atcacttgtc gggcaactca gggcattaga aatgatttag gctgggttca acagaaacca 120
gggaaagtcc ctaaactcct gatctatgct gcatccactt tacacagtgg ggtcccatca 180
aggttcagcg gcagtgcat tggcacagat ttcactctca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag gatttcaatt accctctcac tttcggcgga 300
gggaccaagg tggagatcaa a 321
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<210> 740

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 740

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

<210> 741

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 741

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cagggtgcagc tgggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgcag cgtctggatt tacgttcagg agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcagtt atttggtatg atggaagtaa taaatactat 180
gcagactccg tgaagggcg attcaccatc tccagagaca actccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agccgaggac acggtgtgtg attactgtgc gagcgaata 300
acaattgggg actggttcga cccccgggc cagggaacco tggccaccgt ctctca 357
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<210> 742

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 742

```

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

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<210> 743

<211> 322

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 743

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gccatccaga tgaccagtc tccatctcc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtc gggcattaga aatgatttag gctggatatca gcagaaacca 120
gggaaagccc ctaagctcct gatctatgct gcatccagtt tacaaagtgg ggtcccatca 180
agggtcagcg gcagtgcatc tggcacagat ttcactctca ccatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag gatttcaatt accctctcac ttctggcgga 300
gggaccaagg tggagatcaa ac                                     322

```

<210> 744

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 744

```

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

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65          70          75          80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Asp Phe Asn Tyr Pro Leu
 85          90          95
Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100          105

```

<210> 745

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 745

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caggtcagc tggctgcagc tgggggagc gtggtccagc ctgggaggtc cctgagactc 60
tctgtgttag cctcgggatt caccttcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggtagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggcccg attcaccato tccagagaca attccaagaa caccgtgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300
ttttggagtg gttactttga ctactgggga cagggaaccc tggtcaccgt ctctca 357

```

<210> 746

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 746

```

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

```

<210> 747

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 747

ggattcacct tcagtagata tggc 24

<210> 748

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 748

```

Gly Phe Thr Phe Ser Arg Tyr Gly
 1           5

```

<210> 749

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 749

atatcatatg atggaattaa taaa 24

<210> 750

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 750

```

Ile Ser Tyr Asp Gly Ile Asn Lys
 1           5

```

<210> 751

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 751

gcgaaagggg actttggag tggttactt gactac 36

<210> 752

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 752

Ala Lys Gly Asp Phe Trp Ser Gly Tyr Phe Asp Tyr
1 5 10

<210> 753

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 753

gaaattgtgc tgactcagac tccactctcc tcacctgtca cccttggaca gccggcctcc 60
atctctctga ggctcactca aagcctcgta cacagtgatg gaaacacctt cttgagttgg 120
cttcaccaga gccagcccca gcctccaaga ctctaatatt ataagatttc taaccgggtc 180
cttgggggtc cagacacatt cagtggcagt ggggcagggg cagatttccac actgcaaatc 240
agcagggttg aagctgagga tgcggggatt tattactgca tgcaagctac acaatttccg 300
actttcggcg gagggaccaa ggtggagato aaacga 336

<210> 754

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 754

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

<210> 755

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 755

caaagcctcg tacacagtga tggaaacacc tac 33

<210> 756

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 756

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

<210> 757

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 757

aagatttct 9

<210> 758

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 758

Lys Ile Ser
1

<210> 759

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 759

atgcaagcta cacaatttcc gact 24

<210> 760

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 760

Met Gln Ala Thr Gln Phe Pro Thr
1 5

<210> 761

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 761

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caggtgcagc tgggtggagtc tgggggaggc gtgggtccagc ctggggaggc cctgagactc 60
tcctgtgtag cctctgggatt caccttcagc agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctgggagtg ggtggtagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggggccg attcaccatc tccagagaca attccaagaa caoggtgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300
ttttggagtg gttactttga ctactggggc cagggaaccc tggtcaccgt ctctctca 357

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<210> 762

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 762

```

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

```

<210> 763

<211> 333

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 763

```

gatattgtga tgaccacagac tccactctcc tcacctgtca cccttgagaca gccggcctcc 60
atctcctgca ggtctagctca aagcctcgta cacagtgatg gaaacacctc cttgagttgg 120
cttcacacga ggccagccca gcctccaaga ctctcaattt ataagatttc taaccgggtc 180
tgtgggggtc cagacacatt cagtggcagt ggggcaggga cagatttcac actgcaaato 240
agcagggttg aagctgagga tgtcgggatt tattactgca tgcaagctac acaatttccg 300
actttcggcg gagggaccaaa ggtggagatc aaa 333

```

<210> 764

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 764

```

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

```

```

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

```

<210> 765

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 765

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cagggtgcagc tggltggaglc tgggggaggc ggggtccagc clgggagglc cclgagaclc 60
tcctgtgcag cctotggatt caccotcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggcctggagt ggtggcagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaagggccg attcacoato tccagagaca attccaagaa caccgtgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300
ttttggagtg gttactttga ctactggggc cagggaaccc tggtcaccgt ctctcca 357

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<210> 766

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 766

```

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

```

<210> 767

<211> 334

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 767

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atctcctgca ggtctactca aagcctcgta cacagtgatg gaaacacctc cttgagttgg 120
cttcagcaga ggcacagcca gcctccaaga ctctaatatg ataagatttc taaccgggtc 180
tctgggggtc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggtgg aagctgagga tgtcggggtt tattactgca tgcaagctac acaatttccg 300
actttcggcg gagggaccaa ggtggagatc aaac
334

```

<210> 768

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 768

```

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

```

<210> 769

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 769

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gaggtgcagc tgggtcagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tcctgtgtag cctctggatt caccctcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggcctggagtg gctgatagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggcccg attcaccato tccagagaca attccaagaa caccgtgtat 240
ctgcacaatga acagccctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300
ttttggagtg gatactttga ctactggggc caggaaccc tggtcaccgt ctctca 357

```

<210> 770

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 770

```

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

```

<210> 771

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 771

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ggattcacct tcagtagata tggc      24

```

<210> 772

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 772

Gly Phe Thr Phe Ser Arg Tyr Gly
1 5

<210> 773

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 773

atatcatatg atggaattaa taaa 24

<210> 774

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 774

Ile Ser Tyr Asp Gly Ile Asn Lys
1 5

<210> 775

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 775

gcgaaagggg acttttgag tggatactt gactac 36

<210> 776

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 776

Ala Lys Gly Asp Phe Trp Ser Gly Tyr Phe Asp Tyr
1 5 10

<210> 777

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 777

```

gacatcgtga tgaccacagac tccactctcc tcacctgtca ccttgggaca gccggcctcc 60
atctctctga ggtctagtca aagcctcgtc cacagtgatg gaaacaccta cttgagttgg 120
cttcaccaga ggcacagcca gcctccaaga ctctaatctt ataagatttc taaccgggtc 180
tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgcaaato 240
agcaggggtgg aagctgagga tgtcgggatt tattactgca tgcaaggtag acaatttccg 300
actttcggcg gagggaccaa ggtggagatc aaacga 336

```

<210> 778

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 778

```

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

```

```

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

```

<210> 779

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 779

```

caaagcctcg tacacagtga tggaaacacc tac 33

```

<210> 780

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 780

```

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

```

<210> 781

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 781

```

aagattct 9

```

<210> 782

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 782

Lys Ile Ser
1

<210> 783

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 783

atgcaaggta cacaatttcc gact 24

<210> 784

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 784

Met Gln Gly Thr Gln Phe Pro Thr
1 5

<210> 785

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 785

```

cagggtgcagc tgggtggagtc tggggggaggc gtgggtccagc ctggggaggtc cctgagactc 60
tcctgtgtag cctctggatt caccctcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg gctgatagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgggtgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300
ttttggagtg gatactttga ctactggggc cagggaaccc tggtcaccgt ctctctca 357

```

<210> 786

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 786

```

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

```

Thr Leu Val Thr Val Ser Ser
115

<210> 787

<211> 333

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 787

```

gatatgtga tgaccagac tccactctcc tcacctgtca cccttgga ggcggcctcc 60
atctcctgca ggtctagtca aagcctcgta cacagtgatg gaaacacctt cttgagttgg 120
cttcaccaga ggccaggcca gcctccaaga ctctaatatt ataagatttc taaccgggtc 180
tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgcaaata 240
agcagggtgg aagctgagga tgtcgggatt tattactgca tgcaagggtac acaatttcgg 300
actttcggcg gagggaccaaa ggtggagatc aaa 333

```

<210> 788

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 788

```

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

```

<210> 789

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 789

```

caggtgcagc tgggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tctgtgcagc cctctggatt caccttcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggcccg attcaccato tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300
ttttggagtg gatactttga ctactggggc cagggaaacc tggtcaccgt ctctca 357

```

<210> 790

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 790

```

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

```

<210> 791

<211> 334

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 791

```

gatattgtga tgaccagac tccactctcc tcacctgtca cccttggaac gccggcctcc 60
atctcctgca ggtctagctc aagcctcgta cacagtgatg gaaacaccta cttgagttgg 120
cttcagcaga ggccagccca gctccaaga ctctaatctt ataagatttc taaccggttc 180
tctgggggtcc cagacagatt cagtggcagt ggggcaggga cagatttcac actgaaaatc 240
agcagggtgg aagcagagga tgtcggggtt tattactgca tgcaaggtae acaatttcgc 300
actttcggcg gagggaccaa ggtggagatc aaac
334

```

<210> 792

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 792

```

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

65          70          75          80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85          90          95
Thr Gln Phe Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100          105          110

```

<210> 793

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 793

```

caggtagcagc tgcaggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tctctgtgtag cctcaggatt caccttcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggctggagtg ggtggtagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggccgc attcaccatc tccagagaca attccaagaa caccgtgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300
ttttggagtg gttactttga ctactgggga cagggaaccc tggtcaccgt ctctctca 357

```

<210> 794

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 794

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

<210> 795

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 795

ggattcacct tcagtagata tggc 24

<210> 796

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 796

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

<210> 797

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 797

atatcatatg atggaattaa taaa 24

<210> 798

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 798

```
Ile Ser Tyr Asp Gly Ile Asn Lys
 1           5
```

<210> 799

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 799

gcgaaagggg actttggag tggttactt gactac 36

<210> 800

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 800

Ala Lys Gly Asp Phe Trp Ser Gly Tyr Phe Asp Tyr
1 5 10

<210> 801

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 801

```

gacatccaga tgacccagtc tccatccctc ctgtctgcat ctgtaggaga cagagtcacc 60
atcacttgcc gggcaagtcg gggcattaga aatgatttag gctgggatca gcagaaacca 120
gggaaagccc ctaagccctc gatctatgct gcattccagtt tgc aaagtgg ggtcccatca 180
aggttcagcg gcagggcctc tgggacagaa ttcactotca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataaatagtt accctccgac gttcggccaa 300
gggaccaagg tggagatcaa a 321

```

<210> 802

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 802

```

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

```

<210> 803

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 803

cagggcatta gaaatgat 18

<210> 804

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 804

Gln Gly Ile Arg Asn Asp
1 5

<210> 805

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 805

gctgcatcc 9

<210> 806

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 806

Ala Ala Ser
1

<210> 807

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 807

ctacagcata atagtlaccc tcgacg 27

<210> 808

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 808

Leu Gln His Asn Ser Tyr Pro Pro Thr
1 5

<210> 809

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 809

```

caggtgcagc tgggtggagtc tgggggaggc gtggtccagc ctggggagtc cctgagactc 60
tcctgtgtag cctctggatt cacccttcagt agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggcctggagt ggtggtagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa cacggtgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300
ttttggagtg gttactttga ctactggggc cagggaaacc tggtcaccgt ctctca 357

```

<210> 810

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 810

```

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

```

<210> 811

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 811

```

gacatccaga tgacccagtc tccatccctc ctgtctgcat ctgtaggaga cagagtcacc 60
atcaactigcc gggcaactca gggcattaga aatgatctag gctggtatca gcagaaacca 120
gggaaagccc ctaagccctc gatctatgct gcatccagtt tgcaaaagtgg ggtcccatca 180
aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240
gaagattttg caacttatta ctgtctacag cataatagtt accctccgac gttcggccaa 300
gggaccaagg tggaaatcaa a
321

```

<210> 812

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 812

```

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

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

```

<210> 813
 <211> 357
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 813
 cagggtgcagc tgggtggagtc tggggggaggc gtgggtccagc ctggggaggcc cctgagactc 60
 tcctgtgcag cctctggatt caccttcagt agatatggca tgcactgggt ccgccaggcc 120
 ccaggcaagg ggctggagtg ggtggcagtt atatcatatc atggaattaa taaatactat 180
 gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
 ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300
 ttttggagtg gttacattga ctactggggc cagggaaacc tggtcaccgt ctctca 357

<210> 814
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 814
 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Arg Tyr
 20 25 30
 Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ala Val Ile Ser Tyr Asp Gly Ile Asn Lys Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Lys Gly Asp Phe Trp Ser Gly Tyr Phe Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Leu Val Thr Val Ser Ser
 115

<210> 815
 <211> 322
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 815
 gacatccaga tgaccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60
 atcaactggcc gggcaagtc gggcattaga aatgatattag gctggatatc gcagaaacca 120
 gggaaagccc ctaagcgcc gatctatgct gcattccagtt tgcaaagtgg ggtcccatca 180
 aggttcagcg gcagtggtat tgggacagaa ttcactctca caatcagcag cctgcagcct 240
 gaagattttg caacttatta ctgtctacag cataatagtt accctccgac gttcgcccaa 300
 gggaccaagg tggaaatcaa ac 322

<210> 816
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 816

```

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

```

<210> 817

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 817

```

gaggtgcagc tgggtggagtc tggggggaggc gtgggtccagc ctggggaggtc cctgagactc 60
tctgtgttag cctctgcatt caccttcagtc agatatggca tgcactgggt ccgccaggct 120
ccaggcaagg ggcctggagtg gctgatagtt atatcatatg atggaattaa taaatactat 180
gcagactcgc tgaaggcccg attcaccatc tccagagaca attccaagaa caccgtgtat 240
ctqcaaatga acaqccctga agttgaqqac acqggaqtgt attactgtgc qaaagqqgac 300
ttttggagtg gttactttga ctactggggc cagggaacco tggtcaccgt ctcctca 357

```

<210> 818

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 818

```

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

```

<210> 819

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 819

```

ggattcacct tcagtagata tggc          24

```

<210> 820

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 820

Gly Phe Thr Phe Ser Arg Tyr Gly
1 5

<210> 821

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 821

atatcatatg atggaattaa taaa 24

<210> 822

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 822

Ile Ser Tyr Asp Gly Ile Asn Lys
1 5

<210> 823

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 823

gcgaaagggg actttggag tggttacttt gactac 36

<210> 824

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 824

Ala Lys Gly Asp Phe Trp Ser Gly Tyr Phe Asp Tyr
1 5 10

<210> 825

<211> 327

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 825

gaaattgtgt tgaogcagtc tccaggoacc ctgtctttgt ctccagggga aagagcoacc 60
ctctcccgca gggccagctca gagtgttagc agcagctact tagcctggta ccagcagaaa 120
cctggccagg ctcccaggct cctcatctat ggtgcateca gcagggccac tggcatocca 180
qacaggttca gtggcactgg gtctgggaca gacttcaact tcaccatcaq cagactggag 240
cctgaagatt ttgcagtgtt ttactgtcag cagtatggta gctcaccgtg gacgttgggc 300
caagggacca aggtggaaat caaacga 327

<210> 826

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 826

```

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

```

```

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

```

<210> 827

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 827

cagagtgtta gcagcagcta c 21

<210> 828

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 828

```

Gln Ser Val Ser Ser Tyr
 1             5

```

<210> 829

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 829

ggtgcatcc 9

<210> 830

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 830

```

Gly Ala Ser
 1

```

<210> 831
 <211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 831
 cagcagtatg gtagctcacc gtggacg 27

<210> 832
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 832
 Gln Gln Tyr Gly Ser Ser Pro Trp Thr
 1 5

<210> 833
 <211> 357
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 833
 caggtgcagc tgggtggagtc tgggggaggc gtggtccagc ctggggaggt cctgagactc 60
 tcctgtgtag cctcggcatt caccctcagc agatatggca tgcactgggt ccgccaggct 120
 ccaggcaagg ggcctggagtg gctgatagtt atatcatatg atggaattaa taaatactat 180
 gcagactccg tgaaggcccg attcaccato tccagagaca attccaagaa cacgggtgtat 240
 ctgcaaatga acagcctgag agttgaggac acgggagtggt attactgtgc gaaagggggac 300
 ttttgagatg gttactttga ctactggggc cagggaaacco tggtcaccgt ctctca 357

<210> 834
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 834
 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Ser Arg Tyr
 20 25 30
 Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
 35 40 45
 Ile Val Ile Ser Tyr Asp Gly Ile Asn Lys Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Val Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Gly Val Tyr Tyr Cys
 85 90 95
 Ala Lys Gly Asp Phe Trp Ser Gly Tyr Phe Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Leu Val Thr Val Ser Ser

115

<210> 835
 <211> 324
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic

<400> 835

```

gaaattgtgt tgaagcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
ctctcctgga gggccactca gagggttagc agcagctact tagcctggta ccagcagaaa 120
cttgggccagg ctcccaggct cctcatctat ggtgcateca gcagggccac tggcatocca 180
gacagggtta gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240
cctgaagatt ttgcagtgtg ttactgtcag cagtatggta gctcaccgtg gacgttoggc 300
caagggaacca aggtggaat caaa 324

```

<210> 836

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 836

```

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

```

<210> 837

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 837

```

caggtgcagc tgggtggagt tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60
tctctgtcag cctctggatt caccttcagt agatatggca tgcactgggt ccgccaggct 120
ccaggccaagg ggcctggagt ggtggcagtt atatcatatg atggaattaa taaatactat 180
gcagactccg tgaaggcccg attcaccatc tccagagaca attccaagaa cacgctgtat 240
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaaaggggac 300
ttttggagtg gttactttga ctactggggc cagggaaacc tggtcaccgt ctctctca 357

```

<210> 838

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 838

```

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

```

<210> 839
 <211> 325
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 839
 gaaattgtgt tgaacgagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60
 ctctcctgca gggccactca gagtgttagc agcaqctact tagcctggta ccagcaqaaa 120
 cctggccagg ctcccaggct cctcactat ggtgcatcca gcagggccac tggcatccca 180
 gacaggttca gtggcactgg gtctggggaca gacttcactc tcaccatcag cagactggag 240
 cctgaagatt ttgcagtgtg ttactgtcag cagtatggta gctcacogtg gacgttcggc 300
 caagggacca aggtggaaat caaac 325

<210> 840
 <211> 108
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 840
 Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
 20 25 30
 Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
 35 40 45
 Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
 50 55 60
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
 65 70 75 80
 Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
 85 90 95
 Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 841
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<220>
 <221> VARIANT
 <222> (1)...(1)
 <223> Xaa = Gly

<220>
 <221> VARIANT
 <222> (2)...(2)
 <223> Xaa = Phe

<220>
 <221> VARIANT
 <222> (3)...(3)
 <223> Xaa = Thr

<220>
 <221> VARIANT
 <222> (4)...(4)
 <223> Xaa = Phe

<220>
 <221> VARIANT
 <222> (5)...(5)
 <223> Xaa = Ser or Arg

 <220>
 <221> VARIANT
 <222> (6)...(6)
 <223> Xaa = Ser or Arg

 <220>
 <221> VARIANT
 <222> (7)...(7)
 <223> Xaa = Tyr

 <220>
 <221> VARIANT
 <222> (8)...(8)
 <223> Xaa = Gly, Ala, or Thr

 <400> 841
 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 1 5

 <210> 842
 <211> 8
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Synthetic

 <220>
 <221> VARIANT
 <222> (1)...(1)
 <223> Xaa = Ile

 <220>
 <221> VARIANT
 <222> (2)...(2)
 <223> Xaa = Ser, Gly, or Thr

 <220>
 <221> VARIANT
 <222> (3)...(3)
 <223> Xaa = Tyr, Gly, or Asp

 <220>
 <221> VARIANT
 <222> (4)...(4)
 <223> Xaa = Asp, Gly, or Ser

 <220>
 <221> VARIANT
 <222> (5)...(5)
 <223> Xaa = Gly or Arg

 <220>
 <221> VARIANT
 <222> (6)...(6)
 <223> Xaa = Ile, Gly, or Ala

 <220>

<221> VARIANT
 <222> (7)...(7)
 <223> Xaa = Asn, Ser, Arg, or Gly

<220>
 <221> VARIANT
 <222> (8)...(8)
 <223> Xaa = Lys, Ala, or Thr

<400> 842
 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 1 5

<210> 843
 <211> 12
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<220>
 <221> VARIANT
 <222> (1)...(1)
 <223> Xaa = Ala or Val

<220>
 <221> VARIANT
 <222> (2)...(2)
 <223> Xaa = Lys

<220>
 <221> VARIANT
 <222> (3)...(3)
 <223> Xaa = Gly or Glu

<220>
 <221> VARIANT
 <222> (4)...(4)
 <223> Xaa = Asp or Gly

<220>
 <221> VARIANT
 <222> (5)...(5)
 <223> Xaa = Phe or Asp

<220>
 <221> VARIANT
 <222> (6)...(6)
 <223> Xaa = Trp or Ser

<220>
 <221> VARIANT
 <222> (7)...(7)
 <223> Xaa = Ser or Gly

<220>
 <221> VARIANT
 <222> (8)...(8)
 <223> Xaa = Gly or Tyr

<220>
 <221> VARIANT

<222> (9)...(9)
 <223> Xaa = Tyr or Asp

<220>
 <221> VARIANT
 <222> (10)...(10)
 <223> Xaa = Phe or Leu

<220>
 <221> VARIANT
 <222> (11)...(11)
 <223> Xaa = Asp or Ala

<220>
 <221> VARIANT
 <222> (12)...(12)
 <223> Xaa = Tyr

<400> 843
 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 1 5 10

<210> 844
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<220>
 <221> VARIANT
 <222> (1)...(1)
 <223> Xaa = Gln

<220>
 <221> VARIANT
 <222> (2)...(2)
 <223> Xaa = Ser or Gly

<220>
 <221> VARIANT
 <222> (3)...(3)
 <223> Xaa = Leu or Ile

<220>
 <221> VARIANT
 <222> (4)...(4)
 <223> Xaa = Val or Ser

<220>
 <221> VARIANT
 <222> (5)...(5)
 <223> Xaa = His, Asn, or Thr

<220>
 <221> VARIANT
 <222> (6)...(6)
 <223> Xaa = Ser, Asn, or Tyr

<220>
 <221> VARIANT
 <222> (7)...(7)

<223> Xaa = Asp or absent

<220>

<221> VARIANT

<222> (8)...(8)

<223> Xaa = Gly or absent

<220>

<221> VARIANT

<222> (9)...(9)

<223> Xaa = Asn or absent

<220>

<221> VARIANT

<222> (10)...(10)

<223> Xaa = Thr or absent

<220>

<221> VARIANT

<222> (11)...(11)

<223> Xaa = Tyr or absent

<400> 844

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5 10

<210> 845

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<220>

<221> VARIANT

<222> (1)...(1)

<223> Xaa = Lys or Ala

<220>

<221> VARIANT

<222> (2)...(2)

<223> Xaa = Ile, Ala, or Thr

<220>

<221> VARIANT

<222> (3)...(3)

<223> Xaa = Ser

<400> 845

Xaa Xaa Xaa

1

<210> 846

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<220>

<221> VARIANT
 <222> (1)...(1)
 <223> Xaa = Met or Gln

<220>
 <221> VARIANT
 <222> (2)...(2)
 <223> Xaa = Gln

<220>
 <221> VARIANT
 <222> (3)...(3)
 <223> Xaa = Ala or Tyr

<220>
 <221> VARIANT
 <222> (4)...(4)
 <223> Xaa = Thr or Lys

<220>
 <221> VARIANT
 <222> (5)...(5)
 <223> Xaa = Gln, Ser, or Ile

<220>
 <221> VARIANT
 <222> (6)...(6)
 <223> Xaa = Phe or Ser

<220>
 <221> VARIANT
 <222> (7)...(7)
 <223> Xaa = Pro

<220>
 <221> VARIANT
 <222> (8)...(8)
 <223> Xaa = Thr or Leu

<220>
 <221> VARIANT
 <222> (9)...(9)
 <223> Xaa = Thr or absent

<400> 846
 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
 1 5

<210> 847
 <211> 330
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 847

```

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1      5      10      15
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20     25     30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35     40     45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50     55     60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65     70     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    235    240
Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245    250    255
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260    265    270
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275    280    285
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290    295    300
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305    310    315    320
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325    330

```

<210> 848

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 848

```

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

```

<210> 849

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 849

```

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

```

```

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
 50          55          60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
 65          70          75          80
Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
      85          90          95
Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
      100          105          110
Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
      115          120          125
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
      130          135          140
Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
      145          150          155          160
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
      165          170          175
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
      180          185          190
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
      195          200          205
Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
      210          215          220
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
      225          230          235          240
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
      245          250          255
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
      260          265          270
Thr Thr Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
      275          280          285
Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
      290          295          300
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
      305          310          315          320
Leu Ser Leu Ser Leu Gly Lys
      325

```

<210> 850

<211> 1194

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 850

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atgaggagcc ccagcgcgcc gtgctgctg ggggcccgcc tctgctagc agcctctctc 60
tcctgcagtg gccaccatca aggaaccaat agatcctcta aaggaagaag ccttatttgt 120
aagggtgatg gcacatccca cgtcaactga aaaggagtta cagttgaaac agtcttttct 180
gtggatgagt tttctgcacc tgtcctcact ggaaaactga ccacggtctt ccttccaatt 240
gtctacacaa ttgtgtttgt ggtcggtttg ccaagtaacg qcatggccct gtgggtcttt 300
cttttccgaa ctaagaagaa gcaccctgct gtgatttaca tggccaatct ggccttggtc 360
gacctcctct ctgtcatctg gttccccttg aagattgcct atcacatata tgccaacaa 420
tggatttatg gggaagctct ttgtaatgtg cttattggct tttctatgga caacatgtac 480
tgttccattc tcttcattgc ctgcctcagt gtgcagaggt attgggtcat cgtgaacccc 540
atggggcact ccaggaagaa ggcaaacatt gccattggca tctccctggc aatatggctg 600
ctgattctgc tggtaaccat ccccttgat gtctggaagc agaccatctt cattcctgcc 660
ctgaacatca cgacctgtca tgatgttttg ccggcgagc tcttggtggg agacatgttc 720
aattacttcc tctctctggc cattgggggc tttctgttcc cagccttctt cacagcctct 780
gcctatgtgc tgatgatcag aatgctgcga tcttctgcca tggatgaaaa ctcagagaag 840

```

```

aaaaggaaga gggccatcaa actcaattgt actgtcctgg ccattgacct gatctgcttc 900
actcctagta accttctgct tgtgggcat tattttctga ttaagagcca gggccagagc 960
catgtctatg cctgtacat ttagccctc tgcctctcta cccttaacag ctgcacagac 1020
ccctttgtct attactttgt ttacatgat ttccagggatc atgcaaaaga cgctctcctt 1080
tgccgaagtg tccgactgt aaagcagatg caagtatccc tccctcaaaa gaaacactcc 1140
aggaaatcca gctcttactc ttcaagttca accactgtta agacctccta ttga 1194

```

<210> 851

<211> 397

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 851

```

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

355      360      365
Gln Met Gln Val Ser Leu Thr Ser Lys Lys His Ser Arg Lys Ser Ser
370      375      380
Ser Tyr Ser Ser Ser Ser Thr Thr Val Lys Thr Ser Tyr
385      390      395

```

<210> 852

<211> 18

<212> PRT

<213> Human

<400> 852

```

Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Leu Ile Gly Lys Val Asp
1      5      10      15
Gly Thr

```

<210> 853

<211> 14

<212> PRT

<213> Human

<400> 853

```

Ser Leu Ile Gly Lys Val Asp Gly Thr Ser His Val Thr Gly
1      5      10

```

<210> 854

<211> 6

<212> PRT

<213> Human

<400> 854

```

Ser Leu Ile Gly Lys Val
1      5

```

<210> 855

<211> 276

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 855

```

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

100           105           110
Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr
115           120           125
Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser
130           135           140
Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ala Pro
145           150           155           160
Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln
165           170           175
Val Tyr Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val
180           185           190
Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val
195           200           205
Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu
210           215           220
Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg
225           230           235           240
Val Glu Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val
245           250           255
Val His Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg
260           265           270
Thr Pro Gly Lys
275

```

<210> 856

<211> 20

<212> PRT

<213> Mouse

<400> 856

```

Leu Ala Pro Gly Arg Asn Asn Ser Lys Gly Arg Ser Leu Ile Gly Arg
 1           5           10           15
Leu Glu Thr Gln
 20

```

<210> 857

<211> 18

<212> PRT

<213> Monkey

<400> 857

```

Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Leu Ile Gly Arg Val Asp
 1           5           10           15
Gly Thr

```

<210> 858

<211> 16

<212> PRT

<213> Rat

<400> 858

```

Gly Pro Asn Ser Lys Gly Arg Ser Leu Ile Gly Arg Leu Asp Thr Pro
 1           5           10           15

```

<210> 859

<211> 18

<212> PRT

<213> Rabbit

<400> 859

Gly Thr Asn Lys Thr Ser Lys Gly Arg Ser Leu Ile Gly Arg Asn Thr
1 5 10 15
Gly Ser

<210> 860

<211> 18

<212> PRT

<213> Dog

<400> 860

Gly Thr Asn Arg Thr Ser Lys Gly Arg Ser Leu Ile Gly Lys Thr Asp
1 5 10 15
Ser Ser

<210> 861

<211> 18

<212> PRT

<213> Pig

<400> 861

Gly Thr Ser Arg Pro Ser Lys Gly Arg Ser Leu Ile Gly Lys Ala Asp
1 5 10 15
Asn Thr

<210> 862

<211> 18

<212> PRT

<213> Human

<400> 862

Ala Thr Asn Ala Thr Leu Asp Pro Arg Ser Phe Leu Leu Arg Asn Pro
1 5 10 15
Asn Asp

<210> 863

<211> 18

<212> PRT

<213> Human

<400> 863

Asp Thr Asn Asn Leu Ala Lys Pro Thr Leu Pro Ile Lys Thr Phe Arg
1 5 10 15
Gly Ala

<210> 864

<211> 19

<212> PRT

<213> Human

<400> 864

Glu Ser Gly Ser Thr Gly Gly Gly Asp Asp Ser Thr Pro Ser Ile Leu
1 5 10 15
Pro Ala Pro

<210> 865

<211> 2772

<212> DNA

<213> Mouse

<400> 865

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ggctgctggg aggtatccc cttctggcgg cctcggtctc ctgcagccgg accgagaacc 180
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aaaaaaaa aa

2772

<210> 866

<211> 399

<212> PRT

<213> Mouse

<400> 866

```

Met Arg Ser Leu Ser Leu Ala Trp Leu Leu Gly Gly Ile Thr Leu Leu
1      5      10      15
Ala Ala Ser Val Ser Cys Ser Arg Thr Glu Asn Leu Ala Pro Gly Arg
20     25     30
Asn Asn Ser Lys Gly Arg Ser Leu Ile Gly Arg Leu Glu Thr Gln Pro
35     40     45
Pro Ile Thr Gly Lys Gly Val Pro Val Glu Pro Gly Phe Ser Ile Asp
50     55     60
Glu Phe Ser Ala Ser Ile Leu Thr Gly Lys Leu Thr Thr Val Phe Leu
65     70     75     80
Pro Val Val Tyr Ile Ile Val Phe Val Ile Gly Leu Pro Ser Asn Gly
85     90     95
Met Ala Leu Trp Ile Phe Leu Phe Arg Thr Lys Lys Lys His Pro Ala
100    105    110
Val Ile Tyr Met Ala Asn Leu Ala Leu Ala Asp Leu Leu Ser Val Ile
115    120    125
Trp Phe Pro Leu Ala Ile Ala Tyr His Leu His Gly Asn Asn Trp Val
130    135    140
Tyr Gly Glu Ala Leu Cys Lys Val Leu Ile Gly Phe Phe Tyr Gly Asn
145    150    155    160
Met Tyr Cys Ser Ile Leu Phe Met Thr Cys Leu Ser Val Gln Arg Tyr
165    170    175
Trp Val Ile Val Asn Pro Met Gly His Pro Arg Lys Lys Ala Asn Ile
180    185    190
Ala Val Gly Val Ser Leu Ala Ile Trp Leu Leu Ile Phe Leu Val Thr
195    200    205
Ile Pro Leu Tyr Val Met Lys Gln Thr Ile Tyr Ile Pro Ala Leu Asn
210    215    220
Ile Thr Thr Cys His Asp Val Leu Pro Glu Glu Val Leu Val Gly Asp
225    230    235    240
Met Phe Asn Tyr Phe Leu Ser Leu Ala Ile Gly Val Phe Leu Phe Pro
245    250    255
Ala Ile Leu Thr Ala Ser Ala Tyr Val Leu Met Ile Lys Thr Leu Arg
260    265    270
Ser Ser Ala Met Asp Glu His Ser Glu Lys Lys Arg Gln Arg Ala Ile
275    280    285
Arg Leu Ile Ile Thr Val Leu Ala Met Tyr Phe Ile Cys Phe Ala Pro
290    295    300
Ser Asn Leu Leu Leu Val Val His Tyr Phe Leu Ile Lys Thr Gln Arg
305    310    315    320
Gln Ser His Val Tyr Ala Leu Tyr Leu Val Ala Leu Cys Leu Ser Thr
325    330    335
Leu Asn Ser Cys Ile Asp Pro Phe Val Tyr Tyr Phe Val Ser Lys Asp
340    345    350
Phe Arg Asp His Ala Arg Asn Ala Leu Leu Cys Arg Ser Val Arg Thr
355    360    365
Val Asn Arg Met Gln Ile Ser Leu Ser Ser Asn Lys Phe Ser Arg Lys
370    375    380
Ser Gly Ser Tyr Ser Ser Ser Thr Ser Val Lys Thr Ser Tyr
385    390    395

```

<210> 867

<211> 3011

<212> DNA

<213> Rat

<400> 867

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```

<210> 868

<211> 397

<212> PRT

<213> Rat

<400> 868

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Met Arg Ser Leu Ser Leu Ala Trp Leu Leu Gly Gly Ile Thr Leu Leu
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20     25     30
Ser Lys Gly Arg Ser Leu Ile Gly Arg Leu Asp Thr Pro Pro Pro Ile
35     40     45
Thr Gly Lys Gly Ala Pro Val Glu Pro Gly Phe Ser Val Asp Glu Phe
50     55     60
Ser Ala Ser Val Leu Thr Gly Lys Leu Thr Thr Val Phe Leu Pro Val
65     70     75     80
Ile Tyr Ile Ile Val Phe Val Ile Gly Leu Pro Ser Asn Gly Met Ala
85     90     95
Leu Trp Val Phe Phe Phe Arg Thr Lys Lys Lys His Pro Ala Val Ile
100    105    110
Tyr Met Ala Asn Leu Ala Leu Ala Asp Leu Leu Ser Val Ile Trp Phe
115    120    125
Pro Leu Lys Ile Ser Tyr His Leu His Gly Asn Asp Trp Thr Tyr Gly
130    135    140
Asp Ala Leu Cys Lys Val Leu Ile Gly Phe Phe Tyr Gly Asn Met Tyr
145    150    155    160
Cys Ser Ile Leu Phe Met Thr Cys Leu Ser Val Gln Arg Tyr Trp Val
165    170    175
Ile Val Asn Pro Met Gly His Ser Arg Lys Arg Ala Asn Ile Ala Val
180    185    190
Gly Val Ser Leu Ala Ile Trp Leu Leu Ile Phe Leu Val Thr Ile Pro
195    200    205
Leu Tyr Val Met Arg Gln Thr Ile Tyr Ile Pro Ala Leu Asn Ile Thr
210    215    220
Thr Cys His Asp Val Leu Pro Glu Glu Val Leu Val Gly Asp Met Phe
225    230    235    240
Ser Tyr Phe Leu Ser Leu Ala Ile Gly Val Phe Leu Phe Pro Ala Leu
245    250    255
Leu Thr Ala Ser Ala Tyr Val Leu Met Ile Lys Thr Leu Arg Ser Ser
260    265    270
Ala Met Asp Glu His Ser Glu Lys Lys Arg Arg Arg Ala Ile Arg Leu
275    280    285
Ile Ile Thr Val Leu Ser Met Tyr Phe Ile Cys Phe Ala Pro Ser Asn
290    295    300
Val Leu Leu Val Val His Tyr Phe Leu Ile Lys Ser Gln Arg Gln Ser
305    310    315    320
His Val Tyr Ala Leu Tyr Leu Val Ala Leu Cys Leu Ser Thr Leu Asn
325    330    335
Ser Cys Ile Asp Pro Phe Val Tyr Tyr Phe Val Ser Lys Asp Phe Arg
340    345    350
Asp Gln Ala Arg Asn Ala Leu Leu Cys Arg Ser Val Arg Thr Val Lys
355    360    365
Arg Met Gln Ile Ser Leu Thr Ser Asn Lys Phe Ser Arg Lys Ser Ser
370    375    380
Ser Tyr Ser Ser Ser Ser Thr Ser Val Lys Thr Ser Tyr
385    390    395

```

<210> 869

<211> 22

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 869

```

Gly Pro Asn Ser Lys Gly Arg Ser Leu Ile Gly Arg Leu Asp Thr Pro
1      5      10      15
Gly Gly Gly Gly Ser Lys
20

```

<210> 870

<211> 23

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 870

```

Gly Arg Asn Asn Ser Lys Gly Arg Ser Leu Ile Gly Arg Leu Glu Thr
1      5      10      15
Gln Gly Gly Gly Ser Lys
20

```

<210> 871

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 871

```
Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Leu Ile Gly Lys Val Asp
 1           5           10           15
Gly Thr Gly Gly Gly Gly Ser Lys
                20
```

<210> 872

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 872

```
Gly Thr Asn Arg Ser Ser Lys Ala Arg Ser Leu Ile Gly Lys Val Asp
 1           5           10           15
Gly Thr Gly Gly Gly Gly Ser Lys
                20
```

<210> 873

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 873

```
Gly Thr Asn Arg Ser Ser Lys Gly Ala Ser Leu Ile Gly Lys Val Asp
 1           5           10           15
Gly Thr Gly Gly Gly Gly Ser Lys
                20
```

<210> 874

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 874

```
Gly Thr Asn Arg Ser Ser Lys Gly Arg Ala Leu Ile Gly Lys Val Asp
 1           5           10           15
Gly Thr Gly Gly Gly Gly Ser Lys
                20
```

<210> 875

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 875

```
Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Ala Ile Gly Lys Val Asp
 1           5           10           15
Gly Thr Gly Gly Gly Gly Ser Lys
                20
```

<210> 876

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 876

```
Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Leu Ala Gly Lys Val Asp
 1           5           10          15
Gly Thr Gly Gly Gly Gly Ser Lys
                20
```

<210> 877

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 877

```
Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Leu Ile Ala Lys Val Asp
 1           5           10          15
Gly Thr Gly Gly Gly Gly Ser Lys
                20
```

<210> 878

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 878

```
Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Leu Ile Gly Ala Val Asp
 1           5           10          15
Gly Thr Gly Gly Gly Gly Ser Lys
                20
```

<210> 879

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 879

```
Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Leu Ile Gly Lys Ala Asp
 1           5           10          15
Gly Thr Gly Gly Gly Gly Ser Lys
                20
```

<210> 880

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 880

```
Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Leu Ile Gly Lys Val Ala
 1           5           10          15
Gly Thr Gly Gly Gly Gly Ser Lys
                20
```

<210> 881

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 881

Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Leu Ile Gly Lys Val Asp

1	5	10	15
Ala Thr Gly	Gly Gly Ser Lys		
	20		

<210> 882

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 882

Gly Thr Asn Arg Ser Ser Lys Gly Arg Ser Leu Ile Gly Lys Val Asp

1	5	10	15
Gly Ala Gly	Gly Gly Ser Lys		
	20		

<210> 883

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 883

Gly Arg Asn Asn Ser Lys Gly Arg Ser Leu Ile Gly Arg Leu Glu Thr

1	5	10	15
Gln Pro Pro	Ile		
	20		

<210> 884

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 884

Ser Leu Ile Gly Lys Val Asp Gly Thr Ser His Val Thr Gly Gly Gly

1	5	10	15
Gly Gly Ser	Lys		
	20		

<210> 885

<211> 20

<212> PRT

<213> Artificial Sequence

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<223> Synthetic

<400> 885

Ser Leu Ile Gly Lys Ala Asp Gly Thr Ser His Val Thr Gly Gly Gly

1	5	10	15
Gly Gly Ser	Lys		
	20		

<210> 886

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 886

```

Ser Leu Ile Gly Lys Val Ala Gly Thr Ser His Val Thr Gly Gly Gly
 1           5           10           15
Gly Gly Ser Lys
                20

```

<210> 887

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 887

```

Ser Leu Ile Gly Lys Ala Ala Gly Thr Ser His Val Thr Gly Gly Gly
 1           5           10           15
Gly Gly Ser Lys
                20

```

REFERENCES CITED IN THE DESCRIPTION

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Patentkrav

1. Isoleret humant antistof eller antigen-bindende fragment deraf, der specifikt binder til human PAR-2 (SEQ ID NO: 851) og interagerer med Val-42 og Asp-43
5 af human PAR-2, hvor antistoffet eller det antigen-bindende fragment omfatter komplementaritetsbestemmende regioner (CDR), der omfatter HCDR1-HCDR2-HCDR3 / LCDR1-LCDR2-LCDR3 aminosyresekvenser udvalgt fra gruppen bestående af:
 (a) SEQ ID NO: 100-102-104 / 108-110-112;
10 og (b) SEQ ID NO: 700-702-704 / 708-710-712.
2. Isoleret humant antistof eller antigen-bindende fragment ifølge krav 1, hvor antistoffet eller det antigen-bindende fragment og interagerer med én eller flere rester udvalgt fra gruppen bestående af Ser-37, Leu-38, Ile-39, Gly-40 og Gly-
15 44 af human PAR-2.
3. Isoleret humant antistof eller antigen-bindende fragment ifølge krav 1 eller 2, hvor antistoffet eller det antigen-bindende fragment ikke interagerer med Lys-
20 41 af human PAR-2.
4. Isoleret humant antistof eller antigen-bindende fragment ifølge et hvilket som helst af kravene 1 til 3, hvor antistoffet eller det antigen-bindende fragment interagerer med Ser-37, Leu-38, Ile-39, Gly-40, Val-42 og Asp-43 af human PAR-2, men ikke interagerer med Lys-41 af human PAR-2.
25
5. Isoleret humant antistof eller antigen-bindende fragment ifølge et hvilket som helst af kravene 1 til 4, hvor antistoffet eller det antigen-bindende fragment blokerer trypsin-spaltning af human PAR-2 ved det aktiverende spaltningsted, der befinder sig ved samlingen af resterne Arg-36 og Ser-37 af human PAR-2.
30
6. Isoleret humant antistof eller antigen-bindende fragment ifølge krav 5, hvor antistoffet eller det antigen-bindende fragment ikke blokerer trypsin-spaltning af human PAR-2 ved ét eller flere ikke-aktiverende spaltningsteder udvalgt fra det

ikke-aktiverende spaltningsssted, der befinder sig ved samlingen af resterne Arg-31 og Ser-32 af human PAR-2 og det ikke-aktiverende spaltningsssted, der befinder sig ved samlingen af resterne Lys-34 og Gly-35 af human PAR-2.

- 5 7. Isoleret humant antistof eller antigen-bindende fragment ifølge krav 1, hvor antistoffet eller det antigen-bindende fragment er udvalgt fra gruppen bestående af: (a) et antistof omfattende en variabel tungkædereion (HCVR) med aminosyresekvensen ifølge SEQ ID NO: 714, og en variabel letkædereion (LCVR) med aminosyresekvensen ifølge SEQ ID NO: 692; og (b) et antistof
10 omfattende en HCVR med aminosyresekvensen ifølge SEQ ID NO: 98, og en LCVR med aminosyresekvensen ifølge SEQ ID NO: 106.

8. Farmaceutisk sammensætning omfattende antistoffet eller det antigen-bindende fragment ifølge et hvilket som helst af kravene 1 til 7 og en
15 farmaceutisk acceptabel bærer eller fortynder.

9. Isoleret humant antistof eller antigen-bindende fragment ifølge et hvilket som helst af kravene 1 til 7 eller farmaceutisk sammensætning ifølge krav 8 til anvendelse i en fremgangsmåde til behandling af en patient, hvor patienten
20 udviser ét eller flere symptomer eller tegn på en sygdom eller forstyrrelse forårsaget af PAR-2 aktivitet, hvor sygdommen eller forstyrrelsen forårsaget af PAR-2 aktivitet er en sygdom eller forstyrrelse udvalgt fra gruppen bestående af smerte, pruritus, astma, reumatoid arthritis, fibrose, atopisk dermatitis, inflammatorisk tarmsygdom, ulcerativ colitis, pancreatitis, ulcer, Crohns
25 sygdom, cancer og Nethertons sygdom.

10. Isoleret humant antistof eller antigen-bindende fragment eller sammensætning ifølge krav 9, til anvendelse ifølge krav 9, hvor fremgangsmåde endvidere omfatter administration til patienten af mindst en
30 yderligere terapeutisk aktiv komponent udvalgt fra gruppen bestående af en IL-1-inhibitor, en IL-18-inhibitor, en IL-4-inhibitor, en IL-4-receptorinhibitor, en IL-6-inhibitor, en IL-6-receptorinhibitor, en nervevækstfaktor- (NGF) inhibitor, en

tumornekrosefaktor- (TNF) inhibitor, en TNF-receptorinhibitor, en urinsyresynteseinhibitor og et corticosteroid.

11. Anvendelse af det isolerede antistof eller antigen-bindende fragment ifølge
5 et hvilket som helst af kravene 1 til 7, eller farmaceutisk sammensætning ifølge
krav 8, i fremstillingen af et medikament til anvendelse ved behandling af en
patient, der udviser ét eller flere symptomer eller tegn på en sygdom eller
forstyrrelse forårsaget af PAR-2 aktivitet, hvor sygdommen eller forstyrrelsen
forårsaget af PAR-2 aktivitet er en sygdom eller forstyrrelse udvalgt fra gruppen
10 bestående af smerte, pruritus, astma, rheumatoid arthritis, fibrose, atopisk
dermatitis, inflammatorisk tarmsygdom, ulcerativ colitis, pancreatitis, ulcer,
Crohns sygdom, cancer og Nethertons sygdom.

12. Nukleinsyremolekyle, der koder for et antistof eller antigen-bindende
15 fragment deraf ifølge et hvilket som helst af kravene 1 til 7, en rekombinant
ekspressionsvektor, der bærer nukleinsyren, eller en værtscelle, hvori vektoren
er introduceret.

13. Fremgangsmåde til fremstilling af et antistof eller antigen-bindende
20 fragment deraf ifølge et hvilket som helst af kravene 1 til 7, hvilken
fremgangsmåde omfatter dyrkning af en værtscelle ifølge krav 12 under forhold,
der muliggør fremstilling af antistofferne og indvinding af de producerede
antistoffer.

DRAWINGS

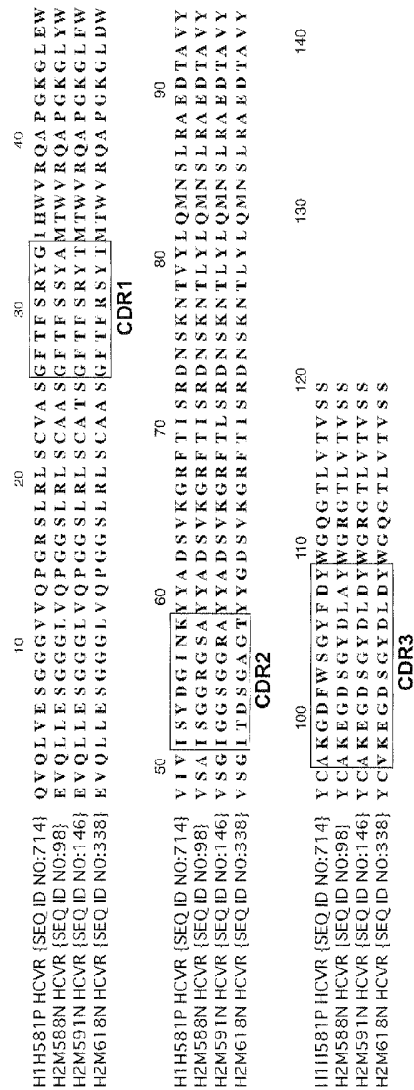


Fig. 1

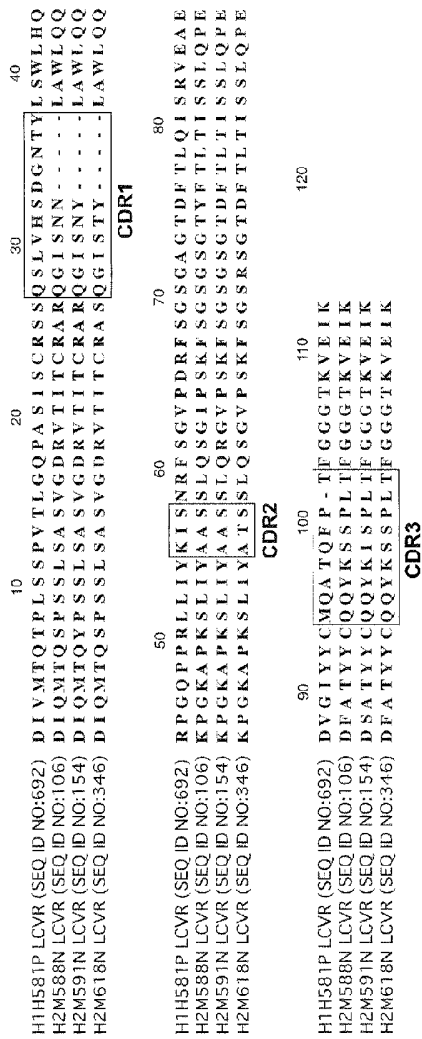


Fig. 2

(A)

		C-terminal Biotin			N-terminal Biotin		
		① ② GTNRSSKGRSLIGKVDGT-B			① ② B-GTNRSSKGRSLIGKVDGT		
No Cleavage		2501 kDa			2373 kDa		
Cleavage @ ①		2073 kDa			988 kDa		
Cleavage @ ②		1558 kDa			N/A		

(B)

Antibody	Time	C-terminal Biotin			N-terminal Biotin		
		2501 kDa	2073 kDa	1558 kDa	2373 kDa	988 kDa	
Neg Ctrl	0	X			X		
Neg Ctrl	5			X			X
Neg Ctrl	15			X			N/D
H4H581P	0	X			X		
H4H581P	5		X				X
H4H581P	15		X				N/D
H4H588N	0	X			X		
H4H588N	5			X			X
H4H588N	15			X			N/D

Fig. 3

(A)		Mouse			Rat			Human		
		①	②	③	①	②	③	①	②	③
		GRNNSKGRSLIGRLLETQPP			GPNSKGRSLIGRLDTP			GTNRSSKGRSLIGKVDTG		
No Cleavage		2556 kDa			2337 kDa			2502 kDa		
Cleavage @ ①		2342 kDa			N/A			2074 kDa		
Cleavage @ ②		1898 kDa			1853 kDa			1772 kDa		
Cleavage @ ③		1686 kDa			1640 kDa			1558 kDa		

(B)													
Antibody	Time	2556 kDa	2342 kDa	1898 kDa	1686 kDa	2337 kDa	1853 kDa	1640 kDa	2502 kDa	2074 kDa	1772 kDa	1558 kDa	
Neg Ctrl	0	X				X			X				
Neg Ctrl	5				X			X				X	
H4H581P	0	X				X			X				
H4H581P	5				X	X		X		X			
H4H588N	0	X				X			X				
H4H588N	5				X			X			X	X	
Comp. Ab	0	X				X			X				
Comp. Ab	5				X			X	X				

Fig. 4

(28)(29)(30)(31)(32)(33)(34)(35)(36)(37)(38)(39)(40)(41)(42)(43)(44)(45) GTNRSSKGRSLIGKVDGT											
Comparator 1:	28	0.1	186	1.5	44	28	2.5	137	152	126	135
Comparator 3:	109	7	21	79	7	8	95	98	120	128	118
H4H581P:	118	106	5	0.2	0.1	24	56	1	20	121	112
H4H588N:	177	140	85	71	22	0.5	84	0.5	4.5	1	64

Fig. 5