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HUMAN ANTIBODIES TO HUMAN DELTA LIKE LIGAND 4

(57) Abstract:

HUMAN ANTIBODIES TO HUMAN DELTA LIKE LIGAND 4

Abstract An isolated human antibody or a fragment of a human antibody which specifically binds to human delta-like ligand 4 (hDII4) and blocks hDII4 binding to a Notch receptor. The human anti hDII4 antibody or antibody fragment binds hDII4 with an affinity of [err] 500 pM, as measured by surface plasmon resonance.

HUMAN ANTIBODIES TO HUMAN DELTA LIKE LIGAND 4

Abstract

An isolated human antibody or a fragment of a human antibody which specifically binds to human delta-like ligand 4 (hDII4) and blocks hDII4 binding to a Notch receptor. The human anti-hDII4 antibody or antibody fragment binds hDII4 with an affinity of ≤ 500 pM, as measured by surface plasmon resonance.

HUMAN ANTIBODIES TO HUMAN DELTA LIKE LIGAND 4

BACKGROUND

[0001] The Notch-signaling pathway is a system for cell-to-cell communication used by a wide range of eukaryotes for many biological processes, such as differentiation, proliferation, and homeostasis. Delta like 4 (Dl4) or delta-like ligand 4 (Dll4) (hereinafter "Dll4") is a member of the Delta family of Notch ligands which exhibits highly selective expression by vascular endothelium (Shutter et al. (2000) *Genes Develop.* 14:1313-1318). Dll4 is a ligand for Notch receptors, including Notch1 and Notch 4. The nucleic acid and amino acid sequences for human Dll4 are shown in SEQ ID NO:1-2, respectively.

[0002] Methods to produce antibodies useful as human therapeutics include generation of chimeric antibodies and humanized antibodies (see, for example, U.S. 6,949,245). See, for example, WO 94/02602 (Abgenix) and U.S. 6,596,541 (Regeneron Pharmaceuticals) describing methods of generating nonhuman transgenic mice capable of producing human antibodies.

[0003] Japanese patent application 2003/047470A2 (Asahi Kasei Kogyo) describes antibodies to the extracellular portion of human Notch ligand protein.

BRIEF SUMMARY OF THE INVENTION

[0004] In a first aspect, the invention provides human antibodies, preferably recombinant human antibodies, that specifically bind human delta-like ligand 4 (hDll4). These antibodies are characterized by binding to hDll4 with high affinity and by the ability to neutralize Dll4 activity. The antibodies of the invention are capable of blocking Dll4 binding to its Notch receptor(s), and thus inhibit signaling by Dll4. The antibodies 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 effect functionality, e.g., to eliminate residual effector functions (Glu which eliminates residual effector functions (Reddy et al. (2000) *J. Immunol.* 164:1925-1933).

[0005] In one embodiment, the antibody of the invention comprises a heavy chain variable region (HCVR) selected from the group consisting of SEQ ID NO:4, 20, 36, 52, 68, 84, 100, 116, 132, 148, 164, 180, 196, 212, 228, 244, 260, 276, 282, 308, 324, 340, 356, 372, 397, 413, 429, 445, 461, 477, 493, 509, 525, 541, 557, 573, 589, 605, 621, 637, 653, 669, 685, 701, 717, 733, 749, 765, 781, 797, 813, 893, 897, 901, 905, 909, 913, 917, 921, 925, 935, 939, 943, and 947 or a substantially identical sequence thereof. In a preferred embodiment, the HCVR is the amino acid sequence of SEQ ID NO:429 or 901.

[0006] In one embodiment, the antibody of the invention comprises a light chain variable region (LCVR) selected from the group consisting of SEQ ID NO:12, 28, 44, 60, 76, 92, 108, 124, 140, 156, 172, 188, 204, 220, 236, 252, 268, 284, 300, 316, 332, 348, 364, 380, 405, 421, 437, 453, 469, 485, 501, 517, 533, 549, 565, 581, 597, 613, 629, 645, 661, 677, 693, 709, 725, 741, 757,

773, 789, 805, 821, 895, 899, 903, 907, 911, 915, 919, 923, 927, 937, 941, 945, and 949 or a substantially identical sequence thereof. In a preferred embodiment, the LCVR is the amino acid sequence of SEQ ID NO:437 or 903.

[0007] In one embodiment, the antibody of the invention comprises a HCVR selected from the group consisting of SEQ ID NO: 4, 20, 36, 52, 68, 84, 100, 116, 132, 148, 164, 180, 196, 212, 228, 244, 260, 276, 292, 308, 324, 340, 356, 372, 397, 413, 429, 445, 461, 477, 493, 509, 525, 541, 557, 573, 589, 605, 621, 637, 653, 669, 685, 701, 717, 733, 749, 765, 781, 797, 813, 893, 897, 901, 905, 909, 913, 917, 921, 925, 935, 939, 943, and 947 or a substantially identical sequence thereof, and a LCVR selected from the group consisting of SEQ ID NO:12, 28, 44, 60, 76, 92, 108, 124, 140, 156, 172, 188, 204, 220, 236, 252, 268, 284, 300, 316, 332, 348, 364, 380, 405, 421, 437, 453, 469, 485, 501, 517, 533, 549, 565, 581, 597, 613, 629, 645, 661, 677, 693, 709, 725, 741, 757, 773, 789, 805, 821, 895, 899, 903, 907, 911, 915, 919, 923, 927, 937, 941, 945, and 949 or a substantially identical sequence thereof. In a preferred embodiment, the HCVR/LCVR are the amino acid sequence pairs SEQ ID NO:429/437 or 901/903.

[0008] In one embodiment, the invention features a human antibody or antibody fragment comprising a heavy chain complementary determining region 1 (CDR1) selected from the group consisting of SEQ ID NO:6, 22, 38, 54, 70, 86, 102, 118, 134, 150, 166, 182, 198, 214, 230, 246, 262, 278, 294, 310, 326, 342, 358, 374, 399, 415, 431, 447, 463, 479, 495, 511, 527, 543, 559, 575, 591, 607, 623, 639, 655, 671, 687, 703, 711119, 735, 751, 767, 783, 799, 815, 831, 847, 863 and 879, or a substantially identical sequence thereof.

[0009] In one embodiment, the invention features a human antibody or antibody fragment comprising a heavy chain CDR2 selected from the group consisting of SEQ ID NO:8, 24, 40, 56, 72, 88, 104, 120, 136, 152, 168, 184, 200, 216, 232, 248, 264, 280, 296, 312, 328, 344, 360, 376, 401, 417, 433, 449, 465, 481, 497, 513, 529, 545, 561, 577, 593, 609, 625, 641, 657, 673, 689, 705, 721, 737, 753, 769, 785, 801, 817, 833, 849, 865 and 881, or a substantially identical sequence thereof.

[0010] In one embodiment, the invention features a human antibody or antibody fragment comprising a heavy chain CDR3 selected from the group consisting of SEQ ID NO:10, 26, 42, 58, 74, 90, 106, 122, 138, 154, 170, 186, 202, 218, 234, 250, 266, 282, 298, 314, 330, 346, 362, 378, 403, 419, 435, 451, 467, 483, 499, 515, 531, 547, 563, 579, 595, 611, 627, 643, 659, 675, 691, 707, 723, 739, 755, 771, 787, 803, 819, 835, 851, 867 and 883, or a substantially identical sequence thereof.

[0011] In one embodiment, the invention features a human antibody or antibody fragment comprising a heavy chain CDR1 selected from the group consisting of SEQ ID NO: 6, 22, 38, 54, 70, 86, 102, 118, 134, 150, 166, 182, 198, 214, 230, 246, 262, 278, 294, 310, 326, 342, 358, 374, 399, 415, 431, 447, 463, 479, 495, 511, 527, 543, 559, 575, 591, 607, 623, 639, 655, 671, 687, 703, 711119, 735, 751, 767, 783, 799, 815, 831, 847, 863 and 879, or a substantially identical sequence thereof; a heavy chain CDR2 selected from the group consisting of SEQ ID

NO: 8, 24, 40, 56, 72, 88, 104, 120, 136, 152, 168, 184, 200, 216, 232, 248, 264, 280, 296, 312, 328, 344, 360, 376, 401, 417, 433, 449, 465, 481, 497, 513, 529, 545, 561, 577, 593, 609, 625, 641, 657, 673, 689, 705, 721, 737, 753, 769, 785, 801, 817, 833, 849, 865 and 881, or a substantially identical sequence thereof; and a heavy chain CDR3 selected from the group consisting of SEQ ID NO: 10, 26, 42, 58, 74, 90, 106, 122, 138, 154, 170, 186, 202, 218, 234, 250, 266, 282, 298, 314, 330, 346, 362, 378, 403, 419, 435, 451, 467, 483, 499, 515, 531, 547, 563, 579, 595, 611, 627, 643, 659, 675, 691, 707, 723, 739, 755, 771, 787, 803, 819, 835, 851, 867 and 883, or a substantially identical sequence thereof. In a preferred embodiment, the antibody or antibody fragment comprises heavy chain CDR1, CDR2 and CDR3 selected from the group consisting of SEQ ID NO: 431/433/435; 374/376/378; 783/785/787; and 799/801/803.

[0012] In one embodiment, the invention features a human antibody or antibody fragment comprising a light chain CDR1 selected from the group consisting of SEQ ID NO: 14, 30, 46, 62, 78, 94, 110, 126, 142, 158, 174, 190, 206, 222, 238, 254, 270, 286, 302, 318, 334, 350, 366, 382, 407, 423, 439, 455, 471, 487, 503, 519, 535, 551, 567, 583, 599, 615, 631, 647, 663, 679, 695, 711, 727, 743, 759, 775, 791, 807, 823, 839, 855, 871 and 887, or a substantially identical sequence thereof.

[0013] In one embodiment, the invention features a human antibody or antibody fragment comprising a light chain CDR2 selected from the group consisting of SEQ ID NO: 16, 32, 48, 64, 80, 96, 112, 128, 144, 160, 176, 192, 208, 224, 240, 256, 272, 288, 304, 320, 336, 352, 368, 384, 409, 425, 441, 457, 473, 489, 505, 521, 537, 553, 569, 585, 601, 617, 633, 649, 665, 681, 697, 713, 729, 745, 761, 777, 793, 809, 825, 841, 857, 873 and 889, or a substantially identical sequence thereof.

[0014] In one embodiment, the invention features a human antibody or antibody fragment comprising a light chain CDR3 selected from the group consisting of SEQ ID NO: 18, 34, 50, 66, 82, 98, 11, 130, 146, 162, 178, 194, 210, 226, 242, 258, 274, 290, 306, 322, 338, 354, 370, 386, 411, 427, 443, 459, 475, 491, 507, 523, 539, 555, 571, 587, 603, 619, 635, 651, 667, 683, 699, 715, 731, 747, 763, 779, 795, 811, 827, 843, 859, 875 and 891, or a substantially identical sequence thereof.

[0015] In one embodiment, the invention features a human antibody or antibody fragment comprising a light chain CDR1 selected from the group consisting of SEQ ID NO: 14, 30, 46, 62, 78, 94, 110, 126, 142, 158, 174, 190, 206, 222, 238, 254, 270, 286, 302, 318, 334, 350, 366, 382, 407, 423, 439, 455, 471, 487, 503, 519, 535, 551, 567, 583, 599, 615, 631, 647, 663, 679, 695, 711, 727, 743, 759, 775, 791, 807, 823, 839, 855, 871 and 887, or a substantially identical sequence thereof; a light chain CDR2 selected from the group consisting of SEQ ID NO: 16, 32, 48, 64, 80, 96, 112, 128, 144, 160, 176, 192, 208, 224, 240, 256, 272, 288, 304, 320, 336, 352, 368, 384, 409, 425, 441, 457, 473, 489, 505, 521, 537, 553, 569, 585, 601, 617, 633, 649, 665, 681, 697, 713, 729, 745, 761, 777, 793, 809, 825, 841, 857, 873 and 889, or a substantially identical sequence thereof; and a light chain CDR3 selected from the group consisting of SEQ

ID NO: 18, 34, 50, 66, 82, 98, 11, 130, 146, 162, 178, 194, 210, 226, 242, 258, 274, 290, 306, 322, 338, 354, 370, 386, 411, 427, 443, 459, 475, 491, 507, 523, 539, 555, 571, 587, 603, 619, 635, 651, 667, 683, 699, 715, 731, 747, 763, 779, 795, 811, 827, 843, 859, 875 and 891, or a substantially identical sequence thereof. In a preferred embodiment, the antibody or antibody fragment comprises the light chain CDR1, CDR2 and CDR3 selected from the group consisting of SEQ ID NO:439/441/443; 382/384/386; 791/793/795; and 807/809/811.

[0016] In a second aspect, the invention provides nucleic acid molecules encoding the antibodies, or antigen-binding portions, of the invention. Recombinant expression vectors carrying the antibody-encoding 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 making the antibodies of the invention by culturing the host cells of the invention.

[0017] In one embodiment, the antibody of the invention comprises a HCVR encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:3, 19, 35, 51, 67, 83, 99, 115, 131, 147, 163, 179, 195, 211, 227, 243, 259, 275, 291, 307, 323, 339, 355, 371, 396, 412, 428, 444, 460, 476, 492, 508, 524, 540, 556, 572, 588, 604, 620, 636, 652, 668, 684, 700, 716, 732, 748, 764, 780, 796, 812, 892, 896, 900, 904, 908, 912, 916, 920, 924, 934, 938, 942, and 946 or a substantially similar sequence having at least 95% homology thereof.

[0018] In one embodiment, the antibody of the invention comprises a LCVR encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:11, 27, 43, 59, 75, 91, 107, 123, 139, 155, 171, 187, 203, 219, 235, 251, 267, 283, 299, 315, 331, 347, 363, 379, 404, 420, 436, 452, 468, 484, 500, 516, 532, 548, 564, 580, 596, 612, 628, 644, 660, 676, 692, 708, 724, 740, 756, 772, 788, 804, 820, 894, 898, 902, 906, 910, 914, 918, 922, 926, 936, 940, 944, and 946 or a substantially similar sequence having at least 95% homology thereof.

[0019] In one embodiment, the antibody of the invention comprises a HCVR encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 3, 19, 35, 51, 67, 83, 99, 115, 131, 147, 163, 179, 195, 211, 227, 243, 259, 275, 291, 307, 323, 339, 355, 371, 396, 412, 428, 444, 460, 476, 492, 508, 524, 540, 556, 572, 588, 604, 620, 636, 652, 668, 684, 700, 716, 732, 748, 764, 780, 796, 812, 892, 896, 900, 904, 908, 912, 916, 920, 924, 934, 938, 942, and 946 or a substantially similar sequence having at least 95% homology thereof, and a LCVR encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 11, 27, 43, 59, 75, 91, 107, 123, 139, 155, 171, 187, 203, 219, 235, 251, 267, 283, 299, 315, 331, 347, 363, 379, 404, 420, 436, 452, 468, 484, 500, 516, 532, 548, 564, 580, 596, 612, 628, 644, 660, 676, 692, 708, 724, 740, 756, 772, 788, 804, 820, 894, 898, 902, 906, 910, 914, 918, 922, 926, 936, 940, 944, and 946 or a substantially similar sequence having at least 95% homology thereof.

[0020] In one embodiment, the invention features a human antibody or antibody fragment comprising a heavy chain CDR1 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:5, 21, 37, 53, 69, 85, 101, 117, 133, 149, 165, 181, 197, 213, 229,

245, 261, 277, 293, 309, 325, 341, 357, 373, 398, 414, 430, 446, 462, 478, 494, 510, 526, 542, 558, 574, 590, 606, 622, 638, 654, 670, 686, 702, 718, 734, 750, 766, 782, 798, 814, 830, 846, 862 and 878, or a substantially similar sequence having at least 95% homology thereof.

[0021] In one embodiment, the invention features a human antibody or antibody fragment comprising a heavy chain CDR2 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:7, 23, 39, 55, 71, 87, 103, 119, 135, 151, 167, 183, 100, 215, 231, 247, 263, 279, 295, 311, 327, 343, 359, 375, 400, 416, 432, 448, 464, 480, 496, 512, 528, 544, 560, 576, 592, 608, 624, 640, 656, 672, 688, 704, 720, 736, 752, 768, 784, 800, 816, 832, 848, 864 and 880, or a substantially similar sequence having at least 95% homology thereof.

[0022] In one embodiment, the invention features a human antibody or antibody fragment comprising a heavy chain CDR3 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:9, 25, 41, 57, 73, 89, 105, 121, 137, 153, 169, 185, 201, 217, 233, 249, 265, 281, 297, 313, 329, 345, 361, 377, 402, 416, 434, 450, 466, 482, 498, 514, 530, 546, 562, 578, 594, 610, 626, 642, 658, 674, 690, 706, 722, 738, 754, 770, 786, 802, 818, 834, 850, 866 and 882, or a substantially similar sequence having at least 95% homology thereof.

[0023] In one embodiment, the invention features a human antibody or antibody fragment comprising a heavy chain CDR1 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:5, 21, 37, 53, 69, 85, 101, 117, 133, 149, 165, 181, 197, 213, 229, 245, 261, 277, 293, 309, 325, 341, 357, 373, 398, 414, 430, 446, 462, 478, 494, 510, 526, 542, 558, 574, 590, 606, 622, 638, 654, 670, 686, 702, 718, 734, 750, 766, 782, 798, 814, 830, 846, 862 and 878, or a substantially similar sequence having at least 95% homology thereof; a heavy chain CDR2 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:7, 23, 39, 55, 71, 87, 103, 119, 135, 151, 167, 183, 100, 215, 231, 247, 263, 279, 295, 311, 327, 343, 359, 375, 400, 416, 432, 448, 464, 480, 498, 512, 528, 544, 560, 576, 592, 608, 624, 640, 656, 672, 688, 704, 720, 736, 752, 768, 784, 800, 816, 832, 848, 864 and 880, or a substantially similar sequence having at least 95% homology thereof; and a heavy chain CDR3 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 9, 25, 41, 57, 73, 89, 105, 121, 137, 153, 169, 185, 201, 217, 233, 249, 265, 281, 297, 313, 329, 345, 361, 377, 402, 416, 434, 450, 466, 482, 498, 514, 530, 546, 562, 578, 594, 610, 626, 642, 658, 674, 690, 706, 722, 738, 754, 770, 786, 802, 818, 834, 850, 866 and 882, or a substantially similar sequence having at least 95% homology thereof. In a preferred embodiment, the antibody or antibody fragment comprises heavy chain CDR1, CDR2 and CDR3 encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:430/432/434; 373/375/377; 782/784/786; and 798/800/802.

[0024] In one embodiment, the invention features a human antibody or antibody fragment comprising a light chain CDR1 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:13, 29, 45, 61, 77, 93, 109, 125, 141, 157, 173, 189, 205, 221, 237, 253, 269, 285, 301, 317, 333, 349, 365, 381, 406, 422, 438, 454, 470, 486, 502, 518, 534, 550,

566, 582, 598, 614, 630, 646, 662, 678, 694, 710, 726, 742, 758, 774, 790, 806, 822, 838, 854, 870 and 886, or a substantially similar sequence having at least 95% homology thereof.

[0025] In one embodiment, the invention features a human antibody or antibody fragment comprising a light chain CDR2 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:15, 31, 47, 63, 79, 95, 111, 127, 143, 159, 175, 191, 207, 223, 239, 255, 271, 287, 303, 319, 335, 351, 367, 383, 408, 424, 440, 456, 472, 488, 504, 520, 536, 552, 568, 584, 600, 616, 632, 648, 664, 680, 696, 712, 728, 744, 760, 776, 792, 808, 824, 840, 856, 872, and 888, or a substantially similar sequence having at least 95% homology thereof.

[0026] In one embodiment, the invention features a human antibody or antibody fragment comprising a light chain CDR3 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:17, 33, 49, 65, 81, 97, 113, 129, 145, 161, 177, 193, 209, 225, 241, 257, 273, 289, 305, 321, 337, 353, 369, 385, 410, 426, 442, 458, 474, 490, 506, 522, 538, 554, 570, 586, 602, 618, 634, 650, 666, 682, 698, 714, 730, 746, 762, 778, 794, 810, 826, 842, 858, 874 and 890, or a substantially similar sequence having at least 95% homology thereof.

[0027] In one embodiment, the invention features a human antibody or antibody fragment comprising a light chain CDR1 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO:13, 29, 45, 61, 77, 93, 109, 125, 141, 157, 173, 189, 205, 221, 237, 253, 269, 285, 301, 317, 333, 349, 365, 381, 406, 422, 438, 454, 470, 486, 502, 518, 534, 550, 566, 582, 598, 614, 630, 646, 662, 678, 694, 710, 726, 742, 758, 774, 790, 806, 822, 838, 854, 870 and 886, or a substantially similar sequence having at least 95% homology thereof; a light chain CDR2 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 15, 31, 47, 63, 79, 95, 111, 127, 143, 159, 175, 191, 207, 223, 239, 255, 271, 287, 303, 319, 335, 351, 367, 383, 408, 424, 440, 456, 472, 488, 504, 520, 536, 552, 568, 584, 600, 616, 632, 648, 664, 680, 696, 712, 728, 744, 760, 776, 792, 808, 824, 840, 856, 872, and 888, or a substantially similar sequence having at least 95% homology thereof; and a light chain CDR3 encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 17, 33, 49, 65, 81, 97, 113, 129, 145, 161, 177, 193, 209, 225, 241, 257, 273, 289, 305, 321, 337, 353, 369, 385, 410, 426, 442, 458, 474, 490, 506, 522, 538, 554, 570, 586, 602, 618, 634, 650, 666, 682, 698, 714, 730, 746, 762, 778, 794, 810, 826, 842, 858, 874 and 890, or a substantially similar sequence having at least 95% homology thereof. In a preferred embodiment, the antibody or antibody fragment comprises the light chain CDR1, CDR2 and CDR3 encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO:438/440/442; 381/383/385; 790/792/794; and 806/808/810.

[0028] In a third aspect, the invention features an isolated antibody or antibody fragment that specifically binds hDII4, comprising a CDR 1, 2 and 3 selected from the group consisting of (a) a heavy chain CDR1 region comprising an amino acid sequence of the formula X¹ – X² – X³ ~ X⁴ – X⁵ – X⁶ – X⁷ – X⁸ (SEQ ID NO:928), wherein X¹ is Gly; X² is Phe or Tyr; X³ is Thr; X⁴ is Phe; X⁵ is Ser, Thr or Asn; X⁶ is Ser, Asn or Tyr; X⁷ is Tyr or Phe; and X⁸ is Gly or Ala; (b) a heavy chain

CDR2 region comprising an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8$ (SEQ ID NO:929), wherein X^1 is Ile or Leu; X^2 is Trp or Ser; X^3 is Tyr, Ala or Gly; X^4 is Asp, Ser or Tyr; X^5 is Gly or Asp; X^6 is Ser, Gly, Thr or Val; X^7 is Asn or Asp; and X^8 is Lys or Arg; (c) a heavy chain CDR3 region comprising an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 - X^9 - X^{10} - X^{11} - X^{12} - X^{13} - X^{14} - X^{15} - X^{16}$ (SEQ ID NO:930), wherein X^1 is Ala or Ser; X^2 is Arg or Lys; X^3 is Asp or Tyr; X^4 is Ser, Gly or His; X^5 is Asp, Ala or Trp; X^6 is Asn, or Phe; X^7 is Tyr, Arg or Lys; X^8 is His or Ser; X^9 is Gly or Trp; X^{10} is Tyr or Phe; X^{11} is Glu or Asp; X^{12} is Gly, His or Pro; X^{13} is Tyr, Trp or absent; X^{14} is Phe or absent; X^{15} is Asp or absent; and X^{16} is Pro or absent.

[0029] In a preferred embodiment, the antibody or antibody fragment comprises heavy chain CDR 1, 2 and 3 selected from the group consisting of (a) a heavy chain CDR1 region comprising an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8$ (SEQ ID NO:928), wherein X^1 is Gly; X^2 is Phe; X^3 is Thr; X^4 is Phe; X^5 is Ser or Asn; X^6 is Ser or Asn; X^7 is Tyr or Phe; and X^8 is Gly or Ala; (b) a heavy chain CDR2 region comprising an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8$ (SEQ ID NO:929), wherein X^1 is Ile or Leu; X^2 is Trp or Ser; X^3 is Tyr or Gly; X^4 is Asp or Ser; X^5 is Gly; X^6 is Ser, Thr or Val; X^7 is Asn or Asp; and X^8 is Lys or Arg; (c) a heavy chain CDR3 region comprising an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7 - X^8 - X^9 - X^{10} - X^{11} - X^{12} - X^{13} - X^{14} - X^{15} - X^{16}$ (SEQ ID NO:930), wherein X^1 is Ala or Ser; X^2 is Arg or Lys; X^3 is Asp; X^4 is Gly or His; X^5 is Asp or Ala; X^6 is Phe; X^7 is Tyr or Arg; X^8 is Ser; X^9 is Gly; X^{10} is Tyr; X^{11} is Glu; X^{12} is Gly or His; X^{13} is Tyr or Trp; X^{14} is Phe or absent; X^{15} is Asp or absent; and X^{16} is Pro or absent.

[0030] In a further embodiment, the isolated antibody or antibody fragment further comprises (d) a light chain CDR1 region comprising an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7$ (SEQ ID NO:931), wherein X^1 is Gln; X^2 is Ser; X^3 is Val; X^4 is Arg, Ser or Thr; X^5 is Ser or Gly; X^6 is Ser or Tyr; and X^7 is Tyr or absent; (e) a light chain CDR2 region comprising an amino acid sequence of the formula $X^1 - X^2 - X^3$ (SEQ ID NO:932), wherein X^1 is Gly or Asp; X^2 is Ala or Thr; and X^3 is Ser; and (f) a light chain CDR3 region comprising 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:933), wherein X^1 is Gln; X^2 is Gln or His; X^3 is Tyr, Arg or Ser; X^4 is Gly, Ser or Ala; X^5 is Ser, Asn or Phe; X^6 is Trp or Ser; X^7 is Pro; X^8 is Trp, Pro or Arg; and X^9 is Thr.

[0031] In a preferred embodiment, the isolated antibody or antibody fragment further comprises (d) a light chain CDR1 region comprising an amino acid sequence of the formula $X^1 - X^2 - X^3 - X^4 - X^5 - X^6 - X^7$ (SEQ ID NO:931), wherein X^1 is Gln; X^2 is Ser; X^3 is Val; X^4 is Arg or Ser; X^5 is Ser; X^6 is Ser or Tyr; and X^7 is Tyr or absent; (e) a light chain CDR2 region comprising an amino acid sequence of the formula $X^1 - X^2 - X^3$ (SEQ ID NO:932), wherein X^1 is Gly or Asp; X^2 is Ala or Thr; and X^3 is Ser; and (f) a light chain CDR3 region comprising 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:933), wherein X^1 is Gln; X^2 is Gln or His; X^3 is Tyr or Arg; X^4 is Gly or Ser; X^5 is Ser or Asn; X^6 is Trp or Ser; X^7

is Pro; X^a is Pro or Arg; and X^b is Thr.

[0032] In a fourth aspect, the invention features a fully human antibody or antibody fragment which binds hDll4 with an IC₅₀ of less than about 10 nM, as measured in *in vitro* assay or ELISA-based Dll4 blocking assay (described below). In a preferred embodiment, the antibody of the invention exhibits an IC₅₀ of about 500 pM or less. In an even more preferred embodiment, the antibody of the invention exhibits an IC₅₀ of about 100 pM or less.

[0033] In one embodiment, the invention provides a fully human monoclonal antibody which specifically binds and inhibits human Dll4 and exhibits an IC₅₀ of less than or equal to about 150 pM, 100 pM, 75 pM, or 50 pM, as measured by Notch-inducible luciferase bioassay with hDll4-Fc. As shown in the experimental section below, the anti-hDll4 antibodies of the invention do not cross-react with closely related delta proteins, such as hDll1 and hDll3.

[0034] In one embodiment, the invention provides an isolated human antibody, or an antigen-binding portion thereof, that binds hDll4 with a K_D of less than about 500 pM, preferably less than about 300 pM, even more preferably less than about 100 pM, less than about 50 pM, less than about 10 pM, as determined by surface plasmon resonance (BIACORE™), for example, using dimeric hDll4 (Table 2).

[0035] The invention encompasses anti-hDll4 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 a galactosylation can be made in order to modify complement dependent cytotoxicity (CDC).

[0036] The invention includes anti-hDll4 antibodies which bind specific epitopes of hDll4 and are capable of blocking the biological activity of hDll4. The extracellular domain of Dll4 is composed of an N-terminal domain, a Delta/Serrate/Lag-2 (DSL) domain, and a tandem of eight epidermal growth factor (EGF)-like repeats. Generally, the EGF domains are recognized as occurring at about amino acid residues 218-251 (domain 1), 252-282 (domain 2), 284-322 (domain 3), 324-360 (domain 4), and 362-400 (domain 5), with the DSL domain at about amino acid residues 173-217 and the N-terminal domain at about amino acid residues 27-172 of hDll4 (SEQ ID NO:2).

[0037] In one embodiment, a blocking antibody of the invention binds within amino acids residues 27 to 524 of SEQ ID NO:2. In a more specific embodiment, a blocking antibody of the invention binds an epitope within the N-terminus-DSL domains 27-217 of SEQ ID NO:2; in an even more specific embodiment, the blocking antibody binds an epitope within about amino acid residues 27-172 (N-terminal domain) or 173-217 (DSL domain). In another embodiment, a blocking antibody of the invention binds the EGF-2 epitope within about amino acids residues 252-282 of SEQ ID NO:2.

[0038] In a fifth aspect, the invention features a composition comprising a recombinant human

anti-human DLL4 antibody and an acceptable carrier. Further included in the invention are vectors and host cells comprising vectors which contain nucleic acid molecules encoding the human anti-hDLL4 antibody of the invention, as well as methods of producing these novel antibodies, comprising growing a host cell comprising nucleic acid encoding the anti-hDLL4 antibody of the invention or an antibody fragment, under conditions permitting production of the protein and recovering the protein so produced.

In a sixth aspect, the Invention features methods for inhibiting hDLL4 activity using an antibody, or antigen-binding portion thereof, of the invention. In one embodiment, the method comprises contacting hDLL4 with the instant antibody or antigen-binding portion thereof, such that hDLL4 is inhibited from binding to Notch receptor, for example Notch-1. In another embodiment, the method comprises administering an antibody or antibody fragment of the invention, to a human subject suffering from a disorder which is ameliorated by inhibition of DLL4 activity. The disorder treated is a disease or condition which is improved, ameliorated, inhibited or prevented by removal, inhibition or reduction of DLL4 activity, for example, pathological vascularization associated with tumor angiogenesis and cancer, immunodeficiency diseases, transplant rejection, or inflammation; and neurodegenerative conditions, e.g., associated with prion disease. The invention also provides for the use of an antibody or antigen-binding fragment of an antibody, as described above, in the manufacture of a medicament for use to attenuate or inhibit a DLL4-mediated disease or disorder in a human.

[0038] Other objects and advantages will become apparent from a review of the ensuing detailed description.

DETAILED DESCRIPTION

[0040] Before the present methods are described, it is to be understood that this invention is not limited to particular methods, and experimental conditions described, as such methods and conditions may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.

[0041] As used in this specification and the appended claims, the singular forms "a", "an", and "the" include plural references unless the context clearly dictates otherwise. Thus for example, a reference to "a method" includes one or more methods, and/or steps of the type described herein and/or which will become apparent to those persons skilled in the art upon reading this disclosure.

[0042] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are now described.

Definitions

[0043] "Delta-like ligand 4", "Dll4", "hDll4" are used interchangeably to refer to the protein encoded by the nucleic acid sequence of SEQ ID NO:1 and the protein having the amino acid sequence of SEQ ID NO:2.

[0044] The term "antibody", as used herein, is intended to refer to immunoglobulin molecules comprised of four polypeptide chains, two heavy (H) chains and two light (L) chains interconnected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as HCVR or VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region (abbreviated herein as LCVR or VL) and a light chain constant region. The light chain constant region is comprised of one domain, CL. The VH and VL regions can be further subdivided into regions of hypervariability, termed complementary determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4.

[0045] The term "high affinity" antibody refers to those antibodies having a binding affinity to hDll4 of at least 10^{-8} M; preferably 10^{-9} M; even more preferably 10^{-10} M, as measured by surface plasmon resonance, e.g., BIACORE™ or solution-affinity ELISA.

[0046] By the term "slow off rate" or "Koff" is meant an antibody that dissociates from hDll4 with a rate constant of 1×10^{-3} s⁻¹ or less, preferably 1×10^{-4} s⁻¹ or less, as determined by surface plasmon resonance, e.g., BIACORE™.

[0047] A "neutralizing" or "blocking" antibody, is intended to refer to an antibody whose binding to Dll4 results in inhibition of the biological activity of Dll4. This inhibition of the biological activity of Dll4 can be assessed by measuring one or more indicators of Dll4 biological activity. These indicators of Dll4 biological activity can be assessed by one or more of several standard *in vitro* or *in vivo* assays known in the art (see examples below). Preferably, the ability of an antibody to neutralize Dll4 activity is assessed by inhibition of Dll4 binding to a Notch receptor.

[0048] The term "antigen-binding portion" of an antibody (or simply "antibody portion" or "antibody fragment"), as used herein, refers to one or more fragments of an antibody that retain the ability to specifically bind to an antigen (e.g., hDll4). It has been shown that the antigen-binding function of an antibody can be performed by fragments of a full-length antibody. Examples of binding fragments encompassed within the term "antigen-binding portion" of an antibody include (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; (ii) a F(ab)₂ fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CH1 domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody; (v) a dAb fragment (Ward et al. (1989) Nature 241:544-546), which consists of a VH domain;

and (vi) an isolated CDR. Furthermore, although the two domains of the Fv fragment, VL and VH, are coded for by separate genes, they can be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single protein chain in which the VL and VH regions pair to form monovalent molecules (known as single chain Fv (scFv); see e.g., Bird et al. (1988) *Science* 242:423-426; and Huston et al. (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883). Such single chain antibodies are also intended to be encompassed within the term "antigen-binding portion" of an antibody. Other forms of single chain antibodies, such as diabodies are also encompassed. Diabodies are bivalent, bispecific antibodies in which VH and VL domains are expressed on a single polypeptide chain, but using a linker that is too short to allow for pairing between the two domains on the same chain, thereby forcing the domains to pair with complementary domains of another chain and creating two antigen binding sites (see e.g., Holliger et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:6444-6448; Poljak et al. (1994) *Structure* 2:1121-1123).

[0049] Still further, an antibody or antigen-binding portion thereof may be part of a larger immunoadhesion molecule, formed by covalent or noncovalent association of the antibody or antibody portion with one or more other proteins or peptides. Examples of such immunoadhesion molecules include use of the streptavidin core region to make a tetrameric scFv molecule (Kipriyanov et al. (1995) *Human Antibodies and Hybridomas* 6:93-101) and use of a cysteine residue, a marker peptide and a C-terminal polyhistidine tag to make bivalent and biotinylated scFv molecules (Kipriyanov et al. (1994) *Mol. Immunol.* 31:1047-1058). Antibody portions, such as Fab and F(ab')₂ fragments, can be prepared from whole antibodies using conventional techniques, such as papain or pepsin digestion, respectively, of whole antibodies. Moreover, antibodies, antibody portions and immunoadhesion molecules can be obtained using standard recombinant DNA techniques, as described herein.

[0050] 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.

[0051] 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*.

[0052] An "isolated antibody", as used herein, is intended to refer to an antibody that is substantially free of other antibodies having different antigenic specificities (e.g., an isolated antibody that specifically binds hDII4 is substantially free of antibodies that specifically bind antigens other than hDII4). An isolated antibody that specifically binds hDII4 may, however, have cross-reactivity to other antigens, such as hDII4 molecules from other species. Moreover, an isolated antibody may be substantially free of other cellular material and/or chemicals.

[0053] The term "surface plasmon resonance", as used herein, refers to an optical phenomenon that allows for the analysis of real-time biospecific interactions by detection of alterations in protein concentrations within a biosensor matrix, for example using the BIACORE™ system (Pharmacia Biosensor AB, Uppsala, Sweden and Piscataway, N.J.).

[0054] The term " K_d ", as used herein, is intended to refer to the dissociation constant of a particular antibody-antigen interaction.

[0055] The term "epitope" includes any determinant, preferably a polypeptide determinant, capable of specific binding to an immunoglobulin or T-cell receptor. In certain embodiments, epitope determinants include chemically active surface groupings of molecules such as amino acids, sugar side chains, phosphoryl groups, or sulfonyl groups, and, in certain embodiments, may have specific three-dimensional structural characteristics, and/or specific charge characteristics. An epitope is a region of an antigen that is bound by an antibody. In certain embodiments, an antibody is said to specifically bind an antigen when it preferentially recognizes its target antigen in a complex mixture of proteins and/or macromolecules. In preferred embodiments, an antibody is said to specifically bind an antigen when the equilibrium dissociation constant is less than or equal to 10^{-8} M, more preferably when the equilibrium dissociation constant is less than or equal to 10^{-9} M, and most preferably when the dissociation constant is less than or equal to 10^{-10} M.

[0056] A protein or polypeptide is "substantially pure," "substantially homogeneous" or "substantially purified" when at least about 60 to 75% of a sample exhibits a single species of polypeptide. The polypeptide or protein may be monomeric or multimeric. A substantially pure polypeptide or protein will typically comprise about 50%, 60, 70%, 80% or 90% W/W of a protein sample, more usually about 95%, and preferably will be over 99% pure. Protein purity or

homogeneity may be indicated by a number of means well known in the art, such as polyacrylamide gel electrophoresis of a protein sample, followed by visualizing a single polypeptide band upon staining the gel with a stain well known in the art. For certain purposes, higher resolution may be provided by using HPLC or other means well known in the art for purification.

[0057] The term "polypeptide analog or variant" as used herein refers to a polypeptide that is comprised of a segment of at least 25 amino acids that has substantial identity to a portion of an amino acid sequence and that has at least one of the following properties: (1) specific binding to hDll4 under suitable binding conditions, or (2) ability to block Dll4 binding to a Notch receptor. Typically, polypeptide analogs or variants comprise a conservative amino acid substitution (or insertion or deletion) with respect to the naturally-occurring sequence. Analogs typically are at least 20 amino acids long, preferably at least 50, 60, 70, 80, 90, 100, 150 or 200 amino acids long or longer, and can often be as long as a full-length naturally-occurring polypeptide.

[0058] Preferred amino acid substitutions are those which: (1) reduce susceptibility to proteolysis, (2) reduce susceptibility to oxidation, (3) alter binding affinity for forming protein complexes, (4) alter binding affinities, and (4) confer or modify other physicochemical or functional properties of such analogs. Analogs can include various mutations of a sequence other than the naturally-occurring peptide sequence. For example, single or multiple amino acid substitutions (preferably conservative amino acid substitutions) may be made in the naturally-occurring sequence (preferably in the portion of the polypeptide outside the domain(s) forming intermolecular contacts. A conservative amino acid substitution should not substantially change the structural characteristics of the parent sequence (e.g., a replacement amino acid should not tend to break a helix that occurs in the parent sequence, or disrupt other types of secondary structure that characterizes the parent sequence). Examples of art-recognized polypeptide secondary and tertiary structures are described in Proteins, Structures and Molecular Principles (Creighton 1984 W. H. Freeman and Company, New York; Introduction to Protein Structure (Bränden & Tooze, eds., 1991, Garland Publishing, NY); and Thornton et al. 1991 Nature 354:105.

[0059] Non-peptide analogs are commonly used in the pharmaceutical industry as drugs with properties analogous to those of the template peptide. These types of non-peptide compound are termed "peptide mimetics" or "peptidomimetics" (see, for example, Fauchere (1986) J. Adv. Drug Res. 15:29; and Evans et al. (1987) J. Med. Chem. 30:1229. Systematic substitution of one or more amino acids of a consensus sequence with a D-amino acid of the same type (e.g., D-lysine in place of L-lysine) may also be used to generate more stable peptides. In addition, constrained peptides comprising a consensus sequence or a substantially identical consensus sequence variation may be generated by methods known in the art (Rizo et al. (1992) Ann. Rev. Biochem. 61:387), for example, by adding internal cysteine residues capable of forming intramolecular disulfide bridges which cyclize the peptide.

[0060] The term "percent sequence identity" in the context of nucleic acid sequences refers to the residues in two sequences which are the same when aligned for maximum correspondence. The length of sequence identity comparison may be over a stretch of at least about nine nucleotides or more, usually at least about 16 nucleotides, more usually at least about 24 nucleotides, typically at least about 26 nucleotides, more typically at least about 32 nucleotides, and preferably at least about 36, 48 or more nucleotides. There are a number of different algorithms known in the art which can be used to measure nucleotide sequence identity. For instance, polynucleotide sequences can be compared using FASTA, Gap or Bestfit, which are programs in Wisconsin Package Version 10.0, Genetics Computer Group (GCG), Madison, Wis. FASTA, which includes, e.g., the programs FASTA2 and FASTA3, provides alignments and percent sequence identity of the regions of the best overlap between the query and search sequences (Pearson (1990) Methods Enzymol. 183:63-98 and (2000) Methods Mol. Biol. 132:185-219). Unless otherwise specified, default parameters for a particular program or algorithm are used. For instance, percent sequence identity between nucleic acid sequences can be determined using FASTA with its default parameters (a word size of 6 and the NOPAM factor for the scoring matrix) or using Gap with its default parameters as provided in GCG Version 6.1.

[0061] A reference to a nucleic acid sequence encompasses its complement unless otherwise specified. Thus, a reference to a nucleic acid molecule having a particular sequence should be understood to encompass its complementary strand, with its complementary sequence. Generally, the art uses the terms "percent sequence identity", "percent sequence similarity" and "percent sequence homology" interchangeably. In this application, these terms shall have the same meaning with respect to nucleic acid sequences.

[0062] The term "substantial similarity", or "substantial sequence similarity," when referring to a nucleic acid or fragment thereof, indicates that, when optimally aligned with appropriate nucleotide insertions or deletions with another nucleic acid (or its complementary strand), there is nucleotide sequence identity in at least about 90%, preferably 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 above.

[0063] As applied to polypeptides, the term "substantial identity" or "substantially identical" means that two peptide sequences, when optimally aligned, such as by the programs GAP or BESTFIT using default gap weights, share at least 80% sequence identity, preferably at least 90% or 95% sequence identity, even more preferably at least 96% 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; and 6) 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: 1443-45. A "moderately conservative" replacement is any change having a nonnegative value in the PAM250 log-likelihood matrix.

[0064] 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 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 mutant 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.

[0065] The length of polypeptide sequences compared for homology will generally be at least about 16 amino acid residues, usually at least about 20 residues, more usually at least about 24 residues, typically at least about 28 residues, and preferably more than about 35 residues. When searching a database containing sequences from a large number of different organisms, it is preferable to compare amino acid sequences.

Preparation of Human Antibodies

[0066] Methods for generating human antibodies include, for example, VELOCIMMUNE® (Regeneron Pharmaceuticals), XENOMOUSE™ technology (Abgenix), the "minilocus" approach, and phage display. The VELOCIMMUNE® technology (U.S. 6,596,541) encompasses a method of generating a high specificity fully human antibody to a select antigen. This technology involves generation of a transgenic mouse having a genome comprising human heavy and light chain variable regions operably linked to endogenous mouse constant region loci such that the mouse produces an antibody comprising a human variable region and a mouse constant region in response to antigenic stimulation. The DNA encoding the variable regions of the heavy and light chains of the antibody are isolated and operably linked to DNA encoding the human heavy and light chain constant regions. The DNA is then expressed in a cell capable of expressing the fully human antibody. In specific embodiment, the cell is a CHO cell.

[0067] The XENOMOUSE™ technology (Green et al. (1994) *Nature Genetics* 7:13-21) generates a mouse having both human variable and constant regions from both the heavy chain and kappa light chain loci. In an alternative approach, others have utilized a 'minilocus' approach in which an exogenous Ig locus is mimicked through inclusion of individual genes from the Ig locus (see, for example, U.S. 5,545,807). The DNA encoding the variable regions can be isolated with or without being operably linked to the DNA encoding the human heavy and light chain constant region.

[0068] Other methods of generating human antibodies, including isolation from a human donor, are known. See, for example, U.S. 6,787,637.

[0069] Antibodies may be therapeutically useful in blocking a ligand-receptor interaction or inhibiting receptor component interaction, rather than by killing cells through fixation of complement and participation in CDC. The constant region of an antibody is important in the ability of an antibody to fix complement and participate in CDC or direct cell killing through antibody-dependent cellular cytotoxicity (ADCC). Thus, the isotype of an antibody may be selected on the basis of the desirability for the antibody to fix complement.

[0070] Human immunoglobulins 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-heavy chain disulfide bonds and a molecule of about 75-80 kDa is formed composed of a single light and heavy chain. These forms have been difficult to separate, even after affinity purification.

[0071] 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. In fact, 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, or modulate effector functions.

[0072] Antibodies of the invention are preferably prepared with the use of VELOCIMMUNE® technology. A transgenic mouse in which the endogenous immunoglobulin heavy and light chain variable regions are replaced with the corresponding human variable regions is challenged with the antigen of interest, and lymphatic cells (such as B-cells) recovered from the mice that express antibodies. The lymphatic cells may be fused with a myeloid-type cell line to prepare immortal hybridoma cell lines, and such hybridoma cell lines are screened and selected to identify hybridoma cell lines that produce antibodies specific to the antigen of interest. DNA encoding the variable regions of the heavy chain and light chain may be isolated and linked to desirable isotypic constant regions of the heavy chain and light chain. Such an antibody protein may be produced in a cell, such as a CHO cell. Alternatively, DNA encoding the antigen-specific chimeric antibodies may be isolated directly from antigen-specific lymphocytes. In various embodiments, the transgenic mouse comprises 12 functional human variable heavy chain genes and 11 functional human variable kappa light chain genes; 25 to 30 human variable heavy chain genes and from 18 to 20 human variable kappa light chain genes; 43 to 48 human variable heavy chain genes and 20 to 22 human variable kappa light chain genes; or about 60 human variable heavy chain genes and about 40 human variable kappa light chain genes.

[0073] In general, the antibodies of the instant invention possess very high affinities, typically possessing K_D of from about 10^9 through about 10^{-11} M, when measured by binding to antigen either immobilized on solid phase or in solution phase. The mouse constant regions are replaced with desired human constant regions to generate the fully human antibodies of the invention, for example wild-type or modified IgG1 or IgG4 (for example, SEQ ID NO:950, 951, or 952). While the constant region selected may vary according to specific use, high affinity antigen-binding and target specificity characteristics reside in the variable region.

[0074] Cancer, infectious diseases, autoimmunity, immunodeficiency, transplants, inflammation, injury and degenerative conditions can be treated by modulation of the immune system. In cases of disease due to inappropriate function or hyperactivity of the immune system, such as autoimmunity or inflammation, can be ameliorated through inhibition of immune cell function or reduction of immune cell numbers. This can be accomplished by blockade of positive signals or stimulation of negative signals on immune cell populations critical to the disease process, such as T, B or NK cells, neutrophils, macrophages, antigen presenting cells, mast cells or other cell types. Overactivity can also be inhibited through elimination of various immune cell populations by stimulation of apoptosis, targeting of specific surface receptors with depleting antibodies or antibody-drug conjugates, or the blockade or alteration of the differentiation of immune cell lineages or specific cell types. Inefficient or reduced immune

function can cause or exacerbate disorders such as cancer, infectious disease, and other immunodeficiencies. Hypoactivity of the immune system can be improved through activation of immune cells by stimulation of positive signals by crosslinking or agonistic antibodies or blockade of negative signals. Immune cell populations can be increased by stimulation of development of some or all immune cell lineages, prevention of apoptosis, or elimination of inhibitory signals. In a specific application, the antibodies of the invention are useful for treatment, inhibition or amelioration of a condition or disease such as, for example, cancer, immunodeficiency, transplant rejection, or inflammation.

Epitope Mapping and Related Technologies

[0075] To screen for antibodies which 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 in Harlow and Lane (1990) *supra* can be performed. Other methods include alanine scanning mutants, peptide blots (Reineke (2004) *Methods Mol Biol* 248:443-63), 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).

[0076] 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.

[0077] 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 (U.S. patent Publication No. 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 hDII4 antibodies of the invention into groups of antibodies binding different epitopes.

[0078] Agents useful for altering the structure of the immobilized antigen are enzymes, such as, for example proteolytic enzymes, for example, trypsin, endoproteinase Glu-C, endoproteinase Asp-N, chymotrypsin, etc. Agents useful for altering the structure of the immobilized antigen may also be chemical agents, such as, succinimidyl esters and their derivatives, primary amine-containing compounds, hydrazines and carbohydrazines, free amino acids, etc.

[0079] The antigen protein may be immobilized on either biosensor chip surfaces or polystyrene beads. The latter can be processed with, for example, an assay such as multiplex LUMINEX™ detection assay (Luminex Corp., Austin, TX). Because of the capacity of LUMINEX™ to handle multiplex analysis with up to 100 different types of beads, LUMINEX™ provides almost unlimited antigen surfaces with various modifications, resulting in improved resolution in antibody epitope profiling over a biosensor assay.

Therapeutic Administration and Formulations

[0080] The administration of therapeutic entities 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 (15th ed, 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. Any of the foregoing mixtures may be appropriate in treatments and therapies in accordance with the present invention, provided that the active ingredient in the formulation is not inactivated by the formulation and the formulation is physiologically compatible and tolerable with the route of administration. See also Powell et al. "Compendium of excipients for parenteral formulations" PDA (1998) J Pharm Sci Technol. 52:238-311 and the citations therein for additional information related to excipients and carriers well known to pharmaceutical chemists.

EXAMPLES

Example 1. Generation of Human Antibodies to Human DI[4].

[0081] Mice may be immunized by any method known in the art (see, for example, Harlow and Lane *supra*). In one embodiment, hDI[4] antigen is administered directly to VELOCIMMUNE® mice comprising DNA loci encoding human Ig heavy chain variable regions and kappa light chain variable regions, with an adjuvant to stimulate the immune response. Such an adjuvant includes complete and incomplete Freund's adjuvant, MPL+TOM adjuvant system (Sigma), or RIBI (muramyl dipeptides) (see O'Hagan 2000 Vaccine Adjuvant, by Human Press, Totowa, NJ). The antibody immune response is monitored by standard antigen specific immunoassay. When a desired immune response is achieved, antibody-expressing B cells were harvested and fused with mouse myeloma cells to preserve their viability, forming hybridoma cell lines. Such hybridoma cell lines are screened and selected to identify cell lines that produce antigen-specific antibodies using assays as described below.

[0082] Alternatively, antigen-specific hybridoma cells may be isolated by flow cytometry.

Briefly, after fusion to myeloma cells, pooled hybridoma cells were grown for 10 days in HAT medium. The cells were then harvested and stained with biotin-labeled Dll4 at 2 mg/ml for one hour, followed by addition of phycoerythrin-streptavidin. The fluorescence-labeled cells were sorted by flow cytometry (single cell per well into 96 well plates containing hybridoma growth medium), cultured for 8-10 days, and conditioned media screened for the presence of functionally desirable monoclonal antibodies, as described below.

[0083] Anti-hDll4 antibodies generated via direct isolation of splenocytes. Antigen-specific antibodies may also be isolated directly from antigen-immunized B cells without fusion to myeloma cells, as described in U.S. Patent Publication 2007/0280945A1. Stable recombinant antibody-expressing CHO cell lines were established from the isolated proper recombinants.

Example 2. Antigen Binding Affinity Determination.

[0084] Equilibrium dissociation constants (K_d values) for antigen binding to the selected antibodies described above were determined by surface kinetics on a real-time biosensor surface plasmon resonance assay (BIACORE™ 2000). The antibody was captured on a goat anti-mouse IgG polyclonal antibody surface created through direct chemical coupling to a BIACORE™ chip to form a captured antibody surface. Varying concentrations of monomeric hDll4 or dimeric hDll4-hFc were injected over the captured antibody surfaces, and antigen-antibody binding and dissociation monitored in real time. Kinetic analysis was performed to calculate K_d , dissociation rate constants, and half-life of antigen/antibody complex dissociation (Table 1). A similar method was applied to measure single B cell-derived monoclonal antibodies modified to contain a human IgG constant domain. Antibodies were presented by goat anti-hFc polyclonal antibody reagent (Jackson Immuno Research Lab) immobilized on BIACORE™ chip, and exposed to either dimeric Dll4-mFc or monomeric Dll4 protein (Table 2).

[0085] Antibody-antigen binding affinity may also be assessed using an ELISA based solution competition assay. Briefly, on a 96-well microtiter plate, antibodies (purified proteins or in conditioned medium) were premixed with serial dilutions of antigen protein (monomeric or dimeric) ranging from 0 to 10 µg/ml with a constant concentration of antibody. After a 2 hr incubation of antigen with antibody, the solutions were transferred to a microtiter plate precoated with antigen for measurement of free antibody (MAXISORB™, VWR, West Chester, PA). The plate was coated with 1 µg/ml hDll4-hFc protein in PBS solution overnight at 4°C and nonspecific binding sites blocked with BSA for 2 hrs. After a 1 hr incubation following transfer, the plate was washed and the plate-bound antibodies were detected with an HRP-conjugated goat anti-mouse IgG polyclonal antibody reagent (Jackson Immuno Laboratory) and developed using colorimetric substrates (OPTEIA™; BD Biosciences Pharmingen, San Diego, CA). The enzymatic reaction was stopped with 1 M phosphoric acid, optical absorptions at 450 nm were recorded and the data were analyzed using a sigmoidal dose-response model and an IC₅₀ values were reported (Table 1).

TABLE 1

Antibody	K_D DII4 (nM)	K_D DII4-Fc (nM)	IC_{50} DII4-Fc (nM)
13B6	2.79	0.188	0.06
15E10	0.55	0.023	0.58
22G12	1.29	0.076	0.03
24C8	0.52	0.047	0.01
VAV 2H4-19	1.51	0.611	0.10
VAV 4H10-9	13.70	0.662	0.30
VAV 7B9-9	0.88	0.021	0.27
VAW 10E4-9	89.00	0.468	0.06
VAW 10G11-2	31.30	1.430	1.66
VAW 1C6-1	45.80	0.092	0.25
VAW 1G2-4	83.80	0.035	0.40
VAW 1H2-2	67.00	0.148	0.30
VAW 2H3-2	0.30	0.150	0.26
VAW 3A7-2	1.64	0.162	0.02
VAW 3A9-5	NA	2.510	16.00
VAW 3F12-8	8.12	0.648	0.07
VAW 6B8-12	0.89	0.060	0.43
VAW 6C6-2	91.70	0.092	0.50
VAW 6G12-10	3.74	0.527	0.19
VAW 7C10-11	17.10	0.853	0.28
VAW 8A10-14	1.41	0.648	0.08
VAW 8G1-12	8.09	8.300	8.60
VAW 9B11-2	62.20	0.048	0.00
VAW 9F12-6	16.00	1.350	0.02
VAW 9G10-1	58.10	0.555	0.10

TABLE 2

Antibody	K_D DII4 (nM)	K_D DII4-Fc (nM)
314266-06F12-B7	2.17	0.075
318518-01A04-D5	0.237	0.244
318518-01A10-D8	0.399	0.016
318518-01B09-C3	0.833	0.180
318518-01B11-D4	0.382	0.088
318518-01E07-H2	0.165	0.238
318518-01G04-F3	0.501	0.107

318518-01G05-B5	1.06	0.196
318518-02A07-B3	0.208	0.148
318518-02B06-E2	2.15	0.193
318518-02B08-F7	N/A	N/A
318518-02C04-D1	0.478	0.331
318518-02F05-D10	1.28	0.035
318518-02G03-F2	1.31	0.042
318518-02G04-B11	0.813	0.048
318518-02G08-F11	N/A	N/A
318518-03A03-B2	0.136	0.124
318518-03C10-F2	1.18	0.131
318518-03D04-B5	0.904	0.136
318518-03D07-G11	3.74	0.163
318518-03F04-A6	0.501	0.088
318518-03F06-A3	0.556	0.037
318518-03H03-F3	6.89	0.084
318518-14A06-E7	4.54	0.282
318518-14A07-C4	0.235	0.035
318518-14D08-G1	0.541	0.046
318518-14H08-A2	6.67	0.128
318518-1H08-E9	0.225	0.050

Example 3. Inhibition of Dll4 and Notch Interaction

[0086] The ability of the antibodies to block Dll4 binding to Notch was evaluated with an ELISA-based immunoassay. Briefly, Notch-hFc recombinant protein was coated on a 96-well plate in PBS buffer overnight at 4°C at 1 mg/ml, and the nonspecific binding sites were blocked with BSA. This plate was used to measure free biotin-Dll4-hFc from antibody titration sample solutions. To make the antibody titration samples, a constant amount of biotin-Dll4-hFc at 25 pM was pre-mixed with varied amounts of antibody, either in crude hybridoma condition medium or as purified antibody protein, ranging from 0 to ~50 nM in serial dilutions, followed by 2 hr incubation at room temperature to allow antibody-antigen binding to reach equilibrium. The equilibrated sample solutions were then transferred to the Notch-hFc coated plates for the measurement of free biotin-Dll4-hFc. After 1 hour binding, the plate was washed and bound biotin-Dll4-hFc was detected using HRP conjugated streptavidin (Poly HRP streptavidin, Pierce Endogen), and developed using TMB substrate (BD Pharmigen). Data was analyzed using GraphPad Prism software and IC₅₀ values were determined as the amount of antibody required to achieve 50% reduction of biotin-Dll4-hFc bound to the plate-coated Notch-Fc (Table 3)

(*conditioned media).

TABLE 3

Antibody	IC ₅₀ (nM)
VAV 2H4-19	0.01
VAW 3A7-2	0.017
VAW 9G10-1	0.019
VAW 10E4-9	0.032
VAW 8A10-11	0.04
VAW 9F12-6	0.059
VAW 3F12-B	0.066
VAW 1C6-1	0.086
VAW 1G2-4	0.11
VAW 6C6-2	0.119
VAW 7B9-4	0.123
VAW 1H2-2	0.154
VAW 2H3-2	0.168
VAW 6B8-12	0.255
VAW 6G12-10	0.257
VAW 7C10-11	0.273
VAW 4H10-9	0.599
VAW 10G11-2	0.931
VAW 3A9-5	3.8
VAW 8G1-12	10.7
VAW 9B11-2	0.069
15E10*	0.04
22G12	0.10
13B6	0.11
24C8	0.031
314266-06F12-B7	0.07
318518-01A04-D5	0.11
318518-01A10-D8	0.05
318518-01B09-C3	0.03
318518-01B11-D4	0.03
318518-01E07-H2	1.17
318518-01G04-F3	0.02
318518-01G05-B5	1.08
318518-02A07-B3	0.03

318518-02B06-E2	0.09
318518-02B08-F7	N/A
318518-02C04-D1	0.60
318518-02F05-D10	0.16
318518-02G03-F2	0.07
318518-02G04-B11	1.09
318518-02G08-F11	N/A
318518-03A03-B2	0.57
318518-03C10-F2	0.12
318518-03D04-B5	0.04
318518-03D07-G11	0.45
318518-03F04-A6	0.01
318518-03F06-A3	0.02
318518-03H03-F3	0.17
318518-14A06-E7	0.04
318518-14A07-C4	0.02
318518-14D08-G1	0.14
318518-14H08-A2	0.25
318518-1H08-E9	0.03

[0087] The ability of selected purified anti-Dll4 antibodies to block Dll4 binding to Notch was also evaluated with the ELISA-based immunoassay described above, modified by replacing 25 pM of biotin-Dll4-hFc with 30 pM of biotin-Dll4-hFc, and reducing antibody-antigen incubation duration from 2 hrs to 1 hr. For convenience, antibody 318518-01A10-D8 was renamed "REGN281" (HCVR/LCVR SEQ ID NOs:429/437 and hIgG1 SEQ ID NO:950). Derived antibodies tested included REGN421 (HCVR/LCVR SEQ ID NO:901/903, hIgG1 SEQ ID NO:950); and REGN422 (HCVR/LCVR SEQ ID NO:901/903, with modified hIgG4 SEQ ID NO:952). Results are shown in Table 4.

TABLE 4

Antibody	IC ₅₀ (nM)
REGN281	0.042
REGN421	0.045
REGN422	0.039

[0088] Ability of antibody to neutralize Dll4 mediated cellular function was also tested *in vitro* using Dll4 expressing human umbilical vein endothelial cells (HUVEC). Inhibition of Notch mediated hHes1 and EphB2 gene expression in HUVEC with the derived antibodies was

monitored as follows: low passage HUVEC were cultured in MCDB-131 media (Vec Technologies). One day prior to analysis, HUVEC cells were seeded at a density of 2×10^5 cells/well in 24-well plates in 1 ml total media volume. The test antibody or other inhibitor was added directly to the individual sample wells in triplicate followed by 5-hour culture at 37°C. At the end of the culture period, media was removed and total RNA was isolated using QIAZOL™ and the RNEASY™ lipid tissue kit (Qiagen). mRNA level quantification was performed by the use of PCR and the fluorogenic 5' nuclease assay (TAQMAM® assay, Applied Biosystems). For each sample, cDNA was synthesized from 1-2 mg of total RNA. cDNA generated from an equivalent amount of starting RNA (typically 25 ng) was loaded in triplicate on ABI PRISM™ optical reaction plates. For each RNA sample a "no RT" control was also run in which no reverse transcriptase was added to allow for subtraction of any potential genomic DNA contributions to the signal. 2x Mastermix (TAQMAM® 2x PCR Mastermix; ABI) was added to each reaction to a final concentration of 1x. Additionally, TAQMAM® probe and primers for the gene of interest were added to each reaction. Each primer was used at a final concentration of 900 nM and the probe was added at a final concentration of 200 nM. Human genomic DNA was used as a standard. The assays were performed under standard TAQMAM® conditions on a ABI 7900HT instrument. Levels of Hes1 and EphrinB2 were measured and normalized to an endogenous control gene (cyclophilin) (Table 5). Probes and primers: human Hes1 probe (SEQ ID NO:387); Oligos: hHes1-869F (SEQ ID NO:388); hHes1-940R (SEQ ID NO:389), human ephrinB2 probe: hEphB2-773T (SEQ ID NO:390); Oligos: hEphB2-752F (SEQ ID NO:391) hEphB2-B12R (SEQ ID NO:392); human cyclophilin: probe: hCyclophilin-343T (SEQ ID NO:393); Oligos: hCyclophilin-323F (SEQ ID NO:394); hCyclophilin-389R (SEQ ID NO:395).

TABLE 5

Antibody	EphrinB2 Expression IC ₅₀ (nM)	Hes1 Expression IC ₅₀ (nM)
22G12	0.379	0.381
15E10	2.56	4.49
VAW 3A7-2	0.409	0.533
314266-06F12-B7	0.239	0.405
318518-01A10-D8	0.305	0.329
318518-01G04-F3	0.088	0.172
318518-01H08-E9	0.413	0.548
318518-02A07-B3	0.398	0.128
318518-03F04-A6	0.158	0.115
318518-03F06-A3	0.304	0.692
318518-014A07-C4	0.175	0.312
318518-014D08-G1	0.510	0.568
hDII4-hFc	0.843	0.974

[0089] HUVEC Proliferation Assay. The ability of antibody to block Dll4 mediated growth inhibition of Human umbilical vein endothelial cells (HUVEC) cells was tested in an *in vitro* cell proliferation assay. Low passage HUVEC cells were obtained and cultured in MCDB-131 media (Vec Technologies). One day prior to analysis 12-well tissue culture plates were coated with hDll4-hFc in PBS at 4°C overnight (0.2 µg/ml; 0.5 ml PBS/well). Plates were washed 1x with PBS and HUVEC cells were seeded at a density of 4x10³ cells/well in 1.0 ml total media volume. Immediately following addition of cells anti-hDll4 antibodies were added in 0.5 ml total volume over a range of concentrations to generate an inhibition curve. Cells were grown for 96-hours at 37°C. Cell number was quantitated using the CCK-8 reagent (Dojindo). All assays were run in triplicate. (Table 6, NB, not blocking).

TABLE 6

Antibody	IC ₅₀ (nM)
15E10	0.284
VAW9B11-2	1.868
VAW8D8-12	NB
13B6	5.01
VAW2H4-19	NB
VAW3A7-2	0.198
VAWBA10-14	0.214
22G12	0.888
318518-06F12-B7	2.067
318518-01A10-D8	0.096
318518-01G04-F3	0.106
318518-01H08-E9	0.188
318518-02A07-B3	0.200
318518-03F04-A8	0.184
318518-03F06-A3	0.188
318518-014A07-C4	0.159
318518-014D08-G1	0.165

[0090] Notch-Inducible Luciferase Assay. A bioassay was developed to determine the ability of selected purified antibodies to neutralize Dll4-mediated cellular function *in vitro* using an engineered HEK293 cell line (ATCC) that constitutively expresses human Notch 1 and contains a Notch-responsive promoter driving luciferase. Inhibition of Notch-inducible luciferase activity was determined as follows: 1 day prior to assay, each well of an opaque 96 well tissue culture plate was coated with 100 µl of either 1 nM or 1.5 nM hDll4-hFc in PBS overnight at 4°C. Cells were seeded onto the coated plates at 2 x10⁴ cells/well in media. Purified antibody protein, in

serial dilutions starting from 2 nM in cell media, was incubated with the cells at 37°C for 24 hrs. Luciferase activity was determined by adding an equal well volume of STEADY-GLO® Substrate (Promega) (Table 7).

TABLE 7

Antibody	IC ₅₀ (pM)	
	1 nM hDll4-hFc	1.5 nM hDll4-hFc
REGN281	50.5	78.7
REGN421	54.4	87.3
REGN422	88.2	131.1

Example 4. Inhibition of Notch1 Cleavage

[0091] The ability of selected anti-hDll4 antibodies to inhibit Notch1 cleavage was tested by examination of total cleaved Notch1 protein by SDS-PAGE/Western blotting. Low passage HUVEC cells were cultured as described above. One day prior to analysis 6-well plates were coated with hDll4-hFc in PBS at 4°C overnight (0.2 µg/ml; 1.0 ml PBS/well). Plates were washed 1x with PBS and HUVEC cells were seeded at 7.5 x 10⁵ cells/well in 2.0 ml total media volume. Immediately following cell seeding, anti-hDll4 antibody was added to each well at 10nM final concentration. Cells were grown for 24 hours at 37°C following which whole cell extracts were prepared and analyzed by SDS-PAGE. Levels of cleaved Notch1 were determined using an anti-cleaved Notch1 (Val1744) antibody (Cell Signaling) and standard western blotting techniques. The anti-hDll4 antibodies were able to entirely block the Notch1 cleavage induced by plate coated hDll4-hFc (data not shown).

Example 5. ADCC and CDC Assays

[0092] Antibody-dependent cell-mediated cytotoxicity (ADCC) induced by two test antibodies (REGN421, REGN422) was assessed using a panel of eight target cell lines with varying hDll4 expression levels. The eight target cell lines were (1) HUVECs; (2) HUVECs stimulated with 10 nM VEGF for 24 hours; (3) Colo205; (4) engineered C6 rat glioma cells expressing eGFP; (5) engineered C6 rat glioma cells expressing hDll4; (6) engineered HT1080 cells expressing eGFP; (7) engineered HT1080 cells expressing hDll4; and (8) HT29. Human DLL4 or eGFP was integrated into the C6 cell or HT1080 genome through retroviral transfection. Briefly, cells from each target cell line (10,000 cells/well in 50 µl) were first mixed with an equal volume of serially diluted REGN421 or REGN422, resulting in a final antibody concentration ranging from 0.169 pM to 10 nM, and incubated for 10 min at room temperature in a 96-well plate format (control = wells without antibody). Separately, human peripheral blood mononuclear cells (PBMCs, effector cells) were prepared following a conventional Ficoll-Hypaque gradient centrifugation enrichment procedure. Approximately 300,000 PBMCs were added to each mixture of antibody and target cells to give a final ratio of effector to target cells of approximately 30:1. The 96-well

plates were then incubated for 4 h at 37°C, 5% CO₂ followed by centrifugation at 250 x g. Supernatants were harvested and assayed for lactate dehydrogenase (LDH) activity using the CYTOTOX 96® Non-Radioactive Cytotoxicity Assay system (Promega). Results are shown in Table 8. REGN421-induced dose dependent cell lysis was only observed in C6 cells expressing hDII4 (col. 5), which exhibited the highest hDII4 expression among all cell lines (as determined by immunoprecipitation/Western blot and flow cytometry). The maximum cell cytotoxicity in the C6-hDII4 cell line ranged from 20% to 60%. No REGN421-induced cell lysis was observed in the remaining seven target cell lines. REGN422 did not induce cell lysis in any of the target cell lines.

TABLE 8

Ab	% Maximum Cytotoxicity							
	1	2	3	4	5	6	7	8
REGN421	0	0	0	0	20-60	0	0	0
REGN422	0	0	0	0	0	0	0	0

[0093] Complement-dependent cytotoxicity (CDC) induced by REGN421 was assessed using the same panel of cells lines described above. Briefly, cells from each of the target cell lines (50,000 cells/well in 50 µl) were first mixed with an equal volume of serially diluted REGN421, resulting in a final antibody concentration ranging from 0.169 pM to 10 nM, and incubated for 10 min at room temperature in a 96-well plate format. Normal human serum, with complement components (Quidel Corp., San Diego, CA) was added to each well to give a final serum concentration of 5%. The plates were then incubated at 37°C, 5% CO₂ for 2 hours followed by addition of CELLTITER-BLUE® reagent (Promega) (controls = wells without antibody and wells with antibody but no serum). The plates were incubated overnight and cell survival (CDC levels) assayed. As a positive control, Daudi cells were treated with rituximab. REGN421 exhibited no CDC toward any of the target cell lines tested (data not shown).

Example 6. Epitope Mapping and Specificity

[0094] In order to determine epitope binding specificity, a series of seven chimeric DII4 proteins were generated in which specific human DII4 domains were substituted into a mouse DII4 protein as follows: #1 contained the human N-terminal and DSL domains (S27-Q218); #2 contained human N-terminal, DSL and EGF-1 domains (S27-N252); #3 contained human N-terminal, DSL, EGF-1 and EGF-2 domains (S27-Q289); #4 contained human N-terminal, DSL, EGF-1, EGF-2, EGF-3, EGF-4 and EGF-5; #5 contained human N-terminal domain (S27-R172); #6 contained human DSL domain (V173-Q218); and #7 contained human EGF-2 domain (E252-D262). The chimeric proteins were fused to a mouse IgG2a-Fc fragment and expressed in CHO-K1 cell. The conditioned media were harvested and protein expression confirmed by western blot.

[0095] Binding specificity of test antibodies to hDll4, mDll4, and chimeric proteins #1, #2, #3, and #4 were tested as follows: purified antibodies 22G12, VAW3A7-2, and 15E10 were amine coupled between 5000- 6000 RU on CM5 chip. Conditioned media from CHO K1 cells containing the chimeric Dll4 proteins, hDll4-mFc, and mDll4-mFc were injected sequentially followed by surface regeneration over antibody-coupled surfaces. A blank amine coupled flowcell surface was used as a control for nonspecific binding of the conditioned media. Results are summarized in Table 9. 22G12 bound an epitope between S27-Q218 of hDll4; VAW3A7-2 bound an epitope between Q283-E400 hDll4; and 15E10 bound an epitope between E252-D282 of hDll4.

TABLE 9

Antibody	hDll4-mFc	mDll4-mFc	Chimeric Proteins			
			#1	#2	#3	#4
22G12	+	-	+	+	+	+
VAW3A7-2	+	-	-	-	-	+
15E10	+	-	-	-	+	+

[0096] Binding specificity of purified test mAb to hDll4, mDll4 and the chimeric proteins (described above) was determined (REGN279 = 314266-6F12-B7; REGN287= 318518-1G04-F3; REGN289= 318518-1H08-E9; REGN290=318518-2A07-B3; REGN306= 318518-3F06-A3). Briefly, each Dll4 protein was captured (70-130 RU) on goat anti-mouse IgG antibody surfaces, followed by injection of test mAb at a concentration of 100 µg/ml. An antibody that bound mDll4-mFc was used as a positive control (positive control= 6C10). The results (Table 10) show that REGN279 bound an epitope between S27-Q218 of hDll4; REGN287 bound between Q283-E400 of hDll4; REGN289, REGN290 and REGN306 bound between S27-E400 of hDll4.

TABLE 10

Antibody	hDll4-mFc	mDll4-mFc	Chimeric human-mouse Dll4 Fusion Proteins						
			#1	#2	#3	#4	#5	#6	#7
REGN279	+	-	+	+	+	+	+	-	-
REGN287	+	-	-	-	-	+	-	-	-
REGN289	+	-	+	+	+	+	-	+	-
REGN290	+	-	+	+	+	+	-	+	-
REGN306	+	-	+	+	+	+	-	+	-
Control	+	+	+	+	+	+	+	+	+

[0097] Further epitope binding specificity determinations were conducted as described above with the following purified test antibodies: REGN281=318518-1A10-D8; REGN305=318518-3F04-A6; REGN309=318518-14A07-C4; REGN310=318518-14D08-G1; REGN421, and REGN422. Briefly, each of the Dll4 proteins was captured (240-470 RU) on goat anti-mouse

IgG antibody surfaces, followed by injection of test antibody at a concentration of 100 µg/ml (Table 11).

TABLE 11

Antibody	hDII4-mFc	mDII4-mFc	Chimeric human-mouse DII4 Fusion Proteins						
			#1	#2	#3	#4	#5	#6	#7
REGN281	+	-	+	+	+	+	+	+	-
REGN305	+	-	-	-	-	+	-	-	-
REGN309	+	-	+	+	+	-	+	+	-
REGN310	+	-	-	-	+	+	-	+	+
REGN421	+	-	+	+	+	+	+	+	-
REGN422	+	-	+	+	+	+	+	+	-

[0100] Western blot analysis. Binding specificity of selected antibodies to chimeric, mouse and human DII4 was determined by Western blot. Briefly, hDII4-mFc (200 ng per lane), mDII4-mFc (200 ng per lane), and chimeric proteins #1 - #7 (approximate 150 ng per lane) were subjected to electrophoresis on duplicate SDS-PAGE gels using non-reducing sample buffer. Each gel was then transferred to a PVDF membrane. Blots were first exposed to REGN421 at 0.2 µg/ml and then to HRP-conjugated anti-hIgG antibody (Pierce). Control blots were exposed to HRP-conjugated anti-mFc antibody (Pierce). Results: REGN421 recognized hDII4-mFc and chimeric proteins containing the human N-terminal domain (#5), a human DSL domain (#6), or both (#1, #2, #3, and #4). REGN421 did not recognize a chimeric protein containing a human EGF-2 domain (#7).

[0101] Protease digestion analysis. Binding between REGN281 and hDII4 was further assessed by protective protease digestion and liquid chromatography/mass spectrometry (LC/MS) using an HPLC1100 (Agilent) and LCQ Classical Ion Trap Mass Spectrometer (Thermo). Briefly, a mixture of hDII4 and REGN281, in a molar ratio of 1:5, or hDII4 alone, was incubated with protease overnight at either 25°C (for GluC protease) or 37°C (for trypsin). Each of the resulting proteolytic digest mixtures was then subjected to LC/MS. Unique peptide peaks present in proteolytic digests performed in the absence of REGN281, which either diminished or disappeared in proteolytic digests performed in the presence of REGN281, indicate potential REGN281 binding sites on hDII4 that were protected from protease digestion by the binding of REGN281 to hDII4. These unique peptide peaks were analyzed by mass spectrometry. The observed mass, predicted mass, and the N-terminal sequences of the peptides are shown in Table 12.

TABLE 12

Peak	Observed Mass	Predicted Mass	hDII4 Peptide (SEQ ID NO:2)	Protease	Domain
G1	521	521.5	Phe37-Glu40	GluC	N-terminal

G2	1362.8	1363.4	Ala121-Glu132	GluC	N-terminal
T1	758	760.8	Pro49-Arg55	Trypsin	N-terminal
T2	587.1	587.2	Tyr169-Arg172	Trypsin	N-terminal
T3	1607.4	1607.6	Val173-Arg186	Trypsin	DSL
T4	1399	1400.7	Gly42-Arg55	Trypsin	N-terminal
T5	569.2	569.3	Thr56-Arg59	Trypsin	N-terminal
T7	2615	2613.4	Ile143-Arg166	Trypsin	N-terminal
T8	1807.2	1806.9	Ser27-Arg41	Trypsin	N-terminal

Example 7. Binding Affinity of Purified Antibodies to Human and Monkey Dll4.

[0102] The binding affinities of selected purified antibodies to hDll4, *M. fascicularis* Dll4 (mfDll4, SEQ ID NO:956), and *M. mulatta* Dll4 (mmDll4, SEQ ID NO:957) monomers were determined using a BIACORE™ 2000 & 3000. Goat anti-hFc polyclonal antibody reagent immobilized on a BIACORE™ chip was used to present REGN281, REGN421, and REGN422. Varying concentrations of each proteins, hDll4 (from 12.5 nM to 100 nM), mfDll4 (from 3.13 nM to 100 nM), or mmDll4 (from 12.5 nM to 100 nM) were used as analyte, and injected over the antibody surfaces. Antigen-antibody binding and dissociation of bound complex were monitored in real time (Table 13).

TABLE 13

	ka (M-1s-1)			kd (s-1)			K _d (nM)		
	hDll4	mfDll4	mmDll4	hDll4	mfDll4	mmDll4	hDll4	mfDll4	mmDll4
REGN281	1.56 x 10 ⁵	6.64 x 10 ⁴	9.27 x 10 ⁴	2.30 x 10 ⁻⁵	2.04 x 10 ⁻⁵	3.05 x 10 ⁻⁵	0.148	0.307	0.329
REGN421	1.63 x 10 ⁵	7.28 x 10 ⁴	9.70 x 10 ⁴	2.17 x 10 ⁻⁵	2.02 x 10 ⁻⁵	3.23 x 10 ⁻⁵	0.133	0.278	0.333
REGN422	1.64 x 10 ⁵	8.01 x 10 ⁴	9.27 x 10 ⁴	2.36 x 10 ⁻⁵	2.88 x 10 ⁻⁵	3.41 x 10 ⁻⁵	0.144	0.380	0.375

[0103] The binding affinities of anti-hDll4 antibodies toward hDll4 and mmDll4 dimers were also determined using a BIACORE™ 2000 and the method describe above, except that hDll4 was replaced with hDll4-mFc (from 3.13 nM to 100 nM), or mmDll4 with mmDll4-mFc (from 0.78 nM to 25 nM) as analyte (Table 14).

TABLE 14

	ka (M-1s-1)		kd (s-1)		K _d (nM)	
	hDll4-mFc	mmDll4-mFc	hDll4-mFc	mmDll4-mFc	hDll4-mFc	mmDll4-mFc
REGN281	3.02 x 10 ⁵	3.16 x 10 ⁵	4.96 x 10 ⁻⁶	4.64 x 10 ⁻⁸	0.0163	0.0147
REGN421	3.43 x 10 ⁵	3.35 x 10 ⁵	4.70 x 10 ⁻⁶	3.80 x 10 ⁻⁸	0.0137	0.013
REGN422	3.46 x 10 ⁵	4.23 x 10 ⁵	4.60 x 10 ⁻⁶	4.15 x 10 ⁻⁸	0.0133	0.0098

Example 8. Cross-Reactivity of Antibodies With hDII1, hDII3, mDII4, or mfDII4.

[0104] Cross-reactivity of the antibodies to human delta-like ligand1 (SEQ ID NO:953) and human delta-like ligand 3 (SEQ ID NO:954) proteins was determined. REGN281, REGN421 and REGN422 were presented by a goat anti-human kappa (hK) polyclonal antibody reagent (Southern Biotech) immobilized on a BIACORE™ chip, and either hDII4-hFc or hDII1-hFc protein at 100 µg/ml were used as analyte injected over the antibody surfaces. All three anti-hDII4 antibodies only bound to hDII4-hFc, and did not bind hDII1-hFc.

[0105] An alternative BIACORE™ format was used to assess cross-reactivity between anti-hDII4 antibody and either hDII1-hFc or hDII3-hFc. Briefly, ligands hDII4-hFc, hDII1-hFc, and hDII3-hFc were each covalently linked to a CM-5 chip, through amine coupling, to an RU range of about 6,000 to 10,000. REGN421, at 300 µg/ml; was injected over the surface of each chip. REGN421 bound only to hDII4-hFc; no binding was observed to either hDII1-hFc or hDII3-hFc. The same result was observed for REGN422 instead of REGN421.

[0106] OCTET™-based binding assays were employed to determine the binding between selected purified anti-hDII4 antibodies and hDII4-hFc, hDII3-hFc, hDII1-hFc, mfDII4-mmh, or mDII4-mFc. Briefly, streptavidin high binding FA biosensors (ForteBio, Inc., Menlo Park, CA) were first incubated with biotin-anti-hK at 5 µg/ml for 10 min at 30°C, to achieve saturation. Biotin-anti-hK-bound biosensors were then incubated with antibodies REGN281, REGN421 or REGN422, at 20 µg/ml for 10 min at 30°C, to achieve saturation. The antibody-bound biosensors were then incubated with either hDII4-hFc or hDII3-hFc, hDII1-hFc, or mDII4-mFc, at 200 nM, or mfDII4-mmh at 100 nM, for 10 min at 30°C. Changes in the thickness of the biological layer after each incubation were measured. Human DII4-hFc and mfDII4-mmh bound to anti-hDII4 antibody-bound biosensors, whereas hDII3-hFc, hDII1-hFc, and mDII4-mFc did not bind to anti-hDII4 antibody-bound biosensors.

Example 9. Effect of Anti-hDII4 Antibody on Tumor Growth

[0107] The effect of REGN421 on tumor growth was evaluated on tumors implanted in Severe Combined Immunodeficiency (SCID) mice expressing a humanized DII4 protein (SCIDxhDII4). Briefly, the humanized DII4 mouse was made by replacing the entire extracellular domain of the mouse DII4 gene with the corresponding extracellular region of the human DII4 gene (7kb) in embryonic stem (ES) cells. Homozygous hDII4 mice were generated and bred into SCID background. Each mouse was then implanted subcutaneously (SC) with 2.5×10^6 human HT1080 tumor cells. After the tumors were established in the mice (~ 100-150 mm³ 18 days after implantation), mice were measured and treated with hFc, hDII4-Fc or REGN421. A total of 7 mice were divided into three groups. The first group (n=3) was treated subcutaneously with hFc at 25 mg/kg; the second group (n=1) was treated with hDII4-Fc at 25 mg/kg; and the third group (n=3) was treated with REGN421 at 10 mg/kg. The treatments were repeated every 48 hours starting at day 18. *In vivo* tumor measurements were obtained three days before the

initial treatment (day 15), on the same day of each treatment (days 18, 20, and 22), and on day 25. Tumor size was calculated using the formula $l \times w^2/2$. Results are shown in Table 15. On day 25, mice were euthanized and each tumor was removed and measured *ex vivo* and calculated (length x width x depth) (Table 16).

[0108] In addition, a group of SCID mice expressing endogenous mDll4 (n=2) was implanted with tumor cells and treated with hDll4-Fc (25 mg/kg) following the same dosing schedule.

TABLE 15

Mouse	Treatment	Tumor Size (mm ³)				
		Day 15	Day 18	Day 20	Day 22	Day 25
SCID	hDll4-hFc	162.0	232.8	320.0	336.0	253.1
SCID	hDll4-hFc	22.5	117.0	117.0	108.0	66.8
SCIDxhDll4	hDll4-hFc	288.0	320.0	352.0	446.0	320.0
SCIDxhDll4	hFc	162.0	288.0	320.0	500.0	550.0
SCIDxhDll4	hFc	162.0	220.5	352.0	662.0	661.5
SCIDxhDll4	hFc	93.8	135.0	179.6	352.0	726.0
SCIDxhDll4	REGN421	144.0	245.0	320.0	162.0	144.0
SCIDxhDll4	REGN421	87.5	162.0	153.0	225.0	135.0
SCIDxhDll4	REGN421	144.0	196.0	272.0	162.0	152.5

TABLE 16

Mouse	Treatment	Tumor Size (mm ³)
SCID	hDll4-hFc	308.0
SCID	hDll4-hFc	105.0
SCIDxhDll4	hDll4-hFc	480.0
SCIDxhDll4	hFc	924.0
SCIDxhDll4	hFc	1020.0
SCIDxhDll4	hFc	792.0
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<400> 15
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<400> 16
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<400> 18
Met Gln Ala Leu His Thr Pro Tyr Thr
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ccctgttagt cccttgtttt caccttagt agctatggta tgacctgggtt ccgcctagggt 120
ccagggaaagg ggctggatgtt gggccaaat taaaacaag alggaaaglga gaaalactat 180
ggggactctg tgaaggcccg attcacatgc tccagagaca acgccaagaa ctccatgtat 240
ctgc当地atgc gcaggccatgtt agccgaggac acggctgtt attatgttc gagagatgg 300
aactatggcc ccgattatcta ctataccac gggttggatgtt tctggggcca agggaccacg 360
gtccatgtt cctcgtt 376

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

Ala Arg Asp Trp Asn Tyr Gly Pro Asp Tyr Tyr Tyr His Gly Leu
100 105 110
Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

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<220>
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<400> 22
Gly Phe Thr Phe Ser Ser Tyr Trp
1 5

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<210> 24
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<400> 24
Ile Lys Gln Asp Gly Ser Glu Lys
1 5

<210> 25
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<400> 25
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Ala Arg Asp Trp Asn Tyr Gly Pro Asp Tyr Tyr Tyr His Gly Leu
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Asp Val

<210> 27
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<212> DNA
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<220>
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alcaatcgcc gggcaagtca gggcattaga aalgttttag gctggltca gcagaaacca 120
gggaaagccc cttaaggccat gatctatgcg tgcatacgatgg ggccatca 180
aggttcagcg gcaglggatc tggacagaa ttcaatcaca caalcagcag ccgtcgcc 240
gaagatttg caacttataa cgttccatcg cataataactt acccgtaaac tttggccag 300
gggaccaagg tggagalcaa ac 322

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<211> 107
<212> PRT
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<220>
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Asp Leu Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Val 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 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 Leu Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Thr Tyr Pro Tyr
85 90 95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 29

<211> 18
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<220>
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<210> 30
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<220>
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<400> 30
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1 5

<210> 31
<211> 9
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<400> 31
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<400> 32
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27

<210> 34
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<400> 37
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<210> 38
<211> 8
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<400> 38
Gly Phe Ser Phe Arg Ser Tyr Gly
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<210> 39
<211> 24
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<220>
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<400> 39
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<210> 40
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<400> 40
Ile Trp Tyr Asp Gly Ser Lys Thr
1 5

<210> 41
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<220>
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<400> 41
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<210> 42
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<400> 42

Ala Ser Gly Phe Ser Val Pro Ala Thr Ile Leu Asp Asn

1 5 10

<210> 43

<211> 322

<212> DNA

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<220>

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<400> 43

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gggaaagccc caaacccgtt gatcttgcg tggaaagggtgg ggtcccalca 180
aggttcagcg gcagtggatc tggcacat ttcacttca caatcagcag cctgcagcca 240
gaagattttg caacttataa ctgttccatc acccgtggac gttcgccaa 300
gggaccaaagg tggaaaatcaa ac 322

<210> 44

<211> 107

<212> PRT

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<220>

<223> Synthetic

<400> 44

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 Phe Gln Gln Lys Pro Gly Lys Ala Pro Asn Arg Leu Ile

35 40 45

Tyr Gly Ala Ser Ser Leu Glu Gly 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 His Asn Ser Tyr Pro Trp

85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

100 105

<210> 45

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 45

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<210> 46

<211> 6

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<400> 46
Gln Gly Ile Arg Asn Asp
1 5

<210> 47
<211> 9
<212> DNA
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<220>
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<400> 47
ggagccalcc 9

<210> 48
<211> 3
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<220>
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<400> 48
Gly Ala Ser
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<210> 49
<211> 27
<212> DNA
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<220>
<223> Synthetic

<400> 49
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<210> 50
<211> 9
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<400> 50
Leu Gln His Asn Ser Tyr Pro Trp Thr
1 5

<210> 51
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<212> DNA
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<220>
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<400> 51

<210> 52

<211> 122

<212> PRT

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<220>

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<400> 52

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 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 Asn Asn Lys Tyr Tyr Ile 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 Arg Gly Tyr Ser Gly Tyr Glu Gly Tyr Phe Asp Leu Trp
 100 105 110
 Gly Arg Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 53

<211> 24

<212> DNA

<213> Artificial Sequence

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<223> Synthetic

<400> 53

ggatccaccttcaggtagctatggc

24

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<211> 8

<212> PRT

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<223> Synthetic

<400> 54

Gly Phe Thr Phe Ser Ser Tyr Gly

1 5

<210> 55
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<400> 55
atatggatcg atggaaataa taaa

24

<210> 56
<211> 8
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<220>
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<400> 56
Ile Trp Tyr Asp Gly Asn Asn Lys
1 5

<210> 57
<211> 45
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<220>
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<400> 57
gcgagagacc gtggatcg tggctacgag ggataactcg atctc 45

<210> 58
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<400> 58
Ala Arg Asp Arg Gly Tyr Ser Gly Tyr Glu Gly Tyr Phe Asp Leu
1 5 10 15

<210> 59
<211> 337
<212> DNA
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<220>
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<400> 59
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ctcaactgta agcccgcca gagtttttta tacagctcca acaataaaga acaatgtatct 120

tggtaccagg agaaaccagg acagccctct aagctgtca ttaclgggc alclacccgg 180
gaatccgggg tccctgaccc atcagtggc agccgggtcg ggacagatct cacttcacc 240
alcaaggcc tgaggctga agatgtggca gttlaitlct gttagcaata ttatctact 300
tggacgtcg ccacaaaggac caaggltggaa alcaaac 337

<210> 60
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<400> 60
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1 5 10 15
Glu Arg Ala Thr Leu Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
20 25 30
Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln 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 Phe Cys Gln Gln
85 90 95
Tyr Tyr Thr Thr Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 61
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<220>
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<400> 61
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<210> 62
<211> 12
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<400> 62
Gln Ser Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr
1 5 10

<210> 63
<211> 9
<212> DNA
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<220>
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<400> 63
tgggcacatc 9

<210> 64
<211> 3
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<400> 64
Trp Ala Ser
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<210> 65
<211> 24
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<400> 65
cagcaatatt atatactatcg gacg 24

<210> 66
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<220>
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<400> 66
Gln Gln Tyr Tyr Thr Thr Trp Thr
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<210> 67
<211> 385
<212> DNA
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<220>
<223> Synthetic

<400> 67
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tcclglgcag ccclgcac cacccatgtt aggcacggca tgcactgggt cggccaggct 120
ccaggcaagg gacggggatg gggggcgtt atatcatacg aatggaaatcaa taaaatactat 180
gttagactcg tgaaggggccg attccacccatccagagaca attcggaaagaa caccgttgtat 240
ctgcaaaalga atagccctgag aacggacgac acggcgtgtt attattgttc gaaagagatla 300
gttaggtttta ctggaaaacct ggtctactac lactaciacg gaalggacgt cggggccaa 360
gggaccacgg tcacccgttc ctcaag 385

<210> 68
<211> 128
<212> PRT

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<400> 68

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

<210> 69

<211> 24

<212> DNA

<213> Artificial Sequence

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<223> Synthetic

<400> 69

gcatccacct tcagtaggca tggc 24

<210> 70

<211> 8

<212> PRT

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<220>

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<400> 70

Ala Ser Thr Phe Ser Arg His Gly

1 5

<210> 71

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 71

atatacalatg atggaaalaa laaa

24

<210> 72

<211> 8

<212> PRT
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<220>
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<400> 72
Ile Ser Tyr Asp Gly Asn Asn Lys
1 5

<210> 73
<211> 63
<212> DNA
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<220>
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<400> 73
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glc 63

<210> 74
<211> 21
<212> PRT
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<220>
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<400> 74
Ser Lys Glu Leu Val Gly Ile Thr Gly Asn Leu Val Tyr Tyr Tyr
1 5 10 15
Tyr Gly Met Asp Val
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<210> 75
<211> 325
<212> DNA
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<220>
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<400> 75
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cclccclgca gggccaglca gactttaaac agcagctact taggcttgta ccagcagaaa 120
cctggccagg ctccccagact cctccalctat ggtgcattca acagggccac tggccalccca 180
gacaglttca gtggcaglgg gtcgggaca gacttcactc tcaccatca gagactggag 240
cclgaagatt tlgcaglglta tactgtcaa cattataaca aclcacccta cactllggc 300
caggggacca agctggagat caaac 325

<210> 76
<211> 108
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<220>
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<400> 76
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1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Ile Asn Ser Ser
20 25 30
Tyr Leu Gly Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Tyr Gly Ala Ser Asn Arg Ala Thr Gly Ile Pro Asp Ser 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 His Tyr Asn Asn Ser Pro
85 90 95
Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 77
<211> 21
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<220>
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<400> 77
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<210> 78
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<212> PRT
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<220>
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<400> 78
Gln Thr Ile Asn Ser Ser Tyr
1 5

<210> 79
<211> 9
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<400> 79
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<210> 80
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<400> 80
Gly Ala Ser
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<210> B1
<211> 27
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<400> 81
caacatata acaacalcacc Itacact 27

<210> 62
<211> 9
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<220>
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<400> 82
Gln His Tyr Asn Asn Ser Pro Tyr Thr
1 5

<210> 83
<211> 361
<212> DNA
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<220>
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<210> 84
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Thr	Leu	Ser	Leu	Thr	Cys	Thr	Val	Ser	Gly	Gly	Ser	Ile	Ser	Ser	Gly	
	20			25			30									
Gly	Tyr	Tyr	Trp	Ser	Trp	Ile	Arg	His	Tyr	Pro	Gly	Lys	Gly	Leu	Glu	
	35			40			45									

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

<210> 85
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<212> DNA
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<400> 85
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<210> 86
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<212> PRT
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<220>
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<400> 86
Gly Gly Ser Ile Ser Ser Gly Gly Tyr Tyr
1 5 10

<210> 87
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<400> 87
gtccattaca gtggaaacac c 21

<210> 88
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<400> 88
Val His Tyr Ser Gly Asn Thr
1 5

<210> 89

<211> 36
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<400> 89
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36

<210> 90
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<400> 90
Ala Arg Ala Pro Arg Gly Tyr His Tyr Phe Ala Tyr
1 5 10

<210> 91
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<400> 91
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cttcctcgca gggcccgatca gaglattgc agcagglaact tagccctggta ccaggcagaaa 120
ccggccagg ctcccggtt ccatactttt gggtcatcca gcaggggccac tggccalacca 180
gacagggttca gggcaggg gtcgtggaca gacilactic tcaccatcaag cagacggag 240
ccigaagttt tgcaggta ttacgtcaag cagtaaggta gtcacccgtt cacttccggc 300
ggagggacca agggggatcaa 325

<210> 92
<211> 108
<212> PRT
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<220>
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<400> 92
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1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Ser Arg
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Phe Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95
Leu Thr Phe Gly Gly Thr Lys Val Glu Ile Lys

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105

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<400> 93
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<210> 94
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<400> 94
Gln Ser Ile Ser Ser Arg Tyr
1 5

<210> 95
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<400> 95
ggtgcatcc

9

<210> 96
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<210> 97
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cagcaglatg gtagtcacc gcctacl

27

<210> 98
<211> 9
<212> PRT
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<400> 98
Gln Gln Tyr Gly Ser Ser Pro Leu Thr
1 5

<210> 99
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<212> DNA
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<400> 99
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acctgcacgt tcctcggtgg ctccalcagtc agtagtggt actactggat ttggatccgc 120
cagcaccggcgg gaaaggccgtt ggaglggatt gggtacgtcc attacaglgg gaacacccac 180
tacagccccgtt ccctcazagag logacttacc alatcagtg acacgttcaa gaaoccagttc 240
tccctgaagc tgagcttgtt gaclgcggcg gacaacggcg lgtallactg tgcgagagcc 300
ccccggat accattactt tgcctactgg ggccaggaa ccctggcac cgttcctca 360
9 361

<210> 100
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 100
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Ser
20 26 30
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Tyr Val His Tyr Ser Gly Asn Thr His Tyr Ser Pro Ser
50 55 60
Leu Lys Ser Arg Leu Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Arg Ala Pro Arg Gly Tyr His Tyr Phe Ala Tyr Trp Gly Gln
100 105 110
Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 101
<211> 30
<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 101

ggggcccca tcagcagtag ggtaclac

30

<210> 102

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 102

Gly Gly Ser Ile Ser Ser Ser Gly Tyr Tyr

1 5 10

<210> 103

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 103

gccccattaca gtgggaacac c

21

<210> 104

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 104

Val His Tyr Ser Gly Asn Thr

1 5

<210> 105

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 105

gcgagagccc ccoglggata ccatacatt gcclac

36

<210> 106

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 106

Ala Arg Ala Pro Arg Gly Tyr His Tyr Phe Ala Tyr
1 5 10

<210> 107

<211> 325

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 107

aaaaatgtgtl tgacgcaglc tocaggcacc ctglctttgl ctcaggggga gagagccacc 60
cttcctcgca gggccagtca gagtaatgc agcagctact tagccctggta ccagcagaaa 120
ccggccagg ctccccaggctt cccalcttl gglicatcca gcagggccac tggcatccca 180
gacaggltca glggcaglgg glctggccca gacticacio tcaccattag gagactggag 240
cclgaagatt ttcgggtgtt ttacgttag cagtttgta gttcacccgtt cacttccggc 300
ggagggacca aggtggatcaa 325

<210> 108

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 108

Lys 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 Ile 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 Phe Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

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

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

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

<210> 109

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 109

cagagtata gcagcagcta c

21

<210> 110

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

<220>
<223> Synthetic

<400> 110
Gln Ser Ile Ser Ser Ser Tyr
1 5

<210> 111
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 111
ggtgccatcc 9

<210> 112
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 112
Gly Ala Ser
1

<210> 113
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 113
cagcaagatg gtagtttacc gctcatl 27

<210> 114
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 114
Gln Gln Tyr Gly Ser Ser Pro Leu Thr
1 5

<210> 115

<211> 358
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 115
caggttcagl tggcgacgtc tggaggcgag glgaagaagc ctggggcclc aglgaaggic 60
tcttgcagg ctttcgttta cacctttcc acctatggla tcagctgggt gogacaggcc 120
ccggacaag ggctlgaglg gatgggatgg atcagcgctt acgacaataa cgccgactal 180
gcacagaact tccaggccag agtcaccalgl accacagaca calccacgac cacagoctac 240
alggagcglga ggaggcccgag atcgtacgac acggccgigt attaalcgtc gaggtalagc 300
tggaacttc actggtcga cccctggggc caggaaaccc tggcacccgl ctcclcag 358

<210> 116
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 116
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Thr Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asp Asn Asn Ala Asp Tyr Ala Gln Asn Phe
50 55 60
Gln Ala Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Ser Trp Asn Phe His Trp Phe Asp Pro Trp Gly Gln Gly
100 105 110
Thr Leu Val Thr Val Ser Ser
115

<210> 117
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 117
ggttacacct ttccaccta tgg 24

<210> 118
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 118
Gly Tyr Thr Phe Ser Thr Tyr Gly
1 5

<210> 119
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 119
alcagcgctt acgacaataa cgcg 24

<210> 120
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 120
Ile Ser Ala Tyr Asp Asn Asn Ala
1 5

<210> 121
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 121
gcgaggatla gcggaaactt tcactggcc gacccc 36

<210> 122
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 122
Ala Arg Tyr Ser Trp Asn Phe His Trp Phe Asp Pro
1 5 10

<210> 123
<211> 325
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 123
gaaatgttgt gacgcagtc tccaggcacc cgttttgtt ctccagggga aagagccacc 60
cttcctgca gggccaglca gagtgtagc agtaccaact tagccgtta ccagcagcaa 120
cttggccagg ctccccaggct cccatctt gglgcalcca gcagggcac lggcatccca 180
gacaggltca gtggcagtgg gtcggaca gacticactt tcaaccatcg cagactggag 240
cttgaagatt ttgcagtgla ttaatgttagt acttaccgtg gacgttcggc 300
caagggacca aggllgaaal caaac 325

<210> 124

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthefic

<400> 124
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 Thr
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln 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 Asn Ser Pro
85 90 95
Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 125

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthefic

<400> 125

cagagtgtta gcagttaccta c

21

<210> 126

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthefic

<400> 126

Gln Ser Val Ser Ser Thr Tyr

1 5

<210> 127

<211> 9

<212> DNA

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 127
ggtgccatcc

9

<210> 128
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 128
Gly Ala Ser
1

<210> 129
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 129
cagcaglatg gtaactcacc gggacg 27

<210> 130
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 130
Gln Gln Tyr Gly Asn Ser Pro Trp Thr
1 5

<210> 131
<211> 358
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 131
caggttcacc tggcgccgtc tggagcttagt gtgaagaaggc cggggccctc agtgaaggcc 60
tcctgcaggc ctcttgttacc aaccttggta tcacctgggtt gggacaggcc 120
ccggacaagg ggcttggatgtt gatgggtatgg alcagccgtt acagggaa cacagactat 180
gcacagaagt tccaggccatg aatcaccatgtt accacagaca cttccacgtc cacagccatc 240
atggaaatgtt gggactgttgc alcgtacgtc acggccgttgtt attacgtgtc gaggttatagtc 300
tggaaatccc acgggttgc cccctggggc caggaaatccc tggtcaccgtt ctcttcgt 358

<210> 132

66

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

<220>
<223> Synthetic

<400> 132
Gln Val His Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Arg Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30
Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Ser Gly Asn Thr Asp Tyr Ala Gln Lys Phe
50 55 60
Gln Ala Arg Ile Thr Met Thr Thr Asp Thr Ser Thr Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Ser Trp Asn Phe His Trp Phe Asp Pro Trp Gly Gln Gly
100 105 110
Thr Leu Val Thr Val Ser Ser
115

<210> 133
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 133
ggttacacct ttaccaacta tgg 24

<210> 134
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 134
Gly Tyr Thr Phe Thr Asn Tyr Gly
1 5

<210> 135
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 135
atcagcgctt acaglggtaa caca 24

<210> 136
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 136
Ile Ser Ala Tyr Ser Gly Asn Thr
1 5

<210> 137
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 137
gcgaggatata gctggaaactt tcaacggttc gaccgg 36

<210> 138
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 138
Ala Arg Tyr Ser Trp Asn Phe His Trp Phe Asp Pro
1 5 10

<210> 139
<211> 325
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 139
gaaattgtgt tgacgcagtc tccaggcacc ctgttttgta ctccaggggaa cagagtccacc 60
cttcctcgta gggccagtc a gagtgtatgt agcagctact tggccggta ccaggcagaaaa 120
ccctggccagg c tccccaggctt cccatctat tggcatccca gcaggggccac tggcatccca 180
gacagggttc a gggcaglgg tgcgggaca gacttcactt tcaaccalcag cagtcggag 240
ccctgaaggatt ttcgcagtgta ttacgttag cagtggtggg gtcacccgtg gacgttcggc 300
caaggggacca ggggtggagat caaac 325

<210> 140
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 140
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Asp Arg Val 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 Ser Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Cys Gly Gly Ser Pro
85 90 95
Trp Thr Phe Gly Gln Gly Thr Arg Val Glu Ile Lys
100 105

<210> 141
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 141
cagagtgtta glagcagcta c 21

<210> 142
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 142
Gln Ser Val Ser Ser Ser Tyr
1 5

<210> 143
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 143
ggtgccatcc 9

<210> 144
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 144

Gly Ala Ser

1

<210> 145

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 145

cagcagtgtg gtggctacc glggacg

27

<210> 146

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 146

Gln Gln Cys Gly Gly Ser Pro Trp Thr

1 5

<210> 147

<211> 358

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 147

caggtaaac tggtgcagtc tgggcctgag gigaagaagc ctggggccctc agtgaaggcg 60
gcgcgcagg cttctggta cacccttacc caatatggtt tcacctgggt gogacaggcc 120
ctctggacaag ggcttgatgg gatggatgg atcagcgctt acatggcaca lacagactat 180
gcacggaaatg lccaggccatg aglaccatcg accacagaca cattcacgac cacagctac 240
atggaaatgtg gtaggcctgag atcgtacgac acggccgtt atatctgtc gagttatagc 300
tggaaatcc acgttgtca cccctggggc caggaaaccc tggcacccgt ctccatcg 358

<210> 148

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 148

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

1 5 10 15

Ser Val Lys Val Ala Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr

20 25 30

Gly Phe Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

35 40 45

Gly Trp Ile Ser Ala Tyr Ser Gly His Thr Asp Tyr Ala Arg Lys Phe

50 55 60

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

<210> 149
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 149
ggttacacct ttaccacata tggt 24

<210> 150
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 150
Gly Tyr Thr Phe Thr His Tyr Gly
1 5

<210> 151
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 151
alcagcgcctt acaglgggca laca 24

<210> 152
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 152
Ile Ser Ala Tyr Ser Gly His Thr
1 5

<210> 153
<211> 36
<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 153

gcgagttata gctggaaactt tcactgggtc gacccc

36

<210> 154

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 154

Ala Ser Tyr Ser Trp Asn Phe His Trp Phe Asp Pro

1 5 10

<210> 155

<211> 325

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 155

caaalttgt tgacgcagtc tccaggcacc ctgcgttgtt ctccaggggga aagagccacc 60
ctcgcgtca gggccatgtca gagtgttagl accaccaclt tagctggta ccagcagaaa 120
ccctggccagg ctcccgatct cccatctat ggacalcca ccaggccac tggcatccca 180
gacaggttca gllggcgttg ggctggact gacttcaclc tcaccatcag cagactggag 240
ccolgaagatt ttgcagtlgl ttaactgtcag cagtgtggtg gclcacccglg gaogttcgcc 300
caagggatcca aggtgaaaal caaac 325

<210> 156

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 156

Gln 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 Thr Thr

20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Ser Leu Leu

35 40 45

Ile Tyr Gly Thr Ser Thr 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 Cys Gly Ser Pro

85 90 95

Trp Thr Phe Gly Gln Gly Thr Lys Val Lys Ile Lys

100 105

<210> 157
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 157
cagagtgta gtaccacca c

21

<210> 158
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 158
Gln Ser Val Ser Thr Thr Tyr
1 5

<210> 159
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 159
ggtagatcc 9

<210> 160
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 160
Gly Thr Ser
1

<210> 161
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 161
cagcagtg gttgttccacc gtggacg

27

<210> 162

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

<220>
<223> Synthetic

<400> 162
Gln Gln Cys Gly Gly Ser Pro Trp Thr
1 5

<210> 163
<211> 367
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 163
 cagglgcagl lgglgcaglc tggggctgag gigaagaagc ctggggccgc tglgaagglc 60
 tcctgcagg ctclggala catgttcacc aglalgtata tcaaclgggc ggcacaggcc 120
 acggacaag ggctgaglg galgggalgg alaaacccta acagtgglaa cacaggclat 180
 gcacagaagt llcaggcgcg agtcaccttg accaggaaca ccclccataag cacagccctac 240
 atggaaactga gcagccctgag alcggggac acggccgtt attaalcgtgc gagagaggg 300
 tatttgtgtg glgatlgcta tgcttttgtt alcggggcc aagggacaal ggcacccgc 360
 lcttcag 367

<210> 164
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 164
 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
 1 5 10 15
 Ala Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
 20 25 30
 Asp Ile Asn Trp Val Arg Gln Ala Thr Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Trp Ile Asn Pro Asn Ser Gly Asn Thr Gly Tyr Ala Gln Lys Phe
 50 55 60
 Gln Gly Arg Val Thr Leu Thr Arg Asn Thr Ser Ile Ser Thr Ala Tyr
 65 70 75 80
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Glu Gly Tyr Cys Gly Gly Asp Cys Tyr Ala Phe Asp Ile Trp
 100 105 110
 Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 165
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 165
ggalacaagt tcaccaggta tgat

24

<210> 166
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 166
Gly Tyr Thr Phe Thr Ser Tyr Asp
1 5

<210> 167
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 167
ataaaacccta acatgttlaa caca

24

<210> 168
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 168
Ile Asn Pro Asn Ser Gly Asn Thr
1 5

<210> 169
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 169
gcgagagagg gatatttggg tggtgatgtc tatgcatttg atatc

45

<210> 170
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 170
Ala Arg Glu Gly Tyr Cys Gly Gly Asp Cys Tyr Ala Phe Asp Ile
1 5 10 15

<210> 171
<211> 325
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 171
 gaaattgtl tgacacaalc tccaggcacc ctglcttgtl ctccagggga aagagccacc 60
 ctctcclgca gggccaglca gaglghtgc agcagcta ltagccctggla ccagcagaaa 120
 cclggccagg ctccccaggctt ctctatctttt ggltcatcca gcaggggccac lggcatccca 180
 gacagggtlca glggcagllg gtctggaca gacticaclc lcaaccatcg cagactggag 240
 cclgaagatt ttgcagtglta tactglcag cagtafgglta gctcacogel cacttcggc 300
 qqaqqqacca aqqlqqaqat caaac 325

<210> 172
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 172
 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 Phe Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
 50 55 60
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
 65 70 75 80
 Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
 85 90 95
 Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 173
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 173
cagaglgtta gcagcgacla c 21

<210> 174
<211> 7
<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 174

Gln Ser Val Ser Ser Ser Tyr

1 5

<210> 175

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 175

ggcgatcc

9

<210> 176

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 176

Gly Ala Ser

1

<210> 177

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 177

cagcgtatg gtagtcacc gcgcact

27

<210> 178

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 178

Gln Gln Tyr Gly Ser Ser Pro Leu Thr

1 5

<210> 179

<211> 361

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 179

cagctgcagc tgcaggagtc gggcccagga cggcggaaac ctccggagac ccgtcccc 60
acccgcacig lctctgggtt ctccatcagc agtagtagtt actaacgggg ctggalccgc 120
cagccccccag ggaaggggctt ggaglggtt gggaglactt alalaglgg gagcacctac 180
tacaaccgtt ccctcaagag tcgagtcacc atatcccgat acacgtccaa gaaccaggtc 240
tcctgaagc tgagcttgtt gacccgcgca gacacggctt tttttttttt tgccggaaac 300
tgggacacg cttttttttt tttttttttt ggccaggaa cttttttttt cttttttttt 360

9 361

<210> 180

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 180

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

<210> 181

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 181

ggggcccca tcagcaglag tagttacac 30

<210> 182

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 182

Gly Gly Ser Ile Ser Ser Ser Ser Tyr Tyr
1 5 10

<210> 183
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 183
atclattata gggggaggcac c 21

<210> 184
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 184
Ile Tyr Tyr Ser Gly Ser Thr
1 5

<210> 185
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 185
gcggcaaaact gggaaagacgc ctcttcgtt gaclac 36

<210> 186
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 186
Ala Ala Asn Trp Asp Asp Ala Phe Phe Phe Asp Tyr
1 5 10

<210> 187
<211> 322
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 187

gacatccaga tgacccagtc tcttccacc cgtcgatc cgttaggaga cagagtacc 60
alcactggcc gggcccgatca gagttagt agctgggtgg cctggtaatca gcagaaacca 120
gggaaaagccca ctatcgatcc galctataag ggcgtcgatc tagaaatggg ggtccccatca 180
aggltcagcg ccaggatggat tggacacaa atcacatca cccacccatca 240
galgttttg caacttataa cgtccaaacag tataatgtt attcgttacat ttggccatca 300
gggaccaaggc tggatcaa ac 322

<210> 188

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 188

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

1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp

20 25 30

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

35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly

50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro

65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Ser Tyr

85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys

100 105

<210> 189

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 189

cagaglatta glagctgg

18

<210> 190

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 190

Gln Ser Ile Ser Ser Trp

1 5

<210> 191

<211> 9

<212> DNA

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 191
aaggccgtct

<210> 192
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 192
Lys Ala Ser
1

<210> 193
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 193
caacatgtata alaglattc gtacact 27

<210> 194
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 194
Gln Gln Tyr Asn Ser Tyr Ser Tyr Thr
1 5

<210> 195
<211> 352
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 195
 cagggtgcagc tgggtgcagtc lggggctgag gigaagaagc ctggggcclc aglgaaggtc 60
 tcclgcaagg ctclggala caccttcacc ggctactata ttcactgggt aogacaggcc 120
 ccggacaag gctttagtg gatgggtatgg alcaacccla acatggggcg cacaaaclat 180
 gcacagaagl tccaggcag ggtcaccalgt accagggaca cgtccatcac cacagccatc 240
 alggagctga gcaggctgtat alclgacgac acggccgtgt allactglgc gagaggaccc 300
 tqgqalltot ttqactactg qqqccqqqqa accctgtolca ccqfctcttc aq 352

<210> 196
<211> 117

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 196
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30
Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Thr Thr Ala Tyr
65 70 75 80
Met Glu Leu Ser Arg Leu Ile Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Gly Pro Trp Asp Phe Phe Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110
Val Thr Val Ser Ser
115

<210> 197
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 197
ggalacacct tcaccggcta cta 24

<210> 198
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 198
Gly Tyr Thr Phe Thr Gly Tyr Tyr
1 5

<210> 199
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 199
alcaacccta acagtgglgg caca 24

<210> 200

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

<220>
<223> Synthetic

<400> 200
Ile Asn Pro Asn Ser Gly Gly Thr
1 5

<210> 201
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 201
gogagaggac octgggattt ctttgactac 30

<210> 202
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 202
Ala Arg Gly Pro Trp Asp Phe Phe Asp Tyr
1 5 10

<210> 203
<211> 340
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 203
gacatgtga tgaccaggc tccagactcc ctggcggtgt ctctggggcga gagggccacc 60
alcaactgcgca aglccagccgca gaglgttta lacagctcca acaalaagaat ctacltagct 120
lgglaccaggc agaaaccaggc acagctctt aagctgcata tttaclgggc atclaccgg 180
gaalccgggg tccctlgaccg attcaglggc agcgggcttg ggacagatctt cacttcacc 240
alcaagcggcc lgeaggctgtga agalgtggca gttttactt gtcaagcaala ttatgtact 300
ccgtacactt tggccaggg gaccaagctg gagalcaaac 340

<210> 204
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 204

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
20 25 30
Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln 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 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> 205
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 205
cagagtgtt tatacagctc caacaataag aactac 36

<210> 206
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 206
Gin Ser Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr
1 5 10

<210> 207
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 207
tgggcacct 9

<210> 208
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 208

Trp Ala Ser

1

<210> 209

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 209

cagcaatatl atagtactcc glacact

27

<210> 210

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 210

Gln Gln Tyr Tyr Ser Thr Pro Tyr Thr

1 5

<210> 211

<211> 352

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 211

caggcgacg tggtgccgtc tggggctgag gtaagaaggc ctggggccgc agtgaaggcc 60
tcctgcagg ctctggata cacccaccg ggctactata tcactgggt aogacaggcc 120
ccggacaag gocttgagtg galgggatgg alcaacccla acaggggtgg cacaacal 180
gcacagaagt tcaggccag ggtcaccatg accaggacca cgccatcatcag cacagccatc 240
alggagctga gcaggctgag atctgacgac acggccgtgt attacgtgtc gagaggaccc 300
tgggattctt ttgaclactg gggccaggga accctggca ccgtccccc ag 352

<210> 212

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 212

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

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Trp Ile Asn Pro Asn Ser Gly Gly 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 Gly Pro Trp Asp Phe Phe Asp Tyr Trp Gly Gln Gly Thr Leu			
100	105	110	
Val Thr Val Ser Ser			
115			

<210> 213
<211> 24
<212> DNA
<213> Artificial Sequences

<220>
<223> Synthetic

<400> 213
ggatacacccl lcaccggc la clal 24

<210> 214
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 214
Gly Tyr Thr Phe Thr Gly Tyr Tyr
1 5

<210> 215
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 215
atcaaccctt acaatgttgtt caca 24

<210> 216
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 216
Ile Asn Pro Asn Ser Gly Gly Thr
1 5

<210> 217
<211> 30

<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 217
gcgagaggac octgggat tttgactac 30

<210> 218
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 218
Ala Arg Gly Pro Trp Asp Phe Phe Asp Tyr
1 5 10

<210> 219
<211> 340
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 219
gacatcgta tgaccaggc lccagactcc cggctgtgt ctctgggcga ggggcacc 60
atcaacgtca agtccagcca gaglgttta tacagtcata acaaalaagaa ctacttagct 120
lgglaccagg agaaaccagg acagccctt aagctgtca ttacggc alctaccgg 180
gaatccgggg tccctgacog atccatggc agcgggcttg ggacagattt cactctacc 240
atcagcagcc lgcaggctga agatggca gtttattact gtcagcaata ttatgtact 300
ccgtacactt tggccaggg gaccaagctg gagatcaaac 340

<210> 220
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 220
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15
Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
20 25 30
Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln 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> 221
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 221
cagaglgtt latacagtc caacaalaag aaciac 36

<210> 222
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 222
Gln Ser Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr
1 5 10

<210> 223
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 223
Igggcalct 9

<210> 224
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 224
Trp Ala Ser
1

<210> 225
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 225

cagcaalatt alaglaclcc glacact

27

<210> 226

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 226

Gln Gln Tyr Tyr Ser Thr Pro Tyr Thr

1 5

<210> 227

<211> 361

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 227

cagggtgcagt tgcaggaggc gggcccagga ctggtaaaggc cttcacacac ccgttcccc 60
acclgcacat ttcgttgg ctcctcgcc aglglgggtt acatcgagg cttggatccgc 120
cagcaccagg gaaaggggcc tggatgggtt gggtaacgccc attacaglgg gaacacccac 180
tacaaccctt cccatcaagag tcgactttcc atataatag acaacgttcaa galccagttc 240
tccctgaaggc tgatgttgtt gactgcccg gacacggccg tttttttttt tgccggagggcc 300
ccccgggtt accatctt tgcctactgg ggcctggggaa ccctggcac cgttccctca 360
9 361

<210> 228

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 228

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

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Gly Ser Gly

20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu

35 40 45

Trp Ile Gly Tyr Val His Tyr Ser Gly Asn Thr His Tyr Asn Pro Ser

50 55 60

Leu Lys Ser Arg Leu Ser Ile Ser Ile Asp Thr Ser Lys Ile Gln Phe

65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr

85 90 95

Cys Ala Arg Ala Pro Arg Gly Tyr His Tyr Phe Ala Tyr Trp Gly Gln

100 105 110

Gly Thr Leu Val Thr Val Ser Ser

115 120

<210> 229

<211> 30

<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 229
ggggccca tggcagttgg tggtaatcac 30

<210> 230
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 230
Gly Gly Ser Ile Gly Ser Gly Gly Tyr Tyr
1 5 10

<210> 231
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 231
gtccattaca gtgggaacac c 21

<210> 232
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 232
Val His Tyr Ser Gly Asn Thr
1 5

<210> 233
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 233
gctttttttt cccgtttttt ccattttttt gttttttt 36

<210> 234
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 234
Ala Arg Ala Pro Arg Gly Tyr His Tyr Phe Ala Tyr
1 5 10

<210> 235
<211> 325
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<210> 236
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 236
 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 Phe Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
 50 55 60
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
 65 70 75 80
 Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
 85 90 95
 Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 237
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 237
caqaqlgta qcaqcaqcla c

<210> 238
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 238
Gln Ser Val Ser Ser Ser Tyr
1 5

<210> 239
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 239
ggtgcatcc 9

<210> 240
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 240
Gly Ala Ser
1

<210> 241
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 241
cagcaglalg gtagtcacc gctact 27

<210> 242
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 242
Gln Gln Tyr Gly Ser Ser Pro Leu Thr
1 5

<210> 243
<211> 361
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 243

caggcgcgc tgccaggagtc gggcccgaga ctggtaaaggc cttcacacgac octglcccc 60
acclgcactg lclclgggtt ctccatcagc aglglgggtt aclacgttgag cggatccgc 120
caglaccagg ggaaggggccl ggaglggatt ggttacgtcc attacaglgg gagcacccac 180
tacaacccgt ccctcaagag tggacttacc atataaatag acacgttcaa gagcccaagt 240
tccclgaagc tgagctelgl gaclgcccgac gacatggcccg tglatlaclg tgccgagagcc 300
ccccgtggat accattactt tgcclactgg ggccagggaa ccctggtcac cgltctccca 360
9 361

<210> 244
<211> 120

<211> 120
<212> PBT

<212> FRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 244

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

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

Trp Ile Gly Tyr Val His Tyr Ser Gly Ser Thr His Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Ile Asp Thr Ser Lys Ser Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Ala Pro Arg Gly Tyr His Tyr Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 245
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 245
qgtqqctcca tcaaccaqlqq tqgllactac

30

<210> 246
<211> 10

<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 246

Gly Gly Ser Ile Ser Ser Gly Gly Tyr Tyr
1 5 10

<210> 247

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 247

gccccattaca gtggggagcac c 21

<210> 248

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 248

Val His Tyr Ser Gly Ser Thr

1 5

<210> 249

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 249

gogagagccc ccccgaggata ccattacctt ggcac 36

<210> 250

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 250

Ala Arg Ala Pro Arg Gly Tyr His Tyr Phe Ala Tyr

1 5 10

<210> 251

<211> 325

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 251

gaaatgtgtl tgacgcagtc tccaggcacc ctgttttglt ctccaggggta aagagccacc 60
ctctctgtca gggccagtca gagtgttagc agcaggact tagccggta ccaggagaaa 120
ccggccagg ctccaggct cctcaclttt gggtcatcca gcagggccac tggcalacca 180
gacagggttca gllgcagtgg gtcggacaa gacticactc tcaccalcaag cagactggag 240
cttgaagat ttgcagtgta ttcgtcagc cagatggta gtcaccgtc cacltcggc 300
ggagggacca aglggagat caaac 325

<210> 252

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 252

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 Arg
20 25 30
Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45
Ile Phe Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95
Leu Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
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<400> 253

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<400> 254

Gln Ser Val Ser Ser Arg Tyr

1 5

<210> 256

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Gly Ala Ser
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27

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<400> 258
 Gln Gln Tyr Gly Ser Ser Pro Leu Thr
 1 5

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<210> 260
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<400> 260
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1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Ile Ile Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Arg Glu Gly Ala Met Val Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110
Leu Val Thr Val Ser Ser
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<210> 262
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<400> 262
Gly Gly Ser Ile Ser Ser Gly Gly Tyr Tyr
1 5 10

<210> 263
<211> 21
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<220>
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<400> 263

alctattaca gggggagcac c

21

<210> 264

<211> 7

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<223> Synthetic

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Ile Tyr Tyr Ser Gly Ser Thr

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30

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<400> 266

Ala Arg Glu Gly Ala Met Val Phe Asp Tyr

1 5 10

<210> 267

<211> 322

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<400> 267

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atcactttgtt gggccaggca gggcatttgc agtttatgg octggatca gaaaaaaacca 120

ggggaaagccc ctaaactctt gatgttgtt gcatccgtt tgccaaatgtgg ggttccatca 180

aggttcagcg gcagtggttc tgggacagaa ttcacccatca ccattcagcag octgcagcc 240

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gggatccaatgc tggatcaa ac

322

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<211> 107

<212> PRT

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<220>

<223> Synthetic

<400> 268
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1 5 10 15
Asp Arg Val Thr Ile Thr Cys Trp Ala Ser Gln Gly Ile Ser Ser Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Ala Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ser Tyr Pro Phe
85 90 95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 269

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<213> Artificial Sequence

<220>

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<400> 269

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18

<210> 270

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<212> PRT

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<400> 270

Gln Gly Ile Ser Ser Tyr

1 5

<210> 271

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Ala Ala Ser

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Gln Gln Leu Asn Ser Tyr Pro Phe Thr

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cagcaccccg ggaaggggct ggaglggatt ggglatcatl attacagtgg gagcacctac 180
tacaacccgt ccclcaagag tgcatttalc alalcaatgtg acacgttcaa gaaccaggtc 240
tccctgaagc tgagcttgtt gaclgcccgccg gacacggcccg tglattatcg tgcgagagaa 300
ggggctatgg ltttgacta cggggccag ggaacccctgg tcaccgttc ctcag 355

<210> 276

<211> 118

<212> PRT

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<220>

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<400> 276

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

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly

20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu

35 40 45

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

<210> 277
<211> 30
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<220>
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<400> 277
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<210> 278
<211> 10
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<220>
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<400> 278
Gly Gly Ser Ile Ser Ser Gly Gly Tyr Tyr
1 5 10

<210> 279
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<400> 279
acatttaca gtgggagcac c 21

<210> 280
<211> 7
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<400> 280
Ile Tyr Tyr Ser Gly Ser Thr
1 5

<210> 281

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<400> 282
 Ala Arg Glu Gly Ala Met Val Phe Asp Tyr
 1 5 10

<210> 283
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<400> 283
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 gggaaagcccc claaacclcll gallttatgcg gcalccgcgt tgcaaaglgg ggtcccca 180
 aggltcagcg gcagtggacl lgggacagaa ttcaclclca ccatcagcag cctgcac 240
 gaagatllg caactttatla ctgtcaacag ctaataatgtt acccgltcac ttllggccag 300
 gggaccaaaacgc tggaalca ac 322

<210> 284
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
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<400> 284
 Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Arg Val Thr Ile Thr Cys Trp Ala Ser Gln Gly Ile Ser Ser Tyr
 20 25 30
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45
 Tyr Ala Ala Ser Ala Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80
 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ser Tyr Pro Phe
 85 90 95
 Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys

100

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<400> 285
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18

<210> 286
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<220>
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<400> 286
Gln Gly Ile Ser Ser Tyr
1 5

<210> 287
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<220>
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<400> 287
gcgcgtcc

9

<210> 288
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<220>
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<400> 288
Ala Ala Ser
1

<210> 289
<211> 27
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<400> 289
caacagctta alagttaacc gttcaat

27

<210> 290
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<220>
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<400> 290
Gln Gln Leu Asn Ser Tyr Pro Phe Thr
1 5

<210> 291
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<212> DNA
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<400> 291
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acctgcacdg tctctgglgg cccalcage aglgggglt aclaclggac cggalccgc 120
cagcacccag ggaaggggccl ggagtggattt gggatcatct attacaglgg gagcaccatc 180
tacaacccgt ccccaagag tggatgtatc alalcaglag acacgtctaa gaaccaggltc 240
tccctgaagc tgagctctgtl gaclgcccg gacacggccg tgatllactg tgogagagaa 300
ggggctalgg tlltgacta cggggccag ggaaccctgg tcaccgtctc ctcag 355

<210> 292
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
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<400> 292
 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
 1 5 10 15
 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
 20 25 30
 Gly Tyr Tyr Trp Thr Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60
 Leu Lys Ser Arg Val Ile Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Ala Arg Glu Gly Ala Met Val Phe Asp Tyr Trp Gly Gln Gly Thr
 100 105 110
 Leu Val Thr Val Ser Ser
 115

<210> 293
<211> 30
<212> DNA
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<400> 293
ggtggctcca tcagcaglgg tggtaatcac 30

<210> 294
<211> 10
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<400> 294
Gly Gly Ser Ile Ser Ser Gly Gly Tyr Tyr
1 5 10

<210> 295
<211> 21
<212> DNA
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<400> 295
atclattaca gllgggagcac c 21

<210> 296
<211> 7
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<220>
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<400> 296
Ile Tyr Tyr Ser Gly Ser Thr
1 5

<210> 297
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<400> 297
gcgagagaag gggclalgggt tttgactac 30

<210> 298
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<220>

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<400> 298

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

<210> 299

<211> 322

<212> DNA

<213> Artificial Sequence

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<223> Synthetic

<400> 299

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gggaaagccc claaactccl galctatgcg gcatccgcgtl tgcaaaatgg ggcccalca 180
agggtcagcg gcaglggatc tgggacagaa ttcactclca caatcagcag ccgcgcgc 240
gaagatltg caacttata ctglcaacag cttatagtl acccgttcac ttggccag 300
gggaccaagc tggagalcaa ac 322

<210> 300

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 300

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

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

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

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

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

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

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

<210> 301

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 301

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<210> 302

<211> 6

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<220>
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<400> 302
Gln Gly Ile Ser Ser Tyr
1 5

<210> 303
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<400> 303
gctgcalcc 9

<210> 304
<211> 3
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<400> 304
Ala Ala Ser
1

<210> 305
<211> 27
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<400> 305
caacagctt atagttaccc gttcact

27

<210> 306
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<400> 306
Gln Gln Leu Asn Ser Tyr Pro Phe Thr
1 5

<210> 307
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<212> DNA

<213> Artificial Sequence

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<400> 307

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acctgcactg tctctggg cccatcagc aglgggggt actactggao clggalccgc 120
cagtaccagg ggaaggggct ggaglggatt ggglacatct altacaglgg gagcacctac 180
tacaaccgI ccccaagag tagagtttc atalcaglag acacgtctaa gaaccaggtc 240
tcctgaggc Iggcgcgtgactggcg gacacggcg tgatlaclg Igcgagagaa 300
ggggclalgg ttIlgacta clggggccag ggaacctclgg Icacctctc clcag 355

<210> 308

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

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<400> 308

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

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly

20 25 30

Gly Tyr Tyr Trp Thr Trp Ile Arg Gln Tyr Pro Gly Lys Gly Leu Glu

35 40 45

Trp Ile Gly Tyr Ile Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser

50 55 60

Leu Lys Ser Arg Val Ile Ile Ser Val Asp Thr Ser Lys Asn Gln Phe

65 70 75 80

Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr

85 90 95

Cys Ala Arg Glu Gly Ala Met Val Phe Asp Tyr Trp Gly Gln Gly Thr

100 105 110

Leu Val Thr Val Ser Ser

115

<210> 309

<211> 30

<212> DNA

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<220>

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<400> 309

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30

<210> 310

<211> 10

<212> PRT

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<220>

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<400> 310

Gly Gly Ser Ile Ser Ser Gly Gly Tyr Tyr
1 5 10

<210> 311
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<400> 311
atcttattaca gtgggagcac c 21

<210> 312
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<400> 312
Ile Tyr Tyr Ser Gly Ser Thr
1 5

<210> 313
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<212> DNA
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<400> 313
gcgagagaag gggctalggI tttgaclac 30

<210> 314
<211> 10
<212> PRT
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<220>
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<400> 314
Ala Arg Glu Gly Ala Met Val Phe Asp Tyr
1 5 10

<210> 315
<211> 322
<212> DNA
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<220>
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<400> 315

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alcacltgct gggccagica gggcatttgc agtttttag cctggatca gcaaaaaacca 120
gggaaagccc ctaagtcctt gatctatgc tgcattcgct tgcaaaglgg ggtccatca 180
aggltcageg gcagttggalc tggacacagaa ttacttcia caatcagcag cctgcagct 240
gaagatttg caacttata ctgtcaacag cttaaatgtt acccgltcac tttggccag 300
gggaccaagc tggagatcaa ac 322

<210> 316
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
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<400> 316
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Trp Ala Ser Gln Gly Ile Ser Ser Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Ala Ala Ser Ala Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Leu Asn Ser Tyr Pro Phe
85 90 95
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 317
<211> 18
<212> DNA
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<220>
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<400> 317
cagggcatca gcaatgtat 18

<210> 318
<211> 6
<212> PRT
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<220>
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<400> 318
Gln Gly Ile Ser Ser Tyr
1 5

<210> 319
<211> 9
<212> DNA
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<220>
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<400> 319
gctlqcaltcc

<210> 320
<211> 3
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<400> 320
Ala Ala Ser
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<210> 321
<211> 27
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<400> 321
caacagctta atagtatccq qltcacl 27

<210> 322
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<220>
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<400> 322
Gln Gln Leu Asn Ser Tyr Pro Phe Thr
1 5

<210> 323
<211> 358
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<220>
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<400> 323
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lccgtgcaggccctcggttaccatcgatccaaatcggtatcccggtlalgcggc 120
ccgtggacaagggctgtggatgtggatcgatccaaatcggtatcccggtlalgcggc 180
gcacagaagtcccggtccatcgatccaaatcggtatcccggtlalgcggc 240
atggaaatcgatcccggtccatcgatccaaatcggtatcccggtlalgcggc 300
tgaaatcgatcccggtccatcgatccaaatcggtatcccggtlalgcggc 358

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<210> 324
<211> 119

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<212> PRT
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<220>
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<400> 324
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1 5 10 15
Ser Val Lys Val Ser Cys Arg Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30
Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Asn Ser Gly Asn Thr Asp Ser Ala Gln Lys Phe
50 55 60
Gln Ala Arg Val Thr Met Thr Thr Asp Thr Ser Thr Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Thr Tyr Ser Trp Asn Phe His Trp Phe Asp Pro Trp Gly Gln Gly
100 105 110
Thr Leu Val Thr Val Ser Ser
115

<210> 325
<211> 24
<212> DNA
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<220>
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<400> 325
ggttacacct ttaccaacta tgg 24

<210> 326
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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<400> 326
Gly Tyr Thr Phe Thr Asn Tyr Gly
1 5

<210> 327
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alcagcgcl a acaglgglaa caca 24

<210> 328

<211> 8
<212> PRT
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<400> 328
Ile Ser Ala Asn Ser Gly Asn Thr
1 5

<210> 329
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
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<400> 329
g c g a c g l a l a g t t g g a a c t t t c a c t g g t c g a c o c c 36

<210> 330
<211> 12
<212> PRT
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<220>
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<400> 330
Ala Thr Tyr Ser Trp Asn Phe His Trp Phe Asp Pro
1 5 10

<210> 331
<211> 325
<212> DNA
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<400> 331
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c t c t c t g c a g g g c a g l c a g a g l t c a g t c a g t c a c t a c l t a a c c t g g l a c c a g c a g a a a a 120
c c l g g c c a g g t c t c a t c t a l g g l g c a l c c a g c a g g g c c a c l g g c a t c c c a 180
g a c a g g l t c a g g g c a g l g g a c a g t c a t t c t c a c c a l c a g a a g l c l g g a g 240
c c l g a a g a t t t g c a g l g t a t a c t g l c a g c a g t g l g g t g g t c a c c g l g g a c g g t c g g c 300
c a a g g g a c c a g g t g g a a a t c a a a c 325

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<400> 332

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

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<211> 21

<212> DNA

<213> Artificial Sequence

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<400> 333

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21

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<211> 7

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Gln Ser Val Ser Thr Asn Tyr

1 5

<210> 335

<211> 9

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9

<210> 336

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<400> 336

Gly Ala Ser

1

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<400> 337
cagcaglgcg gggccacc gtggacg 27

<210> 338
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<400> 338
Gln Gln Cys Gly Gly Ser Pro Trp Thr
1 5

<210> 339
<211> 365
<212> DNA
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<400> 339
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tcctgtcgac cgccggatt cacccatcgat agctatggca tgcactgggt cggccgggt 120
ccaggcaagg gactggggatc gggccggatc atatggatgc atggaaaglaa taataatata 180
ggagactccg tgaaggggccg attcaccatc tccagagaca attcggaa caccgttat 240
cgccaaalga acaggccgtg agccggggac acggccgtat atttactgtgc gagagatgg 300
gttagacgggtg cttttgtat tggggccaa gggacaacgg tcaccgtctc tcag 365

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<211> 118
<212> PRT
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<400> 340
Gln Val Gln Leu Val Glu Ser 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 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
Ala Arg Asp Gly Val Asp Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr
 100 105 110
Thr Val Thr Val Ser Ser
 115

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<220>
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<400> 341
ggatccacct tcaglagata tggc 24

<210> 342
<211> 8
<212> PRT
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<220>
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<400> 342
Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

<210> 343
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<212> DNA
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<220>
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<400> 343
atatggta tgaaaglaa taaa 24

<210> 344
<211> 8
<212> PRT
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<220>
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<400> 344
Ile Trp Tyr Asp Gly Ser Asn Lys
1 5

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<400> 345
gcgagagatg gagtagacgg tgcitlgal att 33

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<400> 346
 Ala Arg Asp Gly Val Asp Gly Ala Phe Asp Ile
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atcacttgtcc gggcaagtca ggacattaga aalgatttag gctlgglatca gcagaaacca 120
gggaaaagccc claaactctt gatcttalgtt gcatccagtt tacaatgggg ggcctccatca 180
aggltcagcg gcaglggatc tggcacagat ttcaactctca ccatacggcag actgcagcc 240
gaagatttt caacttattt ctgtcaacaa gatlaacaatt acctgttatcc ttttgtccag 300
gggaccaacc tggagalcaa ac 322

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<210> 348
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<220>
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<210> 349
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<220>
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<400> 349
caggacatla gaaalgtat

18

<210> 350
<211> 6
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<220>
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<400> 350
Gln Asp Ile Arg Asn Asp
1 5

<210> 351
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<400> 351
gcgcgcattc

9

<210> 352
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<220>
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<400> 352
Ala Ala Ser
1

<210> 353
<211> 27
<212> DNA
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<220>
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<400> 353
caacaagatc acaatttacccl glatacl

27

<210> 354
<211> 9

<212> PRT
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<220>
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<400> 354
Gln Gln Asp Tyr Asn Tyr Leu Tyr Thr
1 5

<210> 356
<211> 364
<212> DNA
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<220>
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<400> 355
gagglgcagl tggggaglc ggggggaggc ttggtocagc ctggggggt cctgagaclc 60
ccctgtgaag ccctgtgatt caccttgat aactttata tgacctgggt cogccagact 120
ccaggaaagg ggctggaglg ggtggccaac alaaaggaaag alggaaalga tagatata 180
glggactctg tgaagggecg ctccaccalc tccagagaca acgccaagca glcactgtt 240
ctacaaaalga acaglctgag acggaggac acggclgtt attaclgtgcc gagagaattt 300
lggaglggcc ctcaclacgg ttggacgic tggggccaag ggaccacggl caccgctcc 360
lcag 364

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<211> 121
<212> PRT
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<220>
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<400> 356
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 Glu Ala Ser Gly Phe Thr Phe Asp Asn Tyr
20 25 30
Tyr Met Thr Trp Val Arg Gln Thr Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Asn Ile Lys Glu Asp Gly Asn Asp Arg Tyr Tyr Val Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Gln Ser Leu Phe
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Glu Phe Trp Ser Gly Pro His Tyr Gly Leu Asp Val Trp Gly
100 105 110
Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 357
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<212> DNA
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<220>

<223> Synthetic

<400> 357

ggattcaccl ttgataacta ttat

24

<210> 358

<211> 8

<212> PRT

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<220>

<223> Synthetic

<400> 358

Gly Phe Thr Phe Asp Asn Tyr Tyr

1 5

<210> 359

<211> 24

<212> DNA

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<220>

<223> Synthetic

<400> 359

ataaaggaaag aiggaaatga taga

24

<210> 360

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 360

Ile Lys Glu Asp Gly Asn Asp Arg

1 5

<210> 361

<211> 42

<212> DNA

<213> Artificial Sequence

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<223> Synthetic

<400> 361

gcgagagaat ttggagtggtt cccctcaclac ggtttgttgcgt tc

42

<210> 362

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 362
Ala Arg Glu Phe Trp Ser Gly Pro His Tyr Gly Leu Asp Val
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<210> 363
<211> 322
<212> DNA
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<220>
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<400> 363
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atcacttgc gggcaagtca ggaatgttgc aataatlagt gctgggtatca gcagaaacca 120
gggaalgtcc ctaataatctt gatctatgtt gcatccatgtt taaaaatggg aatccatca 180
agggtcagcg gcagtggtt tggctcagat ttcaatctca ccattcagcag cctgcagcc 240
gaagatgttgc caacttataa ctgttccatca gatataatcc accctccgac gttcgccag 300
gggaccaagg tggaaatcaa gc 322

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

<220>
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<400> 364
Ala Leu Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Pro Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Arg Asn Asn
20 25 30
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Asn Ala Pro Lys Phe Leu Ile
35 40 45
Tyr Ala Ala Ser Ser Leu Gln Ser Gly Ile Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Ser 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 Pro
85 90 95
Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 365
<211> 18
<212> DNA
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<220>
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<400> 365
caggacgtta gaaaataat 18

<210> 366
<211> 6
<212> PRT
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<220>
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<400> 366
Gln Asp Val Arg Asn Asn
1 5

<210> 367
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 367
gctgcatcc 9

<210> 368
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 368
Ala Ala Ser
1

<210> 369
<211> 27
<212> DNA
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<220>
<223> Synthetic

<400> 369
catacaaggatt acaaatttaccc tccggacg 27

<210> 370
<211> 9
<212> PRT
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<220>
<223> Synthetic

<400> 370
Leu Gln Asp Tyr Asn Tyr Pro Pro Thr
1 5

<210> 371
<211> 370
<212> DNA
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<220>
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<400> 371

<210> 372

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 372

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 Leu Trp Tyr Asp Gly Ser Asn Lys Asn 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 Arg Asp His Asp Phe Arg Ser Gly Tyr Glu Gly Trp Phe Asp Pro
 100 105 110
 Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

210 373

<211> 24

<212> DNA

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<223> Synthetic

<400> 373

ggattcacct tcagtagtta tggc

<210> 374

<211> 8

<212> PRT

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<220>

<223> Synthetic

<400> 374

Gly Phe Thr Phe Ser Ser Tyr Gly

1 5

<210> 375
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<400> 375
ttatggtaa alggaagtaa laaa 24

<210> 376
<211> 8
<212> PRT
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<220>
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<400> 376
Leu Trp Tyr Asp Gly Ser Asn Lys
1 5

<210> 377
<211> 48
<212> DNA
<213> Artificial Sequence

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<400> 377
gcgagagatc acgtttag gaglggtat gaggggllgl tgaccccc 48

<210> 378
<211> 16
<212> PRT
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<220>
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<400> 378
Ala Arg Asp His Asp Phe Arg Ser Gly Tyr Glu Gly Trp Phe Asp Pro
1 5 10 15

<210> 379
<211> 322
<212> DNA
<213> Artificial Sequence

<220>
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<400> 379
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ctclcclgca gggccagtcg gagtgttgc agtacttag cctggatcca acagaaaacct 120
ggccaggctc ccaggctctt catctlalgt gcatccaaaca gggccacgg catcccagcc 180
aggttcgtg gcaaggggtc tggacacatc ttcaatcata ccacagcag cctagatct 240
gaagatlttg cagttatata ctgtcagcac cgtatcaact ggcccccac ttccgggaa 300
gggaccgagg tggaggtaac 322

<210> 380

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

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<400> 380

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

<210> 381

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 381

cagaggttc gcagctac 18

<210> 382

<211> 6

<212> PRT

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<223> Synthetic

<400> 382

Gln Ser Val Arg Ser Tyr

1 5

<210> 383

<211> 9

<212> DNA

<213> Artificial Sequence

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<400> 383
gatgcaccc

9

<210> 384
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<400> 384
Asp Ala Ser
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<210> 385
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<220>
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<400> 385
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27

<210> 386
<211> 9
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<220>
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<400> 386
Gln His Arg Ser Asn Trp Pro Pro Thr
1 5

<210> 387
<211> 16
<212> DNA
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<220>
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<400> 387
taccggctcc cgalgg

16

<210> 388
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<212> DNA
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<220>
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<400> 388
ggcggclaaag ggttttggaa 19

<210> 389
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 389
tgggaalga ggaaagcaaa ct 22

<210> 390
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
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<400> 390
ctgaagtacc ggaggaga 18

<210> 391
<211> 20
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<213> Artificial Sequence

<220>
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<400> 391
atcacgtgg tggtcctctt 20

<210> 392
<211> 16
<212> DNA
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<220>
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<400> 392
gctgcggcgaa ggcctt 16

<210> 393
<211> 23
<212> DNA
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<220>
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<400> 393
tggcaaatgc tggacccaaac aca 23

<210> 394
<211> 19
<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 394

gggtccggc alettgcc

19

<210> 395

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 395

gcagalgaaa aacggaaac ca

22

<210> 396

<211> 372

<212> DNA

<213> Artificial Sequence

<220>

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<400> 396

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accgttgtccca tctccggaga cagtgatccl agtgatagtg ctgttggaa ctggalcagg 120
caglccccat cgaggaggccct tgatggctg ggaaggacat actacaggc caatgtgtat 180
aatgtattatgt cagtatgtt gaaaatgtgtataaacttca acccagatcac atccaaagaaac 240
cacatctcccc tgcagctgaa ctctgtact ccogaggaca cggctatccta ttactgtgc 300
agagaggggg alaaatggaa ttacggctgg ctgcaccctt gggcccgagg aaccacggc 360
accgttgtccca 372

<210> 397

<211> 124

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 397

Gln Val Gln Leu Val Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln

1 5 10 15

Asn Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asp

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 Phe Asn Pro Asp Thr Ser Lys Asn

65 70 75 80

His Ile Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Ile

85 90 95

Tyr Tyr Cys Ala Arg Glu Gly Asp Asn Trp Asn Tyr Gly Trp Leu Asp

100 105 110

Pro Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser

115 120

<210> 398
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 398
ggagacagtg tctctagtga tagtgctgtc 30

<210> 399
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
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<400> 399
Gly Asp Ser Val Ser Ser Asp Ser Ala Ala
1 5 10

<210> 400
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
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<400> 400
acatactaca ggcctaaggc gtataal 27

<210> 401
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 401
Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn
1 5

<210> 402
<211> 42
<212> DNA
<213> Artificial Sequence

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<400> 402
gcaagagagg gggataattg gaattacggc tggctcgacc cc 42

<210> 403
<211> 14
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<220>
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<400> 403
Ala Arg Glu Gly Asp Asn Trp Asn Tyr Gly Trp Leu Asp Pro
1 5 10

<210> 404
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
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<400> 404
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atccctcgca ggtcgaglca gagcccttctt ctttagtaatg gataacaacta ttggaaftgg 120
laccgtcgaga agccaggggca gtcgtccacaa ctccgtatct atttggtttc tagtcgggcc 180
lccggggcgc ctcacagggtt cagttggcagt ggatccggca cagatttac acgtaaaaalc 240
agcagaglgg aggctgagga ttggaaatt tattatgtta tgcaagctcl acaaactccg 300
tacaclttg gccgggggac caaggllggaa ataaaa 336

<210> 405
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 405
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1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu 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 Val Ser Ser 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 Phe Gly Ile Tyr Tyr Cys Met Gln Ala
85 90 95
Leu Gln Thr Pro Tyr Thr Phe Gly Arg Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 406
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 406
cagagccccc ttcttagtaa tggataacaac tat 33

<210> 407
<211> 11
<212> PRT
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<220>
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<400> 407
Gln Ser Leu Leu Leu Ser Asn Gly Tyr Asn Tyr
1 5 10

<210> 408
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthelic

<400> 408
ttggttcl 9

<210> 409
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
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<400> 409
Leu Val Ser
1

<210> 410
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthelic

<400> 410
atgcgaaggcgc lacaaaaccc glacact 27

<210> 411
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 411

Met Gln Ala Leu Gln Thr Pro Tyr Thr

1 5

<210> 412

<211> 360

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 412

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acctgcactg tctctgggtgg cccgtcaggc agtgglaatt actacggag ctggggccgc 120
caacaccagg ggaaggggccl ggaglgglt gggtacatca aaaaacagtgg gggcacctac 180
lacaacccgt ccctcaagag tgcgaaatacc atatcgatag acacgclcaa gaaccaccc 240
lccctgaggc tgagctctat gacggcccg gacacggccg tgtattactg tgcgagagct 300
ggttcgggga gtcactactt tgactactgg ggcgcaggaa ccctggtcac cgtctccca 360

<210> 413

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 413

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

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Val Ser Ser Gly

20 25 30

Asn Tyr Tyr Trp Ser Trp Val Arg Gln His Pro Gly Lys Gly Leu Glu

35 40 45

Trp Phe Gly Tyr Ile Lys Asn Ser Gly Gly Thr Tyr Tyr Asn Pro Ser

50 55 60

Leu Lys Ser Arg Ile Thr Ile Ser Val Asp Thr Ser Lys Asn His Phe

65 70 75 80

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

85 90 95

Cys Ala Arg Ala Gly Ser Gly Ser His Tyr Phe Asp Tyr Trp Gly Gln

100 105 110

Gly Thr Leu Val Thr Val Ser Ser

115 120

<210> 414

<211> 30

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<213> Artificial Sequence

<220>

<223> Synthetic

<400> 414

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30

<210> 415

<211> 10

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<220>
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<400> 415
Gly Gly Ser Val Ser Ser Gly Asn Tyr Tyr
1 5 10

<210> 416
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 416
atcaaaaaca gtgggggcac c 21

<210> 417
<211> 7
<212> PRT
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<220>
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<400> 417
Ile Lys Asn Ser Gly Gly Thr
1 5

<210> 418
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 418
gcgagagc lg gttcgggg ag tcactac lt gactac 36

<210> 419
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 419
Ala Arg Ala Gly Ser Gly Ser His Tyr Phe Asp Tyr
1 5 10

<210> 420
<211> 324

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 420

gacalccagt tgaccaggcacc ctgtcttgtt ctcaggggga aagagccacc 60
cttcgcgtca gggccaggta gagttttagc agcaactact tagccctggta ccagcagaaa 120
ccggccagg ctccccaggct cccatctat ggtgcaccca gcagggccac tggcatccca 180
gacagggtca gggcaggtagg glcgggaca gacllactc tcaccatcgag cagactggag 240
cclgaagatt glgcagtgta ttactglcag caglaoggtt actcacccgal caccctggc 300
caagggacca agctggagal caaa 324

<210> 421

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 421

Asp Ile Gln 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 Asn
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 Cys Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Tyr Ser Pro
85 90 95
Ile Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 422

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 422

cagagtgtta gcagcaacta c

21

<210> 423

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 423

Gln Ser Val Ser Ser Asn Tyr

1 5

<210> 424
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 424
ggtgccatcc 9

<210> 425
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 425
Gly Ala Ser
1

<210> 426
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 426
cagcagtacg gttactcacc gatcacc 27

<210> 427
<211> 9
<212> PRT
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<220>
<223> Synthetic

<400> 427
Gln Gln Tyr Gly Tyr Ser Pro Ile Thr
1 5

<210> 428
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 428
gagggtgcagc tgggtgcagtc tgggggaggc ggggtccagc ctggggaggc cctgagacgc 60
tcctgtcagc cgtctggatt caccttcagt agttttggca tgcaclgggt cggccaggct 120

ccaggcaagg ggctggaglg ggltgtatTT Ttttgttgcgttggaaactaa taaaacat 180
gttagagtcgg tgaaggcccg attcaccatc tcaagagaca attccaagaa talgcgtal 240
ctggaaatga acagccgtgg agccggaggac acggcgtgtl attlactgtgc gagagatcac 300
gatttttagga ggggtttaga ggggggttgc gaccccttggg gcccaggaaac cctggcacc 360
gttcgttca 369

<210> 429
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<210> 430
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 430
ggallccaccc tcaggatgtt taac 24

<210> 431
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 431
Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

<210> 432
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 432
Halgglatg alggaactaa taaa

24

<210> 433
<211> B
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 433
Leu Trp Tyr Asp Gly Thr Asn Lys
1 5

<210> 434
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 434
gcgagagatc acgtatilag gaglggatag gagggggttgtt tagacccc 48

<210> 435
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
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<400> 435
Ala Arg Asp His Asp Phe Arg Ser Gly Tyr Glu Gly Trp Phe Asp Pro
1 5 10 15

<210> 436
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
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<400> 436
 gaaalagtgacgacatccggccaccctgttgttgcctcaggggaaagagccacc 60
 ctctcgcaggccatcgagttgttagcagctacttagccgtgttccacaacaaat 120
 ggccaggcgcctcaggctctcatctalgalgtccatccaaacaggccacatgg 180
 aggttcagtgccaglgggccatcgacatccatctcaatccatcgatccatcgat 240
 gaagatlttcgttgttacatccatcgatccatcgatccatcgatccatcgat 300
 gggaccaaggatggaaalcaa a 321

<210> 437

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

<220>
<223> Synthetic

<400> 437
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Ile
35 40 45
Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Arg Ser Asn Trp Pro Pro
85 90 95
Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 438
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 438
cagaglgta gcagctac 18

<210> 439
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 439
Gln Ser Val Ser Ser Tyr
1 5

<210> 440
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 440
gttgttttttcc 9

<210> 441
<211> 3

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 441

Asp Ala Ser

1

<210> 442
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 442

caaacaccgt a gcaacggcc tcccact

27

<210> 443
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 443

Gln His Arg Ser Asn Trp Pro Pro Thr

1 5

<210> 444
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 444

caggla cagc lgcagc caglc gggcc cagga ctgc lgaa ac ctcc ac a gac cc 60
accc tgc tgc tg tctctggg cc tccca lca gac agtggla alt aca lca ggac ctgg a lccgc 120
cagc acccc ag ggaagg gc g gtagl ggalt gg gla calca aga a cag lgg a a ggc octac 180
lca aalccgl ccc lca aag ag lgc act lacc a lgc aal a g aca cgt lca ga a cacttc 240
tcttgatt tgact tctgl gac lgc ccc gac a cgg cc t ala tla ctg lgc gag a gal 300
gaaa aal a tag c agt tc glca tgcttigal atc lgg ggc a a ggg aca lca g gla ccc glc 360
lcc tca 366

<210> 445
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 445

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

<210> 446
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 446
ggggctcca tcagcagtgg taattaciac 30

<210> 447
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 447
Gly Gly Ser Ile Ser Ser Gly Asn Tyr Tyr
1 5 10

<210> 448
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 448
atcaagaaca gtggaaggcc c 21

<210> 449
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 449
Ile Lys Asn Ser Gly Ser Ala
1 5

<210> 450
<211> 42
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 450
gcgagagalg aaaatatagc agtgcgtcat gctttgata tc 42

<210> 451
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 451
Ala Arg Asp Glu Asn Ile Ala Val Arg His Ala Phe Asp Ile
1 5 10

<210> 452
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 452
gaaalaglgt tgacacagtc tccaggcgcc ctgcgttgtl ctccaggaga aagagccacc 60
cictccgtta gggccatgcg gaclgttgc accagcatac lagccctggta ccaacagaaa 120
ccggccagg ccocccaggctt cccatctat ggatcacatcca gcccggccac lggccatccca 180
gacagggttca gggcagtgg gtcgtggaca gacttcactc tcaccatcac cagacaggag 240
cclgaagatt ttgcaatata ttacgtcag cagtcgtttt acttcacctct cacttcggc 300
ggagggacca agllggaaat caaa 324

<210> 453
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 453
Glu Ile Val Leu Thr Gln Ser Pro Gly Ala Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Arg Thr 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 Thr 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 Thr Arg Leu Glu			
65	70	75	80
Pro Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Ser Gly Tyr Ser Pro			
85	90	95	
Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys			
100	105		

<210> 454
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 454
cggaclgtta gcagcagcta c 21

<210> 455
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 455
Arg Thr Val Ser Ser Ser Tyr
1 5

<210> 456
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 456
gqlacalcc 9

<210> 457
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 457
Gly Thr Ser
1

<210> 458
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetische

<400> 458
cagcaglctg gtlactcacc tclcact

27

<210> 459
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 459
Gln Gln Ser Gly Tyr Ser Pro Leu Thr
1 5

<210> 460
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 460
 cagggtcgcg lgcaggaglc gggcccgagga clggigaagc cticacagac cctglocclc 60
 acclgcaclg tclclgatga ctccalcaac aalgtgaat cctactggac clggatccgc 120
 caacacccag ggaaggggccl ggagtgatt ggtatacalca aatacactgg gggcatccac 180
 talaacccgl cccctcaaaag tcgactcgcc atalcagllg acacglcaaa gaaccaggltc 240
 tccctlgaaaa lgaactlglt gactggcgog gacacggcca aataitactg lgcgagagca 300
 cglggaagic atacttlga tgtclggggc caggggacaa cggtcaccgt clcccta 357

<210> 461
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 461
 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
 1 5 10 15
 Thr Leu Ser Leu Thr Cys Thr Val Ser Asp Asp Ser Ile Asn Asn Val
 20 25 30
 Glu Ser Tyr Trp Thr Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Ile Gly Tyr Ile Lys Tyr Thr Gly Gly Ile His Tyr Asn Pro Ser
 50 55 60
 Leu Lys Ser Arg Leu Ala Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Ser Leu Lys Met Asn Ser Val Thr Ala Ala Asp Thr Ala Lys Tyr Tyr
 85 90 95
 Cys Ala Arg Ala Arg Gly Ser His Thr Phe Asp Val Trp Gly Gln Gly
 100 105 110
 Thr Thr Val Thr Val Ser Ser

<210> 462
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 462
gatgactcca tcaacaatgl tgaatccctac 30

<210> 463
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthelic

<400> 463
Asp Asp Ser Ile Asn Asn Val Glu Ser Tyr
1 5 10

<210> 464
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 464
alcaaalaca ctggggcat c 21

<210> 465
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 465
Ile Lys Tyr Thr Gly Gly Ile
1 5

<210> 466
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 466
gcgagagcac ggaaaglca tacitltgtat gtc 33

<210> 467
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 467
Ala Arg Ala Arg Gly Ser His Thr Phe Asp Val
1 5 10

<210> 468
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 468
 gccalcgggt tgacccagtc tccaggcacc c lglcttggt ctccagggga a a a g a g c c a c c 60
 ctclcclgca gggccaglca gagtgttgc agtaa clact tagcctggla ccagcaga a a a 120
 cctggccagg c l c c c g a c t c c l c a t t a l g g t g c a t c c a g c a g g g l o g c l g g c a t c c a 180
 gacagggttca gtggcagtgg g t c t g g g a c a g a c t t c a c t c l a c c a l c a g c a g a t c g g a g 240
 cctgaagall ttgcaclgla ttatgtcag caalatagta ggtcaccgat c a c t t c g g c 300
 caa g g g a c c a a g c l g g a g a t c a a a 324

<210> 469
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 469
 Ala Ile Arg Leu Thr Gln Ser Pro Gly Thr Leu Ser Trp Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
 20 25 30
 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 Val Ala 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 Leu Tyr Tyr Cys Gln Gln Tyr Ser Arg Ser Pro
 85 90 95
 Ile Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 470
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 470
cagagtta gcaglaacta c 21

<210> 471
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 471
Gln Ser Val Ser Ser Asn Tyr
1 5

<210> 472
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 472
ggtgccatcc 9

<210> 473
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 473
Gly Ala Ser
1

<210> 474
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 474
cagcaataata gtaggtcacc galcacc 27

<210> 475
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 475

Gln Gln Tyr Ser Arg Ser Pro Ile Thr
1 5

<210> 476

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 476

caggcgccgc tgcaggaggc ggccccagga cggcgaaac ctccacagac ccgtcccttc 60
acctgcactg ttcgtgggg cccalcaac aglgttacll actactggac ctggatccgc 120
cagcccccgg ggagggggcc agatgtggatt gggcacatca aatcagttgg gaggcacctac 180
tacaacccgt cccctcaaggg tcgaglcacc atatcaglgg acacgiclaa gaaccaatcc 240
tcccttaaaa tttaactgtgt gactggccgcg gacacggcccg tggttactg tgccgagac 300
tcgttgcgtc alactttaa ttcgtggggc caagggacaa tggtcaccgt ctcccta 357

<210> 477

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 477

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

<210> 478

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 478

ggggcccca tcaacagtgt tacllaclac 30

<210> 479

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 479

Gly Gly Ser Ile Asn Ser Val Thr Tyr Tyr

1 5 10

<210> 480

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 480

alcaaaatca gtgggaggcac c

21

<210> 481

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 481

Ile Lys Phe Ser Gly Ser Thr

1 5

<210> 482

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 482

gcgagagctt cggaaaglca tacttttgat atc

33

<210> 483

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 483

Ala Arg Ala Ser Gly Ser His Thr Phe Asp Ile

1 5 10

<210> 484

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 484

gccccggc tgaccggcacc ctgccttgc cccagggg aagagccacc 60
ccgcgcgc gggccatca gagatggc ggcatatgg ctggatca acagaaact 120
ggccggcgc ccaggccct catctatgc acatctaca gggccaciga cglcccagcc 180
aggtcagtg gcagtgggt tggacagac tcacttcga ccataacaa ccttagagcc 240
gaagatttg cagttatca ctgtcagcag cglagcact ggcgcctag ctccggcaga 300
gggaccaaac tggagalcaa a 321

<210> 485

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 485

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

<210> 486

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 486

cagagatla ggggtat 18

<210> 487

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 487

Gln Ser Ile Ser Gly Tyr

1 5

<210> 488
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 488
gatacalcc 9

<210> 489
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 489
Asp Thr Ser
1

<210> 490
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 490
cagcagcgta ggcgcgtggcc gtcgcagg 27

<210> 491
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 491
Gln Gln Arg Ser Asp Thr Pro Leu Ser
1 5

<210> 492
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 492
caggcgac tgcaggagtc gggccccagga ctggcgaaac cttcacatcgac cctgtccccc 60
accgtcaacg lctcttgtgg ctccatcaac aglgttactt actacggac ctggatccgc 120
cagcaccccg ggaggggcct agaglggtt gggcacatca aatlcaglgtt gggcacccac 180

tacaaccgt ccccaaggc tcgagtccac atalcaggg acaacgtctaa gaacccaattc 240
tccctaaaaa ttaactctgt gactggcgcg gacacggccg lglttlacig lgcgagagct 300
tcggaaagtc atacttttgta tacltgcccc caagggacaa tggtcacccgt ctctctca 357

<210> 493

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 493

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Asn Ser Val
20 25 30

Thr Tyr Tyr Trp Trp Trp Ile Arg Gln His Pro Gly Arg Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Lys Phe Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Gly Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Ile Asn Ser Val Thr Ala Ala Asp Thr Ala Val Phe Tyr
85 90 95

Cys Ala Arg Ala Ser Gly Ser His Thr Phe Asp Ile Trp Gly Gln Gly
100 105 110

Thr Met Val Thr Val Ser Ser
115

<210> 494

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 494

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<210> 495

<211> 10

<212> PRT

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<400> 495

Gly Gly Ser Ile Asn Ser Val Thr Tyr Tyr

1 5 10

<210> 496

<211> 21

<212> DNA

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<220>

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<400> 496

atcaaattca ggggagcac c

21

<210> 497

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 497

Ile Lys Phe Ser Gly Ser Thr

1 5

<210> 498

<211> 33

<212> DNA

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<220>

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33

<210> 499

<211> 11

<212> PRT

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<220>

<223> Synthetic

<400> 499

Ala Arg Ala Ser Gly Ser His Thr Phe Asp Ile

1 5 10

<210> 500

<211> 324

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 500

galatttgc tgaccaggcc tccaggcacc ctgttttgtt ctccaggggaa aagaggccacc 60
ctclocgtca gggccagtc a gagtgttagc aacagctact tagcccgta ccaggcagaaa 120
ccggccagg ctccaggcc tctcatctt ggtgcgtcca gcagggtcac lggccalccc 180
gacagggtca gttggcagg ggctgggaca gacttcactc tcaccatcg cagactggag 240
ccctgaatgtt tggaaatgtt ttactgtcag caglalatgtt ggtccaccat caccttcggc 300
caaggatcca aggtggaaat caaa

324

<210> 501

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 501

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

<210> 502

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 502

cagaglgtta gcaacagcta c 21

<210> 503

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 503

Gln Ser Val Ser Asn Ser Tyr

1 5

<210> 504

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 504

gglgcgllcc

9

<210> 505

<211> 3

<212> PRT

<213> Artificial Sequence

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

<210> 510
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<212> DNA
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<400> 510
gtttaccccttaccaggcttgcgt
24

<210> 511
<211> 8
<212> PRT
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<220>
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<400> 511
Gly Tyr Ser Phe Thr Ser Phe Gly
1 5

<210> 512
<211> 24
<212> DNA
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<220>
<223> Synthetic

<400> 512
alcagcgctt acaglggiga caca 24

<210> 513
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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<400> 513
Ile Ser Ala Tyr Ser Gly Asp Thr
1 5

<210> 514
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 514
qcgcqatala aclqqaacct ccactggtlc gacccc 36

<210> 515
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 515
Ala Arg Tyr Asn Trp Asn Leu His Trp Phe Asp Pro
1 5 10

<210> 516
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 516
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 ctcclcgca gggccagica gaatattaaa agcaactact tagccctggla ccaggcagaaa 120
 cctggccagg ctccccaggct ccicalettt gglacatcca acaggggccac lgccatltca 180
 gacagggtca gllggcagtgg gtctgggaca gacttcattt tcaccalcag cagaclggag 240
 cctcgaagatt ttcagtgta ttactgtcag cagtgatggla acttcaccgtg gacgttcggc 300
 caaggqgacca aagtggalal caaa 324

<210> 517
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
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<400> 517
 Asp Ile Arg Met Thr Gln Ser Pro Gly Ile Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asn Ile Lys Ser Asn
 20 25 30
 Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
 35 40 45
 Ile Phe Gly Thr Ser Asn Arg Ala Thr Ala Ile Ser Asp Arg Phe Ser
 50 55 60
 Gly Ser Gly Ser Gly Thr Asp Phe Leu Phe Thr Ile Ser Arg Leu Glu
 65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Asn Ser Pro
85 90 95
Trp Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
100 105

<210> 518
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
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<400> 518
cagaalatta aaagcaacta c 21

<210> 519
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 519
Gln Asn Ile Lys Ser Asn Tyr
1 5

<210> 520
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 520
ggtaacalcc 9

<210> 521
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 521
Gly Thr Ser
1

<210> 522
<211> 27
<212> DNA
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<220>
<223> Synthetic

<400> 522
caacaaalq qtaaclcacc qloqaco 27

27

<210> 523
<211> 9
<212> PRT
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<220>
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<400> 523
Gln Gln Tyr Gly Asn Ser Pro Trp Thr
1 5

<210> 524
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<212> DNA
<213> Artificial Sequence

<220>
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acclgcaclg tccltgatgg ctccatcaac agtgtlgaat ccacacggac ctggalccgc 120
cagcacccag ggaaggggcc1 ggaglgggat1 ggalacatca aatacactgg gggccalccac 180
tataaccg1 cccctcaagag tcgactlgtcc atalcaglgg acacgtcaaa gaaccagg1lc 240
tcclgaaaaa tgagctgtg acacggccg gacacggccg tglatlaclg lgogagaga 300
cggtggaaagtc alacttlga lgtclggggc caggggacaa lggtcaccgt clctca 357

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<210> 525
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 525
 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
 1 5 10 15
 Thr Leu Ser Leu Thr Cys Thr Val Ser Asp Gly Ser Ile Asn Ser Val
 20 25 30
 Glu Ser Tyr Trp Thr Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Ile Gly Tyr Ile Lys Tyr Thr Gly Gly Ile His Tyr Asn Pro Ser
 50 55 60
 Leu Lys Ser Arg Leu Ala Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Ser Leu Lys Met Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Ala Arg Ala Arg Gly Ser His Thr Phe Asp Val Trp Gly Gln Gly
 100 105 110
 Thr Met Val Thr Val Ser Ser
 115

<210> 526

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

<220>
<223> Synthetic

<400> 526
galggcgcaca tcaacaglgl lgaalccatc 30

<210> 527
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 527
Asp Gly Ser Ile Asn Ser Val Glu Ser Tyr
1 5 10

<210> 528
<211> 21
<212> DNA
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<220>
<223> Synthetic

<400> 528
atcaaalaca cgggggcat c 21

<210> 529
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 529
Ile Lys Tyr Thr Gly Gly Ile
1 5

<210> 530
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 530
gctttttttt gttttttttt 33

<210> 531
<211> 11
<212> PRT

<210> 535
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 535
Gln Ser Ile Ser Ser Asn Tyr
1 5

<210> 536
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 536
ggcgccatcc 9

<210> 537
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 537
Gly Ala Ser
1

<210> 538
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 538
cagcaglata gtagglicacc galcacc 27

<210> 539
<211> 9
<212> PRT
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<220>
<223> Synthetic

<400> 539
Gln Gln Tyr Ser Arg Ser Pro Ile Thr
1 5

<210> 540
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<212> DNA
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<220>
<223> Synthetic

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cagcacccag ggaaggggct ggaglggtl ggglacatca aaaacaglgg gggcacclac 180
lacaaccgt ccctcaagag lcgaatlaac atatcaatcgtag acacgclaa gaaccactlc 240
tcccgaggc lgagcldlat gacggcccgcg gacacggcccg tgtaatlaclg lgcgagagct 300
qqltcqqqgga glcaactactl tgactactlgg ggcacgggaa cooclggtcac cgiclcclca 360

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<210> 541
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 541
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 1 5 10 15
 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Val Ser Ser Gly
 20 25 30
 Asn Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Phe Gly Tyr Ile Lys Asn Ser Gly Gly Thr Tyr Tyr Asn Pro Ser
 50 55 60
 Leu Lys Ser Arg Ile Thr Ile Ser Val Asp Thr Ser Lys Asn His Phe
 65 70 75 80
 Ser Leu Arg Leu Ser Ser Met Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Ala Arg Ala Gly Ser Gly Ser His Tyr Phe Asp Tyr Trp Gly Gln
 100 105 110
 Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 542
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 542
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<210> 543
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 543
Gly Gly Ser Val Ser Ser Gly Asn Tyr Tyr
1 5 10

<210> 544
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 544
alcaaaaaca ggggggcac c 21

<210> 545
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
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<400> 545
Ile Lys Asn Ser Gly Gly Thr
1 5

<210> 546
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 546
gctgagagctg gttcggttggat tcaactatttt gactac 36

<210> 547
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 547
Ala Arg Ala Gly Ser Gly Ser His Tyr Phe Asp Tyr
1 5 10

<210> 548
<211> 324
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 548

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cttcctgca gggccaglca gaglgttagc agcagctact tagcctggla ccagcagaaa 120
cttggccagg ctccccaggcttccatccatggcatccca gcagggccac lggcatccca 180
gacaggctca gggcaglgg gtctgggaca gactcacttccaccatcag cagaclggag 240
cctgaagatt glgcaglgla ttaclgtcg cagttatggtt atctaccatcataccat 300
caagggacca agggaaat caaa 324

<210> 549

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 549

Glu Thr Thr 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 Leu 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 Cys Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Tyr Ser Pro
85 90 95
Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 550

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 550

cagagtgtta gcagcagcta c

21

<210> 551

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 551

Gln Ser Val Ser Ser Ser Tyr

1 5

<210> 552

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

<220>
<223> Synthetic

<400> 552
ggtgccatcc 9

<210> 553
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 553
Gly Ala Ser
1

<210> 554
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 554
cagcagtatg gttacccacc galcacc 27

<210> 555
<211> 9
<212> PRT
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<220>
<223> Synthetic

<400> 555
Gln Gln Tyr Gly Tyr Ser Pro Ile Thr
1 5

<210> 556
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
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<400> 556
gaaglgcagc lggcagtc tggggaggc gtggccagc ctgggaggcc cctgagactc 60
tccgtacag cgctcgat cacccatcg agctalgcctt tgactgggt ccggccaggct 120
ccaggcaagg ggcctggatgt ggtggcagtt atalggatgt atggaaatgtttaaaaactat 180
gcagaccccg tgaaggggcccg attcacccalc tccagagaca attccaagaa cacacgttat 240
ctgcaagtgtt acagccgttgc agccggaggac acggctgttattacgttgttgc gagagatcac 300

gatttttgcatgggtatgcgggggggttcgaccggcggggacccgggcacc 360
gtctctca 369

<210> 557
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 557
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 Thr Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Ala Met Tyr 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 Asn 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 Val Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp His Asp Phe Leu Ser Gly Tyr Glu Gly Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 558
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 558
ggattcaccttcaggtagctatgcc 24

<210> 559
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 559
Gly Phe Thr Phe Ser Ser Tyr Ala
1 5

<210> 560
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 560
atatggta lg alggaagtaa taaa

24

<210> 561
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 561
Ile Trp Tyr Asp Gly Ser Asn Lys
1 5

<210> 562
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 562
gogagagalc acgattttl gagtggtta gagggggggt tcgacccc 48

<210> 563
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
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<400> 563
Ala Arg Asp His Asp Phe Leu Ser Gly Tyr Glu Gly Trp Phe Asp Pro
1 5 10 15

<210> 564
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 564
gaaatttgtgc tgactcagtc tccagccacc ctgtcttgc tccccaggga aagagccacc 60
ctctctctgca gggccagtcgca gagtggttagl agtctacttag octggtagcca acagaaacct 120
ggccaggcgc ccaggcgcct catctalgtat gca tccaaaca gggccacagg catcccgacc 180
aggltcaglg gcaglggggc tgggacagac ttcaclcica ccatcgatag ccctagagcc 240
gaagatttlg cagttatata ctgtcagcaa cgtaccaact ggcccccac ttccggcgga 300
gggacccaaag lggatataa a 321

<210> 565
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 565
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro
85 90 95
Thr Phe Gly Gly Thr Lys Val Asp Ile Lys
100 105

<210> 566
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 566
cagaglgtta glagatac 18

<210> 567
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 567
Gln Ser Val Ser Ser Tyr
1 5

<210> 568
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 568
gatgcabcc 9

<210> 569
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 569
Asp Ala Ser
1

<210> 570
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 570
cagcaacgta gcaacggcc tccact 27

<210> 571
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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<400> 571
Gln Gln Arg Ser Asn Trp Pro Pro Thr
1 5

<210> 572
<211> 375
<212> DNA
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<220>
<223> Synthetic

<400> 572
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tcctgcagg ctctgttttacc acctatggta tcacctgggt gogacagggc 120
ccggacaagg ggcttgatgg galggatgg atcagcgctt tcaalgggtt cacaacacil 180
gcacagaacc tccagaacag aglccacctg accacagaca calccacag cacagccat 240
alggaaactga ggagccgtgg atcgtacgac acggccgttt attacgttgt gagaggggg 300
ggagctcgcc cggggaactt ctcttctac ggtatggatc tctggggcca ggggaccacg 360
glcaccggctt cccta 375

<210> 573
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 573
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Asn Pro Gly Ala
1 5 10 15
Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Tyr

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

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

<220>
<223> Synthetic

<400> 574
ggttacacct taccaccta tggt 24

<210> 575
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 575
Gly Tyr Thr Phe Thr Thr Tyr Gly
1 5

<210> 576
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 576
atcagcgctt tcaalggta caca 24

<210> 577
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 577
Ile Ser Ala Phe Asn Gly Asp Thr
1 5

<210> 578
<211> 54
<212> DNA
<213> Artificial Sequence

<220>
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<400> 578
gctgagagggg gaggagcgc tccggggaaac ttcttttctt acggtaatgg cgtc 54

<210> 579
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 579
Ala Arg Gly Gly Ala Arg Pro Gly Asn Phe Phe Phe Tyr Gly Met
1 5 10 15
Asp Val

<210> 580
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 580
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cttcctcgta gggccatgtca gagtttgtcc agttaatgtt cttggatcca acatggaaacct 120
ggccagggttc ccaggccctt catctatgtt acctccatca gggccacgtgg cgtccccagcc 180
aggttcgttg gcaglgggttc tgggacacgac ttcaatctca acatcagccaa cctggagcc 240
gaagattttt cagtttata ctgtcagccaa cgtggcaact ggccgttcac ttccggcgtt 300
gggacccaaagg tggaaaatcaa a 321

<210> 581
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
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<400> 581
Asp Val Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Phe Ala Ser Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Asp Thr Ser Tyr Arg Ala Thr Gly Val Pro Ala Arg Phe Ser Gly
50 55 60

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

<210> 582
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 582
cagaglltg ccagclac 18

<210> 583
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 583
Gln Ser Phe Ala Ser Tyr
1 5

<210> 584
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 584
galacotcc 9

<210> 585
<211> 3
<212> PRT
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<220>
<223> Synthetic

<400> 585
Asp Thr Ser
1

<210> 586
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 586
cagcaacgtg gcaactggcc gtcacat

27

<210> 587
<211> 9
<212> PRT
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<220>
<223> Synthetic

<400> 587
Gln Gln Arg Gly Asn Trp Pro Leu Thr
1 5

<210> 588
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
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<400> 588
caggcgccgc tggcgccgtc tggaactggg gtgaagaaggc cggggccctc agtggaaaggcc 60
tcctgcggcagg ctctggta cacctttggc tacaatgggtt tcaactgggtt acggacaggcc 120
ccggacaaag ggcttgagtg galggatgg alcagcgctt acggatggtaa cacagaaat 180
gcacagaatgt tccaagacag aalcaccalgt accacagaca calccacgag tacagccatc 240
tggaacatgtt ggagcccttag alcgtacgtc acggccgtctt attacgtgc gaggtatagt 300
tggaacaaacc aclggttgc cccctgggc caggaaaccc tggcacccgt ctccatc 357

<210> 589
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 589
Gln Val Gln Leu Val Gln Ser Gly Thr Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Tyr Asn
20 25 30
Gly Val Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asp Gly Asn Thr Asp Tyr Ala Gln Lys Phe
50 55 60
Gln Asp Arg Ile Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Ser Trp Asn Asn His Trp Phe Asp Pro Trp Gly Gln Gly
100 105 110
Thr Leu Val Thr Val Ser Ser
115

<210> 590
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 590
ggtaacacct ttagctacaa tggt 24

<210> 591
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 591
Gly Tyr Thr Phe Ser Tyr Asn Gly
1 5

<210> 592
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 592
atcagcgctt acgatggtaa caca 24

<210> 593
<211> 8
<212> PRT
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<220>
<223> Synthetic

<400> 593
Ile Ser Ala Tyr Asp Gly Asn Thr
1 5

<210> 594
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 594
gcgaggtaata gtttggaaacaa ccactggttc gacccc 36

<210> 595

<211> 12
<212> PRT
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<220>
<223> Synthetic

<400> 595
Ala Arg Tyr Ser Trp Asn Asn His Trp Phe Asp Pro
1 5 10

<210> 596
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 596
gatattgtga tgactcagtc tccaggcacc cgttcttgc tccaggaga cggggccacc 60
cttcctcgca gggccatca gagtgttcc ggcagctact lagctggta ccagcagaaa 120
cclggccagg ctccccaggct cccatcttgc acaggggcacat tggcatccca 180
gacagggtca ctggcagtgg gtcggaca gacttcaclc taccatcag cagactggag 240
cclgaagat ttgcagtgtat ttcgtcag cagagtgtt ttcacccgtg gacgttcggc 300
caagggacca agcggagat caaa 324

<210> 597
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 597
Asp Ile Val Met Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Asp Gly Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Gly 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 Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Thr
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 Phe Cys Gln Gln Ser Ala Phe Ser Pro
85 90 95
Trp Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 598
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 598
cagagtgtt cccggcaggta c

21

<210> 599
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 599
Gln Ser Val Ser Gly Ser Tyr
1 5

<210> 600
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 600
ggtgccatcc 9

<210> 601
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 601
Gly Ala Ser
1

<210> 602
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 602
cagcagtagtgc tttttcacc gggacg 27

<210> 603
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 603
Gln Gln Ser Ala Phe Ser Pro Trp Thr

176

1 5

<210> 604
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 604
gaagtgca gggcaggc tggcacgc ctggggggc cctgagac 60
tccatgtc ag cctctggatt cacccatcgat atgtacgaca tgcaatgggt ccgc ccaact 120
ataggaaatgg gtcggaglg ggttcagca atggtaatcg cttggacac atataatcca 180
ggcccgatg aggccgatg caccatctcc agagaaaaatg ccaagaactc ctgtttttt 240
caaalgaaca gcctgagagc cggggacacg gctgtttttt actgttgtaa atccggact 300
acagatggg tccatgtc gggccaggga accccggtaa ctgttcclca a 351

<210> 605
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 605
Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Met Tyr
20 25 30
Asp Met His Trp Val Arg Gln Thr Ile Gly Lys Glu Leu Glu Trp Val
35 40 45
Ser Ala Ile Gly Thr Ala Gly Asp Thr Tyr Tyr Pro Gly Ser Val Lys
50 55 60
Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser Leu Phe Leu
65 70 75 80
Gln Met Asn Ser Leu Arg Ala Gly Asp Thr Ala Val Tyr Tyr Cys Val
85 90 95
Arg Ser Gly Thr Thr Glu Trp Phe Asp Pro Trp Gly Gln Gly Thr Pro
100 105 110
Val Thr Val Ser Ser
115

<210> 606
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 606
ggatccatccatgtatcgat cgtac 24

<210> 607
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 607
Gly Phe Thr Phe Ser Met Tyr Asp
1 5

<210> 608
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 608
altggtaclg ctggtgacac a 21

<210> 609
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 609
Ile Gly Thr Ala Gly Asp Thr
1 5

<210> 610
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 610
glaagatcccg ggaclacaga ggggttcgac acc 33

<210> 611
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 611
Val Arg Ser Gly Thr Thr Glu Trp Phe Asp Pro
1 6 10

<210> 612
<211> 321
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthelic

<400> 612

gacalccggc tgaccaggc tccalcgtcc ggctgtccat ctgtgggaga cagagtcacc 60
atcacitgcg ggacgagtcg gggatattgt agctggtagt cctggatca gcagaaacca 120
ggaaaagccc taaacctct galctatgtc gacccatgtt taaaaatgtgg ggtccatca 180
aggttcagcg gcatggatc tggacatcgat tcacatca ccatcagcag ccgtcagcc 240
gaagatttg caacttacta ttttttttttccatcag gctaaccatgttccatc 300
gggaccaagg tggatcaaa a 321

<210> 613

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthelic

<400> 613

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

<210> 614

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 614

caggatata gtagatgg 18

<210> 615

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthelic

<400> 615

Gln Gly Ile Ser Ser Trp

1 5

<210> 616
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 616
gttgttttttccccc

9

<210> 617
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 617
Ala Ala Ser
1

<210> 618
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 618
cttacaggatca acatgtttcccc glacactt

27

<210> 619
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 619
Leu Gln Ala Asn Ser Phe Pro Tyr Thr
1 5

<210> 620
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 620
caggcccgcc tgggtgcagtc tggggggaggc ggggtccagc cggggaggcc octgagaccc 60
tccgtgtcggc cgttgtggatt cacccttcagg tggtaaggca tgcacgtgggtt ccgcgcaggct 120
ccaggccaaagg gggtggggatgtt gggtggcaggtt ttatggatgtt alggaaagttaa taaaatcat 180
gttagaccccg tgaaggggcgg attcaccatc tcaagagaca allccaagaa cacgccttat 240

ctgaaatga acagccgtgg agccggaggac acggctgtgt aatatgtgc gagagatcat 300
gattttagga gtggatgtga ggggtggttc gacccttggg gccaggaaac cctggtcacc 360
glcgcctca 369

<210> 621
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthe

<400> 621
 Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30
 Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ala Val Leu Trp Tyr Asp Gly Ser Asn Lys Asn 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 Arg Asp His Asp Phe Arg Ser Gly Tyr Glu Gly Trp Phe Asp Pro
 100 105 110
 Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 622
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 622
ggatccaccl lcaqlaqta lqqc

<210> 623

<211> 0
<212> PRT
<213> Artificial Sequence

<223> Synthetic

<400> 623
Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

<210> 624
<211> 24
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 624
Matqatalq atqqaaglaa laaa

24

<210> 625
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 625
Leu Trp Tyr Asp Gly Ser Asn Lys
1 5

<210> 626
<211> 48
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 626
ccqaqaqatc atqaltttag gatgttgtt gaggggatgt tcgacccc 48

<210> 627
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 627
 Ala Arg Asp His Asp Phe Arg Ser Gly Tyr Glu Gly Trp Phe Asp Pro
 1 5 10 15

<210> 628
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 628
 gaaatlgc lgacgcaglc lccagccacc ctgttcgtl clccagggg aagagccacc 60
 ctctcclrgca gggcccgaglca gagtgtlrcg agctacttag cctgglacca acagaaaacct 120
 ggccaggcgc ccaggcclct calctatgtat gcatccaaca gggccactgg catccccagcc 180
 aggitcaglg gcagtgggtc lgggacagac ttcactclca ccalcagcg octagagct 240
 gaagatttg caglttata cglcaacac cglagcaact ggcclccac ttccgggga 300
 gggaccaaqg lgaaalcaa a 321

<210> 629
<211> 107
<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 629

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

<210> 630

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 630

cagaglgltc gcagctac 18

<210> 631

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 631

Gln Ser Val Arg Ser Tyr

1 5

<210> 632

<211> 9

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 632

galgcalcc 9

<210> 633

<211> 3

<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic

<400> 633

Asp Ala Ser

1

<210> 634
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 634

caacaccgta gcaacggcc tccccat

27

<210> 635
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 635

Gln His Arg Ser Asn Trp Pro Pro Thr

1 5

<210> 636
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 636

caggtaacat tgaaggagtc gggcccgagga ctggtaaaat cttccggagac ccgttccctc 60
acttgtcacat tctctacatgg cccatccatgc aatgttagttt aatcatgggc ctggatccgc 120
cagccccccat ggaaggggact ggagtggattt gggatgtatcl atatagatgg gagtaaaatlc 180
tacagcccccgtt ccctcaagatg tgagtcacc atatacgatgg acacgtccaa gaatcgttcc 240
tccccgtcaac tgagtcgtgtt gacccgtccat gacacggctg tataatgt tgccgagacag 300
gtccggtgccaa ttttacta ctggggccat ggaaccttgg tccatcgatc ctc 354

<210> 637
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 637

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

1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Thr Gly Ser Ile Ser Ser Ser

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

<210> 638

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 638

acggcgccca tcagcagtag lagttaactac

30

<210> 639

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 639

Thr Gly Ser Ile Ser Ser Ser Ser Tyr Tyr

1 5 10

<210> 640

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 640

atclattala glgggaglaa a

21

<210> 641

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 641

Ile Tyr Tyr Ser Gly Ser Lys

1 5

<210> 642
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 642
gogagacagg tcggcgaaat ctttgactac 30

<210> 643
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 643
Ala Arg Gln Val Gly Ala Ile Phe Asp Tyr
1 5 10

<210> 644
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 644
gccatccgt tgaccgcgc lccctccacc cggcgcgcgc ctgttaggaga cagagtcacc 60
atcctgtcc gggcccgatca gagtattagl agtgggtgg cctggatca gcacaaacca 120
gggaaagccc ctaaacccctc gctctataag gogtcagat tagaaazggg ggtcccatca 180
aggitcagcg gcaatggatc tgggacagag ttcaatcata ccatcagcag cctgcagcc 240
galgatlttg caacttataa cggccaaacag tataatagt atttcggac gtcggccaa 300
gggaccaagg tggagatcaa a 321

<210> 645
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 645
Ala Ile Arg Leu Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
20 25 30
Leu Ala Trp Tyr Gln His Lys Pro Gly Lys Ala Pro Lys Leu Leu Leu
35 40 45
Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

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

<210> 646
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 646
cagagtatata gtagttgg 18

<210> 647
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 647
Gin Ser Ile Ser Ser Trp
1 5

<210> 648
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 648
aaggcgct 9

<210> 649
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 649
Lys Ala Ser
1

<210> 650
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 650
caacagtala alagtttcc tggacg

27

<210> 651
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 651
Gln Gln Tyr Asn Ser Tyr Ser Arg Thr
1 5

<210> 652
<211> 372
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 652
gaggcgccgc tggcgcgc tggagctgag gigaagaagc cggggccgc aglgaaggcc 60
cccgcaagg ccctcggtta cacctttaac atctatggta tcagctgggt acgacaggcc 120
ccggacaag ggcttgaglg galgggalgg atcagcgctt acaaattgtaa cacaaactat 180
gcacagaaac tccaggcccg aglaccalal accacagaaa catccacgac cacagcciac 240
atggatgtga ggagccctgag alcgaecac acggccglll attactglc gagagattct 300
gatggggaa ctccctacca ctatcggt atggacgtcl ggggccaagg gaccacggcc 360
accgtctt ca 372

<210> 653
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 653
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn Ile Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Glu Thr Ser Thr Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Ser Asp Trp Gly Thr Pro Tyr His Tyr Tyr Gly Met Asp
100 105 110
Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 654
<211> 24
<212> DNA
<213> Artificial Sequence

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1 5

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<210> 659
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<400> 659

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<210> 660

<211> 339

<212> DNA

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<400> 660

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tggtaaccgc agaaaaccagg acagccctct aagcctgtca ttactggc atttacccgg 180
aaatccgggg lccclgaccg attcaglggc aeggggtctg ggacagallt caccttacc 240
atcagcagcc tgcaggctga agatglggca gtttatact gtcaagcaata ttataatact 300
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<400> 661

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

20 25 30

Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln

35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Phe Thr Arg Lys 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 Asn Thr Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Asp Ile

100 105 110

Lys

<210> 662

<211> 36

<212> DNA

<213> Artificial Sequence

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36

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<400> 663
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1 5 10

<210> 664
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<212> DNA
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<220>
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<400> 664
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<210> 665
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<400> 665
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27

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Gln Gln Tyr Tyr Asn Thr Pro Arg Thr
1 5

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acccgtca ctgcgttgcg ctccalcaac agtgggtgggt ctactggag ctggatccgc 120
caycaccgg ggaaggggctt ggaglggattt gggtacatca aalacaglgg gggcg tccac 180
lalaacccgl ccccaaggag logaaalcacc atatcaglgg acacgtctaa gaaccatttc 240
tccctgaaaaa tgacclctgt gaclgcgcg gacacggccg tglatttcgt tgccgagagca 300
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<210> 669
<211> 119
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<220>
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<400> 669
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1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Asp Gly Ser Ile Asn Ser Gly
20 25 30
Gly Ser Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Tyr Ile Lys Tyr Ser Gly Gly Val His Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Ile Thr Ile Ser Val Asp Thr Ser Lys Asn His Phe
65 70 75 80
Ser Leu Lys Met Thr Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Phe
85 90 95
Cys Ala Arg Ala Pro Gly Ser His Thr Phe Asp Ile Trp Gly Gln Gly
100 105 110
Thr Met Val Thr Val Ser Ser
115

<210> 670
<211> 30
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<220>
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<211> 10
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<400> 671
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<210> 672
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<400> 672
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<400> 673
Ile Lys Tyr Ser Gly Gly Val
1 5

<210> 674
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<400> 674
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<400> 675
Ala Arg Ala Pro Gly Ser His Thr Phe Asp Ile
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<210> 676

<211> 324
<212> DNA
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<400> 676
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cttcctcgca gggccatcgaa gagtgttagc aacaactact tagccctggta ccaggcagaaa 120
cttggccagg ctccccagact cctccalcat ggtacatcca alaggglcag tggccatcca 180
gacagggtca gggcaglgg gtcgggaca gacttcactc tcaccalcag cagaclggag 240
ccctgaagatt ttaactata ttatgtcag caglalagta ggtcaccgal caccttcggc 300
caagggacac gacggagal laaa 324

<210> 677
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
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<400> 677
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1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Asn Asn
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 Thr Ser Asn Arg Val Ser 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 Glu Leu Tyr Tyr Cys Gln Gln Tyr Ser Arg Ser Pro
85 90 95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 678
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<400> 678
cagagtgtca gcaacaacta c 21

<210> 679
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<220>
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<400> 679
Gln Ser Val Ser Asn Asn Tyr

1 5

<210> 680
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<220>
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<400> 680
ggcacatcc 9

<210> 681
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<400> 681
Gly Thr Ser
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<210> 682
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<400> 682
cagcaglata gtaggtcacc galcacc 27

<210> 683
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<400> 683
Gln Gln Tyr Ser Arg Ser Pro Ile Thr
1 5

<210> 684
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<400> 684
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ccagggaaagg ggcgtggatgtt ggclcaactt attaaglggla glggcgttga cacalactgc 180
gcagaclcgg lgaagggccg gtcaccalc tccagagaca attccaagaaa cacactgtat 240
ctgcaaaalga acagccgttag agccgtggggac acggccglal attiaclgtgc gaaagalggc 300
gccttcataa gtggcclaaga acaclactgg ggcccgaggaa caatggcaca cgttcctca 360

<210> 685
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<400> 685
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 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Asn Phe
 20 25 30
 Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Thr Ile Ser Gly Ser Gly Val Asp Thr Tyr Cys 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 Asp Gly Ala Phe Tyr Ser Gly Tyr Glu His Tyr Trp Gly Gln
 100 105 110
 Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 686
<211> 24
<212> DNA
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<400> 686
ggattcacct ttaacaacctt tgcc 24

<210> 687
<211> 8
<212> PRT
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<220>
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<400> 687
Gly Phe Thr Phe Asn Asn Phe Ala
1 5

<210> 688
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<400> 688

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24

<210> 689

<211> 8

<212> PRT

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<220>

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<400> 689

Ile Ser Gly Ser Gly Val Asp Thr

1 5

<210> 690

<211> 39

<212> DNA

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39

<210> 691

<211> 13

<212> PRT

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<220>

<223> Synthetic

<400> 691

Ala Lys Asp Gly Ala Phe Tyr Ser Gly Tyr Glu His Tyr

1 5 10

<210> 692

<211> 324

<212> DNA

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<220>

<223> Synthetic

<400> 692

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cttggccagg ctccccaggct ctccatcttca gglacatccca acaggggctc lggcalccca 180
gacaggctca ttggcaglgg gtcgggaca gacticacic tcacccatcg cagactggag 240
tcgtaaatgtt tgcagtgtt ttacgttcag caglatggta gtcacctcg gacgttcggc 300
caagggacca aagtggatc caaa 324

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<211> 108
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<220>
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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 Thr Ser Asn Arg Ala Ser Gly Ile Pro Asp Arg Leu Ile
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95
Arg Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
100 105

<210> 694
<211> 21
<212> DNA
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<400> 694
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<210> 695
<211> 7
<212> PRT
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<220>
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<400> 695
Gln Ser Val Ser Ser Ser Tyr
1 5

<210> 696
<211> 9
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<400> 696
ggtacatcc 9

<210> 697

<211> 3
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<220>
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<400> 697
Gly Thr Ser
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<210> 698
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<400> 698
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27

<210> 699
<211> 9
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<400> 699
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1 5

<210> 700
<211> 363
<212> DNA
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<220>
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<210> 701
<211> 121
<212> PRT
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<220>
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<400> 701
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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 Met 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 Ala Tyr Asp Ile Leu Ile Gly Tyr Ser Pro Val Asp Tyr Trp Gly
100 105 110
Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 702
<211> 24
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<400> 702
ggaltcaccl tcaglaglaa tgcc 24

<210> 703
<211> 8
<212> PRT
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<220>
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<400> 703
Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

<210> 704
<211> 24
<212> DNA
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<220>
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<400> 704
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<210> 705
<211> 8
<212> PRT
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<220>
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<400> 705
Ile Trp Tyr Asp Gly Ser Asn Lys
1 5

<210> 706
<211> 42
<212> DNA
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<400> 706
gccccatcgc atatllgtat tggttatcc ccgggttact ac 42

<210> 707
<211> 14
<212> PRT
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<400> 707
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1 5 10

<210> 708
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ggccaggctc ccagactctt cacltalgtat gcatccacca gggccacgg latccccagcc 180
aggtcagtg gcaglgggtc tggcacagaa ttcacgtca ccacgacgag ccgtcgatct 240
gaagatttg caglllattt ctgtcagcag lataataact ggtacacitl tgccagggg 300
accaagctgg agatcaaa 318

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<400> 709
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1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Thr Val Ser Ser Asn
20 25 30
Leu Ala Trp Phe Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

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

<210> 710
<211> 18
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<400> 710
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<210> 711
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<400> 711
Gln Thr Val Ser Ser Asn
1 5

<210> 712
<211> 9
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<220>
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<400> 712
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<210> 713
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<400> 713
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<210> 714
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<210> 718
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<400> 718
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<210> 719
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<400> 719
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<210> 720
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<400> 720
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<210> 721
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<400> 721
 Ile Lys Phe Ser Gly Asn Thr
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<210> 722
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<220>
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<400> 722
 gogagagcac cggaaagtca taacttgac atc 33

<210> 723
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<400> 723
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1 5 10

<210> 724
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<212> DNA
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<400> 724
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cttccttgca gggccaglgl gagttatgtt aalaacttta tagectggta ccagcagaaa 120
ccggccagg ctcccaggcl octcatclat ggfcatcca gcagggccac lggcatccca 180
gacagggtca gllggcaglgg gtcggaca gacttcaclt tcaccalca gaaactggag 240
lclgcagatt tlgcaccgta ttactgtcag caatalagta ggtcaccgat caccttcggc 300
caagggacac gaclggagat taaa 324

<210> 725
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
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<400> 725
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1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Val Ser Ile Ser Asn Asn
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 Arg Arg Leu Glu
65 70 75 80
Ser Ala Asp Phe Ala Pro Tyr Tyr Cys Gln Gln Tyr Ser Arg Ser Pro
85 90 95
Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 726
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<223> Synthetic

<400> 726

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21

<210> 727

<211> 7

<212> PRT

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Val Ser Ile Ser Asn Asn Tyr

1 5

<210> 728

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<400> 728

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<210> 729

<211> 3

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Gly Ala Ser

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27

<210> 731

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<400> 731
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1 5

<210> 732
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 cagccacccagg ggagggggct agagtggtt gggtaatcaaaatcaggg gagcacctac 180
 tacaacccogl ccclcaaggg togagtccacc alatcagttgg acacgjctaa gaaccaatlc 240
 lcccttaaaa ttacilclgl gaclgcccg gacacggccg lglttlaclg lgcgagagcl 300
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<400> 733
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 20 25 30
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 35 40 45
 Trp Ile Gly Tyr Ile Lys Phe Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
 50 55 60
 Leu Lys Gly Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Ser Leu Lys Ile Asn Ser Val Thr Ala Ala Asp Thr Ala Val Phe Tyr
 85 90 95
 Cys Ala Arg Ala Ser Gly Ser His Thr Phe Asp Ile Trp Gly Gln Gly
 100 105 110
 Thr Met Val Thr Val Ser Ser
 115

<210> 734
<211> 30
<212> DNA
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<400> 734
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<210> 735
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<212> PRT
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<400> 735
Gly Gly Ser Ile Asn Ser Val Thr Tyr Tyr
1 5 10

<210> 736
<211> 21
<212> DNA
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<220>
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<400> 736
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<210> 737
<211> 7
<212> PRT
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<220>
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<400> 737
Ile Lys Phe Ser Gly Ser Thr
1 5

<210> 738
<211> 33
<212> DNA
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<220>
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<400> 738
gcgagaggctt cggaaaglca tacttttgat alc 33

<210> 739
<211> 11
<212> PRT
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<220>
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<400> 739
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1 5 10

<210> 740
<211> 324

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<220>
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<400> 740

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 ctgtggcagg ctccccggct ctccatctct ggtgggtccca gcagggtcac lggcatccca 180
 gacagggtca gttggcaglgg gtcgtggaca gacttcactc tcaccatcag cagactggag 240
 cctgtggatgttggaaalgltaa ttagtgcag caglatagta ggltcacatgat caccatcggtc 300
 caaggggacca agctggatgat caaa 324

<210> 741

<211> 108

<212> PRT

<213> Artificial Sequence

220

<223> Synthetic

<400> 741

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

<210> 742

2112 21

<212> DNA

<213> Artificial Sequence

3202

<223> Synthetic

<400> 742

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21

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<220>

<223> Synthetic

<400> 743

Gln Ser Val Ser Asn Ser Tyr

1 5

<210> 744
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<400> 744
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<210> 745
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<400> 745
Gly Ala Ser
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<211> 27
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<220>
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<400> 746
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<210> 747
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<220>
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<400> 747
Gln Gln Tyr Ser Arg Ser Pro Ile Thr
1 5

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ccagggaaagg ggcgggaglg ggllcaagt attagtgga atatggtag tataggctat 180
gcggactcg tgaaggggccg ctccaccatc tccagagaca acggcaagaa ctcctgtat 240
tgcggaaatga acatcgagc agcgaggac acggccctgtt atacatgc aaaagatggg 300
tggaaaccgtt actatcgatc ctatgggc caggaaataa cgglcaccgtt ctccatca 357

<210> 749
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<212> PRT
<213> Artificial Sequence

<220>
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<400> 749
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 Val Thr Leu Asp Asp Tyr
20 25 30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Leu Glu Trp Val
35 40 45
Ser Ser 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 Gly Trp Asn Pro Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly
100 105 110
Ile Thr Val Thr Val Ser Ser
115

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<220>
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<400> 750
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<210> 751
<211> 8
<212> PRT
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<220>
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<400> 751
Gly Val Thr Leu Asp Asp Tyr Ala
1 5

<210> 752
<211> 24
<212> DNA
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<220>
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<400> 752
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<210> 753
<211> 8
<212> PRT
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<220>
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<400> 753
Ile Ser Trp Asn Ser Gly Ser Ile
1 5

<210> 754
<211> 36
<212> DNA
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<220>
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<400> 754
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<210> 755
<211> 12
<212> PRT
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<220>
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<400> 755
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1 5 10

<210> 756
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
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<400> 756
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gggaaagccc ttaagcgcc t gatctatgtt gcaatccgtt tgcaaagggg ggloccatca 180
aggttcagcg tcaglgggatc tgggacagaaa ttcaacttc caalcagcag ctgcagcc 240
gaagatting caacttattt ctgltctacag ctaataatgtt acoccttcac ttccggcgga 300
gggaccaagg tggaaaatcaa a 321

<210> 757
<211> 107

<212> PRT
<213> Artificial Sequence

<220>
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<400> 757
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1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Ser 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 Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 758
<211> 18
<212> DNA
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<220>
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<400> 758
cagggccat ta gaaggat 18

<210> 759
<211> 6
<212> PRT
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<220>
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<400> 759
Gln Gly Ile Arg Ser Asp
1 5

<210> 760
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 760
gc tgca tcc 9

<210> 761
<211> 3
<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 761

Ala Ala Ser

1

<210> 762

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 762

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27

<210> 763

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 763

Leu Gln His Asn Ser Tyr Pro Leu Thr

1 5

<210> 764

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 764

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acctgcgcgg tctctggtga ctccttcggc agtggtaatt acatcggtt cggatccgc 120
caacaccagg ggaaggggctt ggaglggatt ggglacatca agtacacatgg gagcacctac 180
tacaacccgtt ccctcaagag tcgagtattt alatttagtag acacgtctaa gacccaggc 240
tcctgttttttgc tgagtcgttgc gacacggcccg tggatcatgc tgctgagagca 300
cctggaaactt aatgttttgc tggatggggc caagggacaa tggtcaccgtt ctcctca 357

<210> 765

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 765

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

1 5 10 15

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

<210> 766
<211> 30
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<220>
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<400> 766
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<210> 767
<211> 10
<212> PRT
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<220>
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<400> 767
Gly Asp Ser Phe Ser Ser Gly Asn Tyr Tyr
1 5 10

<210> 768
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 768
alcaagtaca ctgggaggcac c 21

<210> 769
<211> 7
<212> PRT
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<220>
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<400> 769
Ile Lys Tyr Thr Gly Ser Thr

1 5

<210> 770
<211> 33
<212> DNA
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<220>
<223> Synthetic

<400> 770
gcgagagcac ctggaaatca lgcatttgat gtt 33

<210> 771
<211> 11
<212> PRT
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<220>
<223> Synthetic

<400> 771
Ala Arg Ala Pro Gly Thr His Ala Phe Asp Val
1 5 10

<210> 772
<211> 324
<212> DNA
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<220>
<223> Synthetic

<400> 772
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cttcctcgca gggccagtcgca gaglgttagc aglagctact tagctggta ccagcagaaaa 120
cctggccagg ctccccggctt ccttcataat gggtcatccca gcagggccac tggcatccca 180
gacaggltca gtggcagtgg gtcgtgaca gaclccactc tcaccalca cagoctggag 240
cctgaagat ttcgtcgatc caglalagta gglcaccat caccttcggc 300
caagggacca agcggatc caaa 324

<210> 773
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
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<400> 773
Glu Thr Thr Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Phe 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 Val Thr Asp Ser Thr Leu Thr Ile Ser Ser Leu Glu

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

<210> 774
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 774
caaaatgtttt acaatgttgc tttttttttt c 21

<210> 775
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
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<400> 775
Gln Ser Val Ser Ser Ser Tyr
1 5

<210> 776
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
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<400> 776
gglgcatacc 9

<210> 777
<211> 3
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<220>
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<400> 777
Gly Ala Ser
1

<210> 778
<211> 27
<212> DNA
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<220>

<223> Synthetic

<400> 778

cagcaglala gtaggtcacc galcacc

27

<210> 779

<211> 9

<212> PRT

<213> Artificial Sequence

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<223> Synthetic

<400> 779

Gln Gln Tyr Ser Arg Ser Pro Ile Thr

1 5

<210> 780

<211> 360

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 780

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ccagggaaagg gcctggagtg ggtctcaact attaglgglia gllggcgltga cacalaclc 180
gcagactccg tgaagggcccgttgcaccatc tccagagaca attccaaagaa cacactgtat 240
ctgcaaalgaa acagccctgag agccgaggac acggccgtat attacgttc gaaagaalggc 300
gcclclata gtggctacga acaclaclgg ggccaggaa ccacggltcac cgclccclca 360

<210> 781

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 781

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

1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Asn Phe

20 25 30

Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

35 40 45

Ser Thr Ile Ser Gly Ser Gly Val Asp Thr Tyr Cys 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

Ser Lys Asp Gly Ala Phe Tyr Ser Gly Tyr Glu His Tyr Trp Gly Gln

100 105 110

Gly Thr Thr Val Thr Val Ser Ser

115 120

<210> 782
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
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<400> 782
ggatccacctttaacaactttgcc 24

<210> 783
<211> 8
<212> PRT
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<400> 783
Gly Phe Thr Phe Asn Asn Phe Ala
1 5

<210> 784
<211> 24
<212> DNA
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<220>
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<400> 784
attagggta gtggcggtga caca 24

<210> 785
<211> 8
<212> PRT
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<220>
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<400> 785
Ile Ser Gly Ser Gly Val Asp Thr
1 5

<210> 786
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 786
tcgaaagatgcgccttcta taglggctac gaacactac 39

<210> 787

<211> 13
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<400> 787
Ser Lys Asp Gly Ala Phe Tyr Ser Gly Tyr Glu His Tyr
1 5 10

<210> 788
<211> 324
<212> DNA
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<400> 788
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cttcctcgca gggccagtcg gagtgttcgc agcagcatac tagctggta ccagcagaaaa 120
ccctggccagg ctcccgatgtt cccatctat ggtacatcca acagggcacac tggccatccca 180
gacagggttcg gllgcaglgg glcgggaca gacttcacac tcaccatcg cagaclggag 240
tctgaatgtt tggcagtgtla ttactgtcag caglatggta gotcacctcg gacgttcggc 300
caaggacca aggllggat caaa 324

<210> 789
<211> 108
<212> PRT
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<220>
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<400> 789
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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 Thr Ser Asn 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
Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95
Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 790
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 790
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21

<210> 791
<211> 7
<212> PRT
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<220>
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<400> 791
Gln Ser Val Ser Ser Ser Tyr
1 5

<210> 792
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
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<400> 792
ggtaacatcc 9

<210> 793
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<220>
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<400> 793
Gly Thr Ser
1

<210> 794
<211> 27
<212> DNA
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<220>
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<400> 794
cagcgatgtg gtagtcacc tcggacg 27

<210> 795
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<220>
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<400> 795
Gln Gln Tyr Gly Ser Ser Pro Arg Thr

22 /

1 5

<210> 796
<211> 357
<212> DNA
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<220>
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<400> 796
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tccgtcaagg ctcctggta caccttacc taclalggta tcagtggat acgacagacc 120
ccctggacaag ggcttgaglg galgggalgg atcagcgctt acgatggtaa cacagactat 180
gcacagaagl lccaagacag aatcacccalgg accacagaca catcclogac cacagcciac 240
atggaaactga ggagccctgag atctgacgac acggccgtct attaclgc gaggtatagt 300
tggaaaca aac actggtcga cccctgggc caggaaacca tggtcaccgl ctctca 357

<210> 797
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 797
Glu Val Gln Leu Val Gln Ser Gly Pro Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Tyr Tyr
20 25 30
Gly Ile Ser Trp Ile Arg Gln Thr Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asp Gly Asn Thr Asp Tyr Ala Gln Lys Phe
50 55 60
Gln Asp Arg Ile Thr Met Thr Thr Asp Thr Ser Ser Thr Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Ser Trp Asn Lys His Trp Phe Asp Pro Trp Gly Gln Gly
100 105 110
Thr Met Val Thr Val Ser Ser
115

<210> 798
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 798
ggllacaccl ttacctacta tggt 24

<210> 799
<211> 8
<212> PRT
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<220>
<223> Synthelic

<400> 799
Gly Tyr Thr Phe Thr Tyr Tyr Gly
1 5

<210> 800
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 800
atcagcgctt acgatgglaa caca 24

<210> 801
<211> 8
<212> PRT
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<220>
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<400> 801
Ile Ser Ala Tyr Asp Gly Asn Thr
1 5

<210> 802
<211> 36
<212> DNA
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<220>
<223> Synthetic

<400> 802
gcgaggllata gttggaaacaa gcaclggtc gacccc 36

<210> 803
<211> 12
<212> PRT
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<220>
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<400> 803
Ala Arg Tyr Ser Trp Asn Lys His Trp Phe Asp Pro
1 5 10

<210> 804
<211> 324
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 804

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cctggccagg ctccccactt cccatcatat ggtgcattca acagggtcac tggcatccca 180
gacagggtca cggcaglgg gtctgggaca gacttcactt tcaccatcg cagaactggag 240
ccctgaagat ttgcagtgta ttcgtcaaa cagtctgtt ttcacccgtg gacgttccgc 300
caggggacca aggtggaaa caaa 324

<210> 805

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 805

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

<210> 806

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 806

cagagtgta ccggcagcta c

21

<210> 807

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 807

Gln Ser Val Thr Gly Ser Tyr

1 5

<210> 808
<211> 9
<212> DNA
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<220>
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<400> 808
gglgcatcc 9

<210> 809
<211> 3
<212> PRT
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<220>
<223> Synthetic

<400> 809
Gly Ala Ser
1

<210> 810
<211> 27
<212> DNA
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<220>
<223> Synthetic

<400> 810
caacagtcgt ctttcacc gggacg 27

<210> 811
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 811
Gln Gln Ser Ala Phe Ser Pro Trp Thr
1 5

<210> 812
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 812
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ccctgtcgac ccctcggtt caccctggat gatattggca tgcactgggt ccggcaatgt 120
ccatggaaagg gcctgggggg ggctcaatgt attatgttggaa alaglgggat tataggctat 180
ggggacgtcg lgaaggggccg cttccaccatc tccatggatc acggccaaatc ctcctgtat 240

cgcggaaalga acagtcgtgag agcgtgaggac acggccgtgl attacgttgtc aaaagatggg 300
tggaaaccgtl aclacattga ctatggggc caggaaalac cggtcacccgt ctctca 357

<210> 813
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 813
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1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Val Thr Leu 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 Ser 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 Gly Trp Asn Pro Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly
100 105 110
Ile Pro Val Thr Val Ser Ser
115

<210> 814
<211> 24
<212> DNA
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<220>
<223> Synthetic

<400> 814
ggagtccaccc tggatgalta tgcc 24

<210> 815
<211> 8
<212> PRT
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<220>
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<400> 815
Gly Val Thr Leu Asp Asp Tyr Ala
1 5

<210> 816
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<212> DNA
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<220>
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<400> 816
attagtggataggtag tata

24

<210> 817
<211> 8
<212> PRT
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<220>
<223> Synthetic

<400> 817
Ile Ser Trp Asn Ser Gly Ser Ile
1 5

<210> 818
<211> 36
<212> DNA
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<220>
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<400> 818
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<210> 819
<211> 12
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<220>
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<400> 819
Ala Lys Asp Gly Trp Asn Pro Tyr Tyr Phe Asp Tyr
1 5 10

<210> 820
<211> 321
<212> DNA
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<400> 820
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atcacitgcc gggcaagtca gggcattaga aglgatttag gcggatgtca gcagaaacca 120
gggaaaagccc claaatgcgtt gatctatgtt gcatccatgtt tgccaaatggg ggtttccatca 180
agglttcaggcg gcagggtggatc tgggacagaa ttccatctca caalccatcgatccatccatca 240
gaagatttt caacatattt ctgtatccatcgatccatcgatccatca acccttcac ttccggatggaa 300
gggatccatcgatccatca a 321

<210> 821
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
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<400> 821
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 Ser 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 Leu
85 90 95
Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 822
<211> 18
<212> DNA
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<220>
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<400> 822
caggccatla gaaglgal 18

<210> 823
<211> 6
<212> PRT
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<220>
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<400> 823
Gln Gly Ile Arg Ser Asp
1 5

<210> 824
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
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<400> 824
gtgtgcaccc 9

<210> 825
<211> 3
<212> PRT
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<220>
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<400> 825
Ala Ala Ser
1

<210> 826
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
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<400> 826
ctacaggata alaqltaccc tctact 27

<210> 827
<211> 9
<212> PRT
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<220>
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<400> 827
Leu Gln His Asn Ser Tyr Pro Leu Thr
1 5

<210> 828
<211> 357
<212> DNA
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<220>
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<210> 829
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
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<400> 829
 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 Val Ser Gly Asp Ser Phe Ser Ser Gly
 25 30 35

<210> 834
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 834
gcgagagcac cggaaacica tggtttgat gtc 33

<210> 835
<211> 11
<212> PRT
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<220>
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<400> 835
Ala Arg Ala Pro Gly Thr His Val Phe Asp Val
1 5 10

<210> 836
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 836
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cgcgcgcgc gggccaglca gaglgttagc agtagctat tagcccggle ccagcagaaaa 120
ccggccagg ctccccaggct cctcaactal ggllgcaccca gcagggccac lggcatccca 180
gacaggltca glggcagtgg gclglgaca gactcaact tcacccatcaag cagccolggag 240
cctgaagalt llgcaglgta ttaclgctag caglatagta ggltcacccat caccctggc 300
caagggacca aggtggagat caaa 324

<210> 837
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
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<400> 837
Asp Ile Gln Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Leu 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 Val Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu
65 70 75 80
Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Ser Arg Ser Pro

65 90 95
Ile Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 838
<211> 21
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<220>
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<400> 838
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<210> 839
<211> 7
<212> PRT
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<220>
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<400> 839
Gln Ser Val Ser Ser Ser Tyr
1 5

<210> 840
<211> 9
<212> DNA
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<220>
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<400> 840
ggtgtcatcc 9

<210> 841
<211> 3
<212> PRT
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<220>
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<400> 841
Gly Ala Ser
1

<210> 842
<211> 27
<212> DNA
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<220>
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<400> 842
cagcaglata gtaggtcaacc galcacc

27

<210> 843
<211> 9
<212> PRT
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<220>
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<400> 843
Gln Gln Tyr Ser Arg Ser Pro Ile Thr
1 5

<210> 844
<211> 363
<212> DNA
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<220>
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<400> 844
caggtgcagc tgcaggagtc gggcccagga ctggtaaagc cticacagac colgtccctc 60
acclgcactg lctctgggg cccatcagc aglggggtt aclacggag ttggatongc 120
cagcacccag ggaaggggctt ggagtggatt gggfacatcc atatacggtt gaacacccac 180
tacaatccoga ccccaagag tagaaatlacc atalcaglag acacglcaa gaaccagllc 240
tccccgggg lgaactctgl gaclgcggcg gacacggcccg tatactgt tgctggagaal 300
alggttcggg gagttcaactg gtcgaccccc tggggccagg gaaccacggt caccgttcc 360
tca 363

<210> 845
<211> 121
<212> PRT
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<220>
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<400> 845
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Tyr Ile His Tyr Ser Gly Asn Thr His Tyr Asn Pro Thr
50 55 60
Leu Lys Ser Arg Ile Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Glu Val Asn Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Arg Asn Met Val Arg Gly Val His Trp Phe Asp Pro Trp Gly
100 105 110
Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 846

<211> 30
<212> DNA
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<220>
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<400> 846
ggggctcca ttagcaglgg tggtaatcac 30

<210> 847
<211> 10
<212> PRT
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<220>
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<400> 847
Gly Gly Ser Ile Ser Ser Gly Gly Tyr Tyr
1 5 10

<210> 848
<211> 21
<212> DNA
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<220>
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<400> 848
atccattala gtgggaacac c 21

<210> 849
<211> 7
<212> PRT
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<220>
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<400> 849
Ile His Tyr Ser Gly Asn Thr
1 5

<210> 850
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
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<400> 850
gcgaggaaata tggtcgggg agttcaactgg ttcgacccc 39

<210> 851
<211> 13
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<213> Artificial Sequence

<220>

<223> Synthetic

<400> 851

Ala Arg Asn Met Val Arg Gly Val His Trp Phe Asp Pro

1 5 10

<210> 852

<211> 324

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 852

gaaalaglgl tgacacagtc tccaggcacc cglcittgl ctccaggggta gagagccacc 60
ctcltcgtt gggccaglcg gagtgttgc agcagctact lagcclggtt ccagcagaaaa 120
cclggccagg ctcccaaggctt cccatctt gglgcaccca gcagggccac tggcatcccc 180
gacaggltca gggcaglgg gtcgggaca gacttcactt tcaccatcag cagaclggag 240
cclgaaggatt ttgcagtata ttclglcaa cagtatagla gtlcaccgct cacttgcgc 300
ggagggacca agctggagal caaa 324

<210> 853

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 853

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 Phe Cys Trp Ala Ser Arg 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 Ser 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 Phe Cys Gln Gln Tyr Ser Ser Ser Pro
85 90 95

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

<210> 854

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 854

cggaglglta gcagcagctt a

<210> 855
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<212> PRT
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<220>
<223> Synthetic

<400> 855
Arg Ser Val Ser Ser Ser Tyr
1 5

<210> 856
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 856
ggtgcatcc 9

<210> 857
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 857
Gly Ala Ser
1

<210> 858
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 858
caacaglala glagttcacc gtcact 27

<210> 859
<211> 9
<212> PRT
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<220>
<223> Synthetic

<400> 859
Gln Gln Tyr Ser Ser Ser Pro Leu Thr
1 5

<210> 860
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<210> 861
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
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<400> 861
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 1 5 10 15
 Thr Leu Ser Leu Thr Cys Thr Val Ser Ser Asp Ser Ile Ser Ser Gly
 20 25 30
 Asn Asn Tyr Trp Thr Trp Ile Arg Gln His Pro Gly Arg Gly Leu Glu
 35 40 45
 Trp Ile Gly Tyr Ile Lys Tyr Thr Gly Ser Ala His Tyr Asn Pro Ser
 50 55 60
 Leu Lys Ser Arg Val Thr Met Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Ser Leu Lys Met Thr Ser Val Thr Asp Ala Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Ala Arg Ala Pro Gly Ser His Ser Phe Asp Ile Trp Gly Arg Gly
 100 105 110
 Thr Met Val Thr Val Ser Ser
 115

<210> 862
<211> 3D
<212> DNA
<213> Artificial Sequence

<220>
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<400> 662
actgacgacca |cggccgttgc taaaatcac 30

<210> 863
<211> 10
<212> PRT
<213> Artificial Sequence

52202

<223> Synthetic

<400> 863

Ser Asp Ser Ile Ser Ser Gly Asn Asn Tyr
1 5 10

<210> 864

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 864

atcaaalaca cggggagcgc c

21

<210> 865

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 865

Ile Lys Tyr Thr Gly Ser Ala
1 5

<210> 866

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 866

gcgaggcgcac cggaaagcca ttcgttgat ala

33

<210> 867

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 867

Ala Arg Ala Pro Gly Ser His Ser Phe Asp Ile
1 5 10

<210> 868

<211> 324

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 868

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cttcctgca gggccatgc gagtgttagc agcagctact tagectggta ccagcagaaa 120
cctggccagg ctccccaggct cctccatcat gggtcatcca gcagggccac tggcatccca 180
gacaggtca gtggcagtgg gtctggaca gacttcaclc tcaacatcgag cagactggag 240
cctgaagat tgcactgla ttacltgagc cgtatlagta gggtcacccat caccttcggc 300
caagggacac gacggagat taata 324

<210> 869

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 869

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

<210> 870

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 870

cagagltta gcagcagcta c 21

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<213> Artificial Sequence

<220>

<223> Synthetic

<400> 871

Gln Ser Val Ser Ser Ser Tyr

1 5

<210> 872

<211> 9

<212> DNA
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<220>
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<400> 872
ggtgcatcc 9

<210> 873
<211> 3
<212> PRT
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<220>
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<400> 873
Gly Ala Ser
1

<210> 874
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 874
cagcaglala gtaggtcacc gatcacc 27

<210> 875
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 875
Gln Gln Tyr Ser Arg Ser Pro Ile Thr
1 5

<210> 876
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 876
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tcctglcgag ccctcggtt cacccttaac aacttgccta tgacctgggt cccgcggct 120
ccagggaaagg gcctggggatg ggcctcaactt attagtggtt gggcggtt cacaactgtt 180
gcagactcgg tgaaggcccg gttcacccatc tccagagaca attcctaaaga cacaactgtt 240
ctgcctaaatgtt acagccgtttt agtgcggggatc acggccgtttt attatgtttt taaaggatggc 300
gccttctata tgggtttttt acactactgg ggcccggtttt cccctggccat cgttctctttt 360

<210> 877
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
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<400> 877
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1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ser Asn Asn Phe
20 25 30
Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ser Thr Ile Ser Gly Ser Gly Val Asp Thr Tyr Cys 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 Val Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Lys Asp Gly Ala Phe Tyr Ser Gly Tyr Glu His Tyr Trp Gly Gln
100 105 110
Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 878
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 878
ggatccacct ctaacaactt tgcc 24

<210> 879
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
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<400> 879
Gly Phe Thr Ser Asn Asn Phe Ala
1 5

<210> 880
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 880
attaglotta qtggcqtlqa caca 24

<210> 881
<211> 8
<212> PRT
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<220>
<223> Synthetic

<400> 881
Ile Ser Gly Ser Gly Val Asp Thr
1 5

<210> 882
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 882
octaaagalo qcoccttclta tagtgcgtac qaacaatc
39

<210> 883
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
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<400> 883
Ala Lys Asp Gly Ala Phe Tyr Ser Gly Tyr Glu His Tyr
1 5 10

<210> 884
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 884
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cttcgcgcga gggccagtca gaggtgttgc agcagctact tagcttgta ccagcggaaa 120
ccggccagg ctccaggctt ctcatctat ggtttatcca acaggggcttc tggcatatcca 180
gacaaggatca ttggcaglgg gtcgtggaca gacttcaccc tccaccalca cagaclggag 240
tctgaagat ttcgttgta ttacgttcag caglalggta gtcacccctgg gacgttcggc 300
caaqqaacca aaqtqgalat caaa 324

<210> B85
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
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<400> 885
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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 Thr Ser Asn Arg Ala Ser Gly Ile Pro Asp Lys Phe Ile
50 55 60
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80
Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95
Arg Thr Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
100 105

<210> 886
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic
<400> 886
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<210> 887
<211> 7
<212> PRT
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<220>
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<400> 887
Gln Ser Val Ser Ser Ser Tyr
1 5

<210> 888
<211> 9
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic
<400> 888
ggtaacatcc 9

<210> 889
<211> 3
<212> PRT
<213> Artificial Sequence

<220> 243

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

<210> 894
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
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<400> 894
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ctgtccctgcc gggccctccca gtcgggtgtcc tccctccacc tggccctggta ccagcagaag 120
ccggccagg ccccccggctt gtgtgtttac ggcgcctccctt cccggggccac cggccatcccc 180
gaccgggttc cccggcccccggcc cccggccacc gacttcaccc tgaccatctc cccggccggag 240
cccgaggact tccgggtgtta ctttgtccag cagtacggctt ccccccctt gaccctccgc 300
ggccggcacca aggtggagal caag 324

<210> 895
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
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<400> 895
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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
Leu Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 896
<211> 369
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 896

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ccggcaagg gcggggatg gggggccgtg ctgggtacg acggcaccaa caagtactac 180
ggcgacloog tgaagggccg gtccaccatc tccgggaca actccaagaa caccctgtac 240
ctgcagatga acccccgtcg ggcggaggac acggcgtgt acacggcgc cgggaccac 300
gactccggt cgggtacga gggctgggtc gacccctggg gcccggcac ctggtgacc 360
ggccccc 369

<210> 897

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 897

Gln Val Gln Leu Val Glu Ser 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 Leu Trp Tyr Asp Gly Thr 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 His Asp Phe Arg Ser Gly Tyr Glu Gly Trp Phe Asp Pro
100 105 110
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 898

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 898

gagatcgatc tgaccatgc cccggccacc ctgtccctgt ccccccggcga gggggcacc 60
ctgtccgtcc gggcccccata gtccgttcc ttctaccctgg ctgggtacca gcaagaagccc 120
ggccaggccc cccggctgt galactacgac gcccacccac gggccacccgg cttcccccac 180
cggttcccg gtcgggttc cggcaccgac tcaccctga ccaccccttc ctggagccc 240
gaggacttcg cccgtatca ctggcagcac cggccaaact ggccccccac ctgggggc 300
ggcaccacgg tggatcaaa g 321

<210> 899

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 899
 Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
 20 25 30
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
 35 40 45
 Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80
 Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Arg Ser Asn Trp Pro Pro
 85 90 95
 Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 900
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<210> 901
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 901
 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
 Ser Phe Leu Trp Tyr Asp Gly Thr Asn Lys Asn Tyr Val Glu Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Met Leu Tyr
 65 70 75 80
 Leu Glu Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Asp His Asp Phe Arg Ser Gly Tyr Glu Gly Trp Phe Asp Pro
 100 105 110
 Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 902
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 902
gaaalaglgt tgacacagtc tccagccacc cglcittgl ctccaggggta aagagccacc 60
ctctccctgca gggccaglca gaglgttagc agtctacitgc cctggtaacc acagaaacol 120
ggccaggcgc ccaggcgccl calclalgt gcalccaaca gggccacigg calcccagec 180
aggltcaitg gcaglgggc lgggacagac ttcaclclca ccatcagcag cctlagagcc 240
gaagalltg cagittatla clgtcaaacac cgtaccaact ggcctccac ttccggcgga 300
gggaccaagg tgaaaatcaa a 321

<210> 903
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 903
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Ile
35 40 45
Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Arg Ser Asn Trp Pro Pro
85 90 95
Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 904
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 904
caggllcgcg lgcaggaglc gggcccagga ctggtaaaggc ttccacagac cctgtccctc 60
acclgcaclg lclclgggtgg ctccalcagc agtgggtgtt acatctggag llggalccgc 120
cagcacccag ggaaggggccl ggagtggatt ggglacalcc attalagtgg gaacacccac 180
tacaatccga ccccaaaatggc lcaaaatacc atatcagtag acacgltcaaa gaaccaggttc 240
tcccttgggg tgaactclgt gactgtccggc gacacggccgc tataactaclg lgcgaggaaal 300
alggttcggg gagttcaclg gllcgaccccc lggggccagg gaaccacggt caccgtcc 360
tca 363

<210> 905
<211> 121

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 905
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45
Trp Ile Gly Tyr Ile His Tyr Ser Gly Asn Thr His Tyr Asn Pro Thr
50 55 60
Leu Lys Ser Arg Ile Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80
Ser Leu Glu Val Asn Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95
Cys Ala Arg Asn Met Val Arg Gly Val His Trp Phe Asp Pro Trp Gly
100 105 110
Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 906
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 906
gaaatagtgt tgacacacgtc tccaggcacc ctgccttgtt ctcaggggga gagagocacc 60
ctcttcgtt gggccagtcg gagtgttagc agcagactact tagcccggtta ccagcagaaaa 120
ccggccagg ctccaggctt ccacatctt ggccalcca gcaggccac tggccalcca 180
gacaggltca gggcagtgg gtcgtggaca gacttcaclc tcaccatcgag cagaclggag 240
cctgaagatt ttgcaglala ttctgtcaa cagtatagta gttcacccgtt cactttccgc 300
ggagggacca agctggagal caaa 324

<210> 907
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 907
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 Phe Cys Trp Ala Ser Arg 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 Ser 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 Phe Cys Gln Gln Tyr Ser Ser Pro

85 90 95
 Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 908
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 908
 caggcgacg tgccaggagtc cggccccggc ctggtaaagc ccgcggcggc cctgtcccttg 60
 acctgcacccg tgcggcgccg cccatctcc tcggccggct acatctggtc ctggatccgg 120
 cagcaccccg gcaaggggctt ggagtggalc ggclacatcc acatctccgg caacacccac 180
 tacaacccctt cccgtgaatgc cccgggtggacc atcccggtgg acacccctccaa gaacctggtc 240
 tccctgtttt ggcgcggccg gacaccggccg ttgtactatcg cgcccccggaaac 300
 atggcgccgg ggcgtgcactg gtccggccccc tggggccagg gcaccccttgtt gaccgtgtcc 360
 loc 363

<210> 909
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 909
 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
 1 5 10 15
 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
 20 25 30
 Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Ile Gly Tyr Ile His Tyr Ser Gly Asn Thr Tyr Tyr Asn Pro Ser
 50 55 60
 Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Ala Arg Asn Met Val Arg Gly Val His Trp Phe Asp Pro Trp Gly
 100 105 110
 Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 910
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

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<400> 910
gagatgtgc tgaccccaigc cccccggcacc ctg|cccclgl ccccccgggaga gggggccacc 60
ctglccgtgcc ggcccccggcgg ctgcgggtcc tccctcttacc lggccgttgta ccaggcagaag 120
cccccccaagg cccccccact acgttttttttccat cccggggccac cggccatcccc 180

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gacogggttc cccggctccgg ctccggcacc gacttcaccc tgaccatctc cccggcgaggag 240
cccgaggact tgcgggtta ctacggccag cagaatccctt ccccccctt gacccggc 300
ggggccacca agggagat caag 324

<210> 911
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 911
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 Arg 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 Ser Ser Ser Pro
85 90 95
Leu Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 912
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 912
caggtgcagc tgcaggagtc gggcclagga ctggtaaage ctccacagac cctggccctc 60
acctgcactg tctctgggtt ccctcatcggc agtgggttgtt acatacgagg ttggalccgc 120
cagcacccag ggaaggccctt ggaglggatt ggglacalcc attalaglgg gaacacccac 180
lacaatccga cccctcaagag tgcatttttttcc alatcgatgg acacgtttttttaa gaaccaggtc 240
tcccttgagg tggaaatgtt gactgcggcg gacacggccgg latactactg tgcgaggaaal 300
atggttcggg gagttcaactg gttagcccccc tggggccagg gaaccccttgtt cacctgttcc 360
tca 363

<210> 913
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 913
Gln Val Gln Leu Gln Glu Ser Gly Leu Gly Leu Val Lys Pro Ser Gln
1 5 10 15
Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30
Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45

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

<210> 914
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 914
ggaaalaglgl tgacacagtc tccaggcacc cgcgttgtl ctccagggga gagagccacc 60
ccttcgtt gggccagtcg gagtttttgc agccatctt laggctggta ccagcagaaaa 120
cctggccagg ctcaggctt cctcatctt gglgcattca gcaggccac tggcatccca 180
gacagggtca gtggcaglgg gtcgggaca gacttcactt tcaccalcag cagaclggag 240
cctgaagatt ttgcagtata ttctgtcaa caglalagta gttcacccgtt cacttcggc 300
ggagggacca aggllgaaat caaa 324

<210> 915
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 915
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 Phe Cys Trp Ala Ser Arg 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 Ser 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 Phe Cys Gln Gln Tyr Ser Ser Ser Pro
85 90 95
Leu Thr Phe Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 916
<211> 367
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

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

<210> 920

<211> 360

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 920

gaggcgac tggggagtc cggggggggc ctggcgac cggcggttc cctgcggc lg 60
 ccctgcggcc octccgggtt cacttcaac aacttgc ca tgcttgggt gggcaggcc 120
 cccggcaagg ggctggatgt ggtgcggcc alicccgtt cggcgllgga cacclactac 180
 ggcgactccg tgaagggccg gttcacccalc tccccggaca actccaagaa caccctgtac 240
 ctgcagatga actccctgcg ggcggaggac acggccglgl actactgttc caaggacggc 300
 gcttctact cggctacga gcaclacgg ggcctgggca ccctggcac cgtgcctcc 360

<210> 921

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 921

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly	
1	5	10	15												
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Asn	Asn	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	Ser	Gly	Ser	Gly	Val	Asp	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													
Ser	Lys	Asp	Gly	Ala	Phe	Tyr	Ser	Gly	Tyr	Glu	His	Tyr	Trp	Gly	Gln
100	105	110													
Gly	Thr	Leu	Val	Thr	Val	Ser	Ser								
115	120														

<210> 922

<211> 324

<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 922
gagatcgac tgaccacgc cccggcacc ctgtccctgtt ccggggcggca gggggccacc 60
ctgtccgtcc gggccctcca gtcgggtgtcc tcccttacc tggccgtta ccaggagaag 120
ccggccagg cccccggct gtgtatcac ggcacccctt cccggggcac cggcatcccc 180
gacgggtttt cgggttcgg ctccggcacc gacttcaccc tgaccatctc cgggttggag 240
cccgaggact tggccgttgta ctactggccag cagtacggct cctccccccg gaccttcggc 300
cagggcacca aglggagat caag 324

<210> 923
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 923
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 Thr 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
Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 924
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 924
caggcgacat tggtcgacgc cggtcgccggag gtaagaaggc cggggccctt cgtttttttt 60
ttttttttttt cccgggtttt caccatccacc taatccggca ttccctgggtt gggccggcc 120
ccggccagg gttttttttt gatggggatgg atcccccattt acggacggaaat caccatccat 180
ggccggaaatc tgcaggccgg ggtttttttt accggccatgg accaccggaca cttccaccctt caccggccat 240
atggggatggc ggcccttggat gtcggacgac accggccgtttt actatcgatggc cgggtttttt 300
ttttttttttt tggggatggc accctggggcc cagggcaccc tggggatggc 357

<210> 925
<211> 119
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic

<400> 925
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Tyr Tyr
20 25 30
Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Ser Ala Tyr Asp Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60
Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Tyr Ser Trp Asn Lys His Trp Phe Asp Pro Trp Gly Gln Gly
100 105 110
Thr Leu Val Thr Val Ser Ser
115

<210> 926

<211> 324

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 926
gagatcgccgcgaccccccggcacc ctgtccccgtccccccggcgg gggggccacc 60
ctgtccgcggccctccca gtcggcggacc ggcccttacc tggccctggta ccaggcagaag 120
cccgccggcagg ccccccggccgtggccatctac ggcggccctccctccggggccac cggccatcccc 180
gaccgggtttccggccggccggccacc gacttcaccc tgaccatcc cccggctggag 240
cccgaggaaatccggccgtttccggccacc gacttcaccc tgaccatcc cccggctggag 300
cagggccacca agggggat caag 324

<210> 927

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 927
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 Thr Gly 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 Ser Ala Phe Ser Pro
85 90 95
Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 928
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<220>
<221> VARIANT
<222> (1)...(8)
<223> Xaa = Any amino acid or absent

<400> 928
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> 929
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<220>
<221> VARIANT
<222> (1)...(8)
<223> Xaa = Any amino acid or absent

<400> 929
Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
1 5

<210> 930
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<220>
<221> VARIANT
<222> (1)...(16)
<223> Xaa = Any amino acid or absent

<400> 930
Xaa
1 5 10 15

<210> 931
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

tcctggaaata tgacclcglt gactggccgcg gacacggccg tglattatgt tgcgagagaca 300
ccttggaaatgc alaactttga calclggggc caaagggacaa tggcgcacccgt ctcttcg 357

<210> 935
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthelic

<400> 935
 Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
 1 5 10 15
 Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Thr Ser Gly
 20 25 30
 Gly Tyr Tyr Trp Thr Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
 35 40 45
 Trp Ile Gly Tyr Ile Lys Phe Ser Gly Asn Thr Tyr Tyr Asn Pro Ser
 50 55 60
 Leu Arg Ser Arg Val Thr Ile Ser Leu Asp Thr Ser Lys Asn Gln Phe
 65 70 75 80
 Ser Leu Asn Met Thr Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Ala Arg Ala Pro Gly Ser His Asn Phe Asp Ile Trp Gly Gln Gly
 100 105 110
 Thr Met Val Thr Val Ser Ser
 115

<210> 936
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 936
 gaaatgtgt tgacccagtc tccagacacc cgtctttgt ctccagggaa aagagccacc 60
 ctclcclgtca gggccaglgt gaglattagt aataacatltl lagcclggla ccagcagaaa 120
 ccggccagg clcccaggct cctcalclat ggtgcaccca gcaggggcac lggcatccca 180
 gacagggttca gtggcagtg glclggaca gactlcactc tcaccatcg aagaclggag 240
 lclgcagatt lfcacccgtta taclgtcag caaatatgtaa ggltcacccgtl caccttcggc 300
 caaggggacac gaclggagal taaa 324

<210> 937
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 937
 Glu Ile Val Leu Thr Gln Ser Pro Asp Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Val Ser Ile Ser Asn Asn
 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 Arg Arg Leu Glu
 65 70 75 80
 Ser Ala Asp Phe Ala Pro Tyr Tyr Cys Gln Gln Tyr Ser Arg Ser Pro
 85 90 95
 Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
 100 105

<210> 938
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 938
 gaagtgcagc lggggggagcc ttggtaacaac cggggggtc cctgagactc 60
 ccctlgcgag cctctggatt cacctttaac aacttgcata tgacclgggt cggccaggct 120
 ccaggggaagg gctctggatg ggctcaactt attagtggtt gtggcgltta cacalactgc 180
 gcagaccccg tgaaggggccg gttcacccalc tccagagaca attccaagaa cacactgtat 240
 ctcggaaatgtt acagccgtt agccgaggac acggccgtttaa attactgtt gaaagatggc 300
 qccttctata qllqqlacqa acactactgg qggccagggtt ccctggtcac cgtctctca 360

<210> 939
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 939
 Glu Val Gln Leu Val Val Ser Gly Gly Ala Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Asn Phe
 20 25 30
 Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Thr Ile Ser Gly Ser Gly Val Asp Thr Tyr Cys 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
 Ser Lys Asp Gly Ala Phe Tyr Ser Gly Tyr Glu His Tyr Trp Gly Gln
 100 105 110
 Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 940
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic

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

<210> 944
 <211> 324
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 944
 gaaaattgtgt tgacacagtc tccaggcacc ctgtttgt ctccagggga cagagccacc 60
 ctctccgtca gggccatgtca gagtgttacc ggcagctact tagccgtta ccaggcagaaa 120
 cctggccagg ctccccatgtca acaggccac tggcatccca 180
 gacagggttca ctggcagttgg gtcgggaca gacttcaccc tcaccatcg cagaclggag 240
 cctgaagatt ttgcgttgta ttctgtcaa cagtcgttt totcaccgtg gacgttcggc 300
 caggggacca agggaaat caaa 324

<210> 945
 <211> 108
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 945
 Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15
 Asp Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Thr Gly 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 Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Thr
 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 Phe Cys Gln Gln Ser Ala Phe Ser Pro
 85 90 95
 Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 946
 <211> 361
 <212> DNA
 <213> Artificial Sequence

220

<223> Synthetic

<400> 946

caggcgcgt tgccggggtc gggccccagga ctggtaago ctgcacagac ccgtccccc 60
 acctgcacgt tctctgggg ctccatggc agtgggtgtt acatcgagg ctggalccgc 120
 cagcaccccg ggaaggggccl ggagtggatt ggglacgtcc attacaglgg gaacaccac 180
 tacaacccgl ccccaaaaggat tgccactttcc atataatag acacgttcaa galcccgatc 240
 lccctgaagc tgaggctcgat gacgtggccgc gacacggccg lgtatcttg tgccgagagcc 300
 ccccgllgal accattactt tgccatcggtt ggccaggaa ccctggtcac cgltctccca 360
 g 361

<210> 347
<211> 120

<211> PBT

<213> Artificial

2202

<223> Synthetic

<400> 947

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

<210> 948

<211> 325

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 948

gaaatlglt lgacacaatc lccaggcacc clglttgc1 clccagggga aagagccacc 60
 ctcctcgca gggccaglca gagtgtlalc agcagctact tagccctgtta ccagcagaaa 120
 cclggccagg clccaggcl ccttcac1ttt ggtgcattca gcaggccac tggcatccca 180
 gacaggltca gtggcaglgg gtc1gggaca gacttcactc tcaccalcaag cagaclggag 240
 cclgaagagt ttcaglgtt tlaactglcag caglalggla gtcacccgtt cacltcggc 300
 ggagggacca aggtggagat caaac 325

<210> 949

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 949

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

<210> 950

<211> 330

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic

<400> 950

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> 951
 <211> 327
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic

<400> 951
 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> 952
<211> 327
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic

<400> 952
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15
Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80
Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95
Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
100 105 110
Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140
Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205
Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285
Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305 310 315 320
Leu Ser Leu Ser Leu Gly Lys
325

<210> 953
<211> 544
<212> PRT
<213> Homo sapiens

<400> 953

Met Gly Ser Arg Cys Ala Leu Ala Leu Ala Val Leu Ser Ala Leu Leu
1 5 10 15
Cys Gln Val Trp Ser Ser Gly Val Phe Glu Leu Lys Leu Gln Glu Phe
20 25 30
Val Asn Lys Lys Gly Leu Leu Gly Asn Arg Asn Cys Cys Arg Gly Gly
35 40 45
Ala Gly Pro Pro Pro Cys Ala Cys Arg Thr Phe Phe Arg Val Cys Leu
50 55 60
Lys His Tyr Gln Ala Ser Val Ser Pro Glu Pro Pro Cys Thr Tyr Gly
65 70 75 80
Ser Ala Val Thr Pro Val Leu Gly Val Asp Ser Phe Ser Leu Pro Asp
85 90 95
Gly Gly Gly Ala Asp Ser Ala Phe Ser Asn Pro Ile Arg Phe Pro Phe
100 105 110
Gly Phe Thr Trp Pro Gly Thr Phe Ser Leu Ile Ile Glu Ala Leu His
115 120 125
Thr Asp Ser Pro Asp Asp Leu Ala Thr Glu Asn Pro Glu Arg Leu Ile
130 135 140
Ser Arg Leu Ala Thr Gln Arg His Leu Thr Val Gly Glu Glu Trp Ser
145 150 155 160
Gln Asp Leu His Ser Ser Gly Arg Thr Asp Leu Lys Tyr Ser Tyr Arg
165 170 175
Phe Val Cys Asp Glu His Tyr Tyr Gly Glu Gly Cys Ser Val Phe Cys
180 185 190
Arg Pro Arg Asp Asp Ala Phe Gly His Phe Thr Cys Gly Glu Arg Gly
195 200 205
Glu Lys Val Cys Asn Pro Gly Trp Lys Gly Pro Tyr Cys Thr Glu Pro
210 215 220
Ile Cys Leu Pro Gly Cys Asp Glu Gln His Gly Phe Cys Asp Lys Pro
225 230 235 240
Gly Glu Cys Lys Cys Arg Val Gly Trp Gln Gly Arg Tyr Cys Asp Glu
245 250 255
Cys Ile Arg Tyr Pro Gly Cys Leu His Gly Thr Cys Gln Gln Pro Trp
260 265 270
Gln Cys Asn Cys Gln Glu Gly Trp Gly Gly Leu Phe Cys Asn Gln Asp
275 280 285
Leu Asn Tyr Cys Thr His His Lys Pro Cys Lys Asn Gly Ala Thr Cys
290 295 300
Thr Asn Thr Gly Gln Gly Ser Tyr Thr Cys Ser Cys Arg Pro Gly Tyr
305 310 315 320
Thr Gly Ala Thr Cys Glu Leu Gly Ile Asp Glu Cys Asp Pro Ser Pro
325 330 335
Cys Lys Asn Gly Gly Ser Cys Thr Asp Leu Glu Asn Ser Tyr Ser Cys
340 345 350
Thr Cys Pro Pro Gly Phe Tyr Gly Lys Ile Cys Glu Leu Ser Ala Met
355 360 365
Thr Cys Ala Asp Gly Pro Cys Phe Asn Gly Gly Arg Cys Ser Asp Ser
370 375 380
Pro Asp Gly Gly Tyr Ser Cys Arg Cys Pro Val Gly Tyr Ser Gly Phe
385 390 395 400
Asn Cys Glu Lys Lys Ile Asp Tyr Cys Ser Ser Ser Pro Cys Ser Asn
405 410 415
Gly Ala Lys Cys Val Asp Leu Gly Asp Ala Tyr Leu Cys Arg Cys Gln
420 425 430
Ala Gly Phe Ser Gly Arg His Cys Asp Asp Asn Val Asp Asp Cys Ala
435 440 445
Ser Ser Pro Cys Ala Asn Gly Gly Thr Cys Arg Asp Gly Val Asn Asp
450 455 460
Phe Ser Cys Thr Cys Pro Pro Gly Tyr Thr Gly Arg Asn Cys Ser Ala

465	470	475	480
Pro Val Ser Arg Cys Glu His Ala Pro Cys His Asn Gly Ala Thr Cys			
485	490	495	
His Glu Arg Gly His Arg Tyr Val Cys Glu Cys Ala Arg Gly Tyr Gly			
500	505	510	
Gly Pro Asn Cys Gln Phe Leu Leu Pro Glu Leu Pro Pro Gly Pro Ala			
515	520	525	
Val Val Asp Leu Thr Glu Lys Leu Glu Gly Gln Gly Gly Pro Phe Pro			
530	535	540	

<210> 954
<211> 490
<212> PRT
<213> Homo sapiens

<400> 954			
Met Val Ser Pro Arg Met Ser Gly Leu Leu Ser Gln Thr Val Ile Leu			
1	5	10	15
Ala Leu Ile Phe Leu Pro Gln Thr Arg Pro Ala Gly Val Phe Glu Leu			
20	25	30	
Gln Ile His Ser Phe Gly Pro Gly Pro Gly Ala Pro Arg Ser			
35	40	45	
Pro Cys Ser Ala Arg Leu Pro Cys Arg Leu Phe Phe Arg Val Cys Leu			
50	55	60	
Lys Pro Gly Leu Ser Glu Glu Ala Ala Glu Ser Pro Cys Ala Leu Gly			
65	70	75	80
Ala Ala Leu Ser Ala Arg Gly Pro Val Tyr Thr Glu Gln Pro Gly Ala			
85	90	95	
Pro Ala Pro Asp Leu Pro Leu Pro Asp Gly Leu Leu Gln Val Pro Phe			
100	105	110	
Arg Asp Ala Trp Pro Gly Thr Phe Ser Phe Ile Ile Glu Thr Trp Arg			
115	120	125	
Glu Glu Leu Gly Asp Gln Ile Gly Gly Pro Ala Trp Ser Leu Leu Ala			
130	135	140	
Arg Val Ala Gly Arg Arg Arg Leu Ala Ala Gly Gly Pro Trp Ala Arg			
145	150	155	160
Asp Ile Gln Arg Ala Gly Ala Trp Glu Leu Arg Phe Ser Tyr Arg Ala			
165	170	175	
Arg Cys Glu Pro Pro Ala Val Gly Thr Ala Cys Thr Arg Leu Cys Arg			
180	185	190	
Pro Arg Ser Ala Pro Ser Arg Cys Gly Pro Gly Leu Arg Pro Cys Ala			
195	200	205	
Pro Leu Glu Asp Glu Cys Glu Ala Pro Pro Val Cys Arg Ala Gly Cys			
210	215	220	
Ser Pro Glu His Gly Phe Cys Glu Gln Pro Gly Glu Cys Arg Cys Leu			
225	230	235	240
Glu Gly Trp Thr Gly Pro Leu Cys Thr Val Pro Val Ser Thr Ser Ser			
245	250	255	
Cys Leu Ser Pro Arg Gly Pro Ser Ser Ala Thr Thr Gly Cys Leu Val			
260	265	270	
Pro Gly Pro Gly Pro Cys Asp Gly Asn Pro Cys Ala Asn Gly Gly Ser			
275	280	285	
Cys Ser Glu Thr Pro Arg Ser Phe Glu Cys Thr Cys Pro Arg Gly Phe			
290	295	300	
Tyr Gly Leu Arg Cys Glu Val Ser Gly Val Thr Cys Ala Asp Gly Pro			
305	310	315	320
Cys Phe Asn Gly Gly Leu Cys Val Gly Gly Ala Asp Pro Asp Ser Ala			
325	330	335	
Tyr Ile Cys His Cys Pro Pro Gly Phe Gln Gly Ser Asn Cys Glu Lys			
340	345	350	

Arg Val Asp Arg Cys Ser Leu Gln Pro Cys Arg Asn Gly Gly Leu Cys
 355 360 365
 Leu Asp Leu Gly His Ala Leu Arg Cys Arg Cys Arg Ala Gly Phe Ala
 370 375 380
 Gly Pro Arg Cys Glu His Asp Leu Asp Asp Cys Ala Gly Arg Ala Cys
 385 390 395 400
 Ala Asn Gly Gly Thr Cys Val Glu Gly Gly Ala His Arg Cys Ser
 405 410 415
 Cys Ala Leu Gly Phe Gly Arg Asp Cys Arg Glu Arg Ala Asp Pro
 420 425 430
 Cys Ala Ala Arg Pro Cys Ala His Gly Gly Arg Cys Tyr Ala His Phe
 435 440 445
 Ser Gly Leu Val Cys Ala Cys Ala Pro Gly Tyr Met Gly Ala Arg Cys
 450 455 460
 Glu Phe Pro Val His Pro Asp Gly Ala Ser Ala Leu Pro Ala Ala Pro
 465 470 475 480
 Pro Gly Leu Arg Pro Gly Asp Pro Gln Arg
 485 490

<210> 955

<211> 527

<212> PRT

<213> *Mus musculus*

<400> 955

Met Thr Pro Ala Ser Arg Ser Ala Cys Arg Trp Ala Leu Leu Leu
 1 5 10 15
 Ala Val Leu Trp Pro Gln Gln Arg Ala Ala Gly Ser Gly Ile Phe Gln
 20 25 30
 Leu Arg Leu Gln Glu Phe Val Asn Gln Arg Gly Met Leu Ala Asn Gly
 35 40 45
 Gln Ser Cys Glu Pro Gly Cys Arg Thr Phe Phe Arg Ile Cys Leu Lys
 50 55 60
 His Phe Gln Ala Thr Phe Ser Glu Gly Pro Cys Thr Phe Gly Asn Val
 65 70 75 80
 Ser Thr Pro Val Leu Gly Thr Asn Ser Phe Val Val Arg Asp Lys Asn
 85 90 95
 Ser Gly Ser Gly Arg Asn Pro Leu Gln Leu Pro Phe Asn Phe Thr Trp
 100 105 110
 Pro Gly Thr Phe Ser Leu Asn Ile Gln Ala Trp His Thr Pro Gly Asp
 115 120 125
 Asp Leu Arg Pro Glu Thr Ser Pro Gly Asn Ser Leu Ile Ser Gln Ile
 130 135 140
 Ile Ile Gln Gly Ser Leu Ala Val Gly Lys Ile Trp Arg Thr Asp Glu
 145 150 155 160
 Gln Asn Asp Thr Leu Thr Arg Leu Ser Tyr Ser Tyr Arg Val Ile Cys
 165 170 175
 Ser Asp Asn Tyr Tyr Gly Glu Ser Cys Ser Arg Leu Cys Lys Lys Arg
 180 185 190
 Asp Asp His Phe Gly His Tyr Glu Cys Gln Pro Asp Gly Ser Leu Ser
 195 200 205
 Cys Leu Pro Gly Trp Thr Gly Lys Tyr Cys Asp Gln Pro Ile Cys Leu
 210 215 220
 Ser Gly Cys His Glu Gln Asn Gly Tyr Cys Ser Lys Pro Asp Glu Cys
 225 230 235 240
 Ile Cys Arg Pro Gly Trp Gln Gly Arg Leu Cys Asn Glu Cys Ile Pro
 245 250 255
 His Asn Gly Cys Arg His Gly Thr Cys Ser Ile Pro Trp Gln Cys Ala
 260 265 270
 Cys Asp Glu Gly Trp Gly Leu Phe Cys Asp Gln Asp Leu Asn Tyr

275	280	285
Cys Thr His His Ser Pro Cys Lys Asn Gly Ser Thr Cys Ser Asn Ser		
290	295	300
Gly Pro Lys Gly Tyr Thr Cys Thr Cys Leu Pro Gly Tyr Thr Gly Glu		
305	310	315
320		
His Cys Glu Leu Gly Leu Ser Lys Cys Ala Ser Asn Pro Cys Arg Asn		
325	330	335
Gly Gly Ser Cys Lys Asp Gln Glu Asn Ser Tyr His Cys Leu Cys Pro		
340	345	350
Pro Gly Tyr Tyr Gly Gln His Cys Glu His Ser Thr Leu Thr Cys Ala		
355	360	365
Asp Ser Pro Cys Phe Asn Gly Gly Ser Cys Arg Glu Arg Asn Gln Gly		
370	375	380
Ser Ser Tyr Ala Cys Glu Cys Pro Pro Asn Phe Thr Gly Ser Asn Cys		
385	390	395
400		
Glu Lys Lys Val Asp Arg Cys Thr Ser Asn Pro Cys Ala Asn Gly Gly		
405	410	415
Gln Cys Gln Asn Arg Gly Pro Ser Arg Thr Cys Arg Cys Arg Pro Gly		
420	425	430
Phe Thr Gly Thr His Cys Glu Leu His Ile Ser Asp Cys Ala Arg Ser		
435	440	445
Pro Cys Ala His Gly Gly Thr Cys His Asp Leu Glu Asn Gly Pro Val		
450	455	460
Cys Thr Cys Pro Ala Gly Phe Ser Gly Arg Arg Cys Glu Val Arg Ile		
465	470	475
480		
Thr His Asp Ala Cys Ala Ser Gly Pro Cys Phe Asn Gly Ala Thr Cys		
485	490	495
Tyr Thr Gly Leu Ser Pro Asn Asn Phe Val Cys Asn Cys Pro Tyr Gly		
500	505	510
Phe Val Gly Ser Arg Cys Glu Phe Pro Val Gly Leu Pro Pro Ser		
515	520	525

<210> 956
<211> 498
<212> PRT
<213> Macaca fascicularis

<400> 956		
Ser Gly Val Phe Gln Leu Gln Leu Gln Glu Phe Val Asn Glu Arg Gly		
1	5	10
15		
Val Leu Ala Ser Gly Arg Pro Cys Glu Pro Gly Cys Arg Thr Phe Phe		
20	25	30
Arg Val Cys Leu Lys His Phe Gln Ala Val Val Ser Pro Gly Pro Cys		
35	40	45
Thr Phe Gly Ser Val Ser Thr Pro Val Leu Gly Thr Asn Ser Phe Ala		
50	55	60
Val Arg Asp Asp Ser Ser Gly Gly Arg Asn Pro Leu Gln Leu Pro		
65	70	75
80		
Phe Asn Phe Thr Trp Pro Gly Thr Phe Ser Leu Ile Ile Glu Ala Trp		
85	90	95
His Ala Pro Gly Asp Asp Leu Arg Pro Glu Ala Leu Pro Pro Asp Ala		
100	105	110
Leu Ile Ser Lys Ile Ala Ile Gln Gly Ser Leu Ala Val Gly Gln Asn		
115	120	125
Trp Leu Leu Asp Glu Gln Thr Ser Thr Leu Thr Arg Leu Arg Tyr Ser		
130	135	140
Tyr Arg Val Ile Cys Ser Asp Asn Tyr Tyr Gly Asp Asn Cys Ser Arg		
145	150	155
160		
Leu Cys Lys Lys Arg Asn Asp His Phe Gly His Tyr Val Cys Gln Pro		
165	170	175

Asp Gly Asn Leu Ser Cys Leu Pro Gly Trp Thr Gly Glu Tyr Cys Gln
 180 185 190
 Gln Pro Ile Cys Leu Ser Gly Cys His Glu Gln Asn Gly Tyr Cys Ser
 195 200 205
 Lys Pro Ala Glu Cys Leu Cys Arg Pro Gly Trp Gln Gly Arg Leu Cys
 210 215 220
 Asn Glu Cys Ile Pro His Asn Gly Cys Arg His Gly Thr Cys Ser Thr
 225 230 235 240
 Pro Trp Gln Cys Thr Cys Asp Glu Gly Trp Gly Gly Leu Phe Cys Asp
 245 250 255
 Gln Asp Leu Asn Tyr Cys Thr His His Ser Pro Cys Lys Asn Gly Ala
 260 265 270
 Thr Cys Ser Asn Ser Gly Gln Arg Ser Tyr Thr Cys Thr Cys Arg Pro
 275 280 285
 Gly Tyr Thr Gly Val Asp Cys Glu Leu Glu Leu Ser Glu Cys Asp Ser
 290 295 300
 Asn Pro Cys Arg Asn Gly Gly Ser Cys Lys Asp Gln Glu Asp Gly Tyr
 305 310 315 320
 His Cys Leu Cys Pro Pro Gly Tyr Tyr Gly Leu His Cys Glu His Ser
 325 330 335
 Thr Leu Ser Cys Ala Asp Ser Pro Cys Phe Asn Gly Gly Ser Cys Arg
 340 345 350
 Glu Arg Asn Gln Gly Ala Ser Tyr Ala Cys Glu Cys Pro Pro Asn Phe
 355 360 365
 Thr Gly Ser Asn Cys Glu Lys Lys Val Asp Arg Cys Thr Ser Asn Pro
 370 375 380
 Cys Ala Asn Gly Gly Gln Cys Leu Asn Arg Gly Pro Ser Arg Met Cys
 385 390 395 400
 Arg Cys Arg Pro Gly Phe Thr Gly Thr Tyr Cys Glu Arg His Val Ser
 405 410 415
 Asp Cys Ala Arg Asn Pro Cys Ala His Gly Gly Thr Cys His Asp Leu
 420 425 430
 Glu Ser Gly Leu Met Cys Thr Cys Pro Ala Gly Phe Ser Gly Arg Arg
 435 440 445
 Cys Glu Val Arg Thr Ser Ile Asp Ala Cys Ala Ser Ser Pro Cys Phe
 450 455 460
 Asn Arg Ala Thr Cys Tyr Thr Asp Leu Ser Thr Asp Thr Phe Val Cys
 465 470 475 480
 Asn Cys Pro Tyr Gly Phe Val Gly Ser Arg Cys Glu Phe Pro Met Gly
 485 490 495
 Leu Pro

<210> 957
 <211> 498
 <212> PRT
 <213> Macaca mulatta

<400> 957
 Ser Gly Val Phe Gln Leu Gln Leu Gln Glu Phe Val Asn Glu Arg Gly
 1 5 10 15
 Val Leu Ala Ser Gly Arg Pro Cys Glu Pro Gly Cys Arg Thr Phe Phe
 20 25 30
 Arg Val Cys Leu Lys His Phe Gln Ala Val Val Ser Pro Gly Pro Cys
 35 40 45
 Thr Phe Gly Ser Val Ser Thr Pro Val Leu Gly Thr Asn Ser Phe Ala
 50 55 60
 Val Arg Asp Asp Ser Ser Gly Gly Arg Asn Pro Leu Gln Leu Pro
 65 70 75 80
 Phe Asn Phe Thr Trp Pro Gly Thr Phe Ser Leu Ile Ile Glu Ala Trp

85	90	95
His Ala Pro Gly Asp Asp Leu Arg Pro Glu Ala Leu Pro Pro Asp Ala		
100	105	110
Leu Ile Ser Lys Ile Ala Ile Gln Gly Ser Leu Ala Val Gly Gln Asn		
115	120	125
Trp Leu Leu Asp Glu Gln Thr Ser Thr Leu Thr Arg Leu Arg Tyr Ser		
130	135	140
Tyr Arg Val Ile Cys Ser Asp Asn Tyr Tyr Gly Asp Asn Cys Ser Arg		
145	150	155
160		
Leu Cys Lys Lys Arg Asn Asp His Phe Gly His Tyr Val Cys Gln Pro		
165	170	175
Asp Gly Asn Leu Ser Cys Leu Pro Gly Trp Thr Gly Glu Tyr Cys Gln		
180	185	190
Gln Pro Ile Cys Leu Ser Gly Cys His Glu Gln Asn Gly Tyr Cys Ser		
195	200	205
Lys Pro Ala Glu Cys Leu Cys Arg Pro Gly Trp Gln Gly Arg Leu Cys		
210	215	220
Asn Glu Cys Ile Pro His Asn Gly Cys Arg His Gly Thr Cys Ser Thr		
225	230	235
240		
Pro Trp Gln Cys Thr Cys Asp Glu Gly Trp Gly Gly Leu Phe Cys Asp		
245	250	255
Gln Asp Leu Asn Tyr Cys Thr His His Ser Pro Cys Lys Asn Gly Ala		
260	265	270
Thr Cys Ser Asn Ser Gly Gln Arg Ser Tyr Thr Cys Thr Cys Arg Pro		
275	280	285
Gly Tyr Thr Gly Val Asp Cys Glu Leu Glu Leu Ser Glu Cys Asp Ser		
290	295	300
Asn Pro Cys Arg Asn Gly Gly Ser Cys Lys Asp Gln Glu Asp Gly Tyr		
305	310	315
320		
His Cys Leu Cys Pro Pro Gly Tyr Tyr Gly Leu His Cys Glu His Ser		
325	330	335
Thr Leu Ser Cys Ala Asp Ser Pro Cys Phe Asn Gly Gly Ser Cys Arg		
340	345	350
Glu Arg Asn Gln Gly Ala Ser Tyr Ala Cys Glu Cys Pro Pro Asn Phe		
355	360	365
Thr Gly Ser Asn Cys Glu Lys Lys Val Asp Arg Cys Thr Ser Asn Pro		
370	375	380
Cys Ala Asn Gly Gly Gln Cys Leu Asn Arg Gly Pro Ser Arg Met Cys		
385	390	395
400		
Arg Cys Arg Pro Gly Phe Thr Gly Thr Tyr Cys Glu Arg His Val Ser		
405	410	415
Asp Cys Ala Arg Asn Pro Cys Ala His Gly Gly Thr Cys His Asp Leu		
420	425	430
Glu Ser Gly Leu Met Cys Thr Cys Pro Ala Gly Phe Ser Gly Arg Arg		
435	440	445
Cys Glu Val Arg Thr Ser Ile Asp Ala Cys Ala Ser Ser Pro Cys Phe		
450	455	460
Asn Arg Ala Thr Cys Tyr Thr Asp Leu Ser Thr Asp Thr Phe Val Cys		
465	470	475
480		
Asn Cys Pro Tyr Gly Phe Val Gly Ser Arg Cys Glu Phe Pro Val Gly		
485	490	495
Leu Pro		

What is claimed is:

1. An isolated nucleic acid molecule encoding an antibody or antibody fragment which specifically binds human delta-like ligand 4 (hDII4), wherein the antibody or antibody fragment comprises heavy chain complementarity determining region (CDR) 1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3, wherein the heavy chain CDR1, CDR2 and CDR3 comprise the amino acid sequences of SEQ ID NOS:431, 433 and 435, respectively.
2. A recombinant expression vector comprising the nucleic acid molecule of claim 1.
3. An isolated host cell comprising the expression vector of claim 1 An isolated nucleic acid molecule encoding an antibody or antibody fragment which specifically binds human delta-like ligand 4 (hDII4), wherein the antibody or antibody fragment comprises heavy chain complementarity determining region CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3, wherein the heavy chain CDR1, CDR2 and CDR3 comprise the amino acid sequences of SEQ ID NOS: 431, 433 and 435, respectively, and the light chain CDR1, CDR2 and CDR3 comprise the amino acid sequences of SEQ ID NOS: 439, 441 and 443, respectively.
4. The nucleic acid molecule of claim 1, wherein the antibody or antibody fragment comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO:429 or 901.
5. The nucleic acid molecule of claim 4 comprising the nucleotide sequence of SEQ ID NO:428 or 900, or a substantially similar sequence having at least 95% homology thereof.
6. The nucleic acid molecule of claim 1, wherein the antibody or antibody fragment comprises a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:437 or 903.
7. The nucleic acid molecule of claim 6 comprising the nucleotide sequence of SEQ ID NO:436 or 902, or a substantially similar sequence having at least 95% homology thereof.
8. An isolated nucleic acid molecule encoding an antibody or antibody fragment which specifically binds human delta-like ligand 4 (hDII4), wherein the antibody or antibody fragment comprises a HCVR comprising the amino acid sequence of SEQ ID NO:901 and a LCVR comprising the amino acid sequence of SEQ ID NO:903.
9. The nucleic acid molecule of claim 8, wherein the HCVR is encoded by a nucleotide sequence comprising SEQ ID NO: 900.
10. The nucleic acid molecule of claim 8, wherein the LCVR is encoded by a nucleotide sequence comprising SEQ ID NO: 902.
11. The nucleic acid molecule of claim 8 comprising the nucleotide sequences of SEQ ID NOS:900 and 902.
12. A method of producing an antibody or antibody fragment which specifically binds human delta-like ligand 4 (hDII4), comprising growing the host cell of claim 3 under conditions permitting production of the antibody or fragment thereof, and recovering the antibody or fragment thereof so produced.
13. A recombinant expression vector comprising the nucleic acid molecule of claim 8.
14. An isolated host cell comprising the expression vector of claim 13.

15. A method of producing an antibody or antibody fragment which specifically binds human delta-like ligand 4 (hDll4), comprising growing the host cell of claim 14 under conditions permitting production of the antibody or fragment thereof, and recovering the antibody or fragment thereof so produced.
16. A recombinant expression vector comprising the nucleic acid molecule of claim 11.
17. An isolated host cell comprising the expression vector of claim 16.
18. A method of producing an antibody or antibody fragment which specifically binds human delta-like ligand 4 (hDll4), comprising growing the host cell of claim 17 under conditions permitting production of the antibody or fragment thereof, and recovering the antibody or fragment thereof so produced.
19. An isolated nucleic acid molecule encoding an antibody or antibody fragment which specifically binds human delta-like ligand 4 (hDll4), wherein the antibody or antibody fragment comprises a HCVR comprising the amino acid sequence of SEQ ID NO:429 and a LCVR comprising the amino acid sequence of SEQ ID NO:437.
20. The nucleic acid molecule of claim 19, wherein the HCVR is encoded by a nucleotide sequence comprising SEQ ID NO: 428.
21. The nucleic acid molecule of claim 19, wherein the LCVR is encoded by a nucleotide sequence comprising SEQ ID NO: 436.
22. The nucleic acid molecule of claim 19 comprising the nucleotide sequences of SEQ ID NOS:428 and 436.