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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF INFLUENZA

(57) Abstract: The present invention provides compositions, vaccines, and methods for diagnosing, treating, and preventing influenza infection using a combination of antibodies raised against the influenza hemagglutinin and the matrix 2 ectodomain polypeptides.

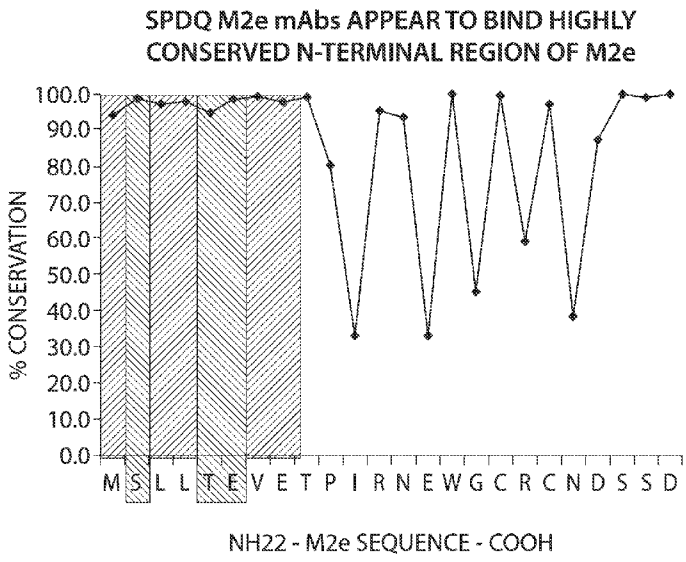


FIG. 8

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COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF INFLUENZA

RELATED APPLICATIONS

[01] This application claims the benefit of provisional application USSN 61/442,733, filed February 14, 2011, the contents of which are herein incorporated by reference in their entirety.

INCORPORATION OF SEQUENCE LISTING

[02] The contents of the text file named "37418-518001WO_ST25.txt," which was created on January 6, 2012 and is 910 KB in size, are hereby incorporated by reference in their entirety.

FIELD OF THE INVENTION

[03] The present invention relates generally to prevention, diagnosis, therapy and monitoring of influenza infection. The invention is more specifically related to compositions containing a combination of human antibodies raised against either the influenza hemagglutinin or matrix 2 protein. Such compositions are useful in pharmaceutical compositions for the prevention and treatment of influenza, and for the diagnosis and monitoring of influenza infection.

BACKGROUND OF THE INVENTION

[04] Influenza virus infects 5-20% of the population and results in 30,000-50,000 deaths each year in the U.S. Disease caused by influenza A viral infections is typified by its cyclical nature. Antigenic drift and shift allow for different A strains to emerge every year. Added to that, the threat of highly pathogenic strains entering into the general population has stressed the need for novel therapies for flu infections.

SUMMARY OF THE INVENTION

[05] The invention provides diagnostic, prophylactic, and therapeutic compositions including a human antibody raised against the Influenza hemagglutinin protein and a human monoclonal antibody raised against the Influenza M2 protein. Moreover, the invention provides diagnostic, prophylactic, and therapeutic compositions including an isolated human antibody raised against an epitope of the Influenza hemagglutinin protein and an isolated human monoclonal antibody raised against an epitope of the Influenza M2 protein.

Furthermore, these compositions are pharmaceutical compositions that include a pharmaceutical carrier. These compositions address a long-felt need in the art for pharmaceutical compositions that both strongly neutralizes Influenza virus infection and recognizes constant regions within proteins common to all Influenza strains.

[06] Specifically, the invention provides a composition including: (a) an isolated human antibody that specifically binds to an epitope of the hemagglutinin (HA) glycoprotein of an influenza virus; and (b) an isolated human monoclonal antibody that specifically binds to an epitope in the extracellular domain of the matrix 2 ectodomain (M2e) polypeptide of an influenza virus. In certain embodiments of this composition, the isolated human monoclonal antibody that specifically binds an epitope of the M2e polypeptide is TCN-032 (8I10), 21B15, TCN-031 (23K12), 3241_G23, 3244_I10, 3243_J07, 3259_J21, 3245_O19, 3244_H04, 3136_G05, 3252_C13, 3255_J06, 3420_I23, 3139_P23, 3248_P18, 3253_P10, 3260_D19, 3362_B11, or 3242_P05. Moreover, the isolated human antibody that specifically binds an epitope of the HA glycoprotein is optionally TCN-522 (3212_I12), TCN-521 (3280_D18), TCN-523 (5248_A17), TCN-563 (5237_B21), TCN-526 (5084_C17), TCN-527 (5086_C06), TCN-528 (5087_P17), TCN-529 (5297_H01), TCN-530 (5248_H10), TCN-531 (5091_H13), TCN-532 (5262_H18), TCN-533 (5256_A17), TCN-534 (5249_B02), TCN-535 (5246_P19), TCN-536 (5095_N01), TCN-537 (3194_D21), TCN-538 (3206_O17), TCN-539 (5056_A08), TCN-540 (5060_F05), TCN-541 (5062_M11), TCN-542 (5079_A16), TCN-543 (5081_G23), TCN-544 (5082_A19), TCN-545 (5082_I15), TCN-546 (5089_L08), TCN-547 (5092_F11), TCN-548 (5092_P01), TCN-549 (5092_P04), TCN-550 (5096_F06), TCN-551 (5243_D01), TCN-552 (5249_I23), TCN-553 (5261_C18), TCN-554 (5277_M05), TCN-555 (5246_L16), TCN-556 (5089_K12), TCN-557 (5081_A04), TCN 558 (5248_H10b), TCN-559 (5097_G08), TCN-560 (5084_P10), TCN-504 (3251_K17), SC06-141, SC06-255, SC06-257, SC06-260, SC06-261, SC06-262, SC06-268, SC06-272, SC06-296, SC06-301, SC06-307, SC06-310, SC06-314, SC06-323, SC06-325, SC06-327, SC06-328, SC06-329, SC06-331, SC06-332, SC06-334, SC06-336, SC06-339, SC06-342, SC06-343, SC06-344, CR6141, CR6255, CR6257, CR6260, CR6261, CR6262, CR6268, CR6272, CR6296, CR6301, CR6307, CR6310, CR6314, CR6323, CR6325, CR6327, CR6328, CR6329, CR6331, CR6332, CR6334, CR6336, CR6339, CR6342, CR6343, CR6344, 2A, D7, D8, F10, G17, H40, A66, D80, E88, E90, or H98.

[07] The epitope of the HA glycoprotein is optionally GVTNKVNSIIDK (SEQ ID NO: 198), GVTNKVNSIINK (SEQ ID NO: 283), GVTNKENSIIDK (SEQ ID NO: 202),

GVTNKVNRIIDK (SEQ ID NO: 201), GITNKVNSVIEK (SEQ ID NO: 281), GITNKENSVIEK (SEQ ID NO: 257), GITNKVNSIIDK (SEQ ID NO: 225), and KITSKVNNIVDK (SEQ ID NO: 216). The influenza hemaglutinin (HA) glycoprotein includes an HA1 and HA2 subunit. Exemplary epitopes of the HA glycoprotein include the HA1 subunit, HA2 subunit, or both the HA1 and HA2 subunits. Alternatively, or in addition, the epitope of the M2e polypeptide is a discontinuous epitope. For example, the epitope of the M2e polypeptide includes the amino acid at positions 2, 5, and 6 of MSLLTEVETPTRNEWGCRCNDSSD (SEQ ID NO: 1) or the amino acid at positions 2, 5, and 6 of SLLTEV (SEQ ID NO: 42).

[08] The invention further provides a composition including: (a) an isolated human anti-HA antibody, or an antigen-binding fragment thereof, including a heavy chain variable region (VH) domain and a light chain variable (VL) domain, wherein the VH domain and the VL domain each contain three complementarity determining regions 1 to 3 (CDR1-3), and wherein each CDR includes the following amino acid sequences: VH CDR1: SEQ ID NOs: 247, 571, 586, 597, 603, 609, 615, 627, 633, 637, 643, 649, 658, 664, 670, 303, 251, 242, or 222; VH CDR2: SEQ ID NOs: 248, 572, 587, 592, 598, 604, 610, 616, 628, 634, 638, 644, 650, 655, 659, 665, 671, 306, 249, 307, or 221; VH CDR3: SEQ ID NOs: 568, 573, 588, 593, 599, 605, 611, 617, 629, 635, 639, 645, 651, 656, 660, 666, 672, 725, 246, 290, or 220; VL CDR1: SEQ ID NOs: 569, 574, 577, 580, 583, 589, 594, 612, 618, 621, 624, 640, 646, 652, 661, 667, 285, 289, 245, 224, or 219; VL CDR2: SEQ ID NOs: 570, 575, 578, 581, 584, 590, 595, 601, 607, 613, 619, 622, 625, 631, 653, 662, 668, 305, 223, or 231;VL CDR3: SEQ ID NOs: 289, 576, 579, 582, 585, 591, 596, 602, 608, 614, 620, 623, 626, 632, 636, 642, 648, 654, 657, 663, 669, 308, 250, 227, or 280; and (b) an isolated anti-matrix 2 ectodomain (M2e) antibody, or antigen-binding fragment thereof, including a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain and the VL domain each contain three complementarity determining regions 1 to 3 (CDR1-3), and wherein each CDR includes the following amino acid sequences: VH CDR1: SEQ ID NOs: 72, 103, 179, 187, 203, 211, 228, 252, 260, 268, 284, 293, or 301; VH CDR2: SEQ ID NOs: 74, 105, 180, 188, 204, 212, 229, 237, 253, 261, 269, 285, or 294; VH CDR3 SEQ ID NOs: 76, 107, 181, 189, 197, 205, 213, 230, 238, 254, 262, 270, 286, or 295; VL CDR1: SEQ ID NOs: 59, 92, 184, 192, 208, 192, 233, 241, 265, or 273; VL CDR2: SEQ ID NOs: 61, 94, 185, 193, 209, 217, 226, 234, 258, 274, or 282; and VL CDR3: SEQ ID NOs: 63, 96, 186, 194, 210, 218, 243, 259, 267, 275, 291, or 300.

Alternatively, or in addition, the invention provides a composition including: (a) an isolated human anti-HA antibody, or an antigen-binding fragment thereof, including a heavy chain variable region (VH) domain and a light chain variable (VL) domain, wherein the VH domain and the VL domain each contain three complementarity determining regions 1 to 3 (CDR1-3), and wherein each CDR includes the following amino acid sequences: VH CDR1: SEQ ID NOs: 247, 571, 586, 597, 603, 609, 615, 627, 633, 637, 643, 649, 658, 664, 670, 303, 251, 242, or 222; VH CDR2: SEQ ID NOs: 248, 572, 587, 592, 598, 604, 610, 616, 628, 634, 638, 644, 650, 655, 659, 665, 671, 306, 249, 307, or 221; VH CDR3: SEQ ID NOs: 568, 573, 588, 593, 599, 605, 611, 617, 629, 635, 639, 645, 651, 656, 660, 666, 672, 725, 246, 290, or 220; VL CDR1: SEQ ID NOs: 569, 574, 577, 580, 583, 589, 594, 612, 618, 621, 624, 640, 646, 652, 661, 667, 285, 289, 245, 224, or 219; VL CDR2: SEQ ID NOs: 570, 575, 578, 581, 584, 590, 595, 601, 607, 613, 619, 622, 625, 631, 653, 662, 668, 305, 223, or 231; VL CDR3: SEQ ID NOs: 289, 576, 579, 582, 585, 591, 596, 602, 608, 614, 620, 623, 626, 632, 636, 642, 648, 654, 657, 663, 669, 308, 250, 227, or 280; and (b) an isolated anti-matrix 2 ectodomain (M2e) antibody, or antigen-binding fragment thereof, including a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain and the VL domain each contain three complementarity determining regions 1 to 3 (CDR1-3), and wherein each CDR includes the following amino acid sequences: VH CDR1: SEQ ID NOs: 109, 112, 182, 190, 206, 214, 239, 255, 263, 271, 287, 296, or 304; VH CDR2: SEQ ID NOs: 110, 113, 183, 191, 207, 215, 232, 240, 256, 264, 272, 288, or 297; VH CDR3 SEQ ID NOs: 76, 107, 181, 189, 197, 205, 213, 230, 238, 254, 262, 270, 286, or 295; VL CDR1: SEQ ID NOs: 59, 92, 184, 192, 208, 192, 233, 241, 265, or 273; VL CDR2: SEQ ID NOs: 61, 94, 185, 193, 209, 217, 226, 234, 258, 274, or 282; and VL CDR3: SEQ ID NOs: 63, 96, 186, 194, 210, 218, 243, 259, 267, 275, 291, or 300.

[09] The invention provides a composition including: (a) an isolated human anti-HA antibody, or an antigen-binding fragment thereof, including a heavy chain variable region (VH) domain, wherein the VH domain includes the following amino acid sequences: SEQ ID NOs 309, 313, 317, 321, 325, 329, 333, 337, 341, 345, 349, 353, 357, 361, 365, 369, 373, 377, 381, 385, 389, 393, 397, 401, 405, 409, 199, 417, 423, 429, 435, 441, 447, 453, 459, 465, 471, 477, 483, 489, 495, 501, 507, 513, 519, 525, 531, 537, 543, 550, 556, or 562, and a light chain variable (VL) domain, wherein the VL domain includes the following amino acid sequences: SEQ ID NOs 310, 314, 318, 322, 326, 330, 334, 338, 342, 346, 350, 354, 358, 362, 366, 370, 374, 378, 382, 386, 390, 394, 398, 402, 406, 410, 414, 420, 426, 432, 438,

444, 450, 456, 462, 468, 474, 480, 486, 492, 498, 504, 510, 516, 522, 528, 534, 540, 547, 553, 559, or 565; and (b) an isolated anti-matrix 2 ectodomain (M2e) antibody, or antigen-binding fragment thereof, including a heavy chain variable (VH) domain, wherein the VH domain includes the following amino acid sequences: SEQ ID NOs 44, 277, 276, 50, 236, 235, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 160, 164, 168, 172, or 176, and a light chain variable (VL) domain, wherein the VL domain includes the following amino acid sequences: SEQ ID NOs 46, 292, 52, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, or 178.

[10] Furthermore, the invention provides a multivalent vaccine composition including any of the compositionsdescribed herein containing an isolated human anti-HA antibody, or an antigen-binding fragment thereof and an isolated anti-matrix 2 ectodomain (M2e) antibody, or antigen-binding fragment thereof. Alternatively, the multivalent vaccine includes antibodies that bind to the epitopes to which the antibodies of the invention bind. Exemplary antibodies of the invention include, but are not limited to, TCN-032 (8I10), 21B15, TCN-031 (23K12), 3241_G23, 3244_I10, 3243_J07, 3259_J21, 3245_O19, 3244_H04, 3136_G05, 3252_C13, 3255_J06, 3420_I23, 3139_P23, 3248_P18, 3253_P10, 3260_D19, 3362_B11, 3242_P05, TCN-522 (3212_I12), TCN-521 (3280_D18), TCN-523 (5248_A17), TCN-563 (5237_B21), TCN-526 (5084_C17), TCN-527 (5086_C06), TCN-528 (5087_P17), TCN-529 (5297_H01), TCN-530 (5248_H10), TCN-531 (5091_H13), TCN-532 (5262_H18), TCN-533 (5256_A17), TCN-534 (5249_B02), TCN-535 (5246_P19), TCN-536 (5095_N01), TCN-537 (3194_D21), TCN-538 (3206_O17), TCN-539 (5056_A08), TCN-540 (5060_F05), TCN-541 (5062_M11), TCN-542 (5079_A16), TCN-543 (5081_G23), TCN-544 (5082_A19), TCN-545 (5082_I15), TCN-546 (5089_L08), TCN-547 (5092_F11), TCN-548 (5092_P01), TCN-549 (5092_P04), TCN-550 (5096_F06), TCN-551 (5243_D01), TCN-552 (5249_I23), TCN-553 (5261_C18), TCN-554 (5277_M05), TCN-555 (5246_L16), TCN-556 (5089_K12), TCN-557 (5081_A04), TCN 558 (5248_H10b), TCN-559 (5097_G08), TCN-560 (5084_P10), TCN-504 (3251_K17), SC06-141, SC06-255, SC06-257, SC06-260, SC06-261, SC06-262, SC06-268, SC06-272, SC06-296, SC06-301, SC06-307, SC06-310, SC06-314, SC06-323, SC06-325, SC06-327, SC06-328, SC06-329, SC06-331, SC06-332, SC06-334, SC06-336, SC06-339, SC06-342, SC06-343, SC06-344, CR6141, CR6255, CR6257, CR6260, CR6261, CR6262, CR6268, CR6272, CR6296, CR6301, CR6307, CR6310, CR6314, CR6323, CR6325, CR6327, CR6328, CR6329, CR6331, CR6332, CR6334, CR6336, CR6339, CR6342, CR6343, CR6344, D7, D8, F10, G17, H40, A66, D80, E88, E90,

and H98. For example, the multivalent vaccine may include one or more of the following epitopes: GVTNKVNSIIDK (SEQ ID NO: 198), GVTNKVNSIINK (SEQ ID NO: 283), GVTNKENSIIDK (SEQ ID NO: 202), GVTNKVNRIIDK (SEQ ID NO: 201), GITNKVNSVIEK (SEQ ID NO: 281), GITNKENSVIEK (SEQ ID NO: 257), GITNKVNSIIDK (SEQ ID NO: 225), KITSKVNNIVDK (SEQ ID NO: 216), MSLLTEVETPTRNEWGCRCNDSSD (SEQ ID NO: 1), and MSLLTEVETPTRNEWGCRCNDSSD (SEQ ID NO: 1) provided in its native conformation.

[11] The multivalent vaccine also includes a composition including: (a) a human antibody that specifically binds to an epitope of the hemagglutinin (HA) glycoprotein of an influenza virus; and (b) a human monoclonal antibody that specifically binds to an epitope in the extracellular domain of the matrix 2 ectodomain (M2e) polypeptide of an influenza virus.

[12] The invention provides a pharmaceutical composition including any one of the compositions described herein. Moreover, the pharmaceutical composition includes a pharmaceutical carrier.

[13] The invention provides a method for stimulating an immune response in a subject, including administering to the subject the pharmaceutical composition described herein. The pharmaceutical composition may administered prior to or after exposure of the subject to an Influenza virus.

[14] The invention also provides a method for the treatment of an influenza virus infection in a subject in need thereof, including administering to the subject the pharmaceutical composition described herein. The subjection may have been exposed to an influenza virus. Alternatively, or in addition, the subject has not been diagnosed with an influenza infection. The pharmaceutical composition may administered prior to or after exposure of the subject to an Influenza virus. Preferably, the pharmaceutical composition is administered at a dose sufficient to promote viral clearance or eliminate influenza infected cells.

[15] The invention further provides a method for the prevention of an influenza virus infection in a subject in need thereof, including administering to the subject a vaccine composition described herein, prior to exposure of the subject to an influenza virus. In certain embodiments of this method, the subject is at risk of contracting an influenza infection. The pharmaceutical composition may administered prior to or after exposure of the subject to an Influenza virus. Preferably, the pharmaceutical composition is administered at a dose sufficient to promote viral clearance or eliminate influenza infected cells.

[16] The treatment and prevention methods provided by the invention further include administering an anti-viral drug, a viral entry inhibitor or a viral attachment inhibitor. Exemplary anti-viral drugs include, but are not limited to, a neuraminidase inhibitor, a HA inhibitor, a sialic acid inhibitor, or an M2 ion channel inhibitor. In certain aspects of these methods, the M2 ion channel inhibitor is amantadine or rimantadine. In other aspects of these methods, the neuraminidase inhibitor is zanamivir or oseltamivir phosphate. The antiviral drug may administered prior to or after exposure of the subject to an Influenza virus.

[17] The treatment and prevention methods provided by the invention further include administering a second anti-Influenza A antibody. The second antibody is optionally an antibody described herein. The second antibody may administered prior to or after exposure of the subject to an Influenza virus.

[18] The invention provides a method for determining the presence of an Influenza virus infection in a subject, including the steps of: (a) contacting a biological sample obtained from the subject with any one of the antibodies or pharmaceutical compositions described herein; (b) detecting an amount of the antibody that binds to the biological sample; and (c) comparing the amount of antibody that binds to the biological sample to a control value, and therefrom determining the presence of the Influenza virus in the subject. Optionally, the control value is determined by contacting a control sample obtained from the subject with any one of the antibodies or pharmaceutical compositions described herein and detecting an amount of the antibody that binds to the control sample.

[19] The invention also provides a diagnostic kit including any one of the antibodies, compositions, or pharmaceutical compositions described herein.

[20] The invention further provides a prophylactic kit including a vaccine composition described herein. Preferably, the vaccine is a multivalent vaccine. The term "multivalent vaccine" describes a single vaccine that elicits an immune response either to more than one infectious agent, *e.g.* the influenza HA glycoprotein and the influenza M2e polypeptide, or to several different epitopes of a molecule, *e.g.* HA epitopes shown in SEQ ID NOs 198, 283, 202, 201, 281, 257, 225, and 216. Alternatively, or in addition, the term multivalent vaccine is meant to describe the administration of a combination of human antibodies raised against more than one infectious agent, *e.g.* the influenza HA glycoprotein and the influenza M2e polypeptide.

[21] Other features and advantages of the invention will be apparent from and are encompassed by the following detailed description and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[22] Figure 1 shows the binding of three antibodies of the present invention and control hu14C2 antibody to 293-HEK cells transfected with an M2 expression construct or control vector, in the presence or absence of free M2 peptide.

[23] Figures 2A and B are graphs showing human monoclonal antibody binding to influenza A/Puerto Rico/8/32.

[24] Figure 3A is a chart showing amino acid sequences of extracellular domains of M2 variants (SEQ ID NOS 1-3, 679 &5-40, respectively, in order of appearance).

[25] Figures 3B and C are bar charts showing binding of human monoclonal anti-influenza antibody binding to M2 variants shown in Figure 3A.

[26] Figures 4A and B are bar charts showing binding of human monoclonal anti-influenza antibody binding to M2 peptides subjected to alanine scanning mutagenesis.

[27] Figure 5 is a series of bar charts showing binding of MAbs 8i10 and 23K12 to M2 protein representing influenza strain A/HK/483/1997 sequence that was stably expressed in the CHO cell line DG44.

[28] Figure 6A is a chart showing cross reactivity binding of anti-M2 antibodies to variant M2 peptides (SEQ ID NOS 680-704, respectively, in order of appearance).

[29] Figure 6B is a chart showing binding activity of M2 antibodies to truncated M2 peptides (SEQ ID NOS 680, 705-724 &19, respectively, in order of appearance).

[30] Figure 7 is a graph showing survival of influenza infected mice treated with human anti-influenza monoclonal antibodies.

[31] Figure 8 is an illustration showing the anti-M2 antibodies bind a highly conserved region in the N-Terminus of M2e (SEQ ID NO: 19).

[32] Figure 9 is a graph showing anti-M2 rHMAb clones from crude supernatant bound to influenza on ELISA, whereas the control anti-M2e mAb 14C2 did not readily bind virus.

[33] Figure 10 is a series of photographs showing anti-M2 rHMAbs bound to cells infected with influenza. MDCK cells were or were not infected with influencza A/PR/8/32 and Ab binding from crude supernatant was tested 24 hours later. Data were gathered from the FMAT plate scanner.

[34] Figure 11 is a graph showing anti-M2 rHMAb clones from crude supernatant bound to cells transfected with the influenza subtypes H3N2, HK483, and VN1203 M2 proteins. Plasmids encoding full length M2 cDNAs corresponding to influenza strains H3N2, HK483,

and VN1203, as well as a mock plasmid control, were transiently transfected into 293 cells. The 14C2, 8i10, 23K12, and 21B15 mABs were tested for binding to the transfectants, and were detected with an AF647-conjugated anti-human IgG secondary antibody. Shown are the mean fluorescence intensities of the specific mAB bound after FACS analysis.

[35] Figures 12A-B are amino acid sequences of the variable regions of anti-M2e mAbs. Framework regions 1-4 (FR 1-4) and complementarity determining regions 1-3 (CDR 1-3) for VH and Vk are shown. FR, CDR, and gene names are defined using the nomenclature in the IMGT database (IMGT®, the International ImMunoGeneTics Information system® http://www.imgt.org). Grey boxes denote identity with the germline sequence which is shown in light blue boxes, hyphens denote gaps, and white boxes are amino acid replacement mutations from the germline.

[36] Figure 13 is a graph depicting the results of a competition binding analysis of a panel of anti-M2e mAbs with TCN-032 Fab. The indicated anti-M2e mAbs were used to bind to the stable CHO transfectant expressing M2 of A/Hong Kong/483/97 that had previously been treated with or without 10 μg/mL TCN-032 Fab fragment. The anti-M2e mAb bound to the cell surface was detected with goat anti-huIgG FcAlexafluor488 FACS and analyzed by flow cytometry. The results are derived from one experiment.

[37] Figure 14A is a graph depicting the ability of anti-M2e mAbs TCN-032 and TCN-031 to bind virus particles and virus-infected cells but not M2e-derived synthetic peptide. Purified influenza virus (A/Puerto Rico/8/34) was coated at 10 μg/ml on ELISA wells and binding of anti-M2e mAbs TCN-031, TCN-032, ch14C2, and the HCMV mAbs 2N9 was evaluated using HRP-labeled goat anti-human Fc. Results shown are representative of 3 experiments.

[38] Figure 14B is a graph depicting the ability of anti-M2e mAbs TCN-032 and TCN-031 to bind virus particles and virus-infected cells but not M2e-derived synthetic peptide. 23mer synthetic peptide of M2 derived from A/Fort Worth/1/50 was coated at 1 μg/ml on ELISA wells and binding of mAbs TCN-031, TCN-032, ch14C2, and 2N9 were evaluated as in panel a. Results shown are representative of 3 experiments.

[39] Figure 14C is a graph depicting the ability of anti-M2e mAbs TCN-032 and TCN-031 to bind virus particles and virus-infected cells but not M2e-derived synthetic peptide. MDCK cells were infected with A/Puerto Rico/8/34 (PR8) and subsequently stained with mAbs TCN-031, TCN-032, ch14C2 and the HCMV mAb 5J12. Binding of antibodies was

detected using Alexafluor 647-conjugated goat anti-Human IgG H&L antibody and quantified by flow cytometry. Results shown are representative of 3 experiments.

[40] Figure 14D is a series of photographs depicting HEK 293 cells stably transfected with the M2 ectodomain of A/Fort Worth /1/50 (D20) were stained with transient transfection supernatant containing mAbs TCN-031, TCN-032, or the control ch14C2 and analyzed by FMAT for binding to M2 in the presence or absence of 5 ug/ml M2e peptide. Mock transfected cells are 293 cells stably transfected with vector alone. Results shown are representative of one experiment.

[41] Figures 15A-D are graphs depicting the Therapeutic efficacy of anti-M2 mAbs TCN-031 and TCN-032 in mice. Mice (n=10) were infected by intranasal inoculation with 5 x $_{LD50}$ A/Vietnam/1203/04 (H5N1) (panels *A-B*) or (n=5) with 5 x $_{LD50}$ A/Puerto Rico 8/34 (H1N1) (panels *C-D)*, followed by 3 intraperitoneal (ip) injections with mAbs at 24, 72, and 120 hours post-infection (a total of 3 mAb injections per mouse) and weighed daily for 14 days. Percentage survival is shown in *a* and *c*, whereas percent weight change of mice is shown in *B* and *D*. The results shown for the treatment study of mice infected with A/Vietnam/1203/04 (H5N1) are representative of 2 experiments.

[42] Figure 16 is a series of graphs depicting the viral titers in lung, liver, and brain of mice treated with anti-M2e mAbs TCN-031 and TCN-032 after challenge with H5N1 A/Vietnam/1203/04. BALB/C mice (n=19) were treated i.p. injection of a 400 μg/200 μL dose of TCN-031, TCN-032, control human mAb 2N9, control chimeric mAb ch14C2, PBS, or left untreated. Tissue viral titers were determined from 3 mice per group at 3 and 6 days post-infection in the lungs (as an indicator of local replication) and in liver and brain (as an indicator of the systemic spread which is characteristic of H5N1 infection).

[43] Figure 17 is a graph depicting the ability of TCN-031 and TCN-032 can potentiate cytolysis by NK cells. MDCK cells were infected with A/Solomon Island/3/2006 (H1N1) virus, and were treated with mAbs TCN-031, TCN-032, or the subclass-matched negative control mAb 2N9. The cells were then challenged with purified human NK cells, and the lactate dehydrogenase released as a result of cell lysis was measured through light absorbance. The results are representative of two separate experiments with two different normal human donors.

[44] Figure 18 is a graph depicting complement-dependent cytolysis (CDC) of M2-expressing cells bound with anti-M2 mAb. The stable transfectant expressing M2 of A/Hong Kong/483/97 and a mock control were treated with the indicated mAbs and subsequently

challenged with human complement. Lysed cells were visualized by Propidium Iodide staining followed by FACS analysis. The data are representative of two experiments.

[45] Figures 19A-C are graphs depicting binding of anti-M2e mAbs TCN-031 and TCN-032 to M2 mutants indicates the epitope is located in the highly conserved N-terminal of M2e. Mutants with alanine substituted at each position of the M2 ectodomain of A/Fort Worth /1/50 (D20)(A) or forty wild-type M2 mutants including A/Vietnam/1203/04 (VN) and A/Hong Kong/483/97 (HK) (*B*) were transiently transfected into 293 cells. The identity of each wild-type M2 mutant is listed in Table 6. Transfected cells were stained with mAbs TCN-031, TCN-032, or the control ch14C2 and analyzed by FACS for binding to M2 at 24 hours post-transfection. mAbs TCN-031 and TCN-032 do not bind variants with amino acid substitutions at positions 1, 4, or 5 of M2e. (*C*) The deduced epitope for TCN-031 and TCN-032 occurs in a highly conserved region of M2e and is distinct from that found for ch14C2. Results shown for (*A*) and (*B*) are representative of 3 experiments.

[46] Figure 20 is a graph depicting mAbs TCN-031 and TCN-032 recognize the same region on M2e. The CHO transfectant stably expressing M2 for A/Hong Kong/483/97 as stained with 10 μg/mL TCN-031, TCN-032, or 2N9, followed by detection with Alexafluor647-labeled TCN-031 (TCN-031AF647) or TCN-032(TCN-032AF647) and analysis by flow cytometry. The results are representative of three experiments.

[47] Figure 21 is a graph depicting anti-M2e mAbs TCN-031 and TCN-032 bind cells that have been infected with H1N1 A/California/4/09. MDCK cells were infected with Influenza A strain H1N1 A/Memphis/14/96, H1N1 A/California/4/09, or mock infected. Twenty four hours post-infection cells were stained with mAbs TCN-031, TCN-032, or the control ch14C2 and analyzed by FACS for binding to M2. Results shown are for one experiment.

DETAILED DESCRIPTION

[48] Influenza viruses consist of three types, A, B and C. Influenza A viruses infect a wide variety of birds and mammals, including humans, horses, marine mammals, pigs, ferrets, and chickens. In animals most influenza A viruses cause mild localized infections of the respiratory and intestinal tract. However, highly pathogenic influenza A strains such as H5N1 exist that cause systemic infections in poultry in which mortality may reach 100%. Animals infected with influenza A often act as a reservoir for the influenza viruses and certain subtypes have been shown to cross the species barrier to humans.

[49] Influenza A viruses can be classified into subtypes based on allelic variations in antigenic regions of two genes that encode surface glycoproteins, namely, hemagglutinin (HA) and neuraminidase (NA) which are required for viral attachment and cellular release. Other major viral proteins include the nucleoprotein, the nucleocapsid structural protein, membrane proteins (M1 and M2), polymerases (PA, PB and PB2) and non-structural proteins (NS1 and NS2). Currently, sixteen subtypes of HA (H1-H16) and nine NA (N1-N9) antigenic variants are known in influenza A virus. Previously, only three subtypes have been known to circulate in humans (H1N1, H1N2, and H3N2).

[50] However, in recent years, the pathogenic H5N1 subtype of avian influenza A has been reported to cross the species barrier and infect humans as documented in Hong Kong in 1997 and 2003, leading to the death of several patients. In humans, the avian influenza virus infects cells of the respiratory tract as well as the intestinal tract, liver, spleen, kidneys and other organs. Symptoms of avian influenza infection include fever, respiratory difficulties including shortness of breath and cough, lymphopenia, diarrhea and difficulties regulating blood sugar levels. In contrast to seasonal influenza, the group most at risk is healthy adults, which make up the bulk of the population. Due to the high pathogenicity of certain avian influenza A subtypes, particularly H5N1, and their demonstrated ability to cross over to infect humans, there is a significant economic and public health risk associated with these viral strains, including a real epidemic and pandemic threat. The scale of the threat is illustrated by the 1918 influenza pandemic which killed over 50 million people.

[51] Currently, no effective vaccines for H5N1 infection are available, so passive immunotherapy with immunoglobulins may be an alternative strategy. Use of passive immunization during the 1918 pandemic reportedly halved the death rate. In view of their therapeutic benefit in humans, there is thus a need for antibodies, preferably human antibodies, capable of neutralizing influenza infection, including H5N1.

[52] The invention provides compositions including human antibodies raised against two influenza proteins, hemagglutinin (HA) and matrix 2 ectodomain (M2e), and shows that these compositions can be used in medicine, in particular for diagnosis, prevention and treatment of influenza infections, including H5N1.

HuM2e Antibodies

[53] The present invention provides fully human monoclonal antibodies specifically directed against M2e. Optionally, the antibody is isolated form a B-cell from a human donor. Exemplary monoclonal antibodies include TCN-032 (8I10), 21B15, TCN-031 (23K12),

3241_G23, 3244_I10, 3243_J07, 3259_J21, 3245_O19, 3244_H04, 3136_G05, 3252_C13, 3255_J06, 3420_I23, 3139_P23, 3248_P18, 3253_P10, 3260_D19, 3362_B11, and 3242_P05.described herein. Alternatively, the monoclonal antibody is an antibody that binds to the same epitope as TCN-032 (8I10), 21B15, TCN-031 (23K12), 3241_G23, 3244_I10, 3243_J07, 3259_J21, 3245_O19, 3244_H04, 3136_G05, 3252_C13, 3255_J06, 3420_I23, 3139_P23, 3248_P18, 3253_P10, 3260_D19, 3362_B11, and 3242_P05. The antibodies respectively referred to herein are huM2e antibodies. The huM2e antibody has one or more of the following characteristics: a) binds to an epitope in the extracellular domain of the matrix 2 ectodomain (M2e) polypeptide of an influenza virus; b) binds to influenza A infected cells; or c) binds to influenza A virus.

[54] The epitope that huM2e antibody binds to is a non-linear epitope of a M2 polypeptide. Preferably, the epitope includes the amino terminal region of the M2e polypeptide. More preferably the epitope wholly or partially includes the amino acid sequence SLLTEV (SEQ ID NO: 42). Most preferably, the epitope includes the amino acid at position 2, 5 and 6 of the M2e polypeptide when numbered in accordance with SEQ ID NO: 1. The amino acid at position 2 is a serine; at position 5 is a threonine; and at position 6 is a glutamic acid.

[55] A huM2e antibody contains a heavy chain variable having the amino acid sequence of SEQ ID NOs: 44, 277, 276, 50, 236, 235, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 160, 164, 168, 172, or 176 and a light chain variable having the amino acid sequence of SEQ ID NOs: 46, 52, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, or 178. Preferably, the three heavy chain CDRs include an amino acid sequence at least 90%, 92%, 95%, 97% 98%, 99% or more identical to the amino acid sequence of SEQ ID NOs: 72, 74, 76, 103, 105, 107, 179, 180, 181, 187, 188, 189, 197, 203, 204, 205, 21, 212, 213, 228, 229, 230, 237, 238, 252, 253, 254, 260, 261, 262, 268, 269, 270, 284, 285, 286, 293, 294, 295, and 301 (as determined by the Kabat method) or SEQ ID NOs: 109, 110, 76, 112, 113, 107, 182, 183, 181, 190, 191, 189, , 197, 206, 207, 205, 214, 215, 213, 232, 230, 239, 240, 238, 255, 256, 254, 263, 264, 262, 271, 272, 270, 287, 288, 286, 296, 297, 295, and 304 (as determined by the Chothia method) and a light chain with three CDRs that include an amino acid sequence at least 90%, 92%, 95%, 97% 98%, 99% or more identical to the amino acid sequence of SEQ ID NOs: 59, 60, 61, 92, 94, 96, 184, 185, 186, 192, 193, 194, 208, 209, 210, , 217, 218, 226, 223, 234, 241, 243, 258, 259, 265, 267, 273, 274, 275, 282, 291, and 300 (as determined by the Kabat method) or SEQ ID NOs: 59, 60, 61, 92, 94, 96, 184, 185, 186, 192, 193, 194, 208, 209, 210, , 217, 218, 226, 223, 234, 241, 243, 258, 259, 265, 267,

273, 274, 275, 282, 291, and 300 (as determined by the Chothia method). The antibody binds M2e.

[56] The heavy chain of a M2e antibody is derived from a germ line V (variable) gene such as, for example, the IgHV4 or the IgHV3 germline gene.

[57] The M2e antibodies of the invention include a variable heavy chain (V_H) region encoded by a human IgHV4 or the IgHV3 germline gene sequence. A IgHV4 germline gene sequence are shown, *e.g.*, in Accession numbers L10088, M29812, M95114, X56360 and M95117. IgHV3 germline gene sequence are shown, *e.g.*, in Accession numbers X92218, X70208, Z27504, M99679 and AB019437. The M2e antibodies of the invention include a V_H region that is encoded by a nucleic acid sequence that is at least 80% homologous to the IgHV4 or the IgHV3 germline gene sequence. Preferably, the nucleic acid sequence is at least 90%, 95%, 96%, 97% homologous to the IgHV4 or the IgHV3 germline gene sequence, and more preferably, at least 98%, 99% homologous to the IgHV4 or the IgHV3 germline gene sequence. The V_H region of the M2e antibody is at least 80% homologous to the amino acid sequence of the V_H region encoded by the IgHV4 or the IgHV3 V_H germline gene sequence. Preferably, the amino acid sequence of V_H region of the M2e antibody is at least 90%, 95%, 96%, 97% homologous to the amino acid sequence encoded by the IgHV4 or the IgHV3 germline gene sequence, and more preferably, at least 98%, 99% homologous to the sequence encoded by the IgHV4 or the IgHV3 germline gene sequence.

[58] The M2e antibodies of the invention also include a variable light chain (V_L) region encoded by a human IgKV1 germline gene sequence. A human IgKV1 V_L germline gene sequence is shown, *e.g.*, Accession numbers X59315, X59312, X59318, J00248, and Y14865. Alternatively, the M2e antibodies include a V_L region that is encoded by a nucleic acid sequence that is at least 80% homologous to the IgKV1 germline gene sequence. Preferably, the nucleic acid sequence is at least 90%, 95%, 96%, 97% homologous to the IgKV1 germline gene sequence, and more preferably, at least 98%, 99% homologous to the IgKV1 germline gene sequence. The V_L region of the M2e antibody is at least 80% homologous to the amino acid sequence of the V_L region encoded the IgKV1 germline gene sequence. Preferably, the amino acid sequence of V_L region of the M2e antibody is at least 90%, 95%, 96%, 97% homologous to the amino acid sequence encoded by the IgKV1 germline gene sequence, and more preferably, at least 98%, 99% homologous to the sequence encoded by e the IgKV1 germline gene sequence.

[59] In another aspect the invention provides a composition including an huM2e antibody according to the invention. In various aspects the composition further includes an anti-viral drug, a viral entry inhibitor or a viral attachment inhibitor. The anti-viral drug is for example a neuraminidase inhibitor, a HA inhibitor, a sialic acid inhibitor or an M2 ion channel inhibitor. The M2 ion channel inhibitor is for example amantadine or rimantadine. The neuraminidase inhibitor for example zanamivir, or oseltamivir phosphate. In a further aspect the composition further includes a second anti-influenza A antibody.

[60] In a further aspect the huM2e antibodies according to the invention are operably-linked to a therapeutic agent or a detectable label.

[61] Additionally, the invention provides methods for stimulating an immune response, treating, preventing or alleviating a symptom of an influenza viral infection by administering an huM2e antibody to a subject

[62] Optionally, the subject is further administered with a second agent such as, but not limited to, an influenza virus antibody, an anti-viral drug such as a neuraminidase inhibitor, a HA inhibitor, a sialic acid inhibitor or an M2 ion channel inhibitor, a viral entry inhibitor or a viral attachment inhibitor. The M2 ion channel inhibitor is, for example, amantadine or rimantadine. The neuraminidase inhibitor is, for example, zanamivir or oseltamivir phosphate. The subject is suffering from or is predisposed to developing an influenza virus infection, such as, for example, an autoimmune disease or an inflammatory disorder.

[63] In another aspect, the invention provides methods of administering the huM2e antibody of the invention to a subject prior to, and/or after exposure to an influenza virus. For example, the huM2e antibody of the invention is used to treat or prevent rejection influenza infection. The huM2e antibody is administered at a dose sufficient to promote viral clearance or eliminate influenza A infected cells.

[64] Also included in the invention is a method for determining the presence of an influenza virus infection in a patient, by contacting a biological sample obtained from the patient with a humM2e antibody; detecting an amount of the antibody that binds to the biological sample; and comparing the amount of antibody that binds to the biological sample to a control value.

[65] The invention further provides a diagnostic kit comprising a huM2e antibody.

[66] Other features and advantages of the invention will be apparent from and are encompassed by the following detailed description and claims.

[67] The present invention provides fully human monoclonal antibodies specific against the extracellular domain of the matrix 2 (M2) polypeptide. The antibodies are respectively referred to herein as huM2e antibodies.

[68] M2 is a 96 amino acid transmembrane protein present as a homotetramer on the surface of influenza virus and virally infected cells. M2 contains a 23 amino acid ectodomain (M2e) that is highly conserved across influenza A strains. Few amino acid changes have occurred since the 1918 pandemic strain thus M2e is an attractive target for influenza therapies. In prior studies, monoclonal antibodies specific to the M2 ectodomain (M2e) were derived upon immunizations with a peptide corresponding to the linear sequence of M2e. In contrast, the present invention provides a novel process whereby full-length M2 is expressed in cell lines, which allows for the identification of human antibodies that bound this cell-expressed M2e. The huM2e antibodies have been shown to bind conformational determinants on the M2-transfected cells, as well as native M2, either on influenza infected cells, or on the virus itself. The huM2e antibodies did not bind the linear M2e peptide, but they do bind several natural M2 variants, also expressed upon cDNA transfection into cell lines. Thus, this invention has allowed for the identification and production of human monoclonal antibodies that exhibit novel specificity for a very broad range of influenza A virus strains. These antibodies may be used diagnostically to identify influenza A infection and therapeutically to treat influenza A infection.

[69] The huM2e antibodies of the invention have one or more of the following characteristics: the huM2e antibody binds a) to an epitope in the extracellular domain of the matrix 2 (M2) polypeptide of an influenza virus; b) binds to influenza A infected cells; and/or c) binds to influenza A virus (i.e., virons). The huM2e antibodies of the invention eliminate influenza infected cells through immune effector mechanisms, such as ADCC, and promote direct viral clearance by binding to influenza virons. The huM2e antibodies of the invention bind to the amino-terminal region of the M2e polypeptide. Preferably, the huM2e antibodies of the invention bind to the amino-terminal region of the M2e polypeptide wherein the N-terminal methionine residue is absent. Exemplary M2e sequences include those sequences listed on Table 1 below

[70] **Table 1**

Type	Name	Subtype	M2E Sequence	SEQ ID NO
A	BREVIG MISSION.1.1918	H1N1	MSLLTEVETPTRNEWGCRCNDSSD	SEQ ID NO: 1
A	FORT MONMOUTH.1.1947	H1N1	MSLLTEVETPTKNEWECRCNDSSD	SEQ ID NO: 2
A	.SINGAPORE.02.2005	H3N2	MSLLTEVETPIRNEWECRCNDSSD	SEQ ID NO: 3
A	WISCONSIN.10.98	H1N1	MSLLTEVETPIRNGWECKCNDSSD	SEQ ID NO: 4
A	WISCONSIN.301.1976	H1N1	MSLLTEVETPIRSEWGCRCNDSSD	SEQ ID NO: 5
A	PANAMA.1.66	H2N2	MSFLPEVETPIRNEWGCRCNDSSD	SEQ ID NO: 6
A	NEW YORK.321.1999	H3N2	MSLLTEVETPIRNEWGCRCNDSSN	SEQ ID NO: 7
A	CARACAS.1.71	H3N2	MSLLTEVETPIRKEWGCRCNDSSD	SEQ ID NO: 8
A	TAIWAN.3.71	H3N2	MSFLTEVETPIRNEWGCRCNDSSD	SEQ ID NO: 9
A	WUHAN.359.95	H3N2	MSLPTEVETPIRSEWGCRCNDSSD	SEQ ID NO: 10
A	HONG KONG.1144.99	H3N2	MSLLPEVETPIRNEWGCRCNDSSD	SEQ ID NO: 11
A	HONG KONG.1180.99	H3N2	MSLLPEVETPIRNGWGCRCNDSSD	SEQ ID NO: 12
A	HONG KONG.1774.99	H3N2	MSLLTEVETPTRNGWECRCSGSSD	SEQ ID NO: 13
A	NEW YORK.217.02	H1N2	MSLLTEVETPIRNEWEYRCNDSSD	SEQ ID NO: 14
A	NEW YORK.300.2003	H1N2	MSLLTEVETPIRNEWEYRCSDSSD	SEQ ID NO: 15
A	SWINE.SPAIN.54008.2004	H3N2	MSLLTEVETPTRNGWECRYSDSSD	SEQ ID NO: 16
A	GUANGZHOU.333.99	H9N2	MSFLTEVETLTRNGWECRCSDSSD	SEQ ID NO: 17
A	HONG KONG.1073.99	H9N2	MSLLTEVETLTRNGWECKCRDSSD	SEQ ID NO: 18
A	HONG KONG.1.68	H3N2	MSLLTEVETPIRNEWGCRCNDSSD	SEQ ID NO: 19
A	SWINE.HONG KONG.126.1982	H3N2	MSLLTEVETPIRSEWGCRCNDSGD	SEQ ID NO: 20
A	NEW YORK.703.1995	H3N2	MSLLTEVETPIRNEWECRCNGSSD	SEQ ID NO: 21
A	SWINE.QUEBEC.192.81	H1N1	MSLPTEVETPIRNEWGCRCNDSSD	SEQ ID NO: 22
A	PUERTO RICO.8.34	H1N1	MSLLTEVETPIRNEWGCRCNGSSD	SEQ ID NO: 23
A	HONG KONG.485.97	H5N1	MSLLTEVDTLTRNGWGCRCSDSSD	SEQ ID NO: 24
A	HONG KONG.542.97	H5N1	MSLLTEVETLTKNGWGCRCSDSSD	SEQ ID NO: 25
A	SILKY CHICKEN.SHANTOU.1826.2004	H9N2	MSLLTEVETPTRNGWECKCSDSSD	SEQ ID NO: 26
A	CHICKEN.TAIWAN.0305.04	H6N1	MSLLTEVETHTRNGWECKCSDSSD	SEQ ID NO: 27
A	QUAIL.ARKANSAS.16309-7.94	H7N3NSA	MSLLTEVKTPTRNGWECKCSDSSD	SEQ ID NO: 28
A	HONG KONG.486.97	H5N1	MSLLTEVETLTRNGWGCRCSDSSD	SEQ ID NO: 29
A	CHICKEN.PENNSYLVANIA.13552-1.98	H7N2NSB	MSLLTEVETPTRDGWECKCSDSSD	SEQ ID NO: 30
A	CHICKEN.HEILONGJIANG.48.01	H9N2	MSLLTEVETPTRNGWGCRCSDSSD	SEQ ID NO: 31
A	SWINE.KOREA.S5.2005	H1N2	MSLLTEVETPTRNGWECKCNDSSD	SEQ ID NO: 32
A	HONG KONG.1073.99	H9N2	MSLLTEVETLTRNGWECKCSDSSD	SEQ ID NO: 33
A	WISCONSIN.3523.88	H1N1	MSLLTEVETPIRNEWGCKCNDSSD	SEQ ID NO: 34
A	X-31 VACCINE STRAIN	H3N2	MSFLTEVETPIRNEWGCRCNGSSD	SEQ ID NO: 35
A	CHICKEN.ROSTOCK.8.1934	H7N1	MSLLTEVETPTRNGWECRCNDSSD	SEQ ID NO: 36
A	ENVIRONMENT.NEW YORK.16326-1.2005	H7N2	MSLLTEVETPIRKGWECNCSDSSD	SEQ ID NO: 37
A	INDONESIA.560H.2006	H5N1	MSLLTEVETPTRNEWECRCSDSSD	SEQ ID NO: 38
A	CHICKEN.HONG KONG.SF1.03	H9N2	MSLLTGVETHTRNGWGCKCSDSSD	SEQ ID NO: 39
A	CHICKEN.HONGKONG.YU427.03	H9N2	MSLLPEVETHTRNGWGCRCSDSSD	SEQ ID NO: 40

[71] In one embodiment, the huM2e antibodies of the invention bind to a M2e that wholly or partially includes the amino acid residues from position 2 to position 7 of M2e when

numbered in accordance with SEQ ID NO: 1. For example, the huM2e antibodies of the invention bind wholly or partially to the amino acid sequence SLLTEVET (SEQ ID NO: 41) Most preferably, the huM2e antibodies of the invention bind wholly or partially to the amino acid sequence SLLTEV (SEQ ID NO: 42). Preferably, the huM2e antibodies of the invention bind to non-linear epitope of the M2e protein. For example, the huM2e antibodies bind to an epitope comprising position 2, 5, and 6 of the M2e polypeptide when numbered in accordance to SEQ ID NO: 1 where the amino acid at a) position 2 is a serine;b) position 5 is a threonine; and c) position 6 is a glutamic acid. Exemplary huM2e monoclonal antibodies that bind to this epitope are the TCN-032 (8I10), 21B15, TCN-031 (23K12), 3241_G23, 3244_I10, 3243_J07, 3259_J21, 3245_O19, 3244_H04, 3136_G05, 3252_C13, 3255_J06, 3420_I23, 3139_P23, 3248_P18, 3253_P10, 3260_D19, 3362_B11, and 3242_P05 antibodies described herein.

[72] The TCN-032 (8I10) antibody includes a heavy chain variable region (SEQ ID NO: 44) encoded by the nucleic acid sequence shown below in SEQ ID NO: 43, a short heavy chain variable region (SEQ ID NO: 277) encoded by the nucleic acid sequence shown below in SEQ ID NO: 278, a long heavy chain variable region (SEQ ID NO: 276) encoded by the nucleic acid sequence shown below in SEQ ID NO: 196, and a light chain variable region (SEQ ID NO: 46) encoded by the nucleic acid sequence shown in SEQ ID NO: 45.

[73] The amino acids encompassing the CDRs as defined by Chothia, C. et al. (1989, Nature, 342: 877-883) are underlined and those defined by Kabat E.A. et al.(1991, Sequences of Proteins of Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Heath and Human Services.) are highlighted in bold in the sequences below.

[74] The heavy chain CDRs of the TCN-032 (8I10) antibody have the following sequences per Kabat definition: NYYWS (SEQ ID NO: 72), FIYYGGNTKYNPSLKS (SEQ ID NO: 74) and ASCSGGYCILD (SEQ ID NO: 76). The light chain CDRs of the TCN-032 (8I10) antibody have the following sequences per Kabat definition: RASQNIYKYLN (SEQ ID NO: 59), AASGLQS (SEQ ID NO: 61) and QQSYSPPLT (SEQ ID NO: 63).

[75] The heavy chain CDRs of the TCN-032 (8I10) antibody have the following sequences per Chothia definition: GSSISN (SEQ ID NO: 109), FIYYGGNTK (SEQ ID NO: 110) and ASCSGGYCILD (SEQ ID NO: 76). The light chain CDRs of the TCN-032 (8I10) antibody have the following sequences per Chothia definition: RASQNIYKYLN (SEQ ID NO: 59), AASGLQS (SEQ ID NO: 61) and QQSYSPPLT (SEQ ID NO: 63).

[76] TCN-032 (8I10) VH nucleotide sequence: (SEQ ID NO: 43)

CAGGTGCAATTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCAC
CTGCACTGTCTCTGGTTCGTCCATCAGTAATTACTACTGGAGCTGGATCCGGCAGTCCCCAG
GGAAGGGACTGGAGTGGATTGGGTTTATCTATTACGGTGGAAACACCAAGTACAATCCCTCC
CTCAAGAGCCGCGTCACCATATCACAAGACACTTCCAAGAGTCAGGTCTCCCTGACGATGAG
CTCTGTGACCGCTGCGGAATCGGCCGTCTATTTCTGTGCGAGAGCGTCTTGTAGTGGTGGTT
ACTGTATCCTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCG

[77] TCN-032 (8I10) VH amino acid sequence: (SEQ ID NO: 44)

Kabat Bold, Chothia underlined

Q	V	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L	T
C	T	V	S	G	S	S	I	S	**N**	**Y**	**Y**	**W**	**S**	W	I	R	Q	S	P	G
K	G	L	E	W	I	G	**F**	**I**	**Y**	**Y**	**G**	**G**	**N**	**T**	**K**	**Y**	**N**	**P**	**S**	**L**
K	**S**	R	V	T	I	S	Q	D	T	S	K	S	Q	V	S	L	T	M	S	S
V	T	A	A	E	S	A	V	Y	F	C	A	R	**A**	**S**	**C**	**S**	**G**	**G**	**Y**	**C**
I	**L**	**D**	Y	W	G	Q	G	T	L	V	T	V	S							

[78] TCN-032 (8I10) VH short nucleotide sequence: (SEQ ID NO: 278)

CAGGTGCAATTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCAC
CTGCACTGTCTCTGGTTCGTCCATCAGTAATTACTACTGGAGCTGGATCCGGCAGTCCCCAG
GGAAGGGACTGGAGTGGATTGGGTTTATCTATTACGGTGGAAACACCAAGTACAATCCCTCC
CTCAAGAGCCGCGTCACCATATCACAAGACACTTCCAAGAGTCAGGTCTCCCTGACGATGAG
CTCTGTGACCGCTGCGGAATCGGCCGTCTATTTCTGTGCGAGAGCGTCTTGTAGTGGTGGTT
ACTGTATCCTTGACTACTGGGGCCAGGGAACCCTGGTCACCGT

[79] TCN-032 (8I10) VH short amino acid sequence: (SEQ ID NO: 277)

Kabat Bold, Chothia underlined

Q	V	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L	T
C	T	V	S	G	S	S	I	S	**N**	**Y**	**Y**	**W**	**S**	W	I	R	Q	S	P	G
K	G	L	E	W	I	G	**F**	**I**	**Y**	**Y**	**G**	**G**	**N**	**T**	**K**	**Y**	**N**	**P**	**S**	**L**
K	**S**	R	V	T	I	S	Q	D	T	S	K	S	Q	V	S	L	T	M	S	S
V	T	A	A	E	S	A	V	Y	F	C	A	R	**A**	**S**	**C**	**S**	**G**	**G**	**Y**	**C**
I	**L**	**D**	Y	W	G	Q	G	T	L	V	T									

[80] TCN-032 (8I10) VH long nucleotide sequence: (SEQ ID NO: 196)

CAGGTGCAATTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCAC
CTGCACTGTCTCTGGTTCGTCCATCAGTAATTACTACTGGAGCTGGATCCGGCAGTCCCCAG
GGAAGGGACTGGAGTGGATTGGGTTTATCTATTACGGTGGAAACACCAAGTACAATCCCTCC
CTCAAGAGCCGCGTCACCATATCACAAGACACTTCCAAGAGTCAGGTCTCCCTGACGATGAG
CTCTGTGACCGCTGCGGAATCGGCCGTCTATTTCTGTGCGAGAGCGTCTTGTAGTGGTGGTT
ACTGTATCCTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC

[81] TCN-032 (8I10) VH long amino acid sequence: (SEQ ID NO: 276)

Kabat Bold, Chothia underlined

Q	V	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L	T
C	T	V	S	G	S	S	I	S	**N**	**Y**	**Y**	**W**	**S**	W	I	R	Q	S	P	G
K	G	L	E	W	I	G	**F**	**I**	**Y**	**Y**	**G**	**G**	**N**	**T**	**K**	**Y**	**N**	**P**	**S**	**L**
K	**S**	R	V	T	I	S	Q	D	T	S	K	S	Q	V	S	L	T	M	S	S
V	T	A	A	E	S	A	V	Y	F	C	A	R	**A**	**S**	**C**	**S**	**G**	**G**	**Y**	**C**
I	**L**	**D**	Y	W	G	Q	G	T	L	V	T	V	S	S						

[82] TCN-032 (8I10) VL nucleotide sequence: (SEQ ID NO: 45)

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCGAGTCAGAACATTTACAAGTATTTAAATTGGTATCAGCAGAGACCAGGGA
AAGCCCCTAAGGGCCTGATCTCTGCTGCATCCGGGTTGCAAAGTGGGGTCCCATCAAGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCACCAGTCTGCAACCTGAAGATTT
TGCAACTTACTACTGTCAACAGAGTTACAGTCCCCCTCTCACTTTCGGCGGAGGGACCAGGG
TGGAGATCAAAC

[83] TCN-032 (8I10) VL amino acid sequence: (SEQ ID NO: 46)

Kabat Bold, Chothia underlined

D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I
T	C	**R**	**A**	**S**	**Q**	**N**	**I**	**Y**	**K**	**Y**	**L**	**N**	W	Y	Q	Q	R	P	G	K
A	P	K	G	L	I	S	**A**	**A**	**S**	**G**	**L**	**Q**	**S**	G	V	P	S	R	F	S
G	S	G	S	G	T	D	F	T	L	T	I	T	S	L	Q	P	E	D	F	A
T	Y	Y	C	**Q**	**Q**	**S**	**Y**	**S**	**P**	**P**	**L**	**T**	F	G	G	G	T	R	V	E
I	K																			

[84] The 21B15 antibody includes a heavy chain variable region (SEQ ID NO: 44) encoded by the nucleic acid sequence shown below in SEQ ID NO: 47, a short heavy chain variable region (SEQ ID NO: 277) encoded by the nucleic acid sequence shown below in SEQ ID NO: 278, a long heavy chain variable region (SEQ ID NO: 276) encoded by the nucleic acid sequence shown below in SEQ ID NO: 196, and a light chain variable region (SEQ ID NO: 46) encoded by the nucleic acid sequence shown in SEQ ID NO: 48.

[85] The amino acids encompassing the CDRs as defined by Chothia et al. 1989, are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[86] The heavy chain CDRs of the 21B15 antibody have the following sequences per Kabat definition: NYYWS (SEQ ID NO: 72), FIYYGGNTKYNPSLKS (SEQ ID NO: 74) and ASCSGGYCILD (SEQ ID NO: 76). The light chain CDRs of the 21B15 antibody have

the following sequences per Kabat definition: RASQNIYKYLN (SEQ ID NO: 59), AASGLQS (SEQ ID NO: 61) and QQSYSPPLT (SEQ ID NO: 63).

[87] The heavy chain CDRs of the 21B15 antibody have the following sequences per Chothia definition: GSSISN (SEQ ID NO: 109), FIYYGGNTK (SEQ ID NO: 110) and ASCSGGYCILD (SEQ ID NO: 76). The light chain CDRs of the 21B15 antibody have the following sequences per Chothia definition: RASQNIYKYLN (SEQ ID NO: 59), AASGLQS (SEQ ID NO: 61) and QQSYSPPLT (SEQ ID NO: 63).

[88] 21B15 VH nucleotide sequence: (SEQ ID NO: 47)

CAGGTGCAATTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCAC
CTGCACTGTCTCTGGTTCGTCCATCAGTAATTACTACTGGAGCTGGATCCGGCAGTCCCCAG
GGAAGGGACTGGAGTGGATTGGGTTTATCTATTACGGTGGAAACACCAAGTACAATCCCTCC
CTCAAGAGCCGCGTCACCATATCACAAGACACTTCCAAGAGTCAGGTCTCCCTGACGATGAG
CTCTGTGACCGCTGCGGAATCGGCCGTCTATTTCTGTGCGAGAGCGTCTTGTAGTGGTGGTT
ACTGTATCCTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCG

[89] 21B15 VH amino acid sequence: (SEQ ID NO: 44)

Kabat Bold, Chothia underlined

Q	V	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L	T
C	T	V	S	G	S	S	I	S	**N**	**Y**	**Y**	**W**	**S**	W	I	R	Q	S	P	G
K	G	L	E	W	I	G	**F**	**I**	**Y**	**Y**	**G**	**G**	**N**	**T**	**K**	**Y**	**N**	**P**	**S**	**L**
K	**S**	R	V	T	I	S	Q	D	T	S	K	S	Q	V	S	L	T	M	S	S
V	T	A	A	E	S	A	V	Y	F	C	A	R	**A**	**S**	**C**	**S**	**G**	**G**	**Y**	**C**
I	**L**	**D**	Y	W	G	Q	G	T	L	V	T	V	S							

[90] 21B15 VH short nucleotide sequence: (SEQ ID NO: 278)

CAGGTGCAATTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCAC
CTGCACTGTCTCTGGTTCGTCCATCAGTAATTACTACTGGAGCTGGATCCGGCAGTCCCCAG
GGAAGGGACTGGAGTGGATTGGGTTTATCTATTACGGTGGAAACACCAAGTACAATCCCTCC
CTCAAGAGCCGCGTCACCATATCACAAGACACTTCCAAGAGTCAGGTCTCCCTGACGATGAG
CTCTGTGACCGCTGCGGAATCGGCCGTCTATTTCTGTGCGAGAGCGTCTTGTAGTGGTGGTT
ACTGTATCCTTGACTACTGGGGCCAGGGAACCCTGGTCACCGT

[91] 21B15 VH short amino acid sequence: (SEQ ID NO: 277)

Kabat Bold, Chothia underlined

Q	V	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L	T
C	T	V	S	G	S	S	I	S	**N**	**Y**	**Y**	**W**	**S**	W	I	R	Q	S	P	G
K	G	L	E	W	I	G	**F**	**I**	**Y**	**Y**	**G**	**G**	**N**	**T**	**K**	**Y**	**N**	**P**	**S**	**L**
K	**S**	R	V	T	I	S	Q	D	T	S	K	S	Q	V	S	L	T	M	S	S
V	T	A	A	E	S	A	V	Y	F	C	A	R	**A**	**S**	**C**	**S**	**G**	**G**	**Y**	**C**
I	**L**	**D**	Y	W	G	Q	G	T	L	V	T									

[92] 21B15 VH long nucleotide sequence: (SEQ ID NO: 196)

CAGGTGCAATTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCAC
CTGCACTGTCTCTGGTTCGTCCATCAGTAATTACTACTGGAGCTGGATCCGGCAGTCCCCAG
GGAAGGGACTGGAGTGGATTGGGTTTATCTATTACGGTGGAAACACCAAGTACAATCCCTCC
CTCAAGAGCCGCGTCACCATATCACAAGACACTTCCAAGAGTCAGGTCTCCCTGACGATGAG
CTCTGTGACCGCTGCGGAATCGGCCGTCTATTTCTGTGCGAGAGCGTCTTGTAGTGGTGGTT
ACTGTATCCTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC

[93] 21B15 VH long amino acid sequence: (SEQ ID NO: 276)

Kabat Bold, Chothia underlined

Q	V	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L	T
C	T	V	S	G	S	S	I	S	**N**	**Y**	**Y**	**W**	**S**	W	I	R	Q	S	P	G
K	G	L	E	W	I	G	**F**	**I**	**Y**	**Y**	**G**	**G**	**N**	**T**	**K**	**Y**	**N**	**P**	**S**	**L**
K	**S**	R	V	T	I	S	Q	D	T	S	K	S	Q	V	S	L	T	M	S	S
V	T	A	A	E	S	A	V	Y	F	C	A	R	**A**	**S**	**C**	**S**	**G**	**G**	**Y**	**C**
I	**L**	**D**	Y	W	G	Q	G	T	L	V	T	V	S	S						

[94] 21B15 VL nucleotide sequence: (SEQ ID NO: 48)

GACATCCAGGTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGCGCGAGTCAGAACATTTACAAGTATTTAAATTGGTATCAGCAGAGACCAGGGA
AAGCCCCTAAGGGCCTGATCTCTGCTGCATCCGGGTTGCAAAGTGGGGTCCCATCAAGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCACCAGTCTGCAACCTGAAGATTT
TGCAACTTACTACTGTCAACAGAGTTACAGTCCCCCTCTCACTTTCGGCGGAGGGACCAGGG
TGGATATCAAAC

[95] 21B15 VL amino acid sequence: (SEQ ID NO: 292)

Kabat Bold, Chothia underlined

D	I	Q	V	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I
T	C	**R**	**A**	**S**	**Q**	**N**	**I**	**Y**	**K**	**Y**	**L**	**N**	W	Y	Q	Q	R	P	G	K
A	P	K	G	L	I	S	**A**	**A**	**S**	**G**	**L**	**Q**	**S**	G	V	P	S	R	F	S
G	S	G	S	G	T	D	F	T	L	T	I	T	S	L	Q	P	E	D	F	A
T	Y	Y	C	**Q**	**Q**	**S**	**Y**	**S**	**P**	**P**	**L**	**T**	F	G	G	G	T	R	V	D
I	K																			

[96] The TCN-031 (23K12) antibody includes a heavy chain variable region (SEQ ID NO: 50) encoded by the nucleic acid sequence shown below in SEQ ID NO: 49, a short heavy chain variable region (SEQ ID NO: 236) encoded by the nucleic acid sequence shown below in SEQ ID NO: 244, a long heavy chain variable region (SEQ ID NO: 195) encoded by the

nucleic acid sequence shown below in SEQ ID NO: 235, and a light chain variable region (SEQ ID NO: 52) encoded by the nucleic acid sequence shown in SEQ ID NO: 51.

[97] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[98] The heavy chain CDRs of the TCN-031 (23K12) antibody have the following sequences per Kabat definition: SNYMS (SEQ ID NO: 103), VIYSGGSTYYADSVK (SEQ ID NO: 105) and CLSRMRGYGLDV (SEQ ID NO: 107). The light chain CDRs of the TCN-031 (23K12) antibody have the following sequences per Kabat definition: RTSQSISSYLN (SEQ ID NO: 92), AASSLQSGVPSRF (SEQ ID NO: 94) and QQSYSMPA (SEQ ID NO: 96).

[99] The heavy chain CDRs of the TCN-031 (23K12) antibody have the following sequences per Chothia definition: GFTVSSN (SEQ ID NO: 112), VIYSGGSTY (SEQ ID NO: 113) and CLSRMRGYGLDV (SEQ ID NO: 107). The light chain CDRs of the TCN-031 (23K12) antibody have the following sequences per Chothia definition: RTSQSISSYLN (SEQ ID NO: 92), AASSLQSGVPSRF (SEQ ID NO: 94) and QQSYSMPA (SEQ ID NO: 96).

[100] TCN-031 (23K12) VH nucleotide sequence: (SEQ ID NO: 49)

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGAATCTC
CTGTGCAGCCTCTGGATTCACCGTCAGTAGCAACTACATGAGTTGGGTCCGCCAGGCTCCAG
GGAAGGGGCTGGAGTGGGTCTCAGTTATTTATAGTGGTGGTAGCACATACTACGCAGACTCC
GTGAAGGGCAGATTCTCCTTCTCCAGAGACAACTCCAAGAACACAGTGTTTCTTCAAATGAA
CAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGATGTCTGAGCAGGATGCGGG
GTTACGGTTTAGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCG

[101] TCN-031 (23K12) VH amino acid sequence: (SEQ ID NO: 50)

Kabat Bold, Chothia underlined

E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	I	S
C	A	A	S	G	F	T	V	S	**S**	**N**	**Y**	**M**	**S**	W	V	R	Q	A	P	G
K	G	L	E	W	V	S	**V**	**I**	**Y**	**S**	**G**	**G**	**S**	**T**	**Y**	**Y**	**A**	**D**	**S**	**V**
K	G	R	F	S	F	S	R	D	N	S	K	N	T	V	F	L	Q	M	N	S
L	R	A	E	D	T	A	V	Y	Y	C	A	R	**C**	**L**	**S**	**R**	**M**	**R**	**G**	**Y**
G	**L**	**D**	**V**	W	G	Q	G	T	T	V	T	V	S							

[102] TCN-031 (23K12) VH short nucleotide sequence: (SEQ ID NO: 244)

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGAATCTC
CTGTGCAGCCTCTGGATTCACCGTCAGTAGCAACTACATGAGTTGGGTCCGCCAGGCTCCAG
GGAAGGGGCTGGAGTGGGTCTCAGTTATTTATAGTGGTGGTAGCACATACTACGCAGACTCC
GTGAAGGGCAGATTCTCCTTCTCCAGAGACAACTCCAAGAACACAGTGTTTCTTCAAATGAA
CAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGATGTCTGAGCAGGATGCGGG
GTTACGGTTTAGACGTCTGGGGCCAAGGGACCACGGTCACCGT

[103] TCN-031 (23K12) VH short amino acid sequence: (SEQ ID NO: 236)

Kabat Bold, Chothia underlined

E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	I	S
C	A	A	S	G	F	T	V	S	**S**	**N**	**Y**	**M**	**S**	W	V	R	Q	A	P	G
K	G	L	E	W	V	S	**V**	**I**	**Y**	**S**	**G**	**G**	**S**	**T**	**Y**	**Y**	**A**	**D**	**S**	**V**
K	G	R	F	S	F	S	R	D	N	S	K	N	T	V	F	L	Q	M	N	S
L	R	A	E	D	T	A	V	Y	Y	C	A	R	**C**	**L**	**S**	**R**	**M**	**R**	**G**	**Y**
G	**L**	**D**	**V**	W	G	Q	G	T	T	V	T	V	S							

[104] TCN-031 (23K12) VH long nucleotide sequence: (SEQ ID NO: 195)

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGAATCTC
CTGTGCAGCCTCTGGATTCACCGTCAGTAGCAACTACATGAGTTGGGTCCGCCAGGCTCCAG
GGAAGGGGCTGGAGTGGGTCTCAGTTATTTATAGTGGTGGTAGCACATACTACGCAGACTCC
GTGAAGGGCAGATTCTCCTTCTCCAGAGACAACTCCAAGAACACAGTGTTTCTTCAAATGAA
CAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGATGTCTGAGCAGGATGCGGG
GTTACGGTTTAGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC

[105] TCN-031 (23K12) VH long amino acid sequence: (SEQ ID NO: 235)

Kabat Bold, Chothia underlined

E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	I	S
C	A	A	S	G	F	T	V	S	**S**	**N**	**Y**	**M**	**S**	W	V	R	Q	A	P	G
K	G	L	E	W	V	S	**V**	**I**	**Y**	**S**	**G**	**G**	**S**	**T**	**Y**	**Y**	**A**	**D**	**S**	**V**
K	G	R	F	S	F	S	R	D	N	S	K	N	T	V	F	L	Q	M	N	S
L	R	A	E	D	T	A	V	Y	Y	C	A	R	**C**	**L**	**S**	**R**	**M**	**R**	**G**	**Y**
G	**L**	**D**	**V**	W	G	Q	G	T	T	V	T	V	S	S						

[106] TCN-031 (23K12) VL nucleotide sequence: (SEQ ID NO: 51)

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGACAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAACTCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCGGTCTGCAACCTGAAGATTT
TGCAACCTACTACTGTCAACAGAGTTACAGTATGCCTGCCTTTGGCCAGGGGACCAAGCTGG
AGATCAAA

[107] TCN-031 (23K12) VL amino acid sequence: (SEQ ID NO: 52)

Kabat Bold, Chothia underlined

D I Q M T Q S P S S L S A S V G D R V T I
T C **R T S Q S I S S Y L N** W Y Q Q K P G K
A P K L L I Y **A A S S L Q S G V P S R F** S
G S G S G T D F T L T I S G L Q P E D F A
T Y Y C **Q Q S Y S M P A** F G Q G T K L E I
K

[108] The 3241_G23 antibody (also referred to herein as G23) includes a heavy chain variable region (SEQ ID NO: 116) encoded by the nucleic acid sequence shown below in SEQ ID NO: 115, and a light chain variable region (SEQ ID NO: 118) encoded by the nucleic acid sequence shown in SEQ ID NO: 117.

[109] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[110] The heavy chain CDRs of the G23 antibody have the following sequences per Kabat definition: GGGYSWN (SEQ ID NO: 179), FMFHSGSPRYNPTLKS (SEQ ID NO: 180) and VGQMDKYYAMDV (SEQ ID NO: 181). The light chain CDRs of the G23 antibody have the following sequences per Kabat definition: RASQSIGAYVN (SEQ ID NO: 184), GASNLQS (SEQ ID NO: 185) and QQTYSTPIT (SEQ ID NO: 186).

[111] The heavy chain CDRs of the G23 antibody have the following sequences per Chothia definition: GGPVSGGG (SEQ ID NO: 182), FMFHSGSPR (SEQ ID NO: 183) and VGQMDKYYAMDV (SEQ ID NO: 181). The light chain CDRs of the G23 antibody have the following sequences per Chothia definition: RASQSIGAYVN (SEQ ID NO: 184), GASNLQS (SEQ ID NO: 185) and QQTYSTPIT (SEQ ID NO: 186).

[112] 3241_G23 VH nucleotide sequence (SEQ ID NO: 115)

CAGGTGCAGCTGCAGCAGTCGGGCCCAGGACTGGTGAAGCCTTCACAGACCCTGTCCCTCAC
TTGCACTGTCTCTGGTGGCCCCGTCAGCGGTGGTGGTTACTCCTGGAACTGGATCCGCCAAC
GCCCAGGACAGGGCCTGGAGTGGGTTGGGTTCATGTTTCACAGTGGGAGTCCCCGCTACAAT
CCGACCCTCAAGAGTCGAATTACCATCTCAGTCGACACGTCTAAGAACCTGGTCTCCCTGAA
GCTGAGCTCTGTGACGGCCGCGGACACGGCCGTGTATTTTTGTGCGCGAGTGGGGCAGATGG
ACAAGTACTATGCCATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC

[113] 3241_G23 VH amino acid sequence (SEQ ID NO: 116)

Kabat Bold, Chothia underlined

QVQLQQSGPGLVKPSQTLSLTCTVSGGPVS**GGGYSWN**WIRQRPGQGLEWVG**FMFHSGSPRYN**
PTLKSRITISVDTSKNLVSLKLSSVTAADTAVYFCAR**VGQMDKYYAMDV**WGQGTTVTVSS

[114] 3241_G23 VL nucleotide sequence (SEQ ID NO: 117)

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTTCCTCTGTCGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGAGCATTGGCGCCTATGTAAATTGGTATCAACAGAAAGCAGGGA
AAGCCCCCCAGGTCCTGATCTTTGGTGCTTCCAATTTACAAAGCGGGGTCCCATCAAGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGACTT
TGCAACTTACTTCTGTCAACAGACTTACAGTACCCCGATCACCTTCGGCCAAGGGACACGAC
TGGAGATTAAACG

[115] 3241_G23 VL amino acid sequence (SEQ ID NO: 118)

Kabat Bold, Chothia underlined

DIQMTQSPSSLSSSVGDRVTITC**RASQSIGAYVN**WYQQKAGKAPQVLIF**GASNLQS**GVPSRF
SGSGSGTDFTLTISSLQPEDFATYFC**QQTYSTPIT**FGQGTRLEIK

[116] The 3244_I10 antibody (also referred to herein as I10) includes a heavy chain variable region (SEQ ID NO: 120) encoded by the nucleic acid sequence shown below in SEQ ID NO: 119, and a light chain variable region (SEQ ID NO: 122) encoded by the nucleic acid sequence shown in SEQ ID NO: 121.

[117] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[118] The heavy chain CDRs of the I10 antibody have the following sequences per Kabat definition: SDYWS (SEQ ID NO: 187), FFYNGGSTKYNPSLKS (SEQ ID NO: 188) and HDAKFSGSYYVAS (SEQ ID NO: 189). The light chain CDRs of the I10 antibody have the following sequences per Kabat definition: RASQSISTYLN (SEQ ID NO: 192), GATNLQS (SEQ ID NO: 193) and QQSYNTPLI (SEQ ID NO: 194).

[119] The heavy chain CDRs of the I10 antibody have the following sequences per Chothia definition: GGSITS (SEQ ID NO: 190), FFYNGGSTK (SEQ ID NO: 191) and HDAKFSGSYYVAS (SEQ ID NO: 189). The light chain CDRs of the I10 antibody have the following sequences per Chothia definition: RASQSISTYLN (SEQ ID NO: 192), GATNLQS (SEQ ID NO: 193) and QQSYNTPLI (SEQ ID NO: 194).

[120] 3244_I10 VH nucleotide sequence (SEQ ID NO: 119)

CAGGTCCAGCTGCAGGAGTCGGGCCCAGGACTGCTGAAGCCTTCGGACACCCTGGCCCTCAC
TTGCACTGTCTCTGGTGGCTCCATCACCAGTGACTACTGGAGCTGGATCCGGCAACCCCCAG
GGAGGGGACTGGACTGGATCGGATTCTTCTATAACGGCGGAAGCACCAAGTACAATCCCTCC
CTCAAGAGTCGAGTCACCATTTCAGCGGACACGTCCAAGAACCAGTTGTCCCTGAAATTGAC

CTCTGTGACCGCCGCAGACACGGGCGTGTATTATTGTGCGAGACATGATGCCAAATTTAGTG
GGAGCTACTACGTTGCCTCCTGGGGCCAGGGAACCCGAGTCACCGTCTCGAGC

[121] 3244_I10 VH amino acid sequence (SEQ ID NO: 120)

QVQLQESGPGLLKPSDTLALTCTVSGGSITSDYWSWIRQPPGRGLDWIGFFYNGGST
KYNPSLKSRVTISADTSKNQLSLKLTSVTAADTGVYYCARHDAKFSGSYYVASWG
QGTRVTVSS

[122] 3244_I10 VL nucleotide sequence (SEQ ID NO: 121)

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CTCTTGCCGGGCAAGTCAGAGCATTAGCACCTATTTAAATTGGTATCAGCAGCAACCTGGGA
AAGCCCCTAAGGTCCTCATTTTTGGTGCAACCAACTTGCAAAGTGGGGTCCCATCTCGCTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTT
TGCAACTTACTACTGTCAACAGAGTTACAATACCCCCCTCATTTTTGGCCAGGGGACCAAGC
TGGAGATCAAACG

[123] 3244_I10 VL amino acid sequence (SEQ ID NO: 122)

DIQMTQSPSSLSASVGDRVTISCRASQSISTYLNWYQQQPGKAPKVLIFGATNLQSG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYNTPLIFGQGTKLEIK

[124] The 3243_J07 antibody (also referred to herein as J07) includes a heavy chain variable region (SEQ ID NO: 124) encoded by the nucleic acid sequence shown below in SEQ ID NO: 123, and a light chain variable region (SEQ ID NO: 126) encoded by the nucleic acid sequence shown in SEQ ID NO: 125.

[125] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[126] The heavy chain CDRs of the J07 antibody have the following sequences per Kabat definition: SDYWS (SEQ ID NO: 187), FFYNGGSTKYNPSLKS (SEQ ID NO: 188) and HDVKFSGSYYVAS (SEQ ID NO: 197). The light chain CDRs of the J07 antibody have the following sequences per Kabat definition: RASQSISTYLN (SEQ ID NO: 192), GATNLQS (SEQ ID NO: 193) and QQSYNTPLI (SEQ ID NO: 194).

[127] The heavy chain CDRs of the J07 antibody have the following sequences per Chothia definition: GGSITS (SEQ ID NO: 190), FFYNGGSTK (SEQ ID NO: 191) and HDVKFSGSYYVAS (SEQ ID NO: 197). The light chain CDRs of the J07 antibody have the following sequences per Chothia definition: RASQSISTYLN (SEQ ID NO: 192), GATNLQS (SEQ ID NO: 193) and QQSYNTPLI (SEQ ID NO: 194).

[128] 3243_J07 VH nucleotide sequence (SEQ ID NO: 123)

CAGGTCCAGCTGCAGGAGTCGGGCCCAGGACTGCTGAAGCCTTCGGACACCCTGGCCCTCAC
TTGCACTGTCTCTGGTGGCTCCATCACCAGTGACTACTGGAGCTGGATCCGGCAACCCCCAG
GGAGGGGACTGGACTGGATCGGATTCTTCTATAACGGCGGGAGCACCAAGTACAATCCCTCC
CTCAAGAGTCGAGTCACCATATCAGCGGACACGTCCAAGAACCAGTTGTCCCTGAAATTGAC
CTCTGTGACCGCCGCAGACACGGGCGTGTATTATTGTGCGAGACATGATGTCAAATTTAGTG
GGAGCTACTACGTTGCCTCCTGGGGCCAGGGAACCCGAGTCACCGTCTCGAGC

[129] 3243_J07 VH amino acid sequence (SEQ ID NO: 124)

QVQLQESGPGLLKPSDTLALTCTVSGGSITSDYWSWIRQPPGRGLDWIGFFYNGGST
KYNPSLKSRVTISADTSKNQLSLKLTSVTAADTGVYYCARHDVKFSGSYYVASWG
QGTRVTVSS

[130] 3243_J07 VL nucleotide sequence (SEQ ID NO: 125)

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CTCTTGCCGGGCAAGTCAGAGCATTAGCACCTATTTAAATTGGTATCAGCAGCAACCTGGGA
AAGCCCCTAAGGTCCTGATCTCTGGTGCAACCAACTTGCAAAGTGGGGTCCCATCTCGCTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTT
TGCAACTTACTACTGTCAACAGAGTTACAATACCCCCCTCATTTTTGGCCAGGGGACCAAGC
TGGAGATCAAACG

[131] 3243_J07 VL amino acid sequence (SEQ ID NO: 126)

DIQMTQSPSSLSASVGDRVTISCRASQSISTYLNWYQQQPGKAPKVLISGATNLQSG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYNTPLIFGQGTKLEIK

[132] The 3259_J21 antibody (also referred to herein as J21) includes a heavy chain variable region (SEQ ID NO: 128) encoded by the nucleic acid sequence shown below in SEQ ID NO: 127, and a light chain variable region (SEQ ID NO: 130) encoded by the nucleic acid sequence shown in SEQ ID NO: 129.

[133] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[134] The heavy chain CDRs of the J21 antibody have the following sequences per Kabat definition: SYNWI (SEQ ID NO: 203), HIYDYGRTFYNSSLQS (SEQ ID NO: 204) and PLGILHYYAMDL (SEQ ID NO: 205). The light chain CDRs of the J21 antibody have the following sequences per Kabat definition: RASQSIDKFLN (SEQ ID NO: 208), GASNLHS (SEQ ID NO: 209) and QQSFSVPA (SEQ ID NO: 210).

[135] The heavy chain CDRs of the J21 antibody have the following sequences per Chothia definition: GGSISS (SEQ ID NO: 206), HIYDYGRTF (SEQ ID NO: 207) and

PLGILHYYAMDL (SEQ ID NO: 205). The light chain CDRs of the J21 antibody have the following sequences per Chothia definition: RASQSIDKFLN (SEQ ID NO: 208), GASNLHS (SEQ ID NO: 209) and QQSFSVPA (SEQ ID NO: 210).

[136] 3259_J21 VH nucleotide sequence (SEQ ID NO: 127)

CAGGTGCAGCTGCAGGAGTCGGGCCCACGAGTGGTGAGGCCTTCGGAGACCCTGTCCCTCAC
CTGCACTGTCTCGGGGGGCTCCATCAGTTCTTACAACTGGATTTGGATCCGGCAGCCCCCTG
GGAAGGGACTGGAGTGGATTGGGCACATATATGACTATGGGAGGACCTTCTACAACTCCTCC
CTCCAGAGTCGACCTACCATATCTGTAGACGCGTCCAAGAATCAGCTCTCCCTGCGATTGAC
CTCTGTGACCGCCTCAGACACGGCCGTCTATTACTGTGCGAGACCTCTCGGTATACTCCACT
ACTACGCGATGGACCTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC

[137] 3259_J21 VH amino acid sequence (SEQ ID NO: 128)

QVQLQESGPRVVRPSETLSLTCTVS<u>GGSISS</u>**YNWI**WIRQPPGKGLEWIG**<u>HIYDYGRTF</u>**
YNSSLQSRPTISVDASKNQLSLRLTSVTASDTAVYYCAR**<u>PLGILHYYAMDL</u>**WGQGT
TVTVSS

[138] 3259_J21 VL nucleotide sequence (SEQ ID NO: 129)

GACATCCAGATGACCCAGTCTCCATTATCCGTGTCTGTATCTGTCGGGGACAGGGTCACCAT
CGCTTGCCGGGCAAGTCAGAGTATTGACAAGTTTTTAAATTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAACTCCTGATCTATGGTGCCTCCAATTTGCACAGTGGGGCCCCATCAAGGTTC
AGTGCCAGTGGGTCTGGGACAGACTTCACTCTAACAATCACCAATATACAGACTGAAGATTT
CGCAACTTACCTCTGTCAACAGAGTTTCAGTGTCCCCGCTTTCGGCGGAGGGACCAAGGTTG
AGATCAAACG

[139] 3259_J21 VL amino acid sequence (SEQ ID NO: 130)

DIQMTQSPLSVSVSVGDRVTIAC**<u>RASQSIDKFLN</u>**WYQQKPGKAPKLLIY**<u>GASNLHS</u>**G
APSRFSASGSGTDFTLTITNIQTEDFATYLC**<u>QQSFSVPA</u>**FGGGTKVEIK

[140] The 3245_O19 antibody (also referred to herein as O19) includes a heavy chain variable region (SEQ ID NO: 132) encoded by the nucleic acid sequence shown below in SEQ ID NO: 131, and a light chain variable region (SEQ ID NO: 134) encoded by the nucleic acid sequence shown in SEQ ID NO: 133.

[141] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[142] The heavy chain CDRs of the O19 antibody have the following sequences per Kabat definition: STYMN (SEQ ID NO: 211), VFYSETRTYYADSVKG (SEQ ID NO: 212) and VQRLSYGMDV (SEQ ID NO: 213). The light chain CDRs of the O19 antibody have the

following sequences per Kabat definition: RASQSISTYLN (SEQ ID NO: 192), GASTLQS (SEQ ID NO: 217) and QQTYSIPL (SEQ ID NO: 218).

[143] The heavy chain CDRs of the O19 antibody have the following sequences per Chothia definition: GLSVSS (SEQ ID NO: 214), VFYSETRTY (SEQ ID NO: 215) and VQRLSYGMDV (SEQ ID NO: 213). The light chain CDRs of the O19 antibody have the following sequences per Chothia definition: RASQSISTYLN (SEQ ID NO: 192), GASTLQS (SEQ ID NO: 217) and QQTYSIPL (SEQ ID NO: 218).

[144] 3245_O19 VH nucleotide sequence (SEQ ID NO:131)

GAGGTGCAACTGGTGGAGTCTGGAGGGGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTC
CTGTACGGCCTCTGGGTTAAGTGTCAGTTCCACCTACATGAACTGGGTCCGCCAGGCTCCAG
GGAAGGGGCTGGAATGGGTCTCAGTTTTTTATAGTGAGACCAGGACGTACTACGCAGACTCC
GTGAAGGGCCGATTCACCGTCTCCAGACACAATTCCAACAACACGCTCTATCTTCAGATGAA
CAGCCTGAGAGTTGAAGACACGGCCGTGTATTATTGTGCGAGAGTCCAGAGATTGTCGTACG
GTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC

[145] 3245_O19 VH amino acid sequence (SEQ ID NO: 132)

EVQLVESGGGLVQPGGSLRLSCTASGLSVSSTYMNWVRQAPGKGLEWVSVFYSET
RTYYADSVKGRFTVSRHNSNNTLYLQMNSLRVEDTAVYYCARVQRLSYGMDVW
GQGTTVTVSS

[146] 3245_O19 VL nucleotide sequence (SEQ ID NO: 133)

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTTGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGAGCATTAGCACCTATTTAAATTGGTATCAGAAGAGACCAGGGA
AAGCCCCTAAACTCCTGGTCTATGGTGCATCCACTTTGCAGAGTGGGGTCCCATCAAGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCGCCAGTCTGCAACCTGAAGATTC
TGCAACTTACTACTGTCAACAGACTTACAGTATCCCCCTCTTCGGCCAGGGGACACGGCTGG
AGATTAAACG

[147] 3245_O19 VL amino acid sequence (SEQ ID NO: 134)

DIQMTQSPSSLSASVGDRVTITCRASQSISTYLNWYQKRPGKAPKLLVYGASTLQSG
VPSRFSGSGSGTDFTLTIASLQPEDSATYYCQQTYSIPLFGQGTRLEIK

[148] The 3244_H04 antibody (also referred to herein as H04) includes a heavy chain variable region (SEQ ID NO: 136) encoded by the nucleic acid sequence shown below in SEQ ID NO: 135, and a light chain variable region (SEQ ID NO: 138) encoded by the nucleic acid sequence shown in SEQ ID NO: 137.

[149] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[150] The heavy chain CDRs of the H04 antibody have the following sequences per Kabat definition: STYMN (SEQ ID NO: 211), VFYSETRTYYADSVKG (SEQ ID NO: 212) and VQRLSYGMDV (SEQ ID NO: 213). The light chain CDRs of the H04 antibody have the following sequences per Kabat definition: RASQSISTYLN (SEQ ID NO: 192), GASSLQS (SEQ ID NO: 226) and QQTYSIPL (SEQ ID NO: 218).

[151] The heavy chain CDRs of the H04 antibody have the following sequences per Chothia definition: GLSVSS (SEQ ID NO: 214), VFYSETRTY (SEQ ID NO: 215) and VQRLSYGMDV (SEQ ID NO: 213). The light chain CDRs of the H04 antibody have the following sequences per Chothia definition: RASQSISTYLN (SEQ ID NO: 192), GASSLQS (SEQ ID NO: 226) and QQTYSIPL (SEQ ID NO: 218).

[152] 3244_H04 VH nucleotide sequence (SEQ ID NO: 135)

GAGGTGCAGCTGGTGGAATCTGGAGGGGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTC
CTGTACAGCCTCTGGGTTAAGCGTCAGTTCCACCTACATGAACTGGGTCCGCCAGGCTCCAG
GGAAGGGGCTGGAATGGGTCTCAGTTTTTTATAGTGAAACCAGGACGTATTACGCAGACTCC
GTGAAGGGCCGATTCACCGTCTCCAGACACAATTCCAACAACACGCTGTATCTTCAAATGAA
CAGCCTGAGAGCTGAAGACACGGCCGTGTATTATTGTGCGAGAGTCCAGAGACTGTCATACG
GTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC

[153] 3244_H04 VH amino acid sequence (SEQ ID NO: 136)

EVQLVESGGGLVQPGGSLRLSCTASGLSVSSTYMNWVRQAPGKGLEWVSVFYSET
RTYYADSVKGRFTVSRHNSNNTLYLQMNSLRAEDTAVYYCARVQRLSYGMDVW
GQGTTVTVSS

[154] 3244_H04 VL nucleotide sequence (SEQ ID NO: 137)

GACATCCAGATGACCCAGTCTCCATCGTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGAGCATTAGCACCTATTTAAATTGGTATCAGAAGAGACCAGGGA
AAGCCCCTAAACTCCTGGTCTATGGTGCATCCAGTTTGCAGAGTGGGGTCCCATCAAGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCGCCAGTCTGCAACCTGAAGATTC
TGCAGTTTATTACTGTCAACAGACTTACAGTATCCCCCTCTTCGGCCAGGGGACACGACTGG
AGATTAAACG

[155] 3244_H04 VL amino acid sequence (SEQ ID NO: 138)

DIQMTQSPSSLSASVGDRVTITCRASQSISTYLNWYQKRPGKAPKLLVYGASSLQSG
VPSRFSGSGSGTDFTLTIASLQPEDSAVYYCQQTYSIPLFGQGTRLEIK

[156] The 3136_G05 antibody (also referred to herein as G05) includes a heavy chain variable region (SEQ ID NO: 140) encoded by the nucleic acid sequence shown below in SEQ ID NO: 139, and a light chain variable region (SEQ ID NO: 142) encoded by the nucleic acid sequence shown in SEQ ID NO: 141.

[157] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[158] The heavy chain CDRs of the G05 antibody have the following sequences per Kabat definition: SDFWS (SEQ ID NO: 228), YVYNRGSTKYSPSLKS (SEQ ID NO: 229) and NGRSSTSWGIDV (SEQ ID NO: 230). The light chain CDRs of the 3136_G05 antibody have the following sequences per Kabat definition: RASQSISTYLH (SEQ ID NO: 233), AASSLQS (SEQ ID NO: 234) and QQSYSPPLT (SEQ ID NO: 63).

[159] The heavy chain CDRs of the 3136_G05 antibody have the following sequences per Chothia definition: GGSISS (SEQ ID NO: 206), YVYNRGSTK (SEQ ID NO: 232) and NGRSSTSWGIDV (SEQ ID NO: 230). The light chain CDRs of the 3136_G05 antibody have the following sequences per Chothia definition: RASQSISTYLH (SEQ ID NO: 233), AASSLQS (SEQ ID NO: 234) and QQSYSPPLT (SEQ ID NO: 63).

[160] 3136_G05 VH nucleotide sequence (SEQ ID NO: 139)

CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCCTCGGAGACCCTGTCCCTCAC
CTGCAGTGTCTCTGGTGGCTCCATTAGTAGTGATTTCTGGAGTTGGATCCGACAGCCCCCAG
GGAAGGGACTGGAGTGGATTGGGTATGTCTATAACAGAGGGAGCACTAAGTACAGTCCCTCC
CTCAAGAGTCGAGTCACCATATCAGCAGACATGTCCAAGAACCAGTTTTCCCTGAATATGAG
TTCTGTGACCGCTGCGGACACGGCCGTGTATTACTGTGCGAAAAATGGTCGAAGTAGCACCA
GTTGGGGCATCGACGTCTGGGGCAAAGGGACCACGGTCACCGTCTCGAGC

[161] 3136_G05 VH amino acid sequence (SEQ ID NO: 140)

QVQLQESGPGLVKPSETLSLTCSVSGGSISSDFWSWIRQPPGKGLEWIGYVYNRGST
KYSPSLKSRVTISADMSKNQFSLNMSSVTAADTAVYYCAKNGRSSTSWGIDVWGK
GTTVTVSS

[162] 3136_G05 VL nucleotide sequence (SEQ ID NO: 141)

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTGGGAGACAGACTCACCAT
CACTTGCCGGGCAAGTCAGAGCATTAGCACCTATTTACATTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAACTCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGTGGCAGTAGATCAGGAACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGATGACTT
TGCAACTTACTACTGTCAACAGAGTTACAGTCCCCCCCTCACTTTCGGCCCTGGGACCAAAG
TGGATATGAAACG

[163] 3136_G05 VL amino acid sequence (SEQ ID NO: 142)

DIQMTQSPSSLSASVGDRLTITCRASQSISTYLHWYQQKPGKAPKLLIYAASSLQSGV
PSRFSGSRSGTDFTLTISSLQPDDFATYYCQQSYSPPLTFGPGTKVDMK

[164] The 3252_C13 antibody (also referred to herein as C13) includes a heavy chain variable region (SEQ ID NO: 144) encoded by the nucleic acid sequence shown below in SEQ ID NO: 143, and a light chain variable region (SEQ ID NO: 146) encoded by the nucleic acid sequence shown in SEQ ID NO: 145.

[165] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[166] The heavy chain CDRs of the C13 antibody have the following sequences per Kabat definition: SDYWS (SEQ ID NO: 187), YIYNRGSTKYTPSLKS (SEQ ID NO: 237) and HVGGHTYGIDY (SEQ ID NO: 238). The light chain CDRs of the C13 antibody have the following sequences per Kabat definition: RASQSISNYLN (SEQ ID NO: 241), AASSLQS (SEQ ID NO: 234) and QQSYNTPIT (SEQ ID NO: 243).

[167] The heavy chain CDRs of the C13 antibody have the following sequences per Chothia definition: GASISS (SEQ ID NO: 239), YIYNRGSTK (SEQ ID NO: 240) and HVGGHTYGIDY (SEQ ID NO: 238). The light chain CDRs of the C13 antibody have the following sequences per Chothia definition: RASQSISNYLN (SEQ ID NO: 241), AASSLQS (SEQ ID NO: 234) and QQSYNTPIT (SEQ ID NO: 243).

[168] 3252_C13 VH nucleotide sequence (SEQ ID NO: 143)

CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCAC
CTGCACTGTCTCTGGTGCCTCCATCAGTAGTGACTACTGGAGCTGGATCCGGCTGCCCCCAG
GGAAGGGACTGGAGTGGATTGGGTATATCTATAATAGAGGGAGTACCAAGTACACCCCCTCC
CTGAAGAGTCGAGTCACCATATCACTAGACACGGCCGAGAACCAGTTCTCCCTGAGGCTGAG
GTCGGTGACCGCCGCAGACACGGCCATCTATTACTGTGCGAGACATGTAGGTGGCCACACCT
ATGGAATTGATTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC

[169] 3252_C13 VH amino acid sequence (SEQ ID NO: 144)

QVQLQESGPGLVKPSETLSLTCTVSGASISSDYWSWIRLPPGKGLEWIGYIYNRGSTK
YTPSLKSRVTISLDTAENQFSLRLRSVTAADTAIYYCARHVGGHTYGIDYWGQGTL
VTVSS

[170] 3252_C13 VL nucleotide sequence (SEQ ID NO: 145)

GACATCCAGATGACCCAGTCTCCATCGTCCCTGTCTGCCTCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGAGCATTAGCAACTATTTAAATTGGTATCAACACAAACCTGGGG
AAGCCCCCAAGCTCCTGAACTATGCTGCGTCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGTGCCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTTCAACCTGAAGATTT
TGCCACTTACTACTGTCAACAGAGTTACAATACTCCGATCACCTTCGGCCAAGGGACACGAC
TGGAAATTAAACG

[171] 3252_C13 VL amino acid sequence (SEQ ID NO: 146)

DIQMTQSPSSLSASVGDRVTITC**RASQSISNYLN**WYQHKPGEAPKLLNY**AASSLQS**G
VPSRFSASGSGTDFTLTISSLQPEDFATYYC**QQSYNTPIT**FGQGTRLEIK

[172] The 3259_J06 antibody (also referred to herein as J06) includes a heavy chain variable region (SEQ ID NO: 148) encoded by the nucleic acid sequence shown below in SEQ ID NO: 147, and a light chain variable region (SEQ ID NO: 150) encoded by the nucleic acid sequence shown in SEQ ID NO: 149.

[173] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[174] The heavy chain CDRs of the J06 antibody have the following sequences per Kabat definition: SDYWS (SEQ ID NO: 187), YIYNRGSTKYTPSLKS (SEQ ID NO: 237) and HVGGHTYGIDY (SEQ ID NO: 238). The light chain CDRs of the J06 antibody have the following sequences per Kabat definition: RASQSISNYLN (SEQ ID NO: 241), AASSLQS (SEQ ID NO: 234) and QQSYNTPIT (SEQ ID NO: 243).

[175] The heavy chain CDRs of the J06 antibody have the following sequences per Chothia definition: GASISS (SEQ ID NO: 239), YIYNRGSTK (SEQ ID NO: 240) and HVGGHTYGIDY (SEQ ID NO: 238). The light chain CDRs of the J06 antibody have the following sequences per Chothia definition: RASQSISNYLN (SEQ ID NO: 241), AASSLQS (SEQ ID NO: 234) and QQSYNTPIT (SEQ ID NO: 243).

[176] 3255_J06 VH nucleotide sequence (SEQ ID NO: 147)

CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCAC
CTGCACTGTCTCTGGTGCCTCCATCAGTAGTGACTACTGGAGCTGGATCCGGCTGCCCCCAG
GGAAGGGACTGGAGTGGATTGGGTATATCTATAATAGAGGGAGTACCAAGTACACCCCCTCC
CTGAAGAGTCGAGTCACCATATCACTAGACACGGCCGAGAACCAGTTCTCCCTGAGGCTGAG
GTCGGTGACCGCCGCAGACACGGCCGTCTATTACTGTGCGAGACATGTGGGTGGCCACACCT
ATGGAATTGATTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC

[177] 3255_J06 VH amino acid sequence (SEQ ID NO: 148)

QVQLQESGPGLVKPSETLSLTCTVS**GASISS**DYWSWIRLPPGKGLEWIG**YIYNRGSTK**
YTPSLKSRVTISLDTAENQFSLRLRSVTAADTAVYYCAR**HVGGHTYGIDY**WGQGT
LVTVSS

[178] 3255_J06 VL nucleotide sequence (SEQ ID NO: 149)

GACATCCAGATGACCCAGTCTCCATCGTCCCTGTCTGCCTCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGAGCATTAGCAACTATTTAAATTGGTATCAACACAAACCTGGGG
AAGCCCCCAAGCTCCTGAACTATGCTGCGTCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGTGCCAGTGGATCTGGGACAGATTTCACTCTCAGCATCAGCGGTCTTCAACCTGAAGATTT
TGCCACTTACTACTGTCAACAGAGCTACAATACTCCGATCACCTTCGGCCCAGGGACACGAC
TGGAAATTAAACG

[179] 3255_J06 VL amino acid sequence (SEQ ID NO: 150)

DIQMTQSPSSLSASVGDRVTITC**RASQSISNYLN**WYQHKPGEAPKLLNY**AASSLQS**G
VPSRFSASGSGTDFTLSISGLQPEDFATYYC**QQSYNTPIT**FGPGTRLEIK

[180] The 3410_I23 antibody (also referred to herein as I23) includes a heavy chain variable region (SEQ ID NO: 152) encoded by the nucleic acid sequence shown below in SEQ ID NO: 151, and a light chain variable region (SEQ ID NO: 154) encoded by the nucleic acid sequence shown in SEQ ID NO: 153.

[181] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[182] The heavy chain CDRs of the 3410_I23 antibody have the following sequences per Kabat definition: SYSWS (SEQ ID NO: 252), YLYYSGSTKYNPSLKS (SEQ ID NO: 253) and TGSESTTGYGMDV (SEQ ID NO: 254). The light chain CDRs of the 3410_I23 antibody have the following sequences per Kabat definition: RASQSISTYLN (SEQ ID NO: 192), AASSLHS (SEQ ID NO: 258) and QQSYSPPIT (SEQ ID NO: 259).

[183] The heavy chain CDRs of the 3410_I23 antibody have the following sequences per Chothia definition: GDSISS (SEQ ID NO: 255), YLYYSGSTK (SEQ ID NO: 256) and TGSESTTGYGMDV (SEQ ID NO: 254). The light chain CDRs of the 3410_I23 antibody have the following sequences per Chothia definition: RASQSISTYLN (SEQ ID NO: 192), AASSLHS (SEQ ID NO: 258) and QQSYSPPIT (SEQ ID NO: 259).

[184] 3420_I23 VH nucleotide sequence (SEQ ID NO: 151)

CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCGTCAC
CTGCAAAGTCTCTGGTGACTCCATCAGTAGTTATTCCTGGAGCTGGATCCGGCAGCCCCCAG
GGAAGGGACTGGAGTGGGTTGGCTATTTGTATTATAGTGGGAGCACCAAGTACAACCCCTCC
CTCAAGAGTCGAACCACCATATCAGTAGACACGTCCACGAACCAGTTGTCCCTGAAGTTGAG
TTTTGTGACCGCCGCGGACACGGCCGTGTATTTCTGTGCGAGAACCGGCTCGGAATCTACTA
CCGGCTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC

[185] 3420_I23 VH amino acid sequence (SEQ ID NO: 152)

QVQLQESGPGLVKPSETLSVTCKVSGDSISSYSWSWIRQPPGKGLEWVGYLYYSGST
KYNPSLKSRTTISVDTSTNQLSLKLSFVTAADTAVYFCARTGSESTTGYGMDVWGQ
GTTVTVSS

[186] 3420_I23 VL nucleotide sequence (SEQ ID NO: 153)

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGAGCATTAGCACCTATTTAAATTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAGCTCCTGATCTATGCTGCATCCAGTTTGCACAGTGGGGTCCCATCAAGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCGCTCTCACCATCAGCAGTCTGCAACCTGAAGATTT
TGCAACTTACTACTGTCAACAGAGTTACAGTCCCCCGATCACCTTCGGCCAAGGGACACGAC
TGGAGATTAAACG

[187] 3420_I23 VL amino acid sequence (SEQ ID NO: 154)

DIQMTQSPSSLSASVGDRVTITCRASQSISTYLNWYQQKPGKAPKLLIYAASSLHSG
VPSRFSGSGSGTDFALTISSLQPEDFATYYCQQSYSPPITFGQGTRLEIK

[188] The 3139_P23 antibody (also referred to herein as P23) includes a heavy chain variable region (SEQ ID NO: 156) encoded by the nucleic acid sequence shown below in SEQ ID NO: 155, and a light chain variable region (SEQ ID NO:158) encoded by the nucleic acid sequence shown in SEQ ID NO:157.

[189] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[190] The heavy chain CDRs of the P23 antibody have the following sequences per Kabat definition: NSFWG (SEQ ID NO: 260), YVYNSGNTKYNPSLKS (SEQ ID NO: 261) and HDDASHGYSIS (SEQ ID NO: 262). The light chain CDRs of the 3139_P23 antibody have the following sequences per Kabat definition: RASQTISTYLN (SEQ ID NO: 265), AASGLQS (SEQ ID NO: 61) and QQSYNTPLT (SEQ ID NO: 267).

[191] The heavy chain CDRs of the 3139_P23 antibody have the following sequences per Chothia definition: GGSISN (SEQ ID NO: 263), YVYNSGNTK (SEQ ID NO: 264) and HDDASHGYSIS (SEQ ID NO: 262). The light chain CDRs of the 3139_P23 antibody have the following sequences per Chothia definition: RASQTISTYLN (SEQ ID NO: 265), AASGLQS (SEQ ID NO: 61) and QQSYNTPLT (SEQ ID NO: 267).

[192] 3139_P23 VH nucleotide sequence (SEQ ID NO: 155)

CAGGTGCAGCTGCAGGAGTCGGGCCCAAGACTGGTGAAGCCTTCGGAGAGCCTGTCCCTCAC
CTGCACTGTCTCTGGTGGCTCCATTAGTAATTCCTTCTGGGGCTGGATCCGGCAGCCCCCAG
GGGAGGGACTGGAGTGGATTGGTTATGTCTATAACAGTGGCAACACCAAGTACAATCCCTCC
CTCAAGAGTCGAGTCACCATTTCGCGCGACACGTCCAAGAGTCAACTCTACATGAAGCTGAG
GTCTGTGACCGCCGCTGACACGGCCGTGTACTACTGTGCGAGGCATGACGACGCAAGTCATG
GCTACAGCATCTCCTGGGGCCACGGAACCCTGGTCACCGTCTCGAGC

[193] 3139_P23 VH amino acid sequence (SEQ ID NO: 156)

QVQLQESGPRLVKPSESLSLTCTVS<u>GGSISN</u>**SFWG**WIRQPPGEGLEWIG<u>**YVYNSGNT**
K</u>**YNPSLKS**RVTISRDTSKSQLYMKLRSVTAADTAVYYCAR<u>**HDDASHGYSIS**</u>WGHG
TLVTVSS

[194] 3139_P23 VL nucleotide sequence (SEQ ID NO: 157)

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGGGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGACCATTAGTACTTATTTAAATTGGTATCAACAGAAATCAGGGA
AAGCCCCTAAGCTCCTGATCTATGCTGCATCCGGTTTGCAAAGTGGAGTCCCATCAAGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTTCAACCTGAAGATTT
TGCAACTTACTTCTGTCAACAGAGTTACAATACTCCCCTGACGTTCGGCCAAGGGACCAAGG
TGGAAATCAAA

[195] 3139_P23 VL amino acid sequence (SEQ ID NO: 158)

DIQMTQSPSSLSASVGDRVTITC<u>**RASQTISTYLN**</u>WYQQKSGKAPKLLIY<u>**AASGLQS**</u>G
VPSRFSGSGSGTDFTLTISSLQPEDFATYFC<u>**QQSYNTPLT**</u>FGQGTKVEIK

[196] The 3248_P18 antibody (also referred to herein as P18) includes a heavy chain variable region (SEQ ID NO: 160) encoded by the nucleic acid sequence shown below in SEQ ID NO: 159, and a light chain variable region (SEQ ID NO: 162) encoded by the nucleic acid sequence shown in SEQ ID NO: 161.

[197] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[198] The heavy chain CDRs of the 3248_P18 antibody have the following sequences per Kabat definition: AYHWS (SEQ ID NO: 268), HIFDSGSTYYNPSLKS (SEQ ID NO: 269) and PLGSRYYYGMDV (SEQ ID NO: 270). The light chain CDRs of the 3248_P18 antibody have the following sequences per Kabat definition: RASQSISRYLN (SEQ ID NO: 273), GASTLQN (SEQ ID NO: 274) and QQSYSVPA (SEQ ID NO: 275).

[199] The heavy chain CDRs of the 3248_P18 antibody have the following sequences per Chothia definition: GGSISA (SEQ ID NO: 271), HIFDSGSTY (SEQ ID NO: 272) and PLGSRYYYGMDV (SEQ ID NO: 270). The light chain CDRs of the 3248_P18 antibody

have the following sequences per Chothia definition: RASQSISRYLN (SEQ ID NO: 273); GASTLQN (SEQ ID NO: 274) and QQSYSVPA (SEQ ID NO: 275).

[200] 3248_P18 VH nucleotide sequence (SEQ ID NO: 159)

CAGGTGCAACTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCAC
CTGCACTGTCTCGGGTGGCTCCATCAGTGCTTACCACTGGAGCTGGATCCGCCAGCCCCCAG
GGAAGGGACTGGAGTGGATTGGGCACATCTTTGACAGTGGGAGCACTTACTACAACCCCTCC
CTTAAGAGTCGAGTCACCATATCACTAGACGCGTCCAAGAACCAGCTCTCCCTGAGATTGAC
CTCTGTGACCGCCTCAGACACGGCCATATATTACTGTGCGAGACCTCTCGGGAGTCGGTACT
ATTACGGAATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC

[201] 3248_P18 VH amino acid sequence (SEQ ID NO: 160)

QVQLQESGPGLVKPSETLSLTCTVSGGSISAYHWSWIRQPPGKGLEWIGHIFDSGST
YYNPSLKSRVTISLDASKNQLSLRLTSVTASDTAIYYCARPLGSRYYYGMDVWGQG
TTVTVSS

[202] 3248_P18 VL nucleotide sequence (SEQ ID NO: 161)

GACATCCAGATGACCCAGTCTCCGTCCTCCCTGTCTGCATCTGTCGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGAGTATTAGCAGGTATTTAAATTGGTATCAGCAGAAACCAGGGA
AAGCCCCTAAGCTCCTGATCTATGGTGCCTCCACTTTGCAAAATGGGGCCCCATCAAGGTTC
AGCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTACAACCTGAAGATTC
CGCAACTTACCTCTGTCAACAGAGTTACAGTGTCCCTGCTTTCGGCGGAGGAACCAAGGTGG
AGGTCAAA

[203] 3248_P18 VL amino acid sequence (SEQ ID NO: 162)

DIQMTQSPSSLSASVGDRVTITCRASQSISRYLNWYQQKPGKAPKLLIYGASTLQNG
APSRFSGSGSGTDFTLTISSLQPEDSATYLCQQSYSVPAFGGGTKVEVK

[204] The 3253_P10 antibody (also referred to herein as P10) includes a heavy chain variable region (SEQ ID NO: 164) encoded by the nucleic acid sequence shown below in SEQ ID NO: 163, and a light chain variable region (SEQ ID NO: 166) encoded by the nucleic acid sequence shown in SEQ ID NO: 165.

[205] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[206] The heavy chain CDRs of the 3253_P10 antibody have the following sequences per Kabat definition: SDYWS (SEQ ID NO: 187), FFYNGGSTKYNPSLKS (SEQ ID NO: 188) and HDAKFSGSYYVAS (SEQ ID NO: 189). The light chain CDRs of the 3253_P10 antibody have the following sequences per Kabat definition: RASQSISTYLN (SEQ ID NO: 192), GATDLQS (SEQ ID NO: 282) and QQSYNTPLI (SEQ ID NO: 194).

[207] The heavy chain CDRs of the 3253_P10 antibody have the following sequences per Chothia definition: GGSITS (SEQ ID NO: 190), FFYNGGSTK (SEQ ID NO: 191) and HDAKFSGSYYVAS (SEQ ID NO: 189). The light chain CDRs of the 3253_P10 antibody have the following sequences per Chothia definition: RASQSISTYLN (SEQ ID NO: 192), GATDLQS (SEQ ID NO: 282) and QQSYNTPLI (SEQ ID NO: 194).

[208] 3253_P10 VH nucleotide sequence (SEQ ID NO: 163)

CAGGTCCAGCTGCAGGAGTCGGGCCCAGGACTGCTGAAGCCTTCGGACACCCTGGCCCTCAC
TTGCACTGTCTCTGGTGGCTCCATCACCAGTGACTACTGGAGCTGGATCCGGCAACCCCCAG
GGAGGGGACTGGACTGGATCGGATTCTTCTATAACGGCGGGAGCACCAAGTACAATCCCTCC
CTCAAGAGTCGAGTCACCATATCAGCGGACACGTCCAAGAACCAGTTGTCCCTGAAATTGAC
CTCTGTGACCGCCGCAGACACGGGCGTGTATTATTGTGCGAGACATGATGCCAAATTTAGTG
GGAGCTACTACGTTGCCTCCTGGGGCCAGGGAACCCGAGTCACCGTCTCGAGC

[209] 3253_P10 VH amino acid sequence (SEQ ID NO: 164)

QVQLQESGPGLLKPSDTLALTCTVS**GGSITS**DYWSWIRQPPGRGLDWIG**FFYNGGST**
KYNPSLKSRVTISADTSKNQLSLKLTSVTAADTGVYYCAR**HDAKFSGSYYVAS**WG
QGTRVTVSS

[210] 3253_P10 VL nucleotide sequence (SEQ ID NO: 165)

GACATCCAGATGACCCAGTCTCCCTCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CTCTTGCCGGGCAAGTCAGAGCATTAGCACCTATTTAAATTGGTATCAGCAGCAACCTGGGA
AAGCCCCTAAGGTCCTGATCTCTGGTGCAACCGACTTGCAAAGTGGGGTCCCATCTCGCTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTT
TGCAACTTACTACTGTCAACAGAGTTACAATACCCCCCTCATTTTTGGCCAGGGGACCAAGC
TGGAGATCAAA

[211] 3253_P10 VL amino acid sequence (SEQ ID NO: 166)

DIQMTQSPSSLSASVGDRVTISC**RASQSISTYLN**WYQQQPGKAPKVLIS**GATDLQS**G
VPSRFSGSGSGTDFTLTISSLQPEDFATYYC**QQSYNTPLI**FGQGTKLEIK

[212] The 3260_D19 antibody (also referred to herein as D19) includes a heavy chain variable region (SEQ ID NO: 168) encoded by the nucleic acid sequence shown below in SEQ ID NO: 167, and a light chain variable region (SEQ ID NO: 170) encoded by the nucleic acid sequence shown in SEQ ID NO: 169.

[213] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[214] The heavy chain CDRs of the 3260_D19 antibody have the following sequences per Kabat definition: DNYIN (SEQ ID NO: 284), VFYSADRTSYADSVKG (SEQ ID NO: 285) and VQKSYYGMDV (SEQ ID NO: 286). The light chain CDRs of the 3260_D19 antibody have the following sequences per Kabat definition: RASQSISRYLN (SEQ ID NO: 273), GASSLQS (SEQ ID NO: 226) and QQTFSIPL (SEQ ID NO: 291).

[215] The heavy chain CDRs of the 3260_D19 antibody have the following sequences per Chothia definition: GFSVSD (SEQ ID NO: 287), VFYSADRTS (SEQ ID NO: 288) and VQKSYYGMDV (SEQ ID NO: 286). The light chain CDRs of the 3260_D19 antibody have the following sequences per Chothia definition: RASQSISRYLN (SEQ ID NO: 273), GASSLQS (SEQ ID NO: 226) and QQTFSIPL (SEQ ID NO: 291).

[216] 3260_D19 VH nucleotide sequence (SEQ ID NO: 167)

GACATGCAGCTGGTGGAGTCTGGAGGAGGCTTGGTCCCGCCGGGGGGGTCCCTGAGACTCTC
CTGCGCAGCCTCTGGGTTTTCCGTCAGTGACAACTACATAAACTGGGTCCGCCAGGCTCCAG
GGAAGGGGCTGGACTGGGTCTCAGTCTTTTATAGTGCTGATAGAACATCCTACGCAGACTCC
GTGAAGGGCCGATTCACCGTCTCCAGCCACGATTCCAAGAACACAGTGTACCTTCAAATGAA
CAGTCTGAGAGCTGAGGACACGGCCGTTTATTACTGTGCGAGAGTTCAGAAGTCCTATTACG
GTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC

[217] 3260_D19 VH amino acid sequence (SEQ ID NO: 168)

DMQLVESGGGLVPPGGSLRLSCAASGFSVS**DNYIN**WVRQAPGKGLDWVS**VFYSADRTSYADS**
VKGRFTVSSHDSKNTVYLQMNSLRAEDTAVYYCAR**VQKSYYGMDV**WGQGTTVTVSS

[218] 3260_D19 VL nucleotide sequence (SEQ ID NO: 169)

GGCATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGAGCATTAGCAGATATTTAAATTGGTATCTGCAGAAACCAGGGA
AAGCCCCTAAGCTCCTGATCTCTGGTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGTGGCACTGGGTCTGGGACAGAATTCACTCTCACCATCAGCAGTTTGCAACCTGAAGATTT
TGCAACTTACTACTGTCAACAGACTTTCAGTATCCCTCTTTTTGGCCAGGGGACCAAGGTGG
AGATCAAA

[219] 3260_D19 VL amino acid sequence (SEQ ID NO: 170)

GIQMTQSPSSLSASVGDRVTITC**RASQSISRYLN**WYLQKPGKAPKLLIS**GASSLQS**GV
PSRFSGTGSGTEFTLTISSLQPEDFATYYC**QQTFSIPL**FGQGTKVEIK

[220] The 3362_B11 antibody (also referred to herein as B11) includes a heavy chain variable region (SEQ ID NO: 172) encoded by the nucleic acid sequence shown below in SEQ ID NO: 171, and a light chain variable region (SEQ ID NO: 174) encoded by the nucleic acid sequence shown in SEQ ID NO: 173.

[221] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[222] The heavy chain CDRs of the B11 antibody have the following sequences per Kabat definition: SGAYYWT (SEQ ID NO: 293), YIYYSGNTYYNPSLKS (SEQ ID NO: 294) and AASTSVLGYGMDV (SEQ ID NO: 295). The light chain CDRs of the B11 antibody have the following sequences per Kabat definition: RASQSISRYLN (SEQ ID NO: 273), AASSLQS (SEQ ID NO: 234) and QQSYSTPLT (SEQ ID NO: 300).

[223] The heavy chain CDRs of the B11 antibody have the following sequences per Chothia definition: GDSITSGA (SEQ ID NO: 296), YIYYSGNTY (SEQ ID NO: 297) and AASTSVLGYGMDV (SEQ ID NO: 295). The light chain CDRs of the B11 antibody have the following sequences per Chothia definition: RASQSISRYLN (SEQ ID NO: 273), AASSLQS (SEQ ID NO: 234) and QQSYSTPLT (SEQ ID NO: 300).

[224] 3362_B11 VH nucleotide sequence (SEQ ID NO: 171)

CAGGTGCAGCTGCAGGCGTCGGGCCCAGGACTGGTGAAGCCTTCAGAGACCCTGTCCCTCAC
CTGCACTGTCTCTGGTGACTCCATCACCAGTGGTGCTTACTACTGGACCTGGATCCGCCAGC
ACCCAGGGAAGGGCCTGGAGTGGATTGGGTACATCTATTACAGTGGGAACACCTACTACAAC
CCGTCCCTCAAGAGTCGAGTTACCATATCACTAGACACGTCTAAGAACCAGTTCTCCCTGAA
GGTGAACTCTGTGACTGCCGCGGACACGGCCGTATATTACTGTGCGCGAGCTGCTTCGACTT
CAGTGCTAGGATACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC

[225] 3362_B11 VH amino acid sequence (SEQ ID NO: 172)

QVQLQASGPGLVKPSETLSLTCTVS<u>GDSITSGA</u>**YYWT**WIRQHPGKGLEWIG<u>**YIYYSG**
NTY</u>**YNPSLKS**RVTISLDTSKNQFSLKVNSVTAADTAVYYCAR<u>**AASTSVLGYGMDV**</u>
WGQGTTVTVSS

[226] 3362_B11 VL nucleotide sequence (SEQ ID NO: 173)

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGAGCATTAGCAGATATTTAAATTGGTATCAGCAGGAACCAGGGA
AGGCCCCTAAGCTCCTGGTCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATAAGCAGTCTTCAACCTGAAGATTT
TGCAACTTACTACTGTCAACAGAGTTATAGTACCCCCCTCACCTTCGGCCAAGGGACACGAC
TGGAGATTAAA

[227] 3362_B11 VH amino acid sequence (SEQ ID NO: 174)

DIQMTQSPSSLSASVGDRVTITC<u>**RASQSISRYLN**</u>WYQQEPGKAPKLLVY<u>**AASSLQS**</u>G
VPSRFSGSGSGTDFTLTISSLQPEDFATYYC<u>**QQSYSTPLT**</u>FGQGTRLEIK

[228] The 3242_P05 antibody (also referred to herein as P05) includes a heavy chain variable region (SEQ ID NO: 176) encoded by the nucleic acid sequence shown below in SEQ ID NO: 175, and a light chain variable region (SEQ ID NO: 178) encoded by the nucleic acid sequence shown in SEQ ID NO: 177.

[229] The amino acids encompassing the CDRs as defined by Chothia et al., 1989 are underlined and those defined by Kabat et al., 1991 are highlighted in bold in the sequences below.

[230] The heavy chain CDRs of the 3242_P05 antibody have the following sequences per Kabat definition: VSDNYIN (SEQ ID NO: 301), VFYSADRTSYADSVKG (SEQ ID NO: 285) and VQKSYYGMDV (SEQ ID NO: 286). The light chain CDRs of the 3242_P05 antibody have the following sequences per Kabat definition: RASQSISRYLN (SEQ ID NO: 273), GASSLQS (SEQ ID NO: 226) and QQTFSIPL (SEQ ID NO: 291).

[231] The heavy chain CDRs of the 3242_P05 antibody have the following sequences per Chothia definition: SGFSV (SEQ ID NO: 304), VFYSADRTS (SEQ ID NO: 288) and VQKSYYGMDV (SEQ ID NO: 286). The light chain CDRs of the 3242_P05 antibody have the following sequences per Chothia definition: The light chain CDRs of the 3242_P05 antibody have the following sequences per Kabat definition: RASQSISRYLN (SEQ ID NO: 273), GASSLQS (SEQ ID NO: 226) and QQTFSIPL (SEQ ID NO: 291).

[232] 3242_P05 VH nucleotide sequence (SEQ ID NO: 175)

GACATGCAGCTGGTGGAGTCTGGAGGAGGCTTGGTCCCGCCGGGGGGGTCCCTGAGACTCTC
CTGCGCAGCCTCTGGGTTTTCCGTCAGTGACAACTACATAAACTGGGTCCGCCAGGCTCCAG
GGAAGGGGCTGGACTGGGTCTCAGTCTTTTATAGTGCTGATAGAACATCCTACGCAGACTCC
GTGAAGGGCCGATTCACCGTCTCCAGCCACGATTCCAAGAACACAGTGTACCTTCAAATGAA
CAGTCTGAGAGCTGAGGACACGGCCGTTTATTACTGTGCGAGAGTTCAGAAGTCCTATTACG
GTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC

[233] 3242_P05 VH amino acid sequence (SEQ ID NO: 176)

DMQLVESGGGLVPPGGSLRLSCAA<u>SGFSV</u>**SDNYIN**WVRQAPGKGLDWVS<u>**VFYSAD**
RTS</u>**YADSVKG**RFTVSSHDSKNTVYLQMNSLRAEDTAVYYCAR<u>**VQKSYYGMDV**</u>W
GQGTTVTVSS

[234] 3242_P05 VL nucleotide sequence (SEQ ID NO: 177)

GGCATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCAT
CACTTGCCGGGCAAGTCAGAGCATTAGCAGATATTTAAATTGGTATCTGCAGAAACCAGGGA
AAGCCCCTAAGCTCCTGATCTCTGGTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTC
AGTGGCACTGGGTCTGGGACAGAATTCACTCTCACCATCAGCAGTTTGCAACCTGAAGATTT

TGCAACTTACTACTGTCAACAGACTTTCAGTATCCCTCTTTTTGGCCAGGGGACCAAGGTGG
AGATCAAA

[235] 3242_P05 VL amino acid sequence (SEQ ID NO: 178)

GIQMTQSPSSLSASVGDRVTITC**RASQSISRYLN**WYLQKPGKAPKLLIS**GASSLQS**GV
PSRFSGTGSGTEFTLTISSLQPEDFATYYC**QQTFSIPL**FGQGTKVEIK

[236] HuM2e antibodies of the invention also include antibodies that include a heavy chain variable amino acid sequence that is at least 90%, 92%, 95%, 97% 98%, 99% or more identical the amino acid sequence of SEQ ID NO: 44, 277, 276, 50, 236, 235, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 160, 164, 168, 172, or 176. and/or a light chain variable amino acid that is at least 90%, 92%, 95%, 97% 98%, 99% or more identical the amino acid sequence of SEQ ID NO: 46, 52, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, 174, 178.

[237] Alternatively, the monoclonal antibody is an antibody that binds to the same epitope as TCN-032 (8I10), 21B15, TCN-031 (23K12), 3241_G23, 3244_I10, 3243_J07, 3259_J21, 3245_O19, 3244_H04, 3136_G05, 3252_C13, 3255_J06, 3420_I23, 3139_P23, 3248_P18, 3253_P10, 3260_D19, 3362_B11, or 3242_P05.

[238] The heavy chain of a M2e antibody is derived from a germ line V (variable) gene such as, for example, the IgHV4 or the IgHV3 germline gene.

[239] The M2e antibodies of the invention include a variable heavy chain (V_H) region encoded by a human IgHV4 or the IgHV3 germline gene sequence. An IgHV4 germline gene sequence is shown, *e.g.*, in Accession numbers L10088, M29812, M95114, X56360 and M95117. An IgHV3 germline gene sequence is shown, *e.g.*, in Accession numbers X92218, X70208, Z27504, M99679 and AB019437. The M2e antibodies of the invention include a V_H region that is encoded by a nucleic acid sequence that is at least 80% homologous to the IgHV4 or the IgHV3 germline gene sequence. Preferably, the nucleic acid sequence is at least 90%, 95%, 96%, 97% homologous to the IgHV4 or the IgHV3 germline gene sequence, and more preferably, at least 98%, 99% homologous to the IgHV4 or the IgHV3 germline gene sequence. The V_H region of the M2e antibody is at least 80% homologous to the amino acid sequence of the V_H region encoded by the IgHV4 or the IgHV3 V_H germline gene sequence. Preferably, the amino acid sequence of V_H region of the M2e antibody is at least 90%, 95%, 96%, 97% homologous to the amino acid sequence encoded by the IgHV4 or the

IgHV3 germline gene sequence, and more preferably, at least 98%, 99% homologous to the sequence encoded by the IgHV4 or the IgHV3 germline gene sequence.

The M2e antibodies of the invention also include a variable light chain (V_L) region encoded by a human IgKV1 germline gene sequence. A human IgKV1 V_L germline gene sequence is shown, *e.g.*, Accession numbers X59315, X59312, X59318, J00248, and Y14865. Alternatively, the M2e antibodies include a V_L region that is encoded by a nucleic acid sequence that is at least 80% homologous to the IgKV1 germline gene sequence. Preferably, the nucleic acid sequence is at least 90%, 95%, 96%, 97% homologous to the IgKV1 germline gene sequence, and more preferably, at least 98%, 99% homologous to the IgKV1 germline gene sequence. The V_L region of the M2e antibody is at least 80% homologous to the amino acid sequence of the V_L region encoded the IgKV1 germline gene sequence. Preferably, the amino acid sequence of V_L region of the M2e antibody is at least 90%, 95%, 96%, 97% homologous to the amino acid sequence encoded by the IgKV1 germline gene sequence, and more preferably, at least 98%, 99% homologous to the sequence encoded by e the IgKV1 germline gene sequence.

HA Antibodies I

[240] The HA antibodies of the invention may also be capable of specifically binding to one or more fragments of influenza virus H5N1, such as the surface glycoproteins, hemagglutinin (HA) and neuraminidase (NA), which are required for viral attachment and cellular release, or membrane proteins (M1 and M2). In a specific embodiment, the HA antibodies of the invention are capable of specifically binding to the HA molecule of H5N1 strains. They may be capable of specifically binding to the HA1 and/or HA2 subunit of the HA molecule. They may be capable of specifically binding to linear or structural and/or conformational epitopes on the HA1 and/or HA2 subunit of the HA molecule. The HA molecule may be purified from viruses or recombinantly produced and optionally isolated before use. Alternatively, HA may be expressed on the surface of cells.

[241] For diagnostic purposes, the HA antibodies may also be capable of specifically binding to proteins not present on the surface of H5N1 including the nucleoprotein, the nucleocapsid structural protein, polymerases (PA, PB and PB2), and non-structural proteins (NS1 and NS2). The nucleotide and/or amino acid sequence of proteins of various H5N1 strains can be found in the GenBank-database, NCBI Influenza Virus Sequence Database,

Influenza Sequence Database (ISD), EMBL-database and/or other databases. It is well within the reach of the skilled person to find such sequences in the respective databases.

In another embodiment the HA antibodies of the invention are capable of specifically binding to a fragment of the above-mentioned proteins and/or polypeptides, wherein the fragment at least includes an antigenic determinant recognized by the HA antibodies of the invention. An "antigenic determinant" as used herein is a moiety that is capable of binding to an HA antibody of the invention with sufficiently high affinity to form a detectable antigen-antibody complex. As used herein, the terms "antigenic determinant" and "epitope" are equivalents. The HA antibodies of the invention may or may not be capable of specifically binding to the extracellular part of HA (also called herein soluble HA (sHA)).

[242] The HA antibodies of the invention can be intact immunoglobulin molecules such as polyclonal or monoclonal antibodies or the HA antibodies can be antigen-binding fragments including, but not limited to, Fab, F(ab'), F(ab')2, Fv, dAb, Fd, complementarity determining region (CDR) fragments, single-chain antibodies (scFv), bivalent single-chain antibodies, single-chain phage antibodies, diabodies, triabodies, tetrabodies, and (poly)peptides that contain at least a fragment of an immunoglobulin that is sufficient to confer specific antigen binding to influenza virus H5N1 strains or a fragment thereof. In a preferred embodiment the HA antibodies are human monoclonal antibodies.

[243] HA antibodies can be used in non-isolated or isolated form. Furthermore, the HA antibodies can be used alone or in a mixture including at least one HA antibody (or variant or fragment thereof). Thus, HA antibodies can be used in combination, e.g., as a pharmaceutical composition comprising two or more antibodies of the invention, variants or fragments thereof. For example, antibodies having different, but complementary activities can be combined in a single therapy to achieve a desired prophylactic, therapeutic or diagnostic effect, but alternatively, antibodies having identical activities can also be combined in a single therapy to achieve a desired prophylactic, therapeutic or diagnostic effect. Optionally, the mixture further includes at least one other therapeutic agent. Preferably, the therapeutic agent such as, e.g., M2 inhibitors (e.g., amantidine, rimantadine) and/or neuraminidase inhibitors (e.g., zanamivir, oseltamivir) is useful in the prophylaxis and/or treatment of an influenza virus H5N1 infection.

[244] Typically, HA antibodies can bind to their binding partners, i.e. influenza virus H5N1 or fragments thereof, with an affinity constant (Kd-value) that is lower than $0.2x10^{-4}$ M, $1.0x10^{-5}$ M, $1.0x10^{-6}$ M, $1.0x10^{-7}$ M, preferably lower than $1.0x10^{-8}$ M, more preferably lower

than $1.0x10^{-9}$ M, more preferably lower than $1.0x10^{-10}$ M, even more preferably lower than $1.0x10^{-11}$ M, and in particular lower than $1.0x10^{-12}$ M. The affinity constants can vary for antibody isotypes. For example, affinity binding for an IgM isotype refers to a binding affinity of at least about $1.0x10^{-7}$ M. Affinity constants can for instance be measured using surface plasmon resonance, for example using the BIACORE system (Pharmacia Biosensor AB, Uppsala, Sweden).

[245] HA antibodies may bind to influenza virus H5N1 or a fragment thereof in soluble form such as for instance in a sample or in suspension or may bind to influenza virus H5N1 or a fragment thereof bound or attached to a carrier or substrate, e.g., microtiter plates, membranes and beads, etc. Carriers or substrates may be made of glass, plastic (e.g., polystyrene), polysaccharides, nylon, nitrocellulose, or Teflon, etc. The surface of such supports may be solid or porous and of any convenient shape. Furthermore, the HA antibodies may bind to influenza virus H5N1 in purified/isolated or non purified/non-isolated form.

[246] HA antibodies exhibit neutralizing activity. Neutralizing activity can for instance be measured as described in International Patent Application PCT/EP2007/059356 (Publication No. WO 2008/028946, the contents of which are incorporated herein in their entirety). Alternative assays measuring neutralizing activity are described in for instance WHO Manual on Animal Influenza Diagnosis and Surveillance, Geneva: World Health Organization, 2005, version 2002.5.

[247] The invention relates to an isolated human HA antibody that recognizes and binds to an epitope in the HA2 subunit of the influenza haemagglutinin protein (HA), characterized in that said HA antibody has neutralizing activity against an influenza virus, for instance, including HA of the H5 subtype. Examples of influenza strains that contain such a HA of the H5 subtype and that are important strains in view of pandemic threats are H5N1, H5N2, H5N8, and H5N9. Particularly preferred are HA antibodies that at least neutralize the H5N1 influenza strain. Preferably, HA antibodies do not depend on an epitope in the HA1 subunit of the HA protein for binding to said HA protein.

Definitions

[248] The term "human HA antibody" describes an intact immunoglobulin including monoclonal antibodies, such as chimeric, humanized or human monoclonal antibodies, or to an antigen-binding and/or variable domain comprising fragment of an immunoglobulin that

competes with the intact immunoglobulin for specific binding to the binding partner of the immunoglobulin, e.g. H5N1. Regardless of structure, the antigen binding fragment binds with the same antigen that is recognized by the intact immunoglobulin. An antigen-binding fragment can comprise a peptide or polypeptide comprising an amino acid sequence of at least 2, 5, 10, 15, 20, 25, 30, 35, 40, 50, 60, 70, 80, 90, 100, 125, 150, 175, 200, or 250 contiguous amino acid residues of the amino acid sequence of the HA antibody.

[249] The term "HA antibody", includes all immunoglobulin classes and subclasses known in the art. Depending on the amino acid sequence of the constant domain of their heavy chains, HA antibodies can be divided into the five major classes of intact antibodies: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgAl, IgA2, IgGl, IgG2, IgG3 and IgG4.

[250] Antigen-binding fragments include, inter alia, Fab, F(ab'), F(ab')2, Fv, dAb, Fd, complementarity determining region (CDR) fragments, single-chain antibodies (scFv), bivalent single-chain antibodies, single-chain phage antibodies, diabodies, triabodies, tetrabodies, (poly)peptides that contain at least a fragment of an immunoglobulin that is sufficient to confer specific antigen binding to the (poly)peptide, etc. The above fragments may be produced synthetically or by enzymatic or chemical cleavage of intact immunoglobulins or they may be genetically engineered by recombinant DNA techniques. The methods of production are well known in the art and are described, for example, in Antibodies: A Laboratory Manual, Edited by: E. Harlow and D, Lane (1988), Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, which is incorporated herein by reference. An HA antibody or antigen-binding fragment thereof may have one or more binding sites. If there is more than one binding site, the binding sites may be identical to one another or they may be different.

[251] With respect to HA antibodies, the term "complementarity determining regions" (CDR) as used herein means sequences within the variable regions of HA antibodies, such as immunoglobulins, that usually contribute to a large extent to the antigen binding site which is complementary in shape and charge distribution to the epitope recognized on the antigen. The CDR regions of HA antibodies can be specific for linear epitopes, discontinuous epitopes, or conformational epitopes of proteins or protein fragments, either as present on the protein in its native conformation or, in some cases, as present on the proteins as denatured, e.g., by solubilization in SDS. Epitopes of HA antibodies may also consist of posttranslational modifications of proteins.

[252] The term "functional variant", as used herein, refers to an HA antibody that includes a nucleotide and/or amino acid sequence that is altered by one or more nucleotides and/or amino acids compared to the nucleotide and/or amino acid sequences of the parental HA antibody and that is still capable of competing for binding to the binding partner, e.g. H5N1, with the parental HA antibody. In other words, the modifications in the amino acid and/or nucleotide sequence of the parental HA antibody do not significantly affect or alter the binding characteristics of the HA antibody encoded by the nucleotide sequence or containing the amino acid sequence, i.e. the antibody is still able to recognize and bind its target. The functional variant may have conservative sequence modifications including nucleotide and amino acid substitutions, additions and deletions. These modifications can be introduced by standard techniques known in the art, such as site-directed mutagenesis and random PCR-mediated mutagenesis, and may include natural as well as non-natural nucleotides and amino acids.

[253] Conservative amino acid substitutions include the ones in which the amino acid residue is replaced with an amino acid residue having similar structural or chemical properties. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., asparagine, glutamine, serine, threonine, tyrosine, cysteine, tryptophan), non-polar side chains (e.g., glycine, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan). It will be clear to the skilled artisan that other classifications of amino acid residue families than the one used above can also be employed. Furthermore, a HA antibody functional variant may have non-conservative amino acid substitutions, e.g., replacement of an amino acid with an amino acid residue having different structural or chemical properties. Similar minor variations may also include amino acid deletions or insertions, or both. Guidance in determining which amino acid residues may be substituted, inserted, or deleted without abolishing immunological activity may be found using computer programs well known in the art.

[254] A mutation in a nucleotide sequence can be a single alteration made at a locus (a point mutation), such as transition or transversion mutations, or alternatively, multiple nucleotides may be inserted, deleted or changed at a single locus. In addition, one or more alterations

may be made at any number of loci within a nucleotide sequence. The mutations may be performed by any suitable method known in the art.

[255] The term "human", when applied to HA antibodies, refers to molecules that are either directly derived from a human or based upon a human sequence. When an HA antibody is derived from or based on a human sequence and subsequently modified, it is still to be considered human as used throughout the specification. In other words, the term human, when applied to HA antibodies is intended to include antibodies having variable and constant regions derived from human germline immunoglobulin sequences or based on variable or constant regions occurring in a human or human lymphocyte and modified in some form. Thus, the human HA antibodies may include amino acid residues not encoded by human germline immunoglobulin sequences, contain substitutions and/or deletions (e.g., mutations introduced by for instance random or site-specific mutagenesis in vitro or by somatic mutation in vivo). "Based on" as used herein refers to the situation that a nucleic acid sequence may be exactly copied from a template, or with minor mutations, such as by error-prone PCR methods, or synthetically made matching the template exactly or with minor modifications. Semi-synthetic molecules based on human sequences are also considered to be human as used herein.

Single Chain HA Antibodies

[256] The heavy chain of an HA antibody is derived from a germ line V (variable) gene such as, for example, the VH1 or VH3 germline gene (*see*, Tomlinson IM, Williams SC, Ignatovitch O, Corbett SJ, Winter G. V-BASE Sequence Directory. Cambridge, United Kingdom: MRC Centre for Protein Engineering (1997)). The HA antibodies of the invention include a V_H region that is encoded by a nucleic acid sequence that is at least 80% homologous to the VH1 or VH3 germline gene sequence. Preferably, the nucleic acid sequence is at least 90%, 95%, 96%, 97% homologous to the VH1 or VH3 germline gene sequence, and more preferably, at least 98%, 99% homologous to the VH1 or VH3 germline gene sequence. The V_H region of the HA antibody is at least 80% homologous to the amino acid sequence of the V_H region encoded by the VH1 or VH3 V_H germline gene sequence. Preferably, the amino acid sequence of V_H region of the HA antibody is at least 90%, 95%, 96%, 97% homologous to the amino acid sequence encoded by the VH1 or VH3 germline gene sequence, and more preferably, at least 98%, 99% homologous to the sequence encoded by the VH1 or VH3 germline gene sequence.

[257] In certain aspects of the invention the VH1 germline gene is VH1 (1-2), VH1 (1-18), VH1 (3-23), or VH1 (1-69). In other aspects of the invention the VH3 germline gene is VH3 (3-21)

[258] The HA antibodies of the invention also include a variable light chain (V_L) region encoded by a human germline gene sequence selected from the group consisting of VKI, VKII, VKIII, VKIV, VL1, VL2, and VL3 (*see*, Tomlinson IM, Williams SC, Ignatovitch O, Corbett SJ, Winter G. V-BASE Sequence Directory. Cambridge, United Kingdom: MRC Centre for Protein Engineering (1997)). Alternatively, the HA antibodies include a V_L region that is encoded by a nucleic acid sequence that is at least 80% homologous to the germline gene sequence of VKI, VKII, VKIII, VKIV, VL1, VL2, or VL3. Preferably, the nucleic acid sequence is at least 90%, 95%, 96%, 97% homologous to the germline gene sequence of VKI, VKII, VKIII, VKIV, VL1, VL2, or VL3, and more preferably, at least 98%, 99% homologous to the germline gene sequence of VKI, VKII, VKIII, VKIV, VL1, VL2, or VL3. The V_L region of the HA antibody is at least 80% homologous to the amino acid sequence of the V_L region encoded the germline gene sequence of VKI, VKII, VKIII, VKIV, VL1, VL2, or VL3. Preferably, the amino acid sequence of V_L region of the HA antibody is at least 90%, 95%, 96%, 97% homologous to the amino acid sequence encoded by the germline gene sequence of VKI, VKII, VKIII, VKIV, VL1, VL2, or VL3, and more preferably, at least 98%, 99% homologous to the sequence encoded by the germline gene sequence of VKI, VKII, VKIII, VKIV, VL1, VL2, or VL3.

[259] In certain aspects of the invention the VKI germline gene is VKI (A20), the VKII germline gene is VKII (A3), the VKIII germline gene is VKIII (A27), and the VKIV germline gene is VKIV (B3). In other aspects of the invention, the VL1 germline gene is VL1 (V1-13), VL1 (V1-16), VL1 (V1-17), or. VL1 (V1-19). Alternatively, the VL2 germline gene is VL2 (V1-3) or VL2 (V1-4). Furthermore, the VL3 germline gene is VL3 (V2-14).

[260] Specific combinations of a VH- and HL-locus are provided for each HA antibody described below.

[261] The CDR regions of the HA antibodies of the invention were determined according to Kabat *et* al. (1991) as described in Sequences of Proteins of Immunological Interest. In certain embodiments of the invention, HA antibodies contain two, three, four, five or all six CDR regions as disclosed herein. Preferably, HA antibodies contain at least two of the CDRs disclosed herein.

[262] The SC06-141 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 309) and a light chain variable region (SEQ ID NO: 310) encoded by the nucleic acid sequence shown in SEQ ID NO: 311 and the amino acid sequence shown in SEQ ID NO: 312. The VH-locus is VH1 (1-18) and the VL locus is HKIV (B3).

[263] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-141 antibody have the following CDR sequences: GYYVY (HCDR1, SEQ ID NO: 247), WISAYNGNTNYAQKFQG (HCDR2, SEQ ID NO: 248) and SRSLDV (HCDR3, SEQ ID NO: 568). The light chain CDRs of the SC06-141 antibody have the following CDR sequences: KSSQSVLYSSNNKNYLA (LCDR1, SEQ ID NO: 569), WASTRES (LCDR2, SEQ ID NO: 570) and QQYYSTPLT (LCDR3, SEQ ID NO: 289).

[264] SC06-141 nucleotide sequence (SEQ ID NO: 311)

```
gaggtccagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc      60
tcctgcaagg cttctgggta caccttcacc ggctactatg tgtactgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat     180
gcacagaagt tccagggcag agtcacgatt accgcggaca aatccacgag cacagcctac     240
atggagctga gcagcctgag atctgaagac acggctgtgt attactgtgc gagaagtaga     300
tccctggacg tctggggcca agggaccacg gtcaccgtct cgagcggtac gggcggttca     360
ggcggaaccg gcagcggcac tggcgggtcg acggatgttg tgatgactca gtctccagac     420
tccctggctg tgtctctggg cgagagggcc accatcaact gcaagtccag ccagagtgtt     480
ttatacagct ccaacaataa gaactactta gcttggtacc agcagaaacc aggacagcct     540
cctaagctgc tcatttactg ggcatctacc cgggaatccg gggtccctga ccgattcagt     600
ggcagcgggt ctgggacaga tttcactctc accatcagca gcctgcaggc tgaagatgtg     660
gcagtttatt actgtcagca atattatagt actcctctca ctttcggcgg agggaccaaa     720
gtggatatca aacgt                                                      735
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[265] SC06-141 amino acid sequence (SEQ ID NO: 312)

EVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYVYWVRQAPGQGLEWMGWISAYNGNTN
YAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCARSRSLDVWGQGTTVTVSSGTGGS
GGTGSGTGGSTDVVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYLAWYQQKPGQPP
KLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSTPLTFGGGTKVDIK
R

[266] SC06-141 VH amino acid sequence (SEQ ID NO: 309)

EVQLVQSGAEVKKPGASVKVSCKASGYTFT**GYYVY**WVRQAPGQGLEWMG**WISAYNGNTN**
YAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCAR**SRSLDV**WGQGTTVTVSS

[267] SC06-141 VL amino acid sequence (SEQ ID NO: 310)

DVVMTQSPDSLAVSLGERATINC**KSSQSVLYSSNNKNYLA**WYQQKPGQPPKLLIY**WAST**
RESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC**QQYYSTPLT**FGGGTKVDIKR

[268] The SC06-255 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 313) and a light chain variable region (SEQ ID NO: 314) encoded by

the nucleic acid sequence shown in SEQ ID NO: 315 and the amino acid sequence shown in SEQ ID NO: 316. The VH-locus is VH1 (1-69) and the VL locus is VL1 (V1-16).

[269] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-255 antibody have the following CDR sequences: SYAIS (HCDR1, SEQ ID NO: 571), GIIPIFGTTKYAPKFQG (HCDR2, SEQ ID NO: 572) and HMGYQVRETMDV (HCDR3, SEQ ID NO: 573). The light chain CDRs of the SC06-255 antibody have the following CDR sequences: SGSTFNIGSNAVD (LCDR1, SEQ ID NO: 574), SNNQRPS (LCDR2, SEQ ID NO: 575) and AAWDDILNVPV (LCDR3, SEQ ID NO: 576).

[270] SC06-255 nucleotide sequence (SEQ ID NO: 315)

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gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc      60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcctgagtg gatgggaggg atcatcccta tttttggtac aacaaaatac     180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac     240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg     300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gtcctatgtg     420
ctgactcagc caccctcagc gtctgggacc cccgggcaga gggtcaccat ctcttgttct     480
ggaagcacgt tcaacatcgg aagtaatgct gtagactggt accggcagct cccaggaacg     540
gcccccaaac tcctcatcta tagtaataat cagcggccct caggggtccc tgaccgattc     600
tctggctcca ggtctggcac ctcagcctcc ctggccatca gtgggctcca gtctgaggat     660
gaggctgatt attactgtgc agcatgggat gacatcctga atgttccggt attcggcgga     720
gggaccaagc tgaccgtcct aggt                                            744
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[271] SC06-255 amino acid sequence (SEQ ID NO: 316)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSSG
TGGSGGTGSGTGGSTSYVLTQPPSASGTPGQRVTISCSGSTFNIGSNAVDWYRQLPGTAPKLLI
YSNNQRPSGVPDRFSGSRSGTSASLAISGLQSEDEADYYCAAWDDILNVPVFGGGTKLTVLG

[272] SC06-255 VH amino acid sequence (SEQ ID NO: 313)

EVQLVESGAEVKKPGSSVKVSCKASGGPFR**SYAIS**WVRQAPGQGPEWMG**GIIPIFGTTKYA**
PKFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAK**HMGYQVRETMDV**WGKG
TTVTVSS

[273] SC06-255 VL amino acid sequence (SEQ ID NO: 314)

SYVLTQPPSASGTPGQRVTISC**SGSTFNIGSNA**VDWYRQLPGTAPKLLIY**SNNQRPS**GVPDRF
SGSRSGTSASLAISGLQSEDEADYYC**AAWDDILNV**PVFGGGTKLTVLG

[274] The SC06-257 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 317) and a light chain variable region (SEQ ID NO: 318) encoded by the nucleic acid sequence shown in SEQ ID NO: 319 and the amino acid sequence shown in SEQ ID NO: 320. The VH-locus is VH1 (1-69) and the VL locus is VL2 (V1-4).

[275] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-257 antibody have the following CDR sequences: SYAIS (HCDR1, SEQ ID NO: 571), GIIPIFGTTKYAPKFQG (HCDR2, SEQ ID NO: 572) and HMGYQVRETMDV (HCDR3, SEQ ID NO: 573). The light chain CDRs of the SC06-257 antibody have the following CDR sequences: TGTSSDVGGYNYVS (LCDR1, SEQ ID NO: 577), EVSNRPS (LCDR2, SEQ ID NO: 578) and SSYTSSSTY (LCDR3, SEQ ID NO: 579).

[276] SC06-257 nucleotide sequence (SEQ ID NO: 319)

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caggtccagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc      60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcctgagtg gatgggaggg atcatcccta tttttggtac aacaaaatac     180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac     240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg     300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gcagtctgcc     420
ctgactcagc ctgccgccgt gtctgggtct cctggacagt cgatcaccat ctcctgcact     480
ggaaccagca gtgacgttgg tggttataac tatgtctcct ggtaccaaca gcacccaggc     540
aaagccccca aactcatgat ttatgaggtc agtaatcggc cctcaggggt ttctaatcgc     600
ttctctggct ccaagtctgg caacacggcc tccctgacca tctctgggct ccaggctgag     660
gacgaggctg attattactg cagctcatat acaagcagca gcacttatgt cttcggaact     720
gggaccaagg tcaccgtcct aggt                                            744
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[277] SC06-257 amino acid sequence (SEQ ID NO: 320)

QVQLVQSGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSSG
TGGSGGTGSGTGGSTQSALTQPAAVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPK
LMIYEVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTYVFGTGTKVTVL
G

[278] SC06-257 VH amino acid sequence (SEQ ID NO: 317)

QVQLVQSGAEVKKPGSSVKVSCKASGGPFR**SYAIS**WVRQAPGQGPEWMG**GIIPIFGTTKYA**
PKFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAK**HMGYQVRETMDV**WGKGTTVTVS
S

[279] SC06-257 VL amino acid sequence (SEQ ID NO: 318)

QSALTQPAAVSGSPGQSITISC**TGTSSDVGGYNYVS**WYQQHPGKAPKLMIY**EVSNRPS**GVSN
RFSGSKSGNTASLTISGLQAEDEADYYC**SSYTSSSTYV**FGTGTKVTVLG

[280] The SC06-260 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 321) and a light chain variable region (SEQ ID NO: 322) encoded by the nucleic acid sequence shown in SEQ ID NO: 323 and the amino acid sequence shown in SEQ ID NO: 324. The VH-locus is VH1 (1-69) and the VL locus is VL1 (V1-17).

[281] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-260 antibody have the following CDR sequences: SYAIS (HCDR1, SEQ ID NO: 571), GIIPIFGTTKYAPKFQG (HCDR2, SEQ ID NO: 572) and HMGYQVRETMDV (HCDR3, SEQ ID NO: 573). The light chain CDRs of the SC06-260antibody have the following CDR sequences: SGSRSNVGDNSVY (LCDR1, SEQ ID NO: 580), KNTQRPS (LCDR2, SEQ ID NO: 581) and VAWDDSVDGYV (LCDR3, SEQ ID NO: 582).

[282] SC06-260 nucleotide sequence (SEQ ID NO: 323)

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gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc      60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttggtac aacaaaatac      180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac     240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg     300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gtcctatgtg     420
ctgactcagc caccctcagt ctctgggacc cccgggcaga gggtcaccat ctcttgctct    480
ggaagccgct ccaacgtcgg agataattct gtatattggt atcaacacgt cccagaaatg     540
gcccccaaac tcctcgtcta taagaatact caacggccct caggagtccc tgcccggttt     600
tccggctcca agtctggcac ttcagcctcc ctggccatca ttggcctcca gtccggcgat     660
gaggctgatt attattgtgt ggcatgggat gacagcgtag atggctatgt cttcggatct     720
gggaccaagg tcaccgtcct aggt                                            744
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[283] SC06-260 amino acid sequence (SEQ ID NO: 324)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSSG
TGGSGGTGSGTGGSTSYVLTQPPSVSGTPGQRVTISCSGSRSNVGDNSVYWYQHVPEMAPKL
LVYKNTQRPSGVPARFSGSKSGTSASLAIIGLQSGDEADYYCVAWDDSVDGYVFGSGTKVTV
LG

[284] SC06-260 VH amino acid sequence (SEQ ID NO: 321)

EVQLVESGAEVKKPGSSVKVSCKASGGPFR**SYAIS**WVRQAPGQGPEWMG**GIIPIFGTTKYA**
PKFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAK**HMGYQVRETMDV**WGKGTTVTVS
S

[285] SC06-260 VL amino acid sequence (SEQ ID NO: 322)

SYVLTQPPSVSGTPGQRVTISC**SGSRSNVGDNSVY**WYQHVPEMAPKLLVY**KNTQRPS**GVPA
RFSGSKSGTSASLAIIGLQSGDEADYYC**VAWDDSVDGY**VFGSGTKVTVLG

[286] The SC06-261 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 325) and a light chain variable region (SEQ ID NO: 326) encoded by the nucleic acid sequence shown in SEQ ID NO: 327 and the amino acid sequence shown in SEQ ID NO: 328. The VH-locus is VH1 (1-69) and the VL locus is VL1 (V1-19).

[287] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-261 antibody have the following CDR sequences: SYAIS (HCDR1, SEQ ID NO: 571), GIIPIFGTTKYAPKFQG (HCDR2, SEQ ID NO: 572) and HMGYQVRETMDV (HCDR3, SEQ ID NO: 573). The light chain CDRs of the SC06-261 antibody have the following CDR sequences: SGSSSNIGNDYVS (LCDR1, SEQ ID NO: 583), DNNKRPS (LCDR2, SEQ ID NO: 584) and ATWDRRPTAYVV (LCDR3, SEQ ID NO: 585).

[288] SC06-261 nucleotide sequence (SEQ ID NO: 327)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc      60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcctgagtg gatgggaggg atcatcccta tttttggtac aacaaaatac     180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac     240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg     300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gcagtctgtg     420
ttgacgcagc cgccctcagt gtctgcggcc ccaggacaga aggtcaccat ctcctgctct     480
ggaagcagct ccaacattgg gaatgattat gtatcctggt accagcagct cccaggaaca     540
gcccccaaac tcctcattta tgacaataat aagcgaccct cagggattcc tgaccgattc     600
tctggctcca agtctggcac gtcagccacc ctgggcatca ccggactcca gactggggac     660
gaggccaact attactgcgc aacatgggat cgccgcccga ctgcttatgt tgtcttcggc     720
ggagggacca agctgaccgt cctaggt                                        747
```

[289] SC06-261 amino acid sequence (SEQ ID NO: 328)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSSG
TGGSGGTGSGTGGSTQSVLTQPPSVSAAPGQKVTISCSGSSSNIGNDYVSWYQQLPGTAPKLL
IYDNNKRPSGIPDRFSGSKSGTSATLGITGLQTGDEANYYCATWDRRPTAYVVFGGGTKLTV
LG

[290] SC06-261 VH amino acid sequence (SEQ ID NO: 325)

EVQLVESGAEVKKPGSSVKVSCKASGGPFR**SYAIS**WVRQAPGQGPEWMG**GIIPIFGTTKYA**
PKFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAK**HMGYQVRETMDV**WGKGTTVTVS
S

[291] SC06-261 VL amino acid sequence (SEQ ID NO: 326)

SVLTQPPSVSAAPGQKVTISC**SGSSSNIGNDYVS**WYQQLPGTAPKLLIY**DNNKRPS**GIPDRFS
GSKSGTSATLGITGLQTGDEANYYC**ATWDRRPTAYVV**FGGGTKLTVLG

[292] The SC06-262 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 329) and a light chain variable region (SEQ ID NO: 330) encoded by the nucleic acid sequence shown in SEQ ID NO: 331 and the amino acid sequence shown in SEQ ID NO: 332. The VH-locus is VH1 (1-69) and the VL locus is VKI (A20).

[293] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-262 antibody have the following CDR sequences: GSAIS (HCDR1, SEQ ID NO: 586), GISPLFGTTNYAQKFQG (HCDR2, SEQ ID NO: 587) and GPKYYSEYMDV (HCDR3, SEQ ID NO: 588). The light chain CDRs of the SC06-262 antibody have the following CDR sequences: RASQGISSYLA (LCDR1, SEQ ID NO: 589), DASTLRS (LCDR2, SEQ ID NO: 590) and QRYNSAPPI (LCDR3, SEQ ID NO: 591).

[294] SC06-262 nucleotide sequence (SEQ ID NO: 331)

```
caggtacagc tgcagcagtc aggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc     60
tcctgcaagg tttccggagt cattttcagc ggcagtgcga tcagctgggt gcgacaggcc    120
cctggacaag gccttgagtg gatgggaggg atcagccctc tctttggcac aacaaattac    180
gcacaaaagt tccagggcag agtcacgatt accgcggacc aatccacgaa cacaacctac    240
atggaggtga acagcctgag atatgaggac acggccgtgt atttctgtgc gcgaggtcca    300
aaatattaca gtgagtacat ggacgtctgg ggcaaaggga ccacggtcac cgtctcgagc    360
ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgga catccagatg    420
acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg    480
gcgagtcagg gcattagcag ttatttagcc tggtatcagc agaagccagg gaaagttcct    540
acactcctga tctatgatgc atccactttg cgatcagggg tcccatctcg cttcagtggc    600
agtggatctg cgacagattt cactctcacc atcagcagcc tgcagcctga agatgttgca    660
acttattact gtcaaaggta taacagtgcc cccccgatca ccttcggcca agggacacga    720
ctggagatta aacgt                                                     735
```

[295] SC06-262 amino acid sequence (SEQ ID NO: 332)

QVQLQQSGAEVKKPGSSVKVSCKVSGVIFSGSAISWVRQAPGQGLEWMGGISPLFGTTNYAQ
KFQGRVTITADQSTNTTYMEVNSLRYEDTAVYFCARGPKYYSEYMDVWGKGTTVTVSSGT
GGSGGTGSGTGGSTDIQMTQSPSSLSASVGDRVTITCRASQGISSYLAWYQQKPGKVPTLLIY
DASTLRSGVPSRFSGSGSATDFTLTISSLQPEDVATYYCQRYNSAPPITFGQGTRLEIKR

[296] SC06-262 VH amino acid sequence (SEQ ID NO: 329)

QVQLQQSGAEVKKPGSSVKVSCKVSGVIF**SGSAIS**WVRQAPGQGLEWM**GGISPLFGTTNYA**
QKFQGRVTITADQSTNTTYMEVNSLRYEDTAVYFCAR**GPKYYSEYMDV**WGKGTTVTVSS

[297] SC06-262 VL amino acid sequence (SEQ ID NO: 330)

DIQMTQSPSSLSASVGDRVTITC**RASQGISSYLA**WYQQKPGKVPTLLIY**DASTLRS**GVPSRFS
GSGSATDFTLTISSLQPEDVATYYC**QRYNSAPPIT**FGQGTRLEIKR

[298] The SC06-268 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 333) and a light chain variable region (SEQ ID NO: 334) encoded by the nucleic acid sequence shown in SEQ ID NO: 335 and the amino acid sequence shown in SEQ ID NO: 336. The VH-locus is VH1 (1-69) and the VL locus is VL3 (V2-14).

[299] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-268 antibody have the following CDR sequences: SYAIS (HCDR1, SEQ ID NO: 571), GIMGMFGTTNYAQKFQG (HCDR2, SEQ ID NO: 592) and SSGYYPEYFQD (HCDR3, SEQ ID NO: 593). The light chain CDRs of the SC06-

268 antibody have the following CDR sequences: SGHKLGDKYVS (LCDR1, SEQ ID NO: 594), QDNRRPS (LCDR2, SEQ ID NO: 595) and QAWDSSTA (LCDR3, SEQ ID NO: 596).

[300] SC06-268 nucleotide sequence (SEQ ID NO: 335)

```
caggtccagc tggtacagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc     60
tcctgcaagg cttctggagg caccttcagt agttatgcta tcagctgggt gcgacaggcc    120
cctggacaag ggcttgagtg gatgggagga atcatgggta tgtttggcac aactaactac    180
gcacagaagt tccagggcag agtcacgatt accgcggacg aattcacgag cgcagcctac    240
atggagctga ggagcctgag atctgaggac acggccgtct actactgtgc gaggtctagt    300
ggttattacc ccgaatactt ccaggactgg ggccagggca ccctggtcac cgtctcgagc    360
ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgca gtctgtgctg    420
actcagccac cctcagagtc cgtgtcccca ggacagacag ccagcgtcac ctgctctgga    480
cataaattgg gggataaata tgtttcgtgg tatcagcaga agccaggcca gtcccctgta    540
ttactcatct atcaagataa caggcggccc tcagggatcc ctgagcgatt cataggctcc    600
aactctggga acacagccac tctgaccatc agcgggaccc aggctctgga tgaggctgac    660
tattactgtc aggcgtggga cagcagcact gcggttttcg gcggagggac caagctgacc    720
gtcctaggt                                                            729
```

[301] SC06-268 amino acid sequence (SEQ ID NO: 336)

QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIMGMFGTTNY
AQKFQGRVTITADEFTSAAYMELRSLRSEDTAVYYCARSSGYYPEYFQDWGQGTLVTVSSG
TGGSGGTGSGTGGSTQSVLTQPPSESVSPGQTASVTCSGHKLGDKYVSWYQQKPGQSPVLLI
YQDNRRPSGIPERFIGSNSGNTATLTISGTQALDEADYYCQAWDSSTAVFGGGTKLTVLG

[302] SC06-268 VH amino acid sequence (SEQ ID NO: 333)

QVQLVQSGAEVKKPGSSVKVSCKASGGTFS**SYAISWVRQAPGQGLEWMGGIMGMFGTTN**
YAQKFQGRVTITADEFTSAAYMELRSLRSEDTAVYYCAR**SSGYYPEYFQD**WGQGTLVTVS
S

[303] SC06-268 VL amino acid sequence (SEQ ID NO: 334)

QSVLTQPPSESVSPGQTASVTC**SGHKLGDKYVSWYQQKPGQSPVLLIYQDNRRPSGIPERFI**
GSNSGNTATLTISGTQALDEADYYCQAWDSSTAVFGGGTKLTVLG

[304] The SC06-272 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 337) and a light chain variable region (SEQ ID NO: 338) encoded by the nucleic acid sequence shown in SEQ ID NO: 339 and the amino acid sequence shown in SEQ ID NO: 340. The VH-locus is VH1 (1-69) and the VL locus is VL2 (V1-3).

[305] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-272 antibody have the following CDR sequences: SYAIT (HCDR1, SEQ ID NO: 597), GIIGMFGSTNYAQNFQG (HCDR2, SEQ ID NO: 598) and STGYYPAYLHH (HCDR3, SEQ ID NO: 599). The light chain CDRs of the SC06-272 antibody have the following CDR sequences: TGTSSDVGGYNYVS (LCDR1,

SEQ ID NO: 577), DVSKRPS (LCDR2, SEQ ID NO: 601) and SSYTSSSTHV (LCDR3, SEQ ID NO: 602).

[306] SC06-272 nucleotide sequence (SEQ ID NO: 339)

```
cagatgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg caccttctcc agttatgcta tcacctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcggta tgtttggttc aacaaactac     180
gcacagaact tccagggcag agtcacgatt accgcggacg aatccacgag cacagcctac     240
atggagctga gcagcctcag atctgaggac acggccgtgt attactgtgc gagaagtact     300
ggttattacc ctgcatacct ccaccactgg ggccagggca ccctggtcac cgtctcgagc     360
ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgca gtctgccctg     420
actcagcctc gctcagtgtc cgggtctcct ggacagtcag tcaccatctc ctgcactgga     480
accagcagtg atgttggtgg ttataactat gtctcctggt accaacagca cccaggcaaa     540
gcccccaaac tcatgattta tgatgtcagt aagcggccct caggggtccc tgatcgcttc     600
tctggctcca agtctggcaa cacggcctcc ctgaccatct ctgggctcca ggctgaggat     660
gaggctgatt attactgcag ctcatataca agcagcagca ctcatgtctt cggaactggg     720
accaaggtca ccgtcctagg t                                               741
```

[307] SC06-272 amino acid sequence (SEQ ID NO: 340)

QMQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAITWVRQAPGQGLEWMGGIIGMFGSTYAQ
NFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARSTGYYPAYLHHWGQGTLVTVS
SGTGGSGGTGSGTGGSTQSALTQPRSVSGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPG
KAPKLMIYDVSKRPSGVPDRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTHVFGTG
TKVTVLG

[308] SC06-272 VH amino acid sequence (SEQ ID NO: 337)

QMQLVQSGAEVKKPGSSVKVSCKASGGTFSS**YAITWVRQAPGQGLEWMGGIIGMFGSTNY**
AQNFQGRVTITADESTSTAYMELSSLRSEDTAVYYCAR**STGYYPAYLHH**WGQGTLVTVSS

[309] SC06-272 VL amino acid sequence (SEQ ID NO: 338)

QSALTQPRSVSGSPGQSVTISC**TGTSSDVGGYNYVSWYQQHPGKAPKLMIYDVSKRPSGVP**
DRFSGSKSGNTASLTISGLQAEDEADYYC**SSYTSSSTH**VFGTGTKVTVLG

[310] The SC06-296 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 341) and a light chain variable region (SEQ ID NO: 342) encoded by the nucleic acid sequence shown in SEQ ID NO: 343 and the amino acid sequence shown in SEQ ID NO: 344. The VH-locus is VH1 (1-2) and the VL locus is VKIII (A27).

[311] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-296 antibody have the following CDR sequences: SYYMH (HCDR1, SEQ ID NO: 603), WINPNSGGTNYAQKFQG (HCDR2, SEQ ID NO: 604) and EGKWGPQAAFDI (HCDR3, SEQ ID NO: 605). The light chain CDRs of the SC06-296 antibody have the following CDR sequences: RASQSVSSSYLA (LCDR1, SEQ ID NO: 646), DASSRAT (LCDR2, SEQ ID NO: 607) and QQYGSSLW (LCDR3, SEQ ID NO: 608).

[312] SC06-296 nucleotide sequence (SEQ ID NO: 343)

```
gaggtgcagc tggtggagac cggggctgag gtgaagaagc ctggggcctc agtgaaggtt      60
tcctgcaagg catctggata caccttcacc agctactata tgcactgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtggtgg cacaaactat     180
gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcag cacagcctac     240
atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gagagagggg     300
aaatggggac ctcaagcggc ttttgatatc tggggccaag ggacaatggt caccgtctcg     360
agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac ggaaattgtg     420
atgacgcagt ctccaggcac cctgtctttg tctccagggg aaagagccac cctctcctgc     480
agggccagtc agagtgttag cagcagctac ttagcctggt accagcagaa acctggccag     540
gctcccaggc tcctcatcta tgatgcatcc agcagggcca ctgacatccc agacaggttc     600
agtggcagtg ggtctgggac agacttcact ctcaccatca gcagactgga gcctgaagat     660
tttgcagtgt attactgtca gcagtatggt agctcacttt ggacgttcgg ccaagggacc     720
aaggtggaga tcaaacgt                                                   738
```

[313] SC06-296 amino acid sequence (SEQ ID NO: 344)

EVQLVETGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGWINPNSGGTN
YAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCAREGKWGPQAAFDIWGQGTMVTV
SSGTGGSGGTGSGTGGSTEIVMTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAP
RLLIYDASSRATDIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSLWTFGQGTKVEIKR

[314] SC06-296VH amino acid sequence (SEQ ID NO: 341)

EVQLVETGAEVKKPGASVKVSCKASGYTFT**SYYMH**WVRQAPGQGLEWMG**WINPNSGGTN**
YAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCA**REGKWGPQAAFDI**WGQGTMVT
VSS

[315] SC06-296 VL amino acid sequence (SEQ ID NO: 342)

EIVMTQSPGTLSLSPGERATLSC**RASQSVSSSYLA**WYQQKPGQAPRLLIY**DASSRAT**DIPDRF
SGSGSGTDFTLTISRLEPEDFAVYYC**QQYGSSLWT**FGQGTKVEIKR

[316] The SC06-301 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 345) and a light chain variable region (SEQ ID NO: 346) encoded by the nucleic acid sequence shown in SEQ ID NO: 347 and the amino acid sequence shown in SEQ ID NO: 348. The VH-locus is VH1 (3-23) and the VL locus is VKII (A3).

[317] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-301 antibody have the following CDR sequences: IYAMS (HCDR1, SEQ ID NO: 609), AISSSGDSTYYADSVKG (HCDR2, SEQ ID NO: 610) and AYGYTFDP (HCDR3, SEQ ID NO: 611). The light chain CDRs of the SC06-301 antibody have the following CDR sequences: RSSQSLLHSNGYNYLD (LCDR1, SEQ ID NO: 612), LGSNRAS (LCDR2, SEQ ID NO: 613) and MQALQTPL (LCDR3, SEQ ID NO: 614).

[318] SC06-301 nucleotide sequence (SEQ ID NO: 347)

```
gaggtgcagc tggtagagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc      60
tcctgtgcag cctctggatt cacctttagc atctatgcca tgagctgggt ccgccaggca     120
ccagggaagg ggctggagtg ggtctcagct attagtagta gtggtgatag cacatactac     180
gcagactccg tgaagggccg gttcaccatc tccagagaca acgccaggaa cacgctgtat     240
ctgcaaatga acagtctgag agccgaggac acggctgtgt attactgtgc gagagcgtat     300
ggctacacgt tcgacccctg gggccaggga accctggtca ccgtctcgag cggtacgggc     360
ggttcaggcg gaaccggcag cggcactggc gggtcgacgg aaattgtgct gactcagtct     420
ccactctccc tgcccgtcac ccctggagag ccggcctcca tctcctgcag gtctagtcag     480
agcctcctgc atagtaatgg atacaactat ttggattggt acctgcagaa gccagggcag     540
tctccacagc tcctgatcta tttgggttct aatcgggcct ccggggtccc tgacaggttc     600
agtggcagtg gatcaggcac agattttaca ctgaaaatca gcagagtgga ggctgaggat     660
gttggggttt attactgcat gcaagctcta caaactcccc tcactttcgg cggagggacc     720
aaggtggaga tcaaacgt                                                   738
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[319] SC06-301 amino acid sequence (SEQ ID NO: 348)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSIYAMSWVRQAPGKGLEWVSAISSSGDSTYYAD
SVKGRFTISRDNARNTLYLQMNSLRAEDTAVYYCARAYGYTFDPWGQGTLVTVSSGTGGSG
GTGSGTGGSTEIVLTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIY
LGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPLTFGGGTKVEIKR

[320] SC06-301 VH amino acid sequence (SEQ ID NO: 345)

EVQLVESGGGLVQPGGSLRLSCAASGFTFS**IYAMS**WVRQAPGKGLEWVS**AISSSGDSTYYA**
DSVKGRFTISRDNARNTLYLQMNSLRAEDTAVYYCAR**AYGYTFDP**WGQGTLVTVSS

[321] SC06-301 VL amino acid sequence (SEQ ID NO: 346)

EIVLTQSPLSLPVTPGEPASISC**RSSQSLLHSNGYNYLD**WYLQKPGQSPQLLIY**LGSNRAS**GV
PDRFSGSGSGTDFTLKISRVEAEDVGVYYC**MQALQTPL**TFGGGTKVEIKR

[322] The SC06-307 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 349) and a light chain variable region (SEQ ID NO: 350) encoded by the nucleic acid sequence shown in SEQ ID NO: 351 and the amino acid sequence shown in SEQ ID NO: 352. The VH-locus is VH3 (3-21) and the VL locus is VKIII (A27).

[323] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-307 antibody have the following CDR sequences: SYSMN (HCDR1, SEQ ID NO: 615), SISSSSSYIYYVDSVKG (HCDR2, SEQ ID NO: 616) and GGGSYGAYEGFDY (HCDR3, SEQ ID NO: 617). The light chain CDRs of the SC06-307 antibody have the following CDR sequences: RASQRVSSYLA (LCDR1, SEQ ID NO: 618), GASTRAA (LCDR2, SEQ ID NO: 619) and QQYGRTPLT (LCDR3, SEQ ID NO: 620).

[324] SC06-307 nucleotide sequence (SEQ ID NO: 351)

```
caggtccagc tggtgcagtc tggggaggc ctggtcaagc ctgggggtc cctgagactc      60
tcctgtgcag cctctggatt caccttcagt agctatagca tgaactgggt ccgccaggct     120
ccagggaagg ggctggagtg ggtctcatcc attagtagta gtagtagtta catatactac     180
gtagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat     240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagaggtggt     300
gggagctacg gggcctacga aggctttgac tactggggcc agggcaccct ggtcaccgtc     360
tcgagcggta cgggcggttc aggcggaacc ggcagcggca ctggcgggtc gacggaaatt     420
gtgctgactc agtctccagg caccctgtct ttgtctccag gggaaagagc caccctctcc     480
tgcagggcca gtcagcgtgt tagcagctac ttagcctggt accaacagaa acctggccag     540
gctcccaggc tcctcatcta tggtgcatcc accagggccg ctggcatccc agacaggttc     600
agtggcagtg ggtctgggac agacttcact ctcaccatca gcagactgga gcctgaagat     660
tctgcagtgt attactgtca gcagtatggt aggcaccgc tcactttcgg cggagggacc      720
aaggtggaga tcaaacgt                                                   738
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[325] SC06-307 amino acid sequence (SEQ ID NO: 352)

QVQLVQSGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSSISSSSSYIYYVD
SVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARGGGSYGAYEGFDYWGQGTLVTVSS
GTGGSGGTGSGTGGSTEIVLTQSPGTLSLSPGERATLSCRASQRVSSYLAWYQQKPGQAPRLL
IYGASTRAAGIPDRFSGSGSGTDFTLTISRLEPEDSAVYYCQQYGRTPLTFGGGTKVEIKR

[326] SC06-307 VH amino acid sequence (SEQ ID NO: 349)

QVQLVQSGGGLVKPGGSLRLSCAASGFTF**SSYSMN**WVRQAPGKGLEWVS**SISSSSSYIYYVD**
SVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYC**ARGGGSYGAYEGFDY**WGQGTLVTVSS

[327] SC06-307 VL amino acid sequence (SEQ ID NO: 350)

EIVLTQSPGTLSLSPGERATLSC**RASQRVSSYLA**WYQQKPGQAPRLLIY**GASTRAAGIPDRFS**
GSGSGTDFTLTISRLEPEDSAVYYC**QQYGRTPLT**FGGGTKVEIKR

[328] The SC06-310 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 353) and a light chain variable region (SEQ ID NO: 354) encoded by the nucleic acid sequence shown in SEQ ID NO: 355 and the amino acid sequence shown in SEQ ID NO: 356. The VH-locus is VH1 (1-69) and the VL locus is VL3 (V2-14).

[329] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-310 antibody have the following CDR sequences: SYAIS (HCDR1, SEQ ID NO: 571), GIIPIFGTTKYAPKFQG (HCDR2, SEQ ID NO: 572) and HMGYQVRETMDV (HCDR3, SEQ ID NO: 573). The light chain CDRs of the SC06-310 antibody have the following CDR sequences: GGNNIGSKSVH (LCDR1, SEQ ID NO: 621), DDSDRPS (LCDR2, SEQ ID NO: 622) and QVWDSSSDHAV (LCDR3, SEQ ID NO: 623).

[330] SC06-310 nucleotide sequence (SEQ ID NO: 355)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc     60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc    120
cctggacaag ggcctgagtg gatgggaggg atcatcccta tttttggtac aacaaaatac    180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac    240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg    300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg    360
agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gtcctatgtg    420
ctgactcagc caccctcggt gtcagtggcc ccaggacaga cggccaggat tacctgtggg    480
ggaaacaaca ttggaagtaa aagtgtgcac tggtaccagc agaagccagg ccaggccccc    540
gtgctggtcg tctatgatga tagcgaccgg ccctcaggga tccctgagcg attctctggc    600
tccaactctg ggaacacggc caccctgacc atcagcaggg tcgaagccgg ggatgaggcc    660
gactattact gtcaggtgtg ggatagtagt agtgatcatg ctgtgttcgg aggaggcacc    720
cagctgaccg tcctcggt                                                  738
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[331] SC06-310 amino acid sequence (SEQ ID NO: 356)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSSG
TGGSGGTGSGTGGSTSYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVV
YDDSDRPSGIPERFSGSNSGNTATLTISRVEAGDEADYYCQVWDSSSDHAVFGGGTQLTVLG

[332] SC06-310 VH amino acid sequence (SEQ ID NO: 353)

EVQLVESGAEVKKPGSSVKVSCKASGGPFR**SYAIS**WVRQAPGQGPEWMG**GIIPIFGTTKYA**
PKFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAK**HMGYQVRETMDV**WGKGTTVTVS
S

[333] SC06-310 VL amino acid sequence (SEQ ID NO: 354)

SYVLTQPPSVSVAPGQTARITC**GGNNIGSKSVH**WYQQKPGQAPVLVVY**DDSDRPS**GIPERFS
GSNSGNTATLTISRVEAGDEADYYC**QVWDSSSDHAV**FGGGTQLTVLG

[334] The SC06-314 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 357) and a light chain variable region (SEQ ID NO: 358) encoded by the nucleic acid sequence shown in SEQ ID NO: 359 and the amino acid sequence shown in SEQ ID NO: 360. The VH-locus is VH1 (1-69) and the VL locus is VL1 (V1-17).

[335] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-314 antibody have the following CDR sequences: SYAIS (HCDR1, SEQ ID NO: 571), GIIPIFGTTKYAPKFQG (HCDR2, SEQ ID NO: 572) and HMGYQVRETMDV (HCDR3, SEQ ID NO: 573). The light chain CDRs of the SC06-314 antibody have the following CDR sequences: SGSSSNIGSNYVY (LCDR1, SEQ ID NO: 624), RDGQRPS (LCDR2, SEQ ID NO: 625) and ATWDDNLSGPV (LCDR3, SEQ ID NO: 626).

[336] SC06-314 nucleotide sequence (SEQ ID NO: 359)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc      60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcctgagtg gatgggaggg atcatcccta tttttggtac aacaaaatac     180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac     240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg     300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gtcctatgtg     420
ctgactcagc caccctcagc gtctgggacc cccgggcaga gggtcaccat ctcttgttct     480
ggaagcagct ccaacatcgg aagtaattat gtatactggt accagcagct cccaggcacg     540
gcccccaaac tcctcatcta tagggatggt cagcggccct caggggtccc tgaccgattc     600
tctggctcca agtctggcac ctcagcctcc ctggccatca gtggactccg gtccgatgat     660
gaggctgatt attactgtgc aacatgggat gacaacctga gtggtccagt attcggcgga     720
gggaccaagc tgaccgtcct aggt                                            744
```

[337] SC06-314 amino acid sequence (SEQ ID NO: 360)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSSG
TGGSGGTGSGTGGSTSYVLTQPPSASGTPGQRVTISCSGSSSNIGSNYVYWYQQLPGTAPKLLI
YRDGQRPSGVPDRFSGSKSGTSASLAISGLRSDDEADYYCATWDDNLSGPVFGGGTKLTVLG

[338] SC06-314 VH amino acid sequence (SEQ ID NO: 357)

EVQLVESGAEVKKPGSSVKVSCKASGGPFR**SYAIS**WVRQAPGQGPEWMG**GIIPIFGTTKYA**
PKFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAK**HMGYQVRETMDV**WGKGTTVTVS
S

[339] SC06-314 VL amino acid sequence (SEQ ID NO: 358)

SYVLTQPPSASGTPGQRVTISC**SGSSSNIGSNYVY**WYQQLPGTAPKLLIY**RDGQRPS**GVPDRF
SGSKSGTSASLAISGLRSDDEADYYC**ATWDDNLSG**PVFGGGTKLTVLG

[340] The SC06-323 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 361) and a light chain variable region (SEQ ID NO: 362) encoded by the nucleic acid sequence shown in SEQ ID NO: 363 and the amino acid sequence shown in SEQ ID NO: 364. The VH-locus is VH1 (1-69) and the VL locus is VKIII (A27).

[341] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-323 antibody have the following CDR sequences: SYGIS (HCDR1, SEQ ID NO: 627), DIIGMFGSTNYAQNFQG (HCDR2, SEQ ID NO: 628) and SSGYYPAYLPH (HCDR3, SEQ ID NO: 629). The light chain CDRs of the SC06-323 antibody have the following CDR sequences: RASQSVSSSYLA (LCDR1, SEQ ID NO: 646), GASSRAT (LCDR2, SEQ ID NO: 631) and QQYGSSPRT (LCDR3, SEQ ID NO: 632).

[342] SC06-323 nucleotide sequence (SEQ ID NO: 363)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc cagggtcctc ggtgaaggtc      60
tcctgtaagg cctctggagg caccttctcc agctatggta tcagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggagac atcatcggta tgtttggttc aacaaactac     180
gcacagaact tccagggcag actcacgatt accgcggacg aatccacgag cacagcctac     240
atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagaagtagt     300
ggttattacc ctgcatacct cccccactgg ggccagggca ccttggtcac cgtctcgagc     360
ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgga aattgtgttg     420
acccagtctc caggcaccct gtctttgtct ccaggggaaa gagccaccct ctcctgcagg     480
gccagtcaga gtgttagcag cagctactta gcctggtacc agcagaaacc tggccaggct     540
cccaggctcc tcatctatgg tgcatccagc agggccactg gcatcccaga caggttcagt     600
ggcagtgggt ctgggacaga cttcactctc accatcagca gactggagcc tgaagatttt     660
gcagtgtatt actgtcagca gtatggtagc tcacccagaa ctttcggcgg agggaccaag     720
gtggagatca aacgt                                                      735
```

[343] SC06-323 amino acid sequence (SEQ ID NO: 364)

EVQLVESGAEVKKPGSSVKVSCKASGGTFSSYGISWVRQAPGQGLEWMGDIIGMFGSTNYA
QNFQGRLTITADESTSTAYMELSSLRSEDTAVYYCARSSGYYPAYLPHWGQGTLVTVSSGTG
GSGGTGSGTGGSTEIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIY
GASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPRTFGGGTKVEIKR

[344] SC06-323 VH amino acid sequence (SEQ ID NO: 361)

EVQLVESGAEVKKPGSSVKVSCKASGGTFSSYGISWVRQAPGQGLEWMGDIIGMFGSTNYA
QNFQGRLTITADESTSTAYMELSSLRSEDTAVYYCARSSGYYPAYLPHWGQGTLVTVSS

[345] SC06-323 VL amino acid sequence (SEQ ID NO: 362)

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFS
GSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPRTFGGGTKVEIKR

[346] The SC06-325 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 365) and a light chain variable region (SEQ ID NO: 366) encoded by the nucleic acid sequence shown in SEQ ID NO: 367 and the amino acid sequence shown in SEQ ID NO: 368. The VH-locus is VH1 (1-69) and the VL locus is VL2 (V1-4).

[347] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-325 antibody have the following CDR sequences: FYSMS (HCDR1, SEQ ID NO: 633), GIIPMFGTTNYAQKFQG (HCDR2, SEQ ID NO: 634) and GDKGIYYYYMDV (HCDR3, SEQ ID NO: 635). The light chain CDRs of the SC06-325 antibody have the following CDR sequences: TGTSSDVGGYNYVS (LCDR1, SEQ ID NO: 577), EVSNRPS (LCDR2, SEQ ID NO: 578) and SSYTSSSTLV (LCDR3, SEQ ID NO: 636).

[348] SC06-325 nucleotide sequence (SEQ ID NO: 367)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc cggggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg caccttcagc ttctattcta tgagctgggt gcgacaggcc     120
cctggacaag gacttgagtg gatgggaggg atcatcccta tgtttggtac aacaaactac     180
gcacagaagt tccagggcag agtcacgatt accgcggtcg aatccacgag cacagcctac     240
atggaggtga gcagcctgag atctgaggac acggccgttt attactgtgc gagaggtgat     300
aagggtatct actactacta catggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gcagtctgcc     420
ctgactcagc ctgcctccgt gtctgggtct cctggacagt cgatcaccat ctcctgcact     480
ggaaccagca gtgacgttgg tggttataac tatgtctcct ggtaccaaca gcacccaggc     540
aaagccccca aactcatgat ttatgaggtc agtaatcggc cctcaggggt ttctaatcgc     600
ttctctggct ccaagtctgg caacacggcc tccctgacca tctctgggct ccaggctgag     660
gacgaggctg attattactg cagctcatat acaagcagca gcactcttgt cttcggaact     720
gggaccaagg tcaccgtcct aggt                                            744
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[349] SC06-325 amino acid sequence (SEQ ID NO: 368)

EVQLVESGAEVKKPGSSVKVSCKASGGTFSFYSMSWVRQAPGQGLEWMGGIIPMFGTTNYA
QKFQGRVTITAVESTSTAYMEVSSLRSEDTAVYYCARGDKGIYYYYMDVWGKGTTVTVSSG
TGGSGGTGSGTGGSTQSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPK
LMIYEVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLVFGTGTKVTVL
G

[350] SC06-325 VH amino acid sequence (SEQ ID NO: 365)

EVQLVESGAEVKKPGSSVKVSCKASGGTFS**FYSMS**WVRQAPGQGLEWMG**GIIPMFGTTNY**
AQKFQGRVTITAVESTSTAYMEVSSLRSEDTAVYYCAR**GDKGIYYYYMDV**WGKGTTVTVS
S

[351] SC06-325 VL amino acid sequence (SEQ ID NO: 366)

QSALTQPASVSGSPGQSITISC**TGTSSDVGGYNYVS**WYQQHPGKAPKLMIY**EVSNRPS**GVSN
RFSGSKSGNTASLTISGLQAEDEADYYC**SSYTSSSTLV**FGTGTKVTVLG

[352] The SC06-327 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 369) and a light chain variable region (SEQ ID NO: 370) encoded by the nucleic acid sequence shown in SEQ ID NO: 371 and the amino acid sequence shown in SEQ ID NO: 372. The VH-locus is VH1 (1-69) and the VL locus is VL3 (V2-14).

[353] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-327 antibody have the following CDR sequences: THAIS (SEQ ID NO: 637), GIIAIFGTANYAQKFQG (SEQ ID NO: 638) and GSGYHISTPFDN (SEQ ID NO: 639). The light chain CDRs of the SC06-327 antibody have the following CDR sequences: GGNNIGSKGVH (SEQ ID NO: 640), DDSDRPS (SEQ ID NO: 622) and QVWDSSSDHVV (SEQ ID NO: 642).

[354] SC06-327 nucleotide sequence (SEQ ID NO: 371)

```
gaggtgcagc tggtggagac cggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cctctggagg caccttcagg acccatgcta tcagttgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcgcta tcttcggaac agcaaactac     180
gcacagaagt tccagggcag aatcacgatt accgcggacg aatccacgag tacagcctac     240
atggagctga gcagcctgag atctgaggac acggccgtgt atttctgtgc gagaggcagt     300
ggttatcata tatcgacacc ctttgacaac tggggccagg gaaccctggt caccgtctcg     360
agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gtcctatgtg     420
ctgactcagc caccctcggt gtcagtggcc ccaggacaga cggccaggat tacctgtggg     480
ggaaacaaca ttggaagtaa aggtgtgcac tggtaccagc agaagcctgg ccaggccct      540
gtgctggtcg tctatgatga tagcgaccgg ccctcaggga tccctgagcg attctctggc     600
tccaactctg ggaacacggc caccctgacc atcagcaggg tcgaagccgg ggatgaggcc     660
gactattact gtcaggtgtg ggatagtagt agtgatcatg tggtattcgg cggagggacc     720
aagctgaccg tcctaggt                                                   738
```

[355] SC06-327 amino acid sequence (SEQ ID NO: 372)

EVQLVETGAEVKKPGSSVKVSCKASGGTFRTHAISWVRQAPGQGLEWMGGIIAIFGTANYA
QKFQGRITITADESTSTAYMELSSLRSEDTAVYFCARGSGYHISTPFDNWGQGTLVTVSSG
TGGSGGTGSGTGGSTSYVLTQPPSVSVAPGQTARITCGGNNIGSKGVHWYQQKPGQAPVLV
VYDDSDRPSGIPERFSGSNSGNTATLTISRVEAGDEADYYCQVWDSSSDHVVFGGGTKLTVL
G

[356] SC06-327 VH amino acid sequence (SEQ ID NO: 369)

EVQLVETGAEVKKPGSSVKVSCKASGGTFR**THAIS**WVRQAPGQGLEWMG**GIIAIFGTANYA**
QKFQGRITITADESTSTAYMELSSLRSEDTAVYFCAR**GSGYHISTPFDN**WGQGTLVTVSS

[357] SC06-327 VL amino acid sequence (SEQ ID NO: 370)

SYVLTQPPSVSVAPGQTARITC**GGNNIGSKGVH**WYQQKPGQAPVLVVY**DDSDRPS**GIPERFS
GSNSGNTATLTISRVEAGDEADYYC**QVWDSSSDHV**VFGGGTKLTVLG

[358] The SC06-328 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 373) and a light chain variable region (SEQ ID NO: 374) encoded by the nucleic acid sequence shown in SEQ ID NO: 375 and the amino acid sequence shown in SEQ ID NO: 376. The VH-locus is VH1 (1-69) and the VL locus is VKIII (A27).

[359] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-328 antibody have the following CDR sequences: GYAIS (HCDR1, SEQ ID NO: 643), GIIPIFGTTNYAQKFQG (HCDR2, SEQ ID NO: 644) and VKDGYCTLTSCPVGWYFDL (HCDR3, SEQ ID NO: 645). The light chain CDRs of the SC06-328 antibody have the following CDR sequences: RASQSVSSSYLA (LCDR1, SEQ ID NO: 646), GASSRAT (LCDR2, SEQ ID NO: 631) and QQYGSSLT (LCDR3, SEQ ID NO: 648).

[360] SC06-328 nucleotide sequence (SEQ ID NO: 375)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggaca catcttcagc ggctatgcaa tcagttgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttggtac aacaaactac     180
gcacagaagt tccagggcag agtcacgatt accgcggacc aatccacgag cacagcctac     240
atggacctga gcaacttgag atctgaggac acggccgtct attactgtgc gagagtgaaa     300
gatggatatt gtactcttac cagctgccct gtcggctggt acttcgatct ctggggccgt     360
ggcaccctgg tcactgtctc gagcggtacg ggcggttcag gcggaaccgg cagcggcact     420
ggcgggtcga cggaaattgt gatgacgcag tctccaggca ccctgtcttt gtctccaggg     480
gaaagagcca ccctctcgtg cagggccagt cagagtgtta gcagcagcta cttagcctgg     540
taccagcaga aacctggcca ggctcccagg ctcctcatct ttggtgcctc cagcagggcc     600
actggcatcc cagacaggtt cagtggcagt gggtctggga cagacttcac tctcaccatc     660
agcagactgg agcctgaaga ttttgcagtg tattactgtc agcagtatgg tagctcactc     720
actttcggcg gagggaccaa gctggagatc aaacgt                               756
```

[361] SC06-328 amino acid sequence (SEQ ID NO: 376)

EVALVESGAEVKKPGSSVKVSCKASGHIFSGYAISWVRQAPGQGLEWMGGIIPIFGTTNYAQ
KFQGRVTITADQSTSTAYMDLSNLRSEDTAVYYCARVKDGYCTLTSCPVGWYFDLWGRGTL
VTVSSGTGGSGGTGSGTGGSTEIVMTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQ
QKPGQAPRLLIFGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSLT
FGGGTKLEIKR

[362] SC06-328 VH amino acid sequence (SEQ ID NO: 373)

EVALVESGAEVKKPGSSVKVSCKASGHIF**SGYAIS**WVRQAPGQGLEWMG**GIIPIFGTTNYA**
QKFQGRVTITADQSTSTAYMDLSNLRSEDTAVYYCAR**VKDGYCTLTSCPVGWYFDL**WGR
GTLVTVSS

[363] SC06-328 VL amino acid sequence (SEQ ID NO: 374)

EIVMTQSPGTLSLSPGERATLSC**RASQSVSSSYLA**WYQQKPGQAPRLLIF**GASSRAT**G
IPDRFSGSGSGTDFTLTISRLEPEDFAVYYC**QQYGSSLT**FGGGTKLEIKR

[364] The SC06-329 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 377) and a light chain variable region (SEQ ID NO: 378) encoded by the nucleic acid sequence shown in SEQ ID NO: 379 and the amino acid sequence shown in SEQ ID NO: 380. The VH-locus is VH1 (1-69) and the VL locus is VKIII (A27).

[365] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-329 antibody have the following CDR sequences: SNSIS (HCDR1, SEQ ID NO: 649), GIFALFGTTDYAQKFQG (HCDR2, SEQ ID NO: 650) and GSGYTTRNYFDY (HCDR3, SEQ ID NO: 651). The light chain CDRs of the SC06-329 antibody have the following CDR sequences: RASQSVSSNYLG (LCDR1, SEQ ID NO: 652), GASSRAS (LCDR2, SEQ ID NO: 653) and QQYGSSPLT (LCDR3, SEQ ID NO: 654).

[366] SC06-329 nucleotide sequence (SEQ ID NO: 379)

```
gaggtccagc tggtacagtc tggggctgag gttaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg catcttcaga agcaattcta tcagttgggt gcgacaggcc     120
cctgggcaag ggcttgagtg gatgggaggg atcttcgctc ttttcggaac aacagactac     180
gcgcagaagt tccagggcag agtcacgatt accgcggacg aatcttcgac cacagtctac     240
ctggagctga gtagcctgac atctgaggac acggccgttt attactgtgc gagaggcagt     300
ggctacacca cacgcaacta ctttgactac tggggccagg gcaccctggt caccgtctcg     360
agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac ggaaattgtg     420
ctgactcagt ctccaggcac cctgtctttg tctccagggg aaagagccac actctcctgc     480
agggccagtc agagtgttag cagcaactac ttaggctggt accagcagaa acctggccag     540
gctcccaggc tcctgatcta tggtgcatcc agcagggcca gtggcatccc agacaggttc     600
agtggcggtg ggtctgggac agacttcact ctcaccatca gcagactgga gcctgaagat     660
tttgcagtgt attactgtca gcagtatggt agctcacccc tcactttcgg cggagggacc     720
aaggtggaga tcaaacgt                                                   738
```

[367] SC06-329 amino acid sequence (SEQ ID NO: 380)

EVQLVQSGAEVKKPGSSVKVSCKASGGIFRSNSISWVRQAPGQGLEWMGGIFALFGTTDYAQ
KFQGRVTITADESSTTVYLELSSLTSEDTAVYYCARGSGYTTRNYFDYWGQGTLVTVSSGTG
GSGGTGSGTGGSTEIVLTQSPGTLSLSPGERATLSCRASQSVSSNYLGWTQQKPGQAPRLLIY
GASSRASGIPDRFSGGGSGTDFTLTISRLEPEDFAVYYCQQYGSSPLTFGGGTKVEIKR

[368] SC06-329 VH amino acid sequence (SEQ ID NO: 377)

EVQLVQSGAEVKKPGSSVKVSCKASGGIFR**SNSIS**WVRQAPGQGLEWMG**GIFALFGTTDYA**
QKFQGRVTITADESSTTVYLELSSLTSEDTAVYYCAR**GSGYTTRNYFDY**WGQGTLVTVSS

[369] SC06-329 VL amino acid sequence (SEQ ID NO: 378)

EIVLTQSPGTLSLSPGERATLSC**RASQSVSSNYLG**WTQQKPGQAPRLLIY**GASSRAS**GIPDRFS
GGGSGTDFTLTISRLEPEDFAVYYC**QQYGSSPLT**FGGGTKVEIKR

[370] The SC06-331 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 381) and a light chain variable region (SEQ ID NO: 382) encoded by the nucleic acid sequence shown in SEQ ID NO: 383 and the amino acid sequence shown in SEQ ID NO: 384. The VH-locus is VH1 (1-69) and the VL locus is VL3 (V2-14).

[371] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-331antibody have the following CDR sequences: SYAIS (HCDR1, SEQ ID NO: 571), GIIGMFGTANYAQKFQG (HCDR2, SEQ ID NO: 655) and GNYYYESSLDY (HCDR3, SEQ ID NO: 656). The light chain CDRs of the SC06-331 antibody have the following CDR sequences: GGNNIGSKSVH (LCDR1, SEQ ID NO: 621), DDSDRPS (LCDR2, SEQ ID NO: 622) and QVWDSSSDH (LCDR3, SEQ ID NO: 657).

[372] SC06-331 nucleotide sequence (SEQ ID NO: 383)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcggta tgttcggtac agcaaactac     180
gcacagaagt tccagggcag agtcacgatt accgcggacg aatttacgag cacagcctac     240
atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagaggaaat     300
tattactatg agagtagtct cgactactgg ggccagggaa ccctggtcac cgtctcgagc     360
ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgca gtctgtcgtg     420
acgcagccgc cctcggtgtc agtggcccca ggacagacgg ccaggattac ctgtggggga     480
aacaacattg gaagtaaaag tgtgcactgg taccagcaga agccaggcca ggcccctgtg     540
ctggtcgtct atgatgatag cgaccggccc tcagggatcc ctgagcgatt ctctggctcc     600
aactctggga acacggccac cctgaccatc agcagggtcg aagccgggga tgaggccgac     660
tattactgtc aggtgtggga tagtagtagt gatcattatg tcttcggaac tgggaccaag     720
gtcaccgtcc taggt                                                      735
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[373] SC06-331 amino acid sequence (SEQ ID NO: 384)

EVQLVESGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIGMFGTANYA
QKFQGRVTITADEFTSTAYMELSSLRSEDTAVYYCARGNYYYESSLDYWGQGTLVTVSSGT
GGSGGTGSGTGGSTQSVVTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVV
YDDSDRPSGIPERFSGSNSGNTATLTISRVEAGDEADYYCQVWDSSSDHYVFGTGTKVTVLG

[374] SC06-331 VH amino acid sequence (SEQ ID NO: 381)

EVQLVESGAEVKKPGSSVKVSCKASGGTFS**SYAIS**WVRQAPGQGLEWMG**GIIGMFGTANY**
AQKFQGRVTITADEFTSTAYMELSSLRSEDTAVYYCAR**GNYYYESSLDY**WGQGTLVTVSS

[375] SC06-331 VL amino acid sequence (SEQ ID NO: 382)

QSVVTQPPSVSVAPGQTARITC**GGNNIGSKSVHW**YQQKPGQAPVLVVY**DDSDRPS**GIPERFS
GSNSGNTATLTISRVEAGDEADYYC**QVWDSSSDHYV**FGTGTKVTVLG

[376] The SC06-332 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 385) and a light chain variable region (SEQ ID NO: 386) encoded by the nucleic acid sequence shown in SEQ ID NO: 387 and the amino acid sequence shown in SEQ ID NO: 388. The VH-locus is VH1 (1-69) and the VL locus is VKI (A20).

[377] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-332 antibody have the following CDR sequences: NFAIN (HCDR1, SEQ ID NO: 658), GIIAVFGTTKYAHKFQG (HCDR2, SEQ ID NO: 659) and GPHYYSSYMDV (HCDR3, SEQ ID NO: 660). The light chain CDRs of the SC06-332 antibody have the following CDR sequences: RASQGISTYLA (LCDR1, SEQ ID NO: 661), AASTLQS (LCDR2, SEQ ID NO: 662) and QKYNSAPS (LCDR3, SEQ ID NO: 663).

[378] SC06-332 nucleotide sequence (SEQ ID NO: 387)

```
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtaaaggtc      60
tcctgcaagg cttctggagg ccccttccgc aattttgcta tcaactgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcgctg tctttgggac gacaaagtac     180
gcacataagt tccagggcag agtcaccatc accgcggacg actccacaaa tacagcttac     240
atggagctgg gcagcctgaa atctgaggac acggccgtgt attactgtgc gagaggtccc     300
cactactact cctcctacat ggacgtctgg ggcgaaggga ccacggtcac cgtctcgagc     360
ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgga catccagttg     420
acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg     480
gcgagtcagg gcattagcac ttatttagcc tggtatcagc agaaacccgg gaaagttcct     540
aaactcctga tctatgctgc atccactttg caatcagggg tcccatctcg gttcagtggc     600
agtggatctg ggacagattt cactctcacc atcagcagcc tgcagcctga agatgttgca     660
acttattact gtcaaaagta taacagtgcc ccttctttcg gccctgggac caaagtggat     720
atcaaacgt                                                             729
```

[379] SC06-332 amino acid sequence (SEQ ID NO: 388)

QVQLVQSGAEVKKPGSSVKVSCKASGGPFRNFAINWVRQAPGQGLEWMGGIIAVFGTTKYA
HKFQGRVTITADDSTNTAYMELGSLKSEDTAVYYCARGPHYYSSYMDVWGEGTTVTVSSGT
GGDGGTGSGTGGSTDIQLTQSPSSLSASVGDRVTITCRASQGISTYLAWYQQKPGKVPKLLIY
AASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCQKYNSAPSFGPGTKVDIKR

[380] SC06-332 VH amino acid sequence (SEQ ID NO: 385)

QVQLVQSGAEVKKPGSSVKVSCKASGGPFR**NFAIN**WVRQAPGQGLEWMG**GIIAVFGTTKY**
AHKFQGRVTITADDSTNTAYMELGSLKSEDTAVYYCAR**GPHYYSSYMDV**WGEGTTVTVSS

[381] SC06-332 VL amino acid sequence (SEQ ID NO: 386)

DIQLTQSPSSLSASVGDRVTITC**RASQGISTYLA**WYQQKPGKVPKLLIY**AASTLQS**GVPSRFS
GSGSGTDFTLTISSLQPEDVATYYC**QKYNSAPS**FGPGTKVDIKR

[382] The SC06-334 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 389) and a light chain variable region (SEQ ID NO: 390) encoded by the nucleic acid sequence shown in SEQ ID NO: 391 and the amino acid sequence shown in SEQ ID NO: 392. The VH-locus is VH1 (1-69) and the VL locus is VL3 (V2-14).

[383] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-334 antibody have the following CDR sequences: SNAVS (HCDR1, SEQ ID NO: 664), GILGVFGSPSYAQKFQG (HCDR2, SEQ ID NO: 665) and GPTYYYSYMDV (HCDR3, SEQ ID NO: 666). The light chain CDRs of the SC06-334 antibody have the following CDR sequences: GGNNIGRNSVH (LCDR1, SEQ ID NO: 667), DDSDRPS (LCDR2, SEQ ID NO: 622) and QVWHSSSDHYV (LCDR3, SEQ ID NO: 669).

[384] SC06-334 nucleotide sequence (SEQ ID NO: 391)

```
gaggtgcagc tggtggagac tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
ccctgcaaat cttctggaag ccccttcagg agtaatgctg tcagctgggt gcgacaggcc     120
cccggacaag ggcttgagtg ggtgggagga atcctcggtg tctttggttc accaagctac     180
gcacagaagt tccagggcag agtcacgatt accgcggacg aatccaccaa cacagtccac     240
atggagctga gaggtttgag atctgaggac acggccgtgt attattgtgc gagaggtcct     300
acctactact actcctacat ggacgtctgg ggcaaaggga ccacggtcac cgtctcgagc     360
ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgtc ctatgtgctg     420
actcagccac cctcggagtc agtggcccca ggacagacgg ccaggattac ctgtggggga     480
aataacattg gaagaaatag tgtgcactgg tatcagcaga agccaggcca ggccccctgtg     540
ctggtcgtgt atgatgatag cgaccggccc tcagggatcc ctgagcgatt ttctggctcc     600
aagtctggga acacggccac cctgattatc agcagggtcg aagtcgggga tgaggccgac     660
tactactgtc aggtgtggca tagtagtagt gatcattatg tcttcggaac tgggaccaag     720
gtcaccgtcc taggt                                                      735
```

[385] SC06-334 amino acid sequence (SEQ ID NO: 392)

EVALVETGAEVKKPGSSVKVPCKSSGSPFRSNAVSWVRQAPGQGLEWVGGILGVFGSPSYA
QKFQGRVTITADESTNTVHMELRGLRSEDTAVYYCARGPTYYYSYMDVWGKGTTVTVSSG
TGGSGGTGSGTGGSTSYVLTQPPSESVAPGQTARITCGGNNIGRNSVHWYQQKPGQAPVLVV
YDDSDRPSGIPERFSGSKSGNTATLIISRVEVGDEADYYCQVWHSSSDHYVFGTGTKVTVLG

[386] SC06-334 VH amino acid sequence (SEQ ID NO: 389)

EVALVETGAEVKKPGSSVKVPCKSSGSPFR**SNAVS**WVRQAPGQGLEWV**GGILGVFGSPSYA**
QKFQGRVTITADESTNTVHMELRGLRSEDTAVYYCAR**GPTYYYSYMDV**WGKGTTVTVSS

[387] SC06-334 VL amino acid sequence (SEQ ID NO: 390)

SYVLTQPPSESVAPGQTARITC**GGNNIGRNSVH**WYQQKPGQAPVLVVY**DDSDRPS**GIPERFS
GSKSGNTATLIISRVEVGDEADYYC**QVWHSSSDHYV**FGTGTKVTVLG

[388] The SC06-336 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 393) and a light chain variable region (SEQ ID NO: 394) encoded by the nucleic acid sequence shown in SEQ ID NO: 395 and the amino acid sequence shown in SEQ ID NO: 396. The VH-locus is VH1 (1-69) and the VL locus is VKIII (A27).

[389] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-336 antibody have the following CDR sequences: SYAIS (HCDR1, SEQ ID NO: 670), GIFGMFGTANYAQKFQG (HCDR2, SEQ ID NO: 671) and SSGYYPQYFQD (HCDR3, SEQ ID NO: 672). The light chain CDRs of the SC06-336 antibody have the following CDR sequences: RASQSVSSSYLA (LCDR1, SEQ ID NO: 646), GASSRAT (LCDR2, SEQ ID NO: 631) and QQYGSSSLT (LCDR3, SEQ ID NO: 308).

[390] SC06-336 nucleotide sequence (SEQ ID NO: 395)

```
cagatgcagc tggtacaatc tggagctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcttcggta tgtttgggac agcaaactac     180
gcgcagaagt tccagggcag agtcacgatt accgcggacg aattcacgag cgcggcctac     240
atggagctga gcagcctggg atctgaggac acggccatgt attactgtgc gaggtctagt     300
ggttattacc cccaatactt ccaggactgg ggccagggca ccctggtcac cgtctcgagc     360
ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgga aattgtgatg     420
acacagtctc caggcaccct gtctttgtct ccagggcaaa gagccaccct ctcctgcagg     480
gccagtcaga gtgttagcag cagctactta gcctggtacc agcagaaacc tggccaggct     540
cccagactcc tcatgtatgg tgcatccagc agggccactg gcatcccaga caggttcagt     600
ggcagtgggt ctgggacaga cttcactctc accatcagca gactggagcc tgaagatttt     660
gcagtgtatt actgtcagca gtatggtagc tcatcgctca ctttcggcgg agggaccaag     720
ctggagatca aacgt                                                      735
```

[391] SC06-336 amino acid sequence (SEQ ID NO: 396)

QMQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIFGMFGTANY
AQKFQGRVTITADEFTSAAYMELSSLGSEDTAMYYCARSSGYYPQYFQDWGQGTLVTVSSG
TGGSGGTGSGTGGSTEIVMTQSPGTLSLSPGQRATLSCRASQSVSSSYLAWYQQKPGQAPRL
LMYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSSLTFGGGTKLEIKR

[392] SC06-336 VH amino acid sequence (SEQ ID NO: 393)

QMQLVQSGAEVKKPGSSVKVSCKASGGTFS**SYAIS**WVRQAPGQGLEWMG**GIFGMFGTAN**
YAQKFQGRVTITADEFTSAAYMELSSLGSEDTAMYYCAR**SSGYYPQYFQD**WGQGTLVTVS
S

[393] SC06-336 VL amino acid sequence (SEQ ID NO: 394)

EIVMTQSPGTLSLSPGQRATLSC**RASQSVSSSYLA**WYQQKPGQAPRLLMY**GASSRAT**GIPDR
FSGSGSGTDFTLTISRLEPEDFAVYYC**QQYGSSSLT**FGGGTKLEIKR

[394] The SC06-339 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 397) and a light chain variable region (SEQ ID NO: 398) encoded by the nucleic acid sequence shown in SEQ ID NO: 399 and the amino acid sequence shown in SEQ ID NO: 400. The VH-locus is VH1 (1-69) and the VL locus is VL3 (V2-14).

[395] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-339 antibody have the following CDR sequences: SYAIS (HCDR1, SEQ ID NO: 303), GIIAIFHTPKYAQKFQG (HCDR2, SEQ ID NO: 306) and GSTYDFSSGLDY (HCDR3, SEQ ID NO: 725). The light chain CDRs of the SC06-339 antibody have the following CDR sequences: GGNNIGSKSVH (LCDR1, SEQ ID NO: 621), DDSDRPS (LCDR2, SEQ ID NO: 622) and QVWDSSSDHVV (LCDR3, SEQ ID NO: 642).

[396] SC06-339 nucleotide sequence (SEQ ID NO: 399)

```
gaggtgcagc tggtggagtc cggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc     60
tcctgcaagg cttctggagg catcttcaac agttatgcta tcagctgggt gcgacaggcc    120
cctggacaag ggcttgagtg gatgggaggc atcatcgcta tctttcatac accaaagtac    180
gcacagaagt tccagggcag agtcacgatt accgcggacg aatccacgaa cacagcctac    240
atggaactga gaagcctgaa atctgaggac acggccctgt attactgtgc gagagggtcc    300
acttacgatt tttcgagtgg ccttgactac tggggccagg gaaccctggt caccgtctcg    360
agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gcaggcaggg    420
ctgactcagc caccctcggt gtcagtggcc ccaggacaga cggccaggat tacctgtggg    480
ggaaacaaca ttggaagtaa aagtgtgcac tggtaccagc agaagccagg ccaggccccc    540
gtcctagtcg tctatgatga tagcgaccgg ccctcaggga tccctgagcg attctctggc    600
tccaactctg ggaacacggc caccctgacc atcagcaggg tcgaagccgg ggatgaggcc    660
gactattact gtcaggtgtg ggatagtagt agtgatcatg tggtattcgg cggagggacc    720
aagctgaccg tcctaggt                                                  738
```

[397] SC06-339 amino acid sequence (SEQ ID NO: 400)

EVQLVESGAEVKKPGSSVKVSCKASGGIFNSYAISWVRQAPGQGLEWMGGIIAIFHTPKYAQ
KFQGRVTITADESTNTAYMELRSLKSEDTALYYCARGSTYDFSSGLDYWGQGTLVTVSSGTG
GSGGTGSGTGGSTQAGLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVY
DDSDRPSGIPERFSGSNSGNTATLTISRVEAGDEADYYCQVWDSSSDHVVFGGGTKLTVLG

[398] SC06-339 VH amino acid sequence (SEQ ID NO: 397)

EVQLVESGAEVKKPGSSVKVSCKASGGIFN**SYAIS**WVRQAPGQGLEWMG**GIIAIFHTPKYA**
QKFQGRVTITADESTNTAYMELRSLKSEDTALYYCAR**GSTYDFSSGLDY**WGQGTLVTVSS

[399] SC06-339 VL amino acid sequence (SEQ ID NO: 398)

QAGLTQPPSVSVAPGQTARITC**GGNNIGSKSVH**WYQQKPGQAPVLVVY**DDSDRPS**GIPERFS
GSNSGNTATLTISRVEAGDEADYYC**QVWDSSSDHVV**FGGGTKLTVLG

[400] The SC06-342 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 401) and a light chain variable region (SEQ ID NO: 402) encoded by the nucleic acid sequence shown in SEQ ID NO: 403 and the amino acid sequence shown in SEQ ID NO: 404. The VH-locus is VH1 (1-69) and the VL locus is VKIV (B3).

[401] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-342 antibody have the following CDR sequences: SYAIS (HCDR1, SEQ ID NO: 251), GVIPIFRTANYAQNFQG (HCDR2, SEQ ID NO: 249) and LNYHDSGTYYNAPRGWFDP (HCDR3, SEQ ID NO: 246). The light chain CDRs of the SC06-342 antibody have the following CDR sequences: KSSQSILNSSNNKNYLA (LCDR1, SEQ ID NO: 245), WASTRES (LCDR2, SEQ ID NO: 570) and QQYYSSPPT (LCDR3, SEQ ID NO: 250).

[402] SC06-342 nucleotide sequence (SEQ ID NO: 403)

```
caggtccagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc     60
tcctgcaagg cttctggagg cttcttcagc agctatgcta tcagctgggt gcgccaggcc    120
cctggacaag gacttgagtg gatgggggg gtcatcccta tctttcgtac agcaaactac    180
gcacagaact tccagggcag agtcaccatt accgcggacg aattcacatc gtatatggag    240
ctgagcagcc tgagatctga cgacacggcc gtgtattact gtgcgaggtt gaattaccat    300
gattcgggga cttattataa cgccccccgg ggctggttcg acccctgggg ccagggaacc    360
ctggtcaccg tctcgagcgg tacgggcggt tcaggcggaa ccggcagcgg cactggcggg    420
tcgacggaca tccagatgac ccagtctcca gactccctgg ctgtgtctct gggcgagaag    480
gccaccatca actgcaagtc cagccagagt attttaaaca gctccaacaa taagaactac    540
ttagcttggt accagcagaa accaggacag cctcctaagc tgctcattta ctgggcatct    600
acccgggaat ccggggtccc tgaccgattc agtggcagcg ggtctgggac agatttcact    660
ctcaccatca gcagcctgca ggctgaagat gtggcagttt attactgtca gcaatattat    720
agtagtccgc cgacgttcgg ccaagggacc aaggtggaaa tcaaacgt                 768
```

[403] SC06-342 amino acid sequence (SEQ ID NO: 404)

QVQLVQSGAEVKKPGSSVKVSCKASGGFFSSYAISWVRQAPGQGLEWMGGVIPIFRTANYA
QNFQGRVTITADEFTSYMELSSLRSDDTAVYYCARLNYHDSGTYYNAPRGWFDPWGQGTLV
TVSSGTGGSGGTGSGTGGSTDIQMTQSPDSLAVSLGEKATINCKSSQSILNSSNNKNYLAWYQ
QKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSSPPTFGQ
GTKVEIKR

[404] SC06-342 VH amino acid sequence (SEQ ID NO: 401)

QVQLVQSGAEVKKPGSSVKVSCKASGGFFSSYAISWVRQAPGQGLEWMGGVIPIFRTANYA
QNFQGRVTITADEFTSYMELSSLRSDDTAVYYCARLNYHDSGTYYNAPRGWFDPWGQGT
LVTVSS

[405] SC06-342 VL amino acid sequence (SEQ ID NO: 402)

DIQMTQSPDSLAVSLGEKATINCKSSQSILNSSNNKNYLAWYQQKPGQPPKLLIYWASTRES
GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSSPPTFGQGTKVEIKR

[406] The SC06-343 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 405) and a light chain variable region (SEQ ID NO: 406) encoded by the nucleic acid sequence shown in SEQ ID NO: 407 and the amino acid sequence shown in SEQ ID NO: 408. The VH-locus is VH1 (1-69) and the VL locus is VL3 (V2-14).

[407] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-343 antibody have the following CDR sequences: YYAMS (HCDR1, SEQ ID NO: 242), GISPMFGTTTYAQKFQG (HCDR2, SEQ ID NO: 307) and SSNYYDSVYDY (HCDR3, SEQ ID NO: 290). The light chain CDRs of the SC06-343 antibody have the following CDR sequences: GGHNIGSNSVH (LCDR1, SEQ ID NO: 224), DNSDRPS (LCDR2, SEQ ID NO: 223) and QVWGSSSDH (LCDR3, SEQ ID NO: 227).

[408] SC06-343 nucleotide sequence (SEQ ID NO: 407)

```
caggtccagc tggtgcagtc tggagctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagt caccttcagt tactatgcta tgagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggagga atcagcccta tgtttgggac aacaacctac     180
gcacagaagt tccagggcag agtcacgatt actgcggacg actccacgag tacagcctac     240
atggaggtga ggagcctgag atctgaggac acggccgtgt attactgtgc gagatcttcg     300
aattactatg atagtgtata tgactactgg ggccagggaa ccctggtcac cgtctcgagc     360
ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgca gtctgtcgtg     420
acgcagccgc cctcggagtc agtggcccca ggacagacgg ccaggattac ctgtggggga     480
cataacattg gaagtaatag tgtgcactgg taccagcaga agccaggcca ggcccctgtg     540
ctggtcgtgt atgataatag cgaccggccc tcagggatcc ctgagcgatt ctctggctcc     600
aactctggga acacggccac cctgaccatc agcagggtcg aagccgggga tgaggccgac     660
tattactgtc aggtgtgggg tagtagtagt gaccattatg tcttcggaac tgggaccaag     720
gtcaccgtcc taggt                                                      735
```

[409] SC06-343 amino acid sequence (SEQ ID NO: 408)

QVQLVQSGAEVKKPGSSVKVSCKASGVTFSYYAMSWVRQAPGQGLEWMGGISPMFGTTTY
AQKFQGRVTITADDSTSTAYMEVRSLRSEDTAVYYCARSSNYYDSVYDYWGQGTLVTVSSG
TGGSGGTGSGTGGSTQSVVTQPPSESVAPGQTARITCGGHNIGSNSVHWYQQKPGQAPVLVV
YDNSDRPSGIPERFSGSNSGNTATLTISRVEAGDEADYYCQVWGSSSDHYVFGTGTKVTVLG

[410] SC06-343 VH amino acid sequence (SEQ ID NO: 405)

QVQLVQSGAEVKKPGSSVKVSCKASGVTFS**YYAMS**WVRQAPGQGLEWMG**GISPMFGTTT**
YAQKFQGRVTITADDSTSTAYMEVRSLRSEDTAVYYCAR**SSNYYDSVYDY**WGQGTLVTVS
S

[411] SC06-343 VL amino acid sequence (SEQ ID NO: 406)

QSVVTQPPSESVAPGQTARITC**GGHNIGSNSVH**WYQQKPGQAPVLVVY**DNSDRPS**GIPERFS
GSNSGNTATLTISRVEAGDEADYYC**QVWGSSSDHYV**FGTGTKVTVLG

[412] The SC06-344 HA-specific single-chain Fv antibody includes a heavy chain variable region (SEQ ID NO: 409) and a light chain variable region (SEQ ID NO: 410) encoded by the nucleic acid sequence shown in SEQ ID NO: 411 and the amino acid sequence shown in SEQ ID NO: 412. The VH-locus is VH1 (1-69) and the VL locus is VL1 (V1-13).

[413] The amino acids encompassing the CDRs are highlighted in bold in the sequences below. The heavy chain CDRs of the SC06-344 antibody have the following CDR sequences: NYAMS (HCDR1, SEQ ID NO: 222), GIIAIFGTPKYAQKFQG (HCDR2, SEQ ID NO: 221) and IPHYNFGSGSYFDY (HCDR3, SEQ ID NO: 220). The light chain CDRs of the SC06-344 antibody have the following CDR sequences: TGSSSNIGAGYDVH (LCDR1, SEQ ID NO: 219), GNSNRPS (LCDR2, SEQ ID NO: 231) and GTWDSSLSAYV (LCDR3, SEQ ID NO: 280).

[414] SC06-344 nucleotide sequence (SEQ ID NO: 411)

```
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgagagtc      60
tcctgcaagg cttctggaag catcttcaga aactatgcta tgagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcgcta tttttgggac accaaagtac     180
gcacagaagt tccagggcag agtcacgatt accgcggacg aatcgacgag cactgtctac     240
atggaactga gcggactgag atctgaggac acggccatgt attactgtgc gaggattccc     300
cactataatt ttggttcggg gagttatttc gactactggg gccagggaac cctggtcacc     360
gtctcgagcg gtacgggcgg ttcaggcgga accggcagcg gcactggcgg gtcgacgact     420
gtgttgacac agccgccctc agtgtctggg gccccagggc agagggtcac catctcctgc     480
actgggagca gctccaacat cggggcaggt tatgatgtac actggtacca gcagcttcca     540
ggaacagccc ccaaactcct catctatggt aacagcaatc ggccctcagg ggtccctgac     600
cgattctctg gctccaagtc tggcacgtca gccaccctgg gcatcaccgg actccagact     660
ggggacgagg ccgattatta ctgcggaaca tgggatagca gcctgagtgc ttatgtcttc     720
ggaactggga ccaaggtcac cgtcctaggt                                      750
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[415] SC06-344 amino acid sequence (SEQ ID NO: 412)

QVQLVQSGAEVKKPGSSVRVSCKASGSIFRNYAMSWVRQAPGQGLEWMGGIIAIFGTPKYA
QKFQGRVTITADESTSTVYMELSGLRSEDTAMYYCARIPHYNFGSGSYFDYWGQGTLVTVSS
GTGGSGGTGSGTGGSTTVLTQPPSVSGAPGQRVTISCTGSSSNIGAGYDVHWYQQLPGTAPK
LLIYGNSNRPSGVPDRFSGSKSGTSATLGITGLQTGDEADYYCGTWDSSLSAYVFGTGTKVT
VLG

[416] SC06-344 VH amino acid sequence (SEQ ID NO: 409)

QVQLVQSGAEVKKPGSSVRVSCKASGSIFR**NYAMS**WVRQAPGQGLEWMG**GIIAIFGTPKY**
AQKFQGRVTITADESTSTVYMELSGLRSEDTAMYYCAR**IPHYNFGSGSYFDY**WGQGTLVT
VSS

[417] SC06-344 VL amino acid sequence (SEQ ID NO: 410)

TVLTQPPSVSGAPGQRVTISC**TGSSSNIGAGYDVH**WYQQLPGTAPKLLIY**GNSNRPS**GVPDR
FSGSKSGTSATLGITGLQTGDEADYYC**GTWDSSLSAYV**FGTGTKVTVLG

IgG HA Antibodies

[418] The CR6141 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 199) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 279 and the heavy chain amino acid sequence shown in SEQ ID NO: 413. The CR6141 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 414) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 415 and the light chain amino acid sequence shown in SEQ ID NO: 416.

[419] CR6141 Heavy Chain nucleotide sequence (SEQ ID NO: 279)

```
gaggtccagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc    60
tcctgcaagg cttctgggta caccttcacc ggctactatg tgtactgggt gcgacaggcc   120
cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat   180
gcacagaagt tccagggcag agtcacgatt accgcggaca aatccacgag cacagcctac   240
atggagctga gcagcctgag atctgaagac acggctgtgt attactgtgc gagaagtaga   300
tccctggacg tctggggcca agggaccacg gtcaccgtct cgagtgctag caccaagggc   360
cccagcgtgt tccccctggc ccccagcagc aagagcacca gcggcggcac agccgccctg   420
ggctgcctgg tgaaggacta cttccccgag cccgtgaccg tgagctggaa cagcggcgcc   480
ttgaccagcg gcgtgcacac cttccccgcc gtgctgcaga gcagcggcct gtacagcctg   540
agcagcgtgg tgaccgtgcc cagcagcagc ctgggcaccc agacctacat ctgcaacgtg   600
aaccacaagc ccagcaacac caaggtggac aaacgcgtgg agcccaagag ctgcgacaag   660
acccacacct gccccccctg ccctgccccc gagctgctgg gcggaccctc cgtgttcctg   720
ttcccccca agcccaagga caccctcatg atcagccgga cccccgaggt gacctgcgtg   780
gtggtggacg tgagccacga ggaccccgag gtgaagttca actggtacgt ggacggcgtg   840
gaggtgcaca acgccaagac caagccccgg gaggagcagt acaacagcac ctaccgggtg   900
gtgagcgtgc tcaccgtgct gcaccaggac tggctgaacg gcaaggagta caagtgcaag   960
gtgagcaaca aggccctgcc tgcccccatc gagaagacca tcagcaaggc caagggccag  1020
ccccgggagc cccaggtgta caccctgccc cccagccggg aggagatgac caagaaccag  1080
gtgtccctca cctgtctggt gaagggcttc taccccagcg acatcgccgt ggagtgggag  1140
agcaacggcc agcccgagaa caactacaag accacccccc ctgtgctgga cagcgacggc  1200
agcttcttcc tgtacagcaa gctcaccgtg gacaagagcc ggtggcagca gggcaacgtg  1260
ttcagctgca gcgtgatgca cgaggccctg cacaaccact acacccagaa gagcctgagc  1320
ctgagccccg gcaag                                                   1335
```

[420] CR6141 Heavy Chain amino acid sequence (SEQ ID NO: 413)

EVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYVYWVRQAPGQGLEWMGWISAYNGNTN
YAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCARSRSLDVWGQGTTVTVSSASTKGP
SVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVV
TVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFL
FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQ
VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGK

[421] CR6141 VH amino acid sequence (SEQ ID NO: 199)

EVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYVYWVRQAPGQGLEWMGWISAYNGNTN
YAQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCARSRSLDVWGQGTTVTVSS

[422] CR6141 Light Chain nucleotide sequence (SEQ ID NO: 415)

```
gatgttgtga tgactcagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc    60
atcaactgca agtccagcca gagtgtttta tacagctcca acaataagaa ctacttagct   120
tggtaccagc agaaaccagg acagcctcct aagctgctca tttactgggc atctacccgg   180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc   240
atcagcagcc tgcaggctga agatgtggca gtttattact gtcagcaata ttatagtact   300
cctctcactt tcggcggagg gaccaaagtg gatatcaaac gtgcggccgc acccagcgtg   360
ttcatcttcc cccctccga cgagcagctg aagagcggca ccgccagcgt ggtgtgcctg   420
ctgaacaact tctaccccg ggaggccaag gtgcagtgga aggtggacaa cgccctgcag   480
agcggcaaca gccaggagag cgtgaccgag caggacagca aggactccac ctacagcctg   540
agcagcaccc tcaccctgag caaggccgac tacgagaagc acaaggtgta cgcctgcgag   600
gtgacccacc agggcctgag cagccccgtg accaagagct tcaaccgggg cgagtgt      657
```

[423] CR6141 Light Chain amino acid sequence (SEQ ID NO: 416)

DVVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYLAWYQQKPGQPPKLLIYWASTRES
GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSTPLTFGGGTKVDIKRAAAPSVFIFPPS

DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSK
ADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

[424] CR6141 VL amino acid sequence (SEQ ID NO: 414)

DVVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYLAWYQQKPGQPPKLLIYWASTRES
GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSTPLTFGGGTKVDIKR

[425] The CR6255 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 417) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 418 and the heavy chain amino acid sequence shown in SEQ ID NO: 419. The CR6255 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 420) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 421 and the light chain amino acid sequence shown in SEQ ID NO: 422.

[426] CR6255 Heavy Chain nucleotide sequence (SEQ ID NO: 418)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc      60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcctgagtg gatgggaggg atcatcccta tttttggtac aacaaaatac     180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac     240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg     300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agtgctagca ccaagggccc cagcgtgttc cccctggccc ccagcagcaa gagcaccagc     420
ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg     480
agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc     540
agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag     600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag     660
cccaagagct gcgacaagac ccacacctgc ccccctgcc ctgccccga gctgctgggc      720
ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc     780
cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac     840
tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac     900
aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc     960
aaggagtaca agtgcaaggt gagcaacaag gccctgcctg cccccatcga gaagaccatc    1020
agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag    1080
gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac    1140
atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac caccccccct    1200
gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg    1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac    1320
acccagaaga gcctgagcct gagccccggc aag                                 1353
```

[427] CR6255 Heavy Chain amino acid sequence (SEQ ID NO: 419)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS
SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLG
GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

[428] CR6255 VH amino acid sequence (SEQ ID NO: 417)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKY
APKFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVS
S

[429] CR6255 Light Chain nucleotide sequence (SEQ ID NO: 421)

```
tcctatgtgc tgactcagcc accctcagcg tctgggaccc ccgggcagag ggtcaccatc      60
tcttgttctg gaagcacgtt caacatcgga agtaatgctg tagactggta ccggcagctc     120
ccaggaacgg ccccaaact cctcatctat agtaataatc agcggccctc aggggtccct      180
gaccgattct ctggctccag gtctggcacc tcagcctccc tggccatcag tgggctccag     240
tctgaggatg aggctgatta ttactgtgca gcatgggatg acatcctgaa tgttccggta     300
ttcggcggag ggaccaagct gaccgtccta ggtgcggccg caggccagcc caaggccgct     360
cccagcgtga ccctgttccc ccctcctcc gaggagctgc aggccaacaa ggccaccctg      420
gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc     480
agccccgtga aggccggcgt ggagaccacc acccccagca agcagagcaa caacaagtac     540
gccgccagca gctacctgag cctcacccc gagcagtgga agagccaccg gagctacagc      600
tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggcccccac cgagtgcagc     660
```

[430] CR6255 Light Chain amino acid sequence (SEQ ID NO: 422)

SYVLTQPPSASGTPGQRVTISCSGSTFNIGSNAVDWYRQLPGTAPKLLIYSNNQRPSGVPDRFS
GSRSGTSASLAISGLQSEDEADYYCAAWDDILNVPVFGGGTKLTVLGAAAGQPKAAPSVTLF
PPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSL
TPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[431] CR6255 VL amino acid sequence (SEQ ID NO: 420)

SYVLTQPPSASGTPGQRVTISCSGSTFNIGSNAVDWYRQLPGTAPKLLIYSNNQRPSGVPDRFS
GSRSGTSASLAISGLQSEDEADYYCAAWDDILNVPVFGGGTKLTVLG

[432] The CR6257 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 423) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 424 and the heavy chain amino acid sequence shown in SEQ ID NO: 425. The CR6257 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 426) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 427 and the light chain amino acid sequence shown in SEQ ID NO: 428.

[433] CR6257 Heavy Chain nucleotide sequence (SEQ ID NO: 424)

```
caggtccagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc      60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcctgagtg gatgggaggg atcatcccta tttttggtac aacaaaatac     180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac     240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg     300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agtgctagca ccaagggccc cagcgtgttc cccctggccc ccagcagcaa gagcaccagc     420
ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg     480
agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc     540
agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag     600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag     660
cccaagagct gcgacaagac ccacacctgc ccccctgcc ctgccccga gctgctgggc      720
ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc     780
cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac     840
tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac     900
aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc     960
aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc     1020
agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag     1080
gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac     1140
atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct      1200
gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg     1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac     1320
acccagaaga gcctgagcct gagccccggc aag                                  1353
```

[434] CR6257 Heavy Chain amino acid sequence (SEQ ID NO: 425)

QVQLVQSGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKY
APKFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVS
SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLF
PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

[435] CR6257 VH amino acid sequence (SEQ ID NO: 423)

QVQLVQSGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKY
APKFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVS
S

[436] CR6257 Light Chain nucleotide sequence (SEQ ID NO: 427)

```
cagtctgccc tgactcagcc tgccgccgtg tctgggtctc ctggacagtc gatcaccatc      60
tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtaccaacag     120
cacccaggca aagcccccaa actcatgatt tatgaggtca gtaatcggcc ctcaggggtt     180
tctaatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc     240
caggctgagg acgaggctga ttattactgc agctcatata caagcagcag cacttatgtc     300
ttcggaactg ggaccaaggt caccgtccta ggtgcggccg caggccagcc caaggccgct     360
cccagcgtga ccctgttccc ccctcctcc gaggagctgc aggccaacaa ggccaccctg      420
gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc     480
agccccgtga aggccggcgt ggagaccacc accccagca agcagagcaa caacaagtac      540
gccgccagca gctacctgag cctcacccgc gagcagtgga agagccaccg gagctacagc     600
tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggcccccac cgagtgcagc     660
```

[437] CR6257 Light Chain amino acid sequence (SEQ ID NO: 428)

QSALTQPAAVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEVSNRPSGVSN
RFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTYVFGTGTKVTVLGAAAGQPKAAPSVTL
FPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSL
TPEQWKSHRSYS CQVTHEGSTVEKTVAPTECS

[438] CR6257 VL amino acid sequence (SEQ ID NO: 426)

QSALTQPAAVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEVSNRPSGVSN
RFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTYVFGTGTKVTVLG

[439] The CR6260 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 429) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 430 and the heavy chain amino acid sequence shown in SEQ ID NO: 431. The CR6260 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 432) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 433 and the light chain amino acid sequence shown in SEQ ID NO: 434.

[440] CR6260 Heavy Chain nucleotide sequence (SEQ ID NO: 430)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc      60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttggtac aacaaaatac      180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac     240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg     300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agtgctagca ccaagggccc cagcgtgttc cccctggccc ccagcagcaa gagcaccagc     420
ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg     480
agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc     540
agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag     600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag     660
cccaagagct gcgacaagac ccacacctgc ccccccctgcc ctgccccga gctgctgggc     720
ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc      780
cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac     840
tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac     900
aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc     960
aaggagtaca agtgcaaggt gagcaacaag gccctgcctg cccccatcga gaagaccatc    1020
agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag    1080
gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac    1140
atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac caccccccct    1200
gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg    1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac    1320
acccagaaga gcctgagcct gagccccggc aag                                 1353
```

[441] CR6260 Heavy Chain amino acid sequence (SEQ ID NO: 431)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL

TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

[442] CR6260 VH amino acid sequence (SEQ ID NO: 429)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSS

[443] CR6260 Light Chain nucleotide sequence (SEQ ID NO: 433)

```
tcctatgtgc tgactcagcc accctcagtc tctgggaccc ccgggcagag ggtcaccatc      60
tcttgctctg gaagccgctc caacgtcgga gataattctg tatattggta tcaacacgtc     120
ccagaaatgg cccccaaact cctcgtctat aagaatactc aacggccctc aggagtccct     180
gcccggtttt ccggctccaa gtctggcact tcagcctccc tggccatcat tggcctccag     240
tccggcgatg aggctgatta ttattgtgtg gcatgggatg acagcgtaga tggctatgtc     300
ttcggatctg ggaccaaggt caccgtccta ggtgcggccg caggccagcc caaggccgct     360
cccagcgtga ccctgttccc cccctcctcc gaggagctgc aggccaacaa ggccaccctg     420
gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc     480
agccccgtga aggccggcgt ggagaccacc accccagca agcagagcaa caacaagtac     540
gccgccagca gctacctgag cctcacccc gagcagtgga agagccaccg gagctacagc     600
tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggcccccac cgagtgcagc     660
```

[444] CR6260 Light Chain amino acid sequence (SEQ ID NO: 434)

SYVLTQPPSVSGTPGQRVTISCSGSRSNVGDNSVYWYQHVPEMAPKLLVYKNTQRPSGVP
ARFSGSKSGTSASLAIIGLQSGDEADYYCVAWDDSVDGYVFGSGTKVTVLGAAAGQPKAAP
SVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKY
AASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[445] CR6260 VL amino acid sequence (SEQ ID NO: 432)

SYVLTQPPSVSGTPGQRVTISCSGSRSNVGDNSVYWYQHVPEMAPKLLVYKNTQRPSGVP
ARFSGSKSGTSASLAIIGLQSGDEADYYCVAWDDSVDGYVFGSGTKVTVLG

[446] The CR6261 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 435) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 436 and the heavy chain amino acid sequence shown in SEQ ID NO: 437. The CR6261 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 438) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 439 and the light chain amino acid sequence shown in SEQ ID NO: 440.

[447] CR6261 Heavy Chain nucleotide sequence (SEQ ID NO: 436)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc      60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcctgagtg gatgggaggg atcatcccta tttttggtac aacaaaatac     180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac     240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg     300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agtgctagca ccaagggccc cagcgtgttc cccctggccc ccagcagcaa gagcaccagc     420
ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg     480
agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc     540
agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag     600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag     660
cccaagagct gcgacaagac ccacacctgc ccccctgcc ctgccccga gctgctgggc      720
ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc      780
cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac     840
tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac     900
aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc     960
aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc     1020
agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag     1080
gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac     1140
atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac caccccccct     1200
gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg     1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac     1320
acccagaaga gcctgagcct gagccccggc aag                                  1353
```

[448] CR6261 Heavy Chain amino acid sequence (SEQ ID NO: 437)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

[449] CR6261 VH amino acid sequence (SEQ ID NO: 435)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSS

[450] CR6261 Light Chain nucleotide sequence (SEQ ID NO: 439)

```
cagtctgtgt tgacgcagcc gccctcagtg tctgcggccc caggacagaa ggtcaccatc      60
tcctgctctg gaagcagctc caacattggg aatgattatg tatcctggta ccagcagctc     120
ccaggaacag ccccaaact cctcatttat gacaataata agcgaccctc agggattcct      180
gaccgattct ctggctccaa gtctggcacg tcagccaccc tgggcatcac cggactccag     240
actggggacg aggccaacta ttactgcgca acatgggatc gccgcccgac tgcttatgtt     300
gtcttcggcg gagggaccaa gctgaccgtc ctaggtgcgg ccgcaggcca gcccaaggcc     360
gctcccagcg tgaccctgtt ccccccctcc tccgaggagc tgcaggccaa caaggccacc     420
ctggtgtgcc tcatcagcga cttctaccct ggcgccgtga ccgtggcctg gaaggccgac     480
agcagccccg tgaaggccgg cgtggagacc accaccccca gcaagcagag caacaacaag     540
tacgccgcca gcagctacct gagcctcacc cccgagcagt ggaagagcca ccggagctac     600
agctgccagg tgacccacga gggcagcacc gtggagaaga ccgtggcccc caccgagtgc     660
```

[451] CR6261 Light Chain amino acid sequence (SEQ ID NO: 440)

QSVLTQPPSVSAAPGQKVTISCSGSSSNIGNDYVSWYQQLPGTAPKLLIYDNNKRPSGIPDRFS
GSKSGTSATLGITGLQTGDEANYYCATWDRRPTAYVVFGGGTKLTVLGAAAGQPKAAPSVT
LFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLS
LTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[452] CR6261VL amino acid sequence (SEQ ID NO: 438)

QSVLTQPPSVSAAPGQKVTISCSGSSSNIGNDYVSWYQQLPGTAPKLLIYDNNKRPSGIPDRFS
GSKSGTSATLGITGLQTGDEANYYCATWDRRPTAYVVFGGGTKLTVLG

[453] The CR6262 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 441) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 442 and the heavy chain amino acid sequence shown in SEQ ID NO: 443. The CR6262 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 444) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 445 and the light chain amino acid sequence shown in SEQ ID NO: 446.

[454] CR6262 Heavy Chain nucleotide sequence (SEQ ID NO: 442)

```
caggtacagc tgcagcagtc aggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg tttccggagt cattttcagc ggcagtgcga tcagctgggt gcgacaggcc     120
cctggacaag gccttgagtg gatgggaggg atcagccctc tctttggcac aacaaattac     180
gcacaaaagt tccagggcag agtcacgatt accgcggacc aatccacgaa cacaacctac     240
atggaggtga acagcctgag atatgaggac acggccgtgt atttctgtgc gcgaggtcca     300
aaatattaca gtgagtacat ggacgtctgg ggcaaaggga ccacggtcac cgtctcgagt     360
gctagcacca agggccccag cgtgttcccc ctggcccccа gcagcaagag caccagcggc     420
ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc     480
tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc     540
ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc     600
tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc     660
aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga     720
ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccсc     780
gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg     840
tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac     900
agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag     960
gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc    1020
aaggccaagg gccagccccg ggagccccag gtgtacaccc tgcccccccag ccgggaggag    1080
atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc    1140
gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccccctgtg    1200
ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg    1260
cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc    1320
cagaagagcc tgagcctgag ccccggcaag                                     1350
```

[455] CR6262 Heavy Chain amino acid sequence (SEQ ID NO: 443)

QVQLQQSGAEVKKPGSSVKVSCKVSGVIFSGSAISWVRQAPGQGLEWMGGISPLFGTTNYAQ
KFQGRVTITADQSTNTTYMEVNSLRYEDTAVYFCARGPKYYSEYMDVWGKGTTVTVSSAST
KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK

GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL
HNHYTQKSLSLSPGK

[456] CR6262 VH amino acid sequence (SEQ ID NO: 441)

QVQLQQSGAEVKKPGSSVKVSCKVSGVIFSGSAISWVRQAPGQGLEWMGGISPLFGTTNYAQ
KFQGRVTITADQSTNTTYMEVNSLRYEDTAVYFCARGPKYYSEYMDVWGKGTTVTVSS

[457] CR6262 Light Chain nucleotide sequence (SEQ ID NO: 445)

```
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgcc gggcgagtca gggcattagc agttatttag cctggtatca gcagaagcca     120
gggaaagttc ctacactcct gatctatgat gcatccactt tgcgatcagg ggtcccatct     180
cgcttcagtg gcagtggatc tgcgacagat ttcactctca ccatcagcag cctgcagcct     240
gaagatgttg caacttatta ctgtcaaagg tataacagtg ccccccgat caccttcggc      300
caagggacac gactggagat taaacgtgcg gccgcaccca gcgtgttcat cttccccccc     360
tccgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac     420
ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag     480
gagagcgtga ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctcacc     540
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc     600
ctgagcagcc ccgtgaccaa gagcttcaac cggggcgagt gt                        642
```

[458] CR6262 Light Chain amino acid sequence (SEQ ID NO: 446)

DIQMTQSPSSLSASVGDRVTITCRASQGISSYLAWYQQKPGKVPTLLIYDASTLRSGVPSRFSG
SGSATDFTLTISSLQPEDVATYYCQRYNSAPPITFGQGTRLEIKRAAAPSVFIFPPSDEQLKSGT
ASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHK
VYACEVTHQGLSSPVTKSFNRGEC

[459] CR6262 VL amino acid sequence (SEQ ID NO: 444)

DIQMTQSPSSLSASVGDRVTITCRASQGISSYLAWYQQKPGKVPTLLIYDASTLRSGVPSRFSG
SGSATDFTLTISSLQPEDVATYYCQRYNSAPPITFGQGTRLEIKR

[460] The CR6268 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 447) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 448 and the heavy chain amino acid sequence shown in SEQ ID NO: 449. The CR6268 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 450) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 451 and the light chain amino acid sequence shown in SEQ ID NO: 452.

[461] CR6268 Heavy Chain nucleotide sequence (SEQ ID NO: 448)

```
caggtccagc tggtacagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg caccttcagt agttatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggagga atcatgggta tgtttggcac aactaactac     180
gcacagaagt tccagggcag agtcacgatt accgcggacg aattcacgag cgcagcctac     240
atggagctga ggagcctgag atctgaggac acggccgtct actactgtgc gaggtctagt     300
ggttattacc ccgaatactt ccaggactgg ggccagggca ccctggtcac cgtctcgagt     360
gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc     420
ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc     480
tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc     540
ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc     600
tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc     660
aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga     720
ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccca     780
gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg     840
tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac     900
agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag     960
gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc    1020
aaggccaagg gccagccccg ggagccccag gtgtacaccc tgcccccag ccgggaggag     1080
atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc    1140
gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccctgtg     1200
ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg    1260
cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc    1320
cagaagagcc tgagcctgag ccccggcaag                                     1350
```

[462] CR6268 Heavy Chain amino acid sequence (SEQ ID NO: 449)

QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIMGMFGTTNY
AQKFQGRVTITADEFTSAAYMELRSLRSEDTAVYYCARSSGYYPEYFQDWGQGTLVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

[463] CR6268 VH amino acid sequence (SEQ ID NO: 447)

QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIMGMFGTTNY
AQKFQGRVTITADEFTSAAYMELRSLRSEDTAVYYCARSSGYYPEYFQDWGQGTLVTVSS

[464] CR6268 Light Chain nucleotide sequence (SEQ ID NO: 451)

```
cagtctgtgc tgactcagcc accctcagag tccgtgtccc caggacagac agccagcgtc      60
acctgctctg gacataaatt gggggataaa tatgtttcgt ggtatcagca gaagccaggc     120
cagtcccctg tattactcat ctatcaagat aacaggcggc cctcagggat ccctgagcga     180
ttcataggct ccaactctgg gaacacagcc actctgacca tcagcgggac ccaggctctg     240
gatgaggctg actattactg tcaggcgtgg gacagcagca ctgcggtttt cggcggaggg     300
accaagctga ccgtcctagg tgcggccgca ggccagccca aggccgctcc cagcgtgacc     360
ctgttccccc cctcctccga ggagctgcag gccaacaagg ccaccctggt gtgcctcatc     420
agcgacttct accctggcgc cgtgaccgtg gcctggaagg ccgacagcag ccccgtgaag     480
gccggcgtgg agaccaccac ccccagcaag cagagcaaca acaagtacgc cgccagcagc     540
tacctgagcc tcacccccga gcagtggaag agccaccgga gctacagctg ccaggtgacc     600
cacgagggca gcaccgtgga gaagaccgtg gcccccaccg agtgcagc                  648
```

[465] CR6268 Light Chain amino acid sequence (SEQ ID NO: 452)

QSVLTQPPSESVSPGQTASVTCSGHKLGDKYVSWYQQKPGQSPVLLIYQDNRRPSGIPERFIG
SNSGNTATLTISGTQALDEADYYCQAWDSSTAVFGGGTKLTVLGAAAGQPKAAPSVTLFPPS
SEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSLTPE
QWKSHRSYSCQVTHEGSTVEKTVAPTECS

[466] CR6268 VL amino acid sequence (SEQ ID NO: 450)

QSVLTQPPSESVSPGQTASVTCSGHKLGDKYVSWYQQKPGQSPVLLIYQDNRRPSGIPERFIG
SNSGNTATLTISGTQALDEADYYCQAWDSSTAVFGGGTKLTVLG

[467] The CR6272 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 453) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 454 and the heavy chain amino acid sequence shown in SEQ ID NO: 455. The CR6272 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 456) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 457 and the light chain amino acid sequence shown in SEQ ID NO: 458.

[468] CR6272 Heavy Chain nucleotide sequence (SEQ ID NO: 454)

```
cagatgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg caccttctcc agttatgcta tcacctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcggta tgtttggttc aacaaactac     180
gcacagaact tccagggcag agtcacgatt accgcggacg aatccacgag cacagcctac     240
atggagctga gcagcctcag atctgaggac acggccgtgt attactgtgc gagaagtact     300
ggttattacc ctgcatacct ccaccactgg ggccagggca ccctggtcac cgtctcgagt     360
gctagcacca agggccccag cgtgttcccc ctggcccccа gcagcaagag caccagcggc     420
ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc     480
tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc     540
ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc     600
tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc     660
aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga     720
ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccсc     780
gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg     840
tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac     900
agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag     960
gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc    1020
aaggccaagg gccagccccg ggagccccag gtgtacaccc tgcccccсag ccgggaggag    1080
atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc    1140
gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccccctgtg    1200
ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg    1260
cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc    1320
cagaagagcc tgagcctgag ccccggcaag                                     1350
```

[469] CR6272 Heavy Chain amino acid sequence (SEQ ID NO: 455)

QMQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAITWVRQAPGQGLEWMGGIIGMFGSTNYA
QNFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARSTGYYPAYLHHWGQGTLVTVSSAST
KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK

GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL
HNHYTQKSLSLSPGK

[470] CR6272 VH amino acid sequence (SEQ ID NO: 453)

QMQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAITWVRQAPGQGLEWMGGIIGMFGSTNYA
QNFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARSTGYYPAYLHHWGQGTLVTVSS

[471] CR6272 Light Chain nucleotide sequence (SEQ ID NO: 457)

```
cagtctgccc tgactcagcc tcgctcagtg tccgggtctc ctggacagtc agtcaccatc      60
tcctgcactg gaaccagcag tgatgttggt ggttataact atgtctcctg gtaccaacag     120
cacccaggca aagccccaa actcatgatt tatgatgtca gtaagcggcc ctcaggggtc     180
cctgatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc     240
caggctgagg atgaggctga ttattactgc agctcatata caagcagcag cactcatgtc     300
ttcggaactg ggaccaaggt caccgtccta ggtgcggccg caggccagcc caaggccgct     360
cccagcgtga ccctgttccc cccctcctcc gaggagctgc aggccaacaa ggccacccctg     420
gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc     480
agccccgtga aggccggcgt ggagaccacc accccagca agcagagcaa caacaagtac     540
gccgccagca gctacctgag cctcacccc gagcagtgga agagccaccg gagctacagc     600
tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggccccac cgagtgcagc     660
```

[472] CR6272 Light Chain amino acid sequence (SEQ ID NO: 458)

QSALTQPRSVSGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYDVSKRPSGVPD
RFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTHVFGTGTKVTVLGAAAGQPKAAPSVTL
FPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSL
TPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[473] CR6272 VL amino acid sequence (SEQ ID NO: 456)

GSALTQPRSVSGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYDVSKRPSGVPD
RFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTHVFGTGTKVTVLG

[474] The CR696 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 459) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 460 and the heavy chain amino acid sequence shown in SEQ ID NO: 461. The CR6296 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 462) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 463 and the light chain amino acid sequence shown in SEQ ID NO: 464.

[475] CR6296 Heavy Chain nucleotide sequence (SEQ ID NO: 460)

```
gaggtgcagc tggtggagac cggggctgag gtgaagaagc ctggggcctc agtgaaggtt      60
tcctgcaagg catctggata caccttcacc agctactata tgcactgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtggtgg cacaaactat     180
gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcag cacagcctac     240
atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gagagagggg     300
aaatggggac ctcaagcggc ttttgatatc tggggccaag ggacaatggt caccgtctcg     360
agtgctagca ccaagggccc cagcgtgttc cccctggccc ccagcagcaa gagcaccagc     420
ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg     480
agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc     540
agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag     600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag     660
cccaagagct gcgacaagac ccacacctgc ccccccctgcc ctgccccga gctgctgggc     720
ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc     780
cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac     840
tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac     900
aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc     960
aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc    1020
agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag    1080
gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac    1140
atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct     1200
gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg    1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac    1320
acccagaaga gcctgagcct gagccccggc aag                                 1353
```

[476] CR6296 Heavy Chain amino acid sequence (SEQ ID NO: 461)

EVQLVETGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGWINPNSGGTN
YAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCAREGKWGPQAAFDIWGQGTMVTV
SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG
LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFL
FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVV
SVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL
TCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

[477] CR6296 VH amino acid sequence (SEQ ID NO: 459)

EVQLVETGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGWINPNSGGTN
YAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCAREGKWGPQAAFDIWGQGTMVTV
SS

[478] CR6296 Light Chain nucleotide sequence (SEQ ID NO: 463)

```
gaaattgtga tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc      60
ctctcctgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa     120
cctggccagg ctcccaggct cctcatctat gatgcatcca gcagggccac tgacatccca     180
gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag     240
cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcactttg gacgttcggc     300
caagggacca aggtggagat caaacgtgcg gccgcaccca gcgtgttcat cttcccccc      360
tccgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac     420
ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag     480
gagagcgtga ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctcacc     540
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc     600
ctgagcagcc ccgtgaccaa gagcttcaac cggggcgagt gt                        642
```

[479] CR6296 Light Chain amino acid sequence (SEQ ID NO: 464)

EIVMTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYDASSRATDIPDRFS
GSGSGTDFTLTISRLEPEDFAVYYCQQYGSSLWTFGQGTKVEIKRAAAPSVFIFPPSDEQLKSG
TASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKH
KVYACEVTHQGLSSPVTKSFNRGEC

[480] CR6296 VL amino acid sequence (SEQ ID NO: 462)

EIVMTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYDASSRATDIPDRFS
GSGSGTDFTLTISRLEPEDFAVYYCQQYGSSLWTFGQGTKVEIKR

[481] The CR6301 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 465) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 466 and the heavy chain amino acid sequence shown in SEQ ID NO: 467. The CR6301 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 468) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 469 and the light chain amino acid sequence shown in SEQ ID NO: 470.

[482] CR6301 Heavy Chain nucleotide sequence (SEQ ID NO: 466)

```
gaggtgcagc tggtagagtc tgggggaggc ttggtacagc ctgggggGTC cctgagactc      60
tcctgtgcag cctctggatt cacctttagc atctatgcca tgagctgggt ccgccaggca     120
ccagggaagg ggctggagtg ggtctcagct attagtagta gtggtgatag cacatactac     180
gcagactccg tgaagggccg gttcaccatc tccagagaca acgccaggaa cacgctgtat     240
ctgcaaatga acagtctgag agccgaggac acggctgtgt attactgtgc gagagcgtat     300
ggctacacgt tcgacccctg gggccaggga accctggtca ccgtctcgag tgctagcacc     360
aagggcccca gcgtgttccc cctggccccc agcagcaaga gcaccagcgg cggcacagcc     420
gccctgggct gcctggtgaa ggactacttc cccgagcccg tgaccgtgag ctggaacagc     480
ggcgccttga ccagcggcgt gcacaccttc cccgccgtgc tgcagagcag cggcctgtac     540
agcctgagca gcgtggtgac cgtgcccagc agcagcctgg gcacccagac ctacatctgc     600
aacgtgaacc acaagcccag caacaccaag gtggacaaac gcgtggagcc caagagctgc     660
gacaagaccc acacctgccc cccctgccct gccccgagc tgctgggcgg accctccgtg     720
ttcctgttcc ccccaagcc caaggacacc ctcatgatca gccggacccc cgaggtgacc     780
tgcgtggtgg tggacgtgag ccacgaggac cccgaggtga agttcaactg gtacgtggac     840
ggcgtggagg tgcacaacgc caagaccaag ccccgggagg agcagtacaa cagcacctac     900
cgggtggtga gcgtgctcac cgtgctgcac caggactggc tgaacggcaa ggagtacaag     960
tgcaaggtga gcaacaaggc cctgcctgcc cccatcgaga agaccatcag caaggccaag    1020
ggccagcccc gggagcccca ggtgtacacc ctgccccca gccgggagga gatgaccaag    1080
aaccaggtgt ccctcacctg tctggtgaag ggcttctacc ccagcgacat cgccgtggag    1140
tgggagagca acggccagcc cgagaacaac tacaagacca ccccccctgt gctggacagc    1200
gacggcagct tcttcctgta cagcaagctc accgtggaca agagccggtg gcagcagggc    1260
aacgtgttca gctgcagcgt gatgcacgag gccctgcaca accactacac ccagaagagc    1320
ctgagcctga gccccggcaa g                                              1341
```

[483] CR6301 Heavy Chain amino acid sequence (SEQ ID NO: 467)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSIYAMSWVRQAPGKGLEWVSAISSSGDSTYYAD
SVKGRFTISRDNARNTLYLQMNSLRAEDTAVYYCARAYGYTFDPWGQGTLVTVSSASTKGP
SVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVV
TVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDT
LMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ

DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN
HYTQKSLSLSPGK

[484] CR6301 VH amino acid sequence (SEQ ID NO: 465)

EVQLVESGGGLVQPGGSLRLSCAASGFTFSIYAMSWVRQAPGKGLEWVSAISSSGDSTYYAD
SVKGRFTISRDNARNTLYLQMNSLRAEDTAVYYCARAYGYTFDPWGQGTLVTVSS

[485] CR6301 Light Chain nucleotide sequence (SEQ ID NO: 469)

```
gaaattgtgc tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc     60
atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg    120
tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc    180
tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc    240
agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactccc    300
ctcactttcg gcggagggac caaggtggag atcaaacgtg cggccgcacc cagcgtgttc    360
atcttccccc cctccgacga gcagctgaag agcggcaccg ccagcgtggt gtgcctgctg    420
aacaacttct acccccggga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc    480
ggcaacagcc aggagagcgt gaccgagcag gacagcaagg actccaccta cagcctgagc    540
agcaccctca ccctgagcaa ggccgactac gagaagcaca aggtgtacgc ctgcgaggtg    600
acccaccagg gcctgagcag ccccgtgacc aagagcttca accggggcga gtgt           654
```

[486] CR6301 Light Chain amino acid sequence (SEQ ID NO: 470)

EIVLTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVP
DRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPLTFGGGTKVEIKRAAAPSVFIFPPSDE
QLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA
DYEKHKVYACEVTHQGLSSPVTKSFNRGEC

[487] CR6301 VL amino acid sequence (SEQ ID NO:468)

EIVLTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVP
DRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPLTFGGGTKVEIKR

[488] The CR6307 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 471) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 472 and the heavy chain amino acid sequence shown in SEQ ID NO: 473. The CR6307 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 474) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 475 and the light chain amino acid sequence shown in SEQ ID NO: 476.

[489] CR6307 Heavy Chain nucleotide sequence (SEQ ID NO: 472)

```
caggtccagc tggtgcagtc tgggggaggc ctggtcaagc ctgggggGtc cctgagactc      60
tcctgtgcag cctctggatt caccttcagt agctatagca tgaactgggt ccgccaggct     120
ccagggaagg ggctggagtg ggtctcatcc attagtagta gtagtagtta catatactac     180
gtagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat     240
ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagaggtggt     300
gggagctacg gggcctacga aggctttgac tactggggcc agggcaccct ggtcaccgtc     360
tcgagtgcta gcaccaaggg ccccagcgtg ttccccctgg cccccagcag caagagcacc     420
agcggcggca cagccgccct gggctgcctg gtgaaggact acttccccga gcccgtgacc     480
gtgagctgga acagcggcgc cttgaccagc ggcgtgcaca ccttccccgc cgtgctgcag     540
agcagcggcc tgtacagcct gagcagcgtg gtgaccgtgc ccagcagcag cctgggcacc     600
cagacctaca tctgcaacgt gaaccacaag cccagcaaca ccaaggtgga caaacgcgtg     660
gagcccaaga gctgcgacaa gacccacacc tgccccccct gccctgcccc cgagctgctg     720
ggcggaccct ccgtgttcct gttccccccc aagcccaagg acaccctcat gatcagccgg     780
acccccgagg tgacctgcgt ggtggtggac gtgagccacg aggaccccga ggtgaagttc     840
aactggtacg tggacggcgt ggaggtgcac aacgccaaga ccaagccccg ggaggagcag     900
tacaacagca cctaccgggt ggtgagcgtg ctcaccgtgc tgcaccagga ctggctgaac     960
ggcaaggagt acaagtgcaa ggtgagcaac aaggccctgc ctgccccat cgagaagacc     1020
atcagcaagg ccaagggcca gccccgggag ccccaggtgt acaccctgcc ccccagccgg     1080
gaggagatga ccaagaacca ggtgtccctc acctgtctgg tgaagggctt ctaccccagc     1140
gacatcgccg tggagtggga gagcaacggc cagcccgaga acaactacaa gaccacccc      1200
cctgtgctgg acagcgacgg cagcttcttc ctgtacagca agctcaccgt ggacaagagc     1260
cggtggcagc agggcaacgt gttcagctgc agcgtgatgc acgaggccct gcacaaccac     1320
tacacccaga agagcctgag cctgagcccc ggcaag                               1356
```

[490] CR6307 Heavy Chain amino acid sequence (SEQ ID NO: 473)

QVQLVQSGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSSISSSSSYIYYVD
SVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARGGGSYGAYEGFDYWGQGTLVTVSS
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY
SLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFP
PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV
LTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

[491] CR6307 VH amino acid sequence (SEQ ID NO: 471)

QVQLVQSGGGLVKPGGSLRLSCAASGFTFSSYSMNWVRQAPGKGLEWVSSISSSSSYIYYVD
SVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARGGGSYGAYEGFDYWGQGTLVTVSS

[492] CR6307 Light Chain nucleotide sequence (SEQ ID NO: 475)

```
gaaattgtgc tgactcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc      60
ctctcctgca gggccagtca gcgtgttagc agctacttag cctggtacca acagaaacct     120
ggccaggctc ccaggctcct catctatggt gcatccacca gggccgctgg catcccagac     180
aggttcagtg gcagtgggtc tgggacagac ttcactctca ccatcagcag actggagcct     240
gaagattctg cagtgtatta ctgtcagcag tatggtagga caccgctcac tttcggcgga     300
gggaccaagg tggagatcaa acgtgcggcc gcacccagcg tgttcatctt ccccccctcc     360
gacgagcagc tgaagagcgg caccgccagc gtggtgtgcc tgctgaacaa cttctacccc     420
cgggaggcca aggtgcagtg gaaggtggac aacgccctgc agagcggcaa cagccaggag     480
agcgtgaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctcaccctg     540
agcaaggccg actacgagaa gcacaaggtg tacgcctgcg aggtgaccca ccagggcctg     600
agcagccccg tgaccaagag cttcaaccgg ggcgagtgt                             639
```

[493] CR6307 Light Chain amino acid sequence (SEQ ID NO: 476)

EIVLTQSPGTLSLSPGERATLSCRASQRVSSYLAWYQQKPGQAPRLLIYGASTRAAGIPDRFSG
SGSGTDFTLTISRLEPEDSAVYYCQQYGRTPLTFGGGTKVEIKRAAAPSVFIFPPSDEQLKSGT
ASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHK
VYACEVTHQGLSSPVTKSFNRGEC

[494] CR6307 VL amino acid sequence (SEQ ID NO: 474)

EIVLYQSPGTLSLSPGERATLSCRASQRVSSYLAWYQQKPGQAPRLLIYGASTRAAGIPDRFS
GSGSGTDFTLTISRLEPEDSAVYYCQQYGRTPLTFGGGTKVEIKR

[495] The CR6310 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 477) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 478 and the heavy chain amino acid sequence shown in SEQ ID NO: 479. The CR6310 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 480) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 481 and the light chain amino acid sequence shown in SEQ ID NO: 482.

[496] CR6310 Heavy Chain nucleotide sequence (SEQ ID NO: 478)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc     60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc    120
cctggacaag ggcctgagtg gatgggaggg atcatcccta tttttggtac aacaaaatac    180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac    240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg    300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg    360
agtgctagca ccaagggccc cagcgtgttc ccctggccc ccagcagcaa gagcaccagc    420
ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg    480
agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc    540
agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag    600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag    660
cccaagagct gcgacaagac ccacacctgc ccccctgcc ctgcccccga gctgctgggc    720
ggaccctccg tgttcctgtt ccccccccaag cccaaggaca ccctcatgat cagccggacc    780
cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac    840
tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac    900
aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc    960
aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc   1020
agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag   1080
gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac   1140
atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac caccccccct   1200
gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg   1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac   1320
acccagaaga gcctgagcct gagccccggc aag                                1353
```

[497] CR6310 Heavy Chain amino acid sequence (SEQ ID NO: 479)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
```
```

VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

[498] CR6310 VH amino acid sequence (SEQ ID NO: 477)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSS

[499] CR6310 Light Chain nucleotide sequence (SEQ ID NO: 481)

```
tcctatgtgc tgactcagcc accctcggtg tcagtggccc caggacagac ggccaggatt      60
acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc     120
caggcccctg tgctggtcgt ctatgatgat agcgaccggc cctcagggat ccctgagcga     180
ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg     240
gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgc tgtgttcgga     300
ggaggcaccc agctgaccgt cctcggtgcg gccgcaggcc agcccaaggc cgctcccagc     360
gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc     420
ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc     480
gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc     540
agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag     600
gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc           654
```

[500] CR6310 Light Chain amino acid sequence (SEQ ID NO: 482)

SYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPSGIPERFSG
SNSGNTATLTISRVEAGDEADYYCQVWDSSSDHAVFGGGTQLTVLGAAAGQPKAAPSVTLF
PPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSL
TPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[501] CR6310 VL amino acid sequence (SEQ ID NO: 480)

SYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPSGIPERFSG
SNSGNTATLTISRVEAGDEADYYCQVWDSSSDHAVFGGGTQLTVLG

[502] The CR6314 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 483) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 484 and the heavy chain amino acid sequence shown in SEQ ID NO: 485. The CR6314 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 486) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 487 and the light chain amino acid sequence shown in SEQ ID NO: 488.

[503] CR6314 Heavy Chain nucleotide sequence (SEQ ID NO: 484)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc      60
tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcctgagtg gatgggaggg atcatcccta tttttggtac aacaaaatac     180
gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac     240
atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg     300
gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agtgctagca ccaagggccc cagcgtgttc cccctggccc ccagcagcaa gagcaccagc     420
ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg     480
agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc     540
agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag     600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag     660
cccaagagct gcgacaagac ccacacctgc ccccccctgcc ctgccccga gctgctgggc     720
ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc      780
cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac     840
tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac     900
aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc     960
aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc     1020
agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag     1080
gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac     1140
atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac caccccccct     1200
gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg     1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac     1320
acccagaaga gcctgagcct gagccccggc aag                                  1353
```

[504] CR6314 Heavy Chain amino acid sequence (SEQ ID NO: 485)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

[505] CR6314 VH amino acid sequence (SEQ ID NO: 483)

EVQLVESGAEVKKPGSSVKVSCKASGGPFRSYAISWVRQAPGQGPEWMGGIIPIFGTTKYAP
KFQGRVTITADDFAGTVYMELSSLRSEDTAMYYCAKHMGYQVRETMDVWGKGTTVTVSS

[506] CR6314 Light Chain nucleotide sequence (SEQ ID NO: 487)

```
tcctatgtgc tgactcagcc accctcagcg tctgggaccc ccgggcagag ggtcaccatc      60
tcttgttctg gaagcagctc caacatcgga agtaattatg tatactggta ccagcagctc     120
ccaggcacgg ccccaaact cctcatctat agggatggtc agcggccctc agggggtccct     180
gaccgattct ctggctccaa gtctggcacc tcagcctcct tggccatcag tggactccgg     240
tccgatgatg aggctgatta ttactgtgca acatgggatg acaacctgag tggtccagta     300
ttcggcggag ggaccaagct gaccgtccta ggtgcggccg caggccagcc caaggccgct     360
cccagcgtga ccctgttccc ccctcctcc gaggagctgc aggccaacaa ggccaccctg      420
gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc     480
agccccgtga aggccggcgt ggagaccacc accccagca agcagagcaa caacaagtac      540
gccgccagca gctacctgag cctcacccgc gagcagtgga agagccaccg gagctacagc     600
tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggcccccac cgagtgcagc     660
```

[507] CR6314 Light Chain amino acid sequence (SEQ ID NO: 488)

SYVLTQPPSASGTPGQRVTISCSGSSSNIGSNYVYWYQQLPGTAPKLLIYRDGQRPSGVPDRFS
GSKSGTSASLAISGLRSDDEADYYCATWDDNLSGPVFGGGTKLTVLGAAAQPKAAPSVTLFP
PSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSLT
PGQWKSHRSYSCQVTHEGSTVEKTVAPTECSG

[508] CR6314 VL amino acid sequence (SEQ ID NO: 486)

SYVLTQPPSASGTPGQRVTISCSGSSSNIGSNYVYWYQQLPGTAPKLLIYRDGQRPSGVPDRFS
GSKSGTSASLAISGLRSDDEADYYCATWDDNLSGPVFGGGTKLTVLG

[509] The CR6323 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 489) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 490 and the heavy chain amino acid sequence shown in SEQ ID NO: 491. The CR6323 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 492) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 493 and the light chain amino acid sequence shown in SEQ ID NO: 494.

[510] CR6323 Heavy Chain nucleotide sequence (SEQ ID NO: 490)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc cagggtcctc ggtgaaggtc      60
tcctgtaagg cctctggagg caccttctcc agctatggta tcagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggagac atcatcggta tgtttggttc aacaaactac     180
gcacagaact tccagggcag actcacgatt accgcggacg aatccacgag cacagcctac     240
atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagaagtagt     300
ggttattacc ctgcatacct ccccactgg ggccagggca ccttggtcac cgtctcgagt      360
gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc     420
ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagccgt gaccgtgagc      480
tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc     540
ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc     600
tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc     660
aagagctgcg acaagaccca cacctgcccc ccctgcccctg ccccgagct gctgggcgga     720
ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccccc     780
gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg     840
tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac     900
agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag     960
gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc    1020
aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag    1080
atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc    1140
gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccctgtg     1200
ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg    1260
cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc    1320
cagaagagcc tgagcctgag ccccggcaag                                     1350
```

[511] CR6323 Heavy Chain amino acid sequence (SEQ ID NO: 491)

EVQLVESGAEVKKPGSSVKVSCKASGGTFSSYGISWVRQAPGQGLEWMGDIIGMFGSTNYA
QNFQGRLTITADESTSTAYMELSSLRSEDTAVYYCARSSGYYPAYLPHWGQGTLVTVSSAST
KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV

LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL
HNHYTQKSLSLSPGK

[512] CR6323 VH amino acid sequence (SEQ ID NO: 489)

EVQLVESGAEVKKPGSSVKVSCKASGGTFSSYGISWVRQAPGQGLEWMGDIIGMFGSTNYA
QNFQGRLTITADESTSTAYMELSSLRSEDTAVYYCARSSGYYPAYLPHWGQGTLVTVSS

[513] CR6323 Light Chain nucleotide sequence (SEQ ID NO: 493)

```
gaaattgtgt tgacccagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc      60
ctctcctgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa     120
cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca     180
gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag     240
cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcacccag aactttcggc     300
ggagggacca aggtggagat caaacgtgcg gccgcaccca gcgtgttcat cttcccccca     360
tccgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac     420
ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag     480
gagagcgtga ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctcacc     540
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc     600
ctgagcagcc ccgtgaccaa gagcttcaac cggggcgagt gt                        642
```

[514] CR6323 Light Chain amino acid sequence (SEQ ID NO: 494)

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFS
GSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPRTFGGGTKVEIKRAAAPSVFIFPPSDEQLKSG
TASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKH
KVYACEVTHQGLSSPVTKSFNRGEC

[515] CR6323 VL amino acid sequence (SEQ ID NO: 492)

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFS
GSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPRTFGGGTKVEIKR

[516] The CR6325 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 495) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 496 and the heavy chain amino acid sequence shown in SEQ ID NO: 497. The CR6325 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 498) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 499 and the light chain amino acid sequence shown in SEQ ID NO: 500.

[517] CR6325 Heavy Chain nucleotide sequence (SEQ ID NO: 496)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc cggggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg caccttcagc ttctattcta tgagctgggt gcgacaggcc     120
cctggacaag gacttgagtg gatgggaggg atcatcccta tgtttggtac aacaaactac     180
gcacagaagt tccagggcag agtcacgatt accgcggtcg aatccacgag cacagcctac     240
atggaggtga gcagcctgag atctgaggac acggccgttt attactgtgc gagaggtgat     300
aagggtatct actactacta catggacgtc tggggcaaag ggaccacggt caccgtctcg     360
agtgctagca ccaagggccc cagcgtgttc cccctggccc ccagcagcaa gagcaccagc     420
ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg     480
agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc     540
agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag     600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag     660
cccaagagct gcgacaagac ccacacctgc ccccccctgc ctgcccccga gctgctgggc     720
ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc      780
cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac     840
tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac     900
aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc     960
aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc     1020
agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag     1080
gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac     1140
atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac caccccccct     1200
gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg     1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac     1320
acccagaaga gcctgagcct gagccccggc aag                                  1353
```

[518] CR6325 Heavy Chain amino acid sequence (SEQ ID NO: 497)

EVQLVESGAEVKKPGSSVKVSCKASGGTFSFYSMSWVRQAPGQGLEWMGGIIPMFGTTNYA
QKFQGRVTITAVESTSTAYMEVSSLRSEDTAVYYCARGDKGIYYYYMDVWGKGTTVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

[519] CR6325 VH amino acid sequence (SEQ ID NO: 495)

EVQLVESGAEVKKPGSSVKVSCKASGGTFSFYSMSWVRQAPGQGLEWMGGIIPMFGTTNYA
QKFQGRVTITAVESTSTAYMEVSSLRSEDTAVYYCARGDKGIYYYYMDVWGKGTTVTVSS

[520] CR6325 Light Chain nucleotide sequence (SEQ ID NO: 499)

```
cagtctgccc tgactcagcc tgcctccgtg tctgggtctc ctggacagtc gatcaccatc      60
tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtaccaacag     120
cacccaggca aagccccaa actcatgatt tatgaggtca gtaatcggcc ctcaggggtt      180
tctaatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc     240
caggctgagg acgaggctga ttattactgc agctcatata caagcagcag cactcttgtc     300
ttcggaactg ggaccaaggt caccgtccta ggtgcggccg caggccagcc caaggccgct     360
cccagcgtga ccctgttccc ccctcctcc gaggagctgc aggccaacaa ggccacccctg     420
gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc     480
agccccgtga aggccggcgt ggagaccacc accccagca agcagagcaa caacaagtac      540
gccgccagca gctacctgag cctcacccc gagcagtgga agagccaccg gagctacagc      600
tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggcccccac cgagtgcagc     660
```

[521] CR6325 Light Chain amino acid sequence (SEQ ID NO: 500)

QSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEVSNRPSGVSNR
FSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLVFGTGTKVTVLGAAAGQPKAAPSVTLF
PPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSL
TPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[522] CR6325 VL amino acid sequence (SEQ ID NO: 498)

QSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEVSNRPSGVSNR
FSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLVFGTGTKVTVLG

[523] The CR6327 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 501) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 502 and the heavy chain amino acid sequence shown in SEQ ID NO: 503. The CR6327 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 504) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 505 and the light chain amino acid sequence shown in SEQ ID NO: 506.

[524] CR6327 Heavy Chain nucleotide sequence (SEQ ID NO: 502)

```
gaggtgcagc tggtggagac cggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cctctggagg caccttcagg acccatgcta tcagttgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcgcta tcttcggaac agcaaactac     180
gcacagaagt tccagggcag aatcacgatt accgcggacg aatccacgag tacagcctac     240
atggagctga gcagcctgag atctgaggac acggccgtgt atttctgtgc gagaggcagt     300
ggttatcata tatcgacacc ctttgacaac tggggccagg gaaccctggt caccgtctcg     360
agtgctagca ccaagggccc cagcgtgttc cccctggccc ccagcagcaa gagcaccagc     420
ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg     480
agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc     540
agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag     600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag     660
cccaagagct gcgacaagac ccacacctgc ccccctgcc ctgccccga gctgctgggc      720
ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc      780
cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac     840
tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac     900
aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc     960
aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc     1020
agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag     1080
gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac     1140
atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct      1200
gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg     1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac     1320
acccagaaga gcctgagcct gagccccggc aag                                  1353
```

[525] CR6327 Heavy Chain amino acid sequence (SEQ ID NO: 503)

EVQLVETGAEVKKPGSSVKVSCKASGGTFRTHAISWVRQAPGQGLEWMGGIIAIFGTANYA
QKFQGRITITADESTSTAYMELSSLRSEDTAVYFCARGSGYHISTPFDNWGQGTLVTVSSAST
KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV

LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL
HNHYTQKSLSLSPGK

[526] CR6327 VH amino acid sequence (SEQ ID NO: 501)

EVQLVETGAEVKKPGSSVKVSCKASGGTFRTHAISWVRQAPGQGLEWMGGIIAIFGTANYA
QKFQGRITITADESTSTAYMELSSLRSEDTAVYFCARGSGYHISTPFDNWGQGTLVTVSS

[527] CR6327 Light Chain nucleotide sequence (SEQ ID NO: 505)

```
tcctatgtgc tgactcagcc accctcggtg tcagtggccc caggacagac ggccaggatt      60
acctgtgggg gaaacaacat tggaagtaaa ggtgtgcact ggtaccagca gaagcctggc     120
caggcccctg tgctggtcgt ctatgatgat agcgaccggc cctcagggat ccctgagcga     180
ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg     240
gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgt ggtattcggc     300
ggagggacca agctgaccgt cctaggtgcg gccgcaggcc agcccaaggc cgctcccagc     360
gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc     420
ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc     480
gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc     540
agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag     600
gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc           654
```

[528] CR6327 Light Chain amino acid sequence (SEQ ID NO: 506)

SYVLTQPPSVSVAPGQTARITCGGNNIGSKGVHWYQQKPGQAPVLVVYDDSDRPSGIPERFS
GSNSGNTATLTISRVEAGDEADYYCQVWDSSSDHVVFGGGTKLTVLGAAAGQPKAAPSVTL
FPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSL
TPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[529] CR6327 VL amino acid sequence (SEQ ID NO: 504)

SYVLTQPPSVSVAPGQTARITCGGNNIGSKGVHWYQQKPGQAPVLVVYDDSDRPSGIPERFS
GSNSGNTATLTISRVEAGDEADYYCQVWDSSSDHVVFGGGTKLTVLG

[530] The CR6328 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 507) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 508 and the heavy chain amino acid sequence shown in SEQ ID NO: 509. The CR6328 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 510) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 511 and the light chain amino acid sequence shown in SEQ ID NO: 512.

[531] CR6328 Heavy Chain nucleotide sequence (SEQ ID NO: 508)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggaca catcttcagc ggctatgcaa tcagttgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttggtac aacaaactac     180
gcacagaagt tccagggcag agtcacgatt accgcggacc aatccacgag cacagcctac     240
atggacctga gcaacttgag atctgaggac acggccgtct attactgtgc gagagtgaaa     300
gatggatatt gtactcttac cagctgccct gtcggctggt acttcgatct ctggggccgt     360
ggcaccctgg tcactgtctc gagtgctagc accaagggcc ccagcgtgtt ccccctggcc     420
cccagcagca agagcaccag cggcggcaca gccgccctgg gctgcctggt gaaggactac     480
ttccccgagc ccgtgaccgt gagctggaac agcggcgcct tgaccagcgg cgtgcacacc     540
ttccccgccg tgctgcagag cagcggcctg tacagcctga gcagcgtggt gaccgtgccc     600
agcagcagcc tgggcaccca gacctacatc tgcaacgtga accacaagcc cagcaacacc     660
aaggtggaca aacgcgtgga gcccaagagc tgcgacaaga cccacacctg ccccccctgc     720
cctgcccccg agctgctggg cggaccctcc gtgttcctgt tccccccaa gcccaaggac     780
accctcatga tcagccggac ccccgaggtg acctgcgtgg tggtggacgt gagccacgag     840
gaccccgagg tgaagttcaa ctggtacgtg gacggcgtgg aggtgcacaa cgccaagacc     900
aagccccggg aggagcagta caacagcacc taccgggtgg tgagcgtgct caccgtgctg     960
caccaggact ggctgaacgg caaggagtac aagtgcaagg tgagcaacaa ggccctgcct    1020
gccccatcg agaagaccat cagcaaggcc aagggccagc cccgggagcc ccaggtgtac     1080
accctgcccc ccagccggga ggagatgacc aagaaccagg tgtccctcac ctgtctggtg    1140
aagggcttct accccagcga catcgccgtg gagtgggaga gcaacggcca gcccgagaac    1200
aactacaaga ccacccccc tgtgctggac agcgacggca gcttcttcct gtacagcaag     1260
ctcaccgtgg acaagagccg gtggcagcag ggcaacgtgt tcagctgcag cgtgatgcac    1320
gaggccctgc acaaccacta cacccagaag agcctgagcc tgagccccgg caag          1374
```

[532] CR6328 Heavy Chain amino acid sequence (SEQ ID NO: 509)

EVQLVESGAEVKKPGSSVKVSCKASGHIFSGYAISWVRQAPGQGLEWMGGIIPIFGTTNYAQ
KFQGRVTITADQSTSTAYMDLSNLRSEDTAVYYCARVKDGYCTLTSCPVGWYFDLWGRGTL
VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ
SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPS
VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQ
VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPGK

[533] CR6328 VH amino acid sequence (SEQ ID NO: 507)

EVQLVESGAEVKKPGSSVKVSCKASGHIFSGYAISWVRQAPGQGLEWMGGIIPIFGTTNYAQ
KFQGRVTITADQSTSTAYMDLSNLRSEDTAVYYCARVKDGYCTLTSCPVGWYFDLWGRGTL
VTVSS

[534] CR6328 Light Chain nucleotide sequence (SEQ ID NO: 511)

```
gaaattgtga tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc      60
ctctcgtgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa     120
cctggccagg ctcccaggct cctcatcttt ggtgcctcca gcagggccac tggcatccca     180
gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag     240
cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcactcac tttcggcgga     300
gggaccaagc tggagatcaa acgtgcggcc gcacccagcg tgttcatctt ccccccctcc     360
gacgagcagc tgaagagcgg caccgccagc gtggtgtgcc tgctgaacaa cttctacccc     420
cgggaggcca aggtgcagtg gaaggtggac aacgccctgc agagcggcaa cagccaggag     480
agcgtgaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctcaccctg     540
agcaaggccg actacgagaa gcacaaggtg tacgcctgcg aggtgaccca ccagggcctg     600
agcagccccg tgaccaagag cttcaaccgg ggcgagtgt                             639
```

[535] CR6328 Light Chain amino acid sequence (SEQ ID NO: 512)

EIVMTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIFGASSRATGIPDRFS
GSGSGTDFTLTISRLEPEDFAVYYCQQYGSSLTFGGGTKLEIKRAAAPSVFIFPPSDEQLKSGT
ASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHK
VYACEVTHQGLSSPVTKSFNRGEC

[536] CR6328 VL amino acid sequence (SEQ ID NO: 510)

EIVMTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIFGASSRATGIPDRFS
GSGSGTDFTLTISRLEPEDFAVYYCQQYGSSLTFGGGTKLEIKR

[537] The CR6329 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 513) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 514 and the heavy chain amino acid sequence shown in SEQ ID NO: 515. The CR6329 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 516) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 517 and the light chain amino acid sequence shown in SEQ ID NO: 518.

[538] CR6329 Heavy Chain nucleotide sequence (SEQ ID NO: 514)

```
gaggtccagc tggtacagtc tggggctgag gttaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg catcttcaga agcaattcta tcagttgggt gcgacaggcc     120
cctgggcaag ggcttgagtg gatgggaggg atcttcgctc ttttcggaac aacagactac     180
gcgcagaagt tccagggcag agtcacgatt accgcggacg aatcttcgac cacagtctac     240
ctggagctga gtagcctgac atctgaggac acggccgttt attactgtgc gagaggcagt     300
ggctacacca cacgcaacta ctttgactac tggggccagg gcaccctggt caccgtctcg     360
agtgctagca ccaagggccc cagcgtgttc cccctggccc ccagcagcaa gagcaccagc     420
ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg     480
agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc     540
agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag     600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag     660
cccaagagct gcgacaagac ccacacctgc ccccctgcc ctgccccga gctgctgggc      720
ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc     780
cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac     840
tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac     900
aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc     960
aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc     1020
agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag     1080
gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac     1140
atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac caccccccct     1200
gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg     1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac     1320
acccagaaga gcctgagcct gagccccggc aag                                  1353
```

[539] CR6329 Heavy Chain amino acid sequence (SEQ ID NO: 515)

EVQLVQSGAEVKKPGSSVKVSCKASGGIFRSNSISWVRQAPGQGLEWMGGIFALFGTTDYAQ
KFQGRVTITADESSTTVYLELSSLTSEDTAVYYCARGSGYTTRNYFDYWGQGTLVTVSSAST
KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP

KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL
HNHYTQKSLSLSPGK

[540] CR6329 VH amino acid sequence (SEQ ID NO: 513)

EVQLVQSGAEVKKPGSSVKVSCKASGGIFRSNSISWVRQAPGQGLEWMGGIFALFGTTDYAQ
KFQGRVTITADESSTTVYLELSSLTSEDTAVYYCARGSGYTTRNYFDYWGQGTLVTVSS

[541] CR6329 Light Chain nucleotide sequence (SEQ ID NO: 517)

```
gaaattgtgc tgactcagtc tccaggcacc ctgtctttgt ctccagggga aagagccaca      60
ctctcctgca gggccagtca gagtgttagc agcaactact taggctggta ccagcagaaa     120
cctggccagg ctcccaggct cctgatctat ggtgcatcca gcagggccag tggcatccca     180
gacaggttca gtggcggtgg gtctgggaca gacttcactc tcaccatcag cagactggag     240
cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcaccccc cactttcggc     300
ggagggacca aggtggagat caaacgtgcg gccgcaggcc agcccaaggc cgctcccagc     360
gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc     420
ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc     480
gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc     540
agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag     600
gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc           654
```

[542] CR6329 Light Chain amino acid sequence (SEQ ID NO: 518)

EIVLTQSPGTLSLSPGERATLSCRASQSVSSNYLGWYQQKPGQAPRLLIYGASSRASGIPDRFS
GGGSGTDFTLTISRLEPEDFAVYYCQQYGSSPLTFGGGTKVEIKRAAAGQPKAAPSVTLFPPSS
EELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSLTPEQ
WKSHRSYSCQVTHEGSTVEKTVAPTECS

[543] CR6329 VL amino acid sequence (SEQ ID NO: 516)

EIVLTQSPGTLSLSPGERATLSCRASQSVSSNYLGWYQQKPGQAPRLLIYGASSRASGIPDRFS
GGGSGTDFTLTISRLEPEDFAVYYCQQYGSSPLTFGGGTKVEIKR

[544] The CR6331 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 519) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 520 and the heavy chain amino acid sequence shown in SEQ ID NO: 521. The CR6331 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 522) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 523 and the light chain amino acid sequence shown in SEQ ID NO: 524.

[545] CR6331 Heavy Chain nucleotide sequence (SEQ ID NO: 520)

```
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcggta tgttcggtac agcaaactac     180
gcacagaagt tccagggcag agtcacgatt accgcggacg aatttacgag cacagcctac     240
atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagaggaaat     300
tattactatg agagtagtct cgactactgg ggccagggaa ccctggtcac cgtctcgagt     360
gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc     420
ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc     480
tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc     540
ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc     600
tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc     660
aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga     720
ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccccc     780
gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg     840
tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac     900
agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag     960
gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc    1020
aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag    1080
atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc    1140
gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccccctgtg    1200
ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg    1260
cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc    1320
cagaagagcc tgagcctgag ccccggcaag                                     1350
```

[546] CR6331 Heavy Chain amino acid sequence (SEQ ID NO: 521)

EVQLVESGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIGMFGTANYA
QKFQGRVTITADEFTSTAYMELSSLRSEDTAVYYCARGNYYYESSLDYWGQGTLVTVSSAST
KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL
HNHYTQKSLSLSPGK

[547] CR6331 VH amino acid sequence (SEQ ID NO: 519)

EVQLVESGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIGMFGTANYA
QKFQGRVTITADEFTSTAYMELSSLRSEDTAVYYCARGNYYYESSLDYWGQGTLVTVSS

[548] CR6331 Light Chain nucleotide sequence (SEQ ID NO: 523)

```
cagtctgtcg tgacgcagcc gccctcggtg tcagtggccc caggacagac ggccaggatt      60
acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc     120
caggcccctg tgctggtcgt ctatgatgat agcgaccggc cctcagggat ccctgagcga     180
ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg     240
gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatta tgtcttcgga     300
actgggacca aggtcaccgt cctaggtgcg gccgcaggcc agcccaaggc cgctcccagc     360
gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc     420
ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc     480
gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc     540
agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag     600
gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc           654
```

[549] CR6331 Light Chain amino acid sequence (SEQ ID NO: 524)

QSVVTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPSGIPERFS
GSNSGNTATLTISRVEAGDEADYYCQVWDSSSDHYVFGTGTKVTVLGAAAGQPKAAPSVTL
FPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSL
TPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[550] CR6331 VL amino acid sequence (SEQ ID NO: 522)

QSVVTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPSGIPERFS
GSNSGNTATLTISRVEAGDEADYYCQVWDSSSDHYVFGTGTKVTVLG

[551] The CR6332 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 525) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 526 and the heavy chain amino acid sequence shown in SEQ ID NO: 527. The CR6332 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 528) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 529 and the light chain amino acid sequence shown in SEQ ID NO: 530.

[552] CR6332 Heavy Chain nucleotide sequence (SEQ ID NO: 526)

```
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtaaaggtc      60
tcctgcaagg cttctggagg ccccttccgc aattttgcta tcaactgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcgctg tctttgggac gacaaagtac     180
gcacataagt tccagggcag agtcaccatc accgcggacg actccacaaa tacagcttac     240
atggagctgg gcagcctgaa atctgaggac acggccgtgt attactgtgc gagaggtccc     300
cactactact cctcctacat ggacgtctgg ggcgaaggga ccacggtcac cgtctcgagt     360
gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc     420
ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc     480
tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc     540
ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc     600
tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc     660
aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga     720
ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccccc     780
gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg     840
tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac     900
agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag     960
gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc    1020
aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag    1080
atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc    1140
gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccccctgtg    1200
ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg    1260
cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc    1320
cagaagagcc tgagcctgag ccccggcaag                                     1350
```

[553] CR6332 Heavy Chain amino acid sequence (SEQ ID NO: 527)

QVQLVQSGAEVKKPGSSVKVSCKASGGPFRNFAINWVRQAPGQGLEWMGGIIAVFGTTKYA
HKFQGRVTITADDSTNTAYMELGSLKSEDTAVYYCARGPHYYSSYMDVWGEGTTVTVSSAS
TKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL
SSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK
PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT

VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLSPGK

[554] CR6332 VH amino acid sequence (SEQ ID NO: 525)

QVQLVQSGAEVKKPGSSVKVSCKASGGPFRNFAINWVRQAPGQGLEWMGGIIAVFGTTKYA
HKFQGRVTITADDSTNTAYMELGSLKSEDTAVYYCARGPHYYSSYMDVWGEGTTVTVSS

[555] CR6332 Light Chain nucleotide sequence (SEQ ID NO: 529)

```
gacatccagt tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc      60
atcacttgcc gggcgagtca gggcattagc acttatttag cctggtatca gcagaaaccc     120
gggaaagttc ctaaactcct gatctatgct gcatccactt tgcaatcagg ggtcccatct     180
cggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct     240
gaagatgttg caacttatta ctgtcaaaag tataacagtg ccccttcttt cggccctggg     300
accaaagtgg atatcaaacg tgcggccgca cccagcgtgt tcatcttccc ccctccgac      360
gagcagctga agagcggcac cgccagcgtg gtgtgcctgc tgaacaactt ctaccccgg      420
gaggccaagg tgcagtggaa ggtggacaac gccctgcaga gcggcaacag ccaggagagc     480
gtgaccgagc aggacagcaa ggactccacc tacagcctga gcagcaccct caccctgagc     540
aaggccgact acgagaagca caaggtgtac gcctgcgagg tgacccacca gggcctgagc     600
agccccgtga ccaagagctt caaccggggc gagtgt                               636
```

[556] CR6332 Light Chain amino acid sequence (SEQ ID NO: 530)

DIQLTQSPSSLSASVGDRVTITCRASQGISTYLAWYQQKPGKVPKLLIYAASTLQSGVPSRFSG
SGSGTDFTLTISSLQPEDVATYYCQKYNSAPSFGPGTKVDIKRAAAPSVFIFPPSDEQLKSGTA
SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV
YACEVTHQGLSSPVTKSFNRGEC

[557] CR6332 VL amino acid sequence (SEQ ID NO: 528)

DIQLTQSPSSLSASVGDRVTITCRASQGISTYLAWYQQKPGKVPKLLIYAASTLQSGVPSRFSG
SGSGTDFTLTISSLQPEDVATYYCQKYNSAPSFGPGTKVDIKR

[558] The CR6334 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 531) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 532 and the heavy chain amino acid sequence shown in SEQ ID NO: 533. The CR6334 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 534) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 535 and the light chain amino acid sequence shown in SEQ ID NO: 536.

[559] CR6334 Heavy Chain nucleotide sequence (SEQ ID NO: 532)

```
gaggtgcagc tggtggagac tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
ccctgcaaat cttctggaag ccccttcagg agtaatgctg tcagctgggt gcgacaggcc     120
cccggacaag ggcttgagtg ggtgggagga atcctcggtg tctttggttc accaagctac     180
gcacagaagt tccagggcag agtcacgatt accgcggacg aatccaccaa cacagtccac     240
atggagctga gaggtttgag atctgaggac acggccgtgt attattgtgc gagaggtcct     300
acctactact actcctacat ggacgtctgg ggcaaaggga ccacggtcac cgtctcgagt     360
gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc     420
ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc     480
tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc     540
ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc     600
tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc     660
aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga     720
ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccccc     780
gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg     840
tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac     900
agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag     960
gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc    1020
aaggccaagg gccagccccg ggagccccag gtgtacaccc tgcccccccag ccgggaggag    1080
atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc    1140
gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccccctgtg    1200
ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg    1260
cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc    1320
cagaagagcc tgagcctgag ccccggcaag                                     1350
```

[560] CR6334 Heavy Chain amino acid sequence (SEQ ID NO: 533)

EVQLVETGAEVKKPGSSVKVPCKSSGSPFRSNAVSWVRQAPGQGLEWVGGILGVFGSPSYA
QKFQGRVTITADESTNTVHMELRGLRSEDTAVYYCARGPTYYYSYMDVWGKGTTVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

[561] CR6334 VH amino acid sequence (SEQ ID NO: 531)

EVQLVETGAEVKKPGSSVKVPCKSSGSPFRSNAVSWVRQAPGQGLEWVGGILGVFGSPSYA
QKFQGRVTITADESTNTVHMELRGLRSEDTAVYYCARGPTYYYSYMDVWGKGTTVTVSS

[562] CR6334 Light Chain nucleotide sequence (SEQ ID NO: 535)

```
tcctatgtgc tgactcagcc accctcggag tcagtggccc caggacagac ggccaggatt      60
acctgtgggg gaaataacat tggaagaaat agtgtgcact ggtatcagca gaagccaggc     120
caggcccctg tgctggtcgt gtatgatgat agcgaccggc cctcagggat ccctgagcga     180
ttttctggct ccaagtctgg gaacacggcc accctgatta tcagcagggt cgaagtcggg     240
gatgaggccg actactactg tcaggtgtgg catagtagta gtgatcatta tgtcttcgga     300
actgggacca aggtcaccgt cctaggtgcg gccgcaggcc agcccaaggc cgctcccagc     360
gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc     420
ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc     480
gtgaaggccg gcgtggagac caccacccca agcaagcaga gcaacaacaa gtacgccgcc     540
agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag     600
gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc           654
```

[563] CR6334 Light Chain amino acid sequence (SEQ ID NO: 536)

SYVLTQPPSESVAPGQTARITCGGNNIGRNSVHWYQQKPGQAPVLVVYDDSDRPSGIPERFSG
SKSGNTATLIISRVEVGDEADYYCQVWHSSSDHYVFGTGTKVTVLGAAAGQPKAAPSVTLFP
PSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSLT
PEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[564] CR6334 VL amino acid sequence (SEQ ID NO: 534)

SYVLTQPPSESVAPGQTARITCGGNNIGRNSVHWYQQKPGQAPVLVVYDDSDRPSGIPERFSG
SKSGNTATLIISRVEVGDEADYYCQVWHSSSDHYVFGTGTKVTVLG

[565] The CR6336 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 537) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 538 and the heavy chain amino acid sequence shown in SEQ ID NO: 539. The CR6336 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 540) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 541 and the light chain amino acid sequence shown in SEQ ID NO: 542.

[566] CR6336 Heavy Chain nucleotide sequence (SEQ ID NO: 538)

```
cagatgcagc tggtacaatc tggagctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcttcggta tgtttgggac agcaaactac     180
gcgcagaagt tccagggcag agtcacgatt accgcggacg aattcacgag cgcggcctac     240
atggagctga gcagcctggg atctgaggac acggccatgt attactgtgc gaggtctagt     300
ggttattacc cccaatactt ccaggactgg ggccagggca ccctggtcac cgtctcgagt     360
gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc     420
ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc     480
tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc     540
ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc     600
tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc     660
aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga     720
ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggaccccc     780
gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg     840
tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac     900
agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag     960
gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc    1020
aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag    1080
atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc    1140
gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccctgtg     1200
ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg    1260
cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc    1320
cagaagagcc tgagcctgag ccccggcaag                                     1350
```

[567] CR6336 Heavy Chain amino acid sequence (SEQ ID NO: 539)

QMQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIFGMFGTANY
AQKFQGRVTITADEFTSAAYMELSSLGSEDTAMYYCARSSGYYPQYFQDWGQGTLVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL

TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

[568] CR6336 VH amino acid sequence (SEQ ID NO: 537)

QMQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIFGMFGTANY
AQKFQGRVTITADEFTSAAYMELSSLGSEDTAMYYCARSSGYYPQYFQDWGQGTLVTVSS

[569] CR6336 Light Chain nucleotide sequence (SEQ ID NO: 541)

```
gaaattgtga tgacacagtc tccaggcacc ctgtctttgt ctccagggca aagagccacc      60
ctctcctgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa     120
cctggccagg ctcccagact cctcatgtat ggtgcatcca gcagggccac tggcatccca     180
gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag     240
cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcatcgct cactttcggc     300
ggagggacca agctggagat caaacgtgcg gccgcaccca gcgtgttcat cttccccccc     360
tccgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac     420
ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag     480
gagagcgtga ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctcacc     540
ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc     600
ctgagcagcc ccgtgaccaa gagcttcaac cggggcgagt gt                        642
```

[570] CR6336 Light Chain amino acid sequence (SEQ ID NO: 542)

EIVMTQSPGTLSLSPGQRATLSCRASQSVSSSYLAWYQQKPGQAPRLLMYGASSRATGIPDRF
SGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSSLTFGGGTKLEIKRAAAPSVFIFPPSDEQLKSG
TASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKH
KVYACEVTHQGLSSPVTKSFNRGEC

[571] CR6336 VL amino acid sequence (SEQ ID NO: 540)

EIVMTQSPGTLSLSPGQRATLSCRASQSVSSSYLAWYQQKPGQAPRLLMYGASSRATGIPDRF
SGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSSLTFGGGTKLEIKR

[572] The CR6339 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 543) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 545 and the heavy chain amino acid sequence shown in SEQ ID NO: 546. The CR6339 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 547) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 548 and the light chain amino acid sequence shown in SEQ ID NO: 549.

[573] CR6339 Heavy Chain nucleotide sequence (SEQ ID NO: 545)

```
gaggtgcagc tggtggagtc cggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg catcttcaac agttatgcta tcagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggc atcatcgcta tctttcatac accaaagtac     180
gcacagaagt tccagggcag agtcacgatt accgcggacg aatccacgaa cacagcctac     240
atggaactga gaagcctgaa atctgaggac acggccctgt attactgtgc gagagggtcc     300
acttacgatt tttcgagtgg ccttgactac tggggccagg gaaccctggt caccgtctcg     360
agtgctagca ccaagggccc cagcgtgttc cccctggccc ccagcagcaa gagcaccagc     420
ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg     480
agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc     540
agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag     600
acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag     660
cccaagagct gcgacaagac ccacacctgc cccccctgcc ctgcccccga gctgctgggc     720
ggaccctccg tgttcctgtt ccccccccaag cccaaggaca ccctcatgat cagccggacc     780
cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac     840
tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac     900
aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc     960
aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc    1020
agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag    1080
gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac    1140
atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct     1200
gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg    1260
tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac    1320
acccagaaga gcctgagcct gagccccggc aag                                 1353
```

[574] CR6339 Heavy Chain amino acid sequence (SEQ ID NO: 546)

EVQLVESGAEVKKPGSSVKVSCKASGGIFNSYAISWVRQAPGQGLEWMGGIIAIFHTPKYAQ
KFQGRVTITADESTNTAYMELRSLKSEDTALYYCARGSTYDFSSGLDYWGQGTLVTVSSAST
KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS
SVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

[575] CR6339 VH amino acid sequence (SEQ ID NO: 543)

EVQLVESGAEVKKPGSSVKVSCKASGGIFNSYAISWVRQAPGQGLEWMGGIIAIFHTPKYAQ
KFQGRVTITADESTNTAYMELRSLKSEDTALYYCARGSTYDFSSGLDYWGQGTLVTVSS

[576] CR6339 Light Chain nucleotide sequence (SEQ ID NO: 548)

```
caggcagggc tgactcagcc accctcggtg tcagtggccc caggacagac ggccaggatt      60
acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc     120
caggcccctg tcctagtcgt ctatgatgat agcgaccggc cctcagggat ccctgagcga     180
ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg     240
gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgt ggtattcggc     300
ggagggacca agctgaccgt cctaggtgcg gccgcaggcc agcccaaggc cgctcccagc     360
gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc     420
ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc     480
gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc     540
agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag     600
gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc           654
```

[577] CR6339 Light Chain amino acid sequence (SEQ ID NO: 549)

QAGLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPSGIPERFS
GSNSGNTATLTISRVEAGDEADYYCQVWDSSSDHVVFGGGTKLTVLGAAAGQPKAAPSVTL
FPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSL
TPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[578] CR6339 VL amino acid sequence (SEQ ID NO: 547)

QAGLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPVLVVYDDSDRPSGIPERFS
GSNSGNTATLTISRVEAGDEADYYCQVWDSSSDHVVFGGGTKLTVLG

[579] The CR6342 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 550) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 551 and the heavy chain amino acid sequence shown in SEQ ID NO: 552. The CR6342 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 553) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 554 and the light chain amino acid sequence shown in SEQ ID NO: 555.

[580] CR6342 Heavy Chain nucleotide sequence (SEQ ID NO: 551)

```
caggtccagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagg cttcttcagc agctatgcta tcagctgggt gcgccaggcc     120
cctggacaag gacttgagtg gatgggggag gtcatcccta tctttcgtac agcaaactac     180
gcacagaact tccagggcag agtcaccatt accgcggacg aattcacatc gtatatggag     240
ctgagcagcc tgagatctga cgacacggcc gtgtattact gtgcgaggtt gaattaccat     300
gattcgggga cttattataa cgccccccgg ggctggttcg acccctgggg ccagggaacc     360
ctggtcaccg tctcgagtgc tagcaccaag ggccccagcg tgttccccct ggccccccagc     420
agcaagagca ccagcggcgg cacagccgcc ctgggctgcc tggtgaagga ctacttcccc     480
gagcccgtga ccgtgagctg gaacagcggc gccttgacca gcggcgtgca caccttcccc     540
gccgtgctgc agagcagcgg cctgtacagc ctgagcagcg tggtgaccgt gcccagcagc     600
agcctgggca cccagaccta catctgcaac gtgaaccaca agcccagcaa caccaaggtg     660
gacaaacgcg tggagcccaa gagctgcgac aagacccaca cctgcccccc ctgccctgcc     720
cccgagctgc tgggcggacc ctccgtgttc ctgttccccc ccaagcccaa ggacaccctc     780
atgatcagcc ggacccccga ggtgacctgc gtggtggtgg acgtgagcca cgaggacccc     840
gaggtgaagt tcaactggta cgtggacggc gtggaggtgc acaacgccaa gaccaagccc     900
cgggaggagc agtacaacag cacctaccgg gtggtgagcg tgctcaccgt gctgcaccag     960
gactggctga acggcaagga gtacaagtgc aaggtgagca acaaggccct gcctgccccc    1020
atcgagaaga ccatcagcaa ggccaagggc cagccccggg agccccaggt gtacaccctg    1080
cccccagcc gggaggagat gaccaagaac caggtgtccc tcacctgtct ggtgaagggc    1140
ttctacccca gcgacatcgc cgtggagtgg gagagcaacg gccagcccga gaacaactac    1200
aagaccaccc cccctgtgct ggacagcgac ggcagcttct tcctgtacag caagctcacc    1260
gtggacaaga gccggtggca gcagggcaac gtgttcagct gcagcgtgat gcacgaggcc    1320
ctgcacaacc actacaccca gaagagcctg agcctgagcc ccggcaag                1368
```

[581] CR6342 Heavy Chain amino acid sequence (SEQ ID NO: 552)

QVQLVQSGAEVKKPGSSVKVSCKASGGFFSSYAISWVRQAPGQGLEWMGGVIPIFRTANYA
QNFQGRVTITADEFTSYMELSSLRSDDTAVYYCARLNYHDSGTYYNAPRGWFDPWGQGTLV
TVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS
SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPS

VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQ
VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPGK

[582] CR6342 VH amino acid sequence (SEQ ID NO: 550)

QVQLVQSGAEVKKPGSSVKVSCKASGGFFSSYAISWVRQAPGQGLEWMGGVIPIFRTANYA
QNFQGRVTITADEFTSYMELSSLRSDDTAVYYCARLNYHDSGTYYNAPRGWFDPWGQGTLV
TVSS

[583] CR6342 Light Chain nucleotide sequence (SEQ ID NO: 554)

```
gacatccaga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gaaggccacc      60
atcaactgca agtccagcca gagtatttta aacagctcca acaataagaa ctacttagct     120
tggtaccagc agaaaccagg acagcctcct aagctgctca tttactgggc atctacccgg     180
gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc     240
atcagcagcc tgcaggctga agatgtggca gtttattact gtcagcaata ttatagtagt     300
ccgccgacgt tcggccaagg gaccaaggtg gaaatcaaac gtgcggccgc acccagcgtg     360
ttcatcttcc ccccctccga cgagcagctg aagagcggca ccgccagcgt ggtgtgcctg     420
ctgaacaact tctaccccag ggaggccaag gtgcagtgga aggtggacaa cgccctgcag     480
agcggcaaca gccaggagag cgtgaccgag caggacagca aggactccac ctacagcctg     540
agcagcaccc tcaccctgag caaggccgac tacgagaagc acaaggtgta cgcctgcgag     600
gtgacccacc agggcctgag cagccccgtg accaagagct tcaaccgggg cgagtgt        657
```

[584] CR6342 Light Chain amino acid sequence (SEQ ID NO: 555)

DIQMTQSPDSLAVSLGEKATINCKSSQSILNSSNNKNYLAWYQQKPGQPPKLLIYWASTRESG
VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSSPPTFGQGTKVEIKRAAAPSVFIFPPSD
EQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA
DYEKHKVYACEVTHQGLSSPVTKSFNRGEC

[585] CR6342 VL amino acid sequence (SEQ ID NO: 553)

DIQMTQSPDSLAVSLGEKATINCKSSQSILNSSNNKNYLAWYQQKPGQPPKLLIYWASTRESG
VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSSPPTFGQGTKVEIKR

[586] The CR6343 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 556) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 557 and the heavy chain amino acid sequence shown in SEQ ID NO: 558. The CR6343 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 559) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 560 and the light chain amino acid sequence shown in SEQ ID NO: 561.

[587] CR6343 Heavy Chain nucleotide sequence (SEQ ID NO: 557)

```
caggtccagc tggtgcagtc tggagctgag gtgaagaagc ctgggtcctc ggtgaaggtc      60
tcctgcaagg cttctggagt caccttcagt tactatgcta tgagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggagga atcagcccta tgtttgggac aacaacctac     180
gcacagaagt tccagggcag agtcacgatt actgcggacg actccacgag tacagcctac     240
atggaggtga ggagcctgag atctgaggac acggccgtgt attactgtgc gagatcttcg     300
aattactatg atagtgtata tgactactgg ggccagggaa ccctggtcac cgtctcgagt     360
gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc     420
ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc     480
tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc     540
ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc     600
tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc     660
aagagctgcg acaagaccca cacctgcccc ccctgccctg ccccgagct gctgggcgga     720
ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccc      780
gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg     840
tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac     900
agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag     960
gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc    1020
aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag    1080
atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc    1140
gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccctgtg     1200
ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg    1260
cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc    1320
cagaagagcc tgagcctgag ccccggcaag                                     1350
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[588] CR6343 Heavy Chain amino acid sequence (SEQ ID NO: 558)

QVQLVQSGAEVKKPGSSVKVSCKASGVTFSYYAMSWVRQAPGQGLEWMGGISPMFGTTTY
AQKFQGRVTITADDSTSTAYMEVRSLRSEDTAVYYCARSSNYYDSVYDYWGQGTLVTVSSA
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLSPGK

[589] CR6343 VH amino acid sequence (SEQ ID NO: 556)

QVQLVQSGAEVKKPGSSVKVSCKASGVTFSYYAMSWVRQAPGQGLEWMGGISPMFGTTTY
AQKFQGRVTITADDSTSTAYMEVRSLRSEDTAVYYCARSSNYYDSVYDYWGQGTLVTVSS

[590] CR6343 Light Chain nucleotide sequence (SEQ ID NO: 560)

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cagtctgtcg tgacgcagcc gccctcggag tcagtggccc caggacagac ggccaggatt      60
acctgtgggg gacataacat tggaagtaat agtgtgcact ggtaccagca gaagccaggc     120
caggcccctg tgctggtcgt gtatgataat agcgaccggc cctcagggat ccctgagcga     180
ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg     240
gatgaggccg actattactg tcaggtgtgg ggtagtagta gtgaccatta tgtcttcgga     300
actgggacca aggtcaccgt cctaggtgcg gccgcaggcc agcccaaggc cgctcccagc     360
gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc     420
ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc     480
gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc     540
agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag     600
gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc           654
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[591] CR6343 Light Chain amino acid sequence (SEQ ID NO: 561)

QSVVTQPPSESVAPGQTARITCGGHNIGSNSVHWYQQKPGQAPVLVVYDNSDRPSGIPERFSG
SNSGNTATLTISRVEAGDEADYYCQVWGSSSDHYVFGTGTKVTVLGAAAGQPKAAPSVTLF
PPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSL
TPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[592] CR6343 VL amino acid sequence (SEQ ID NO: 559)

QSVVTQPPSESVAPGQTARITCGGHNIGSNSVHWYQQKPGQAPVLVVYDNSDRPSGIPERFSG
SNSGNTATLTISRVEAGDEADYYCQVWGSSSDHYVFGTGTKVTVLG

[593] The CR6344 HA-specific IgG antibody includes a heavy chain variable region (SEQ ID NO: 562) encoded by the heavy chain nucleotide sequence shown in SEQ ID NO: 563 and the heavy chain amino acid sequence shown in SEQ ID NO: 564. The CR6344 HA-specific IgG antibody also includes a light chain variable region (SEQ ID NO: 565) encoded by the light chain nucleotide sequence shown in SEQ ID NO: 566 and the light chain amino acid sequence shown in SEQ ID NO: 567.

[594] CR6344 Heavy Chain nucleotide sequence (SEQ ID NO: 563)

```
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgagagtc      60
tcctgcaagg cttctggaag catcttcaga aactatgcta tgagctgggt gcgacaggcc     120
cctggacaag ggcttgagtg gatgggaggg atcatcgcta tttttgggac accaaagtac     180
gcacagaagt tccagggcag agtcacgatt accgcggacg aatcgacgag cactgtctac     240
atggaactga gcggactgag atctgaggac acggccatgt attactgtgc gaggattccc     300
cactataatt ttggttcggg gagttatttc gactactggg gccagggaac cctggtcacc     360
gtctcgagtg ctagcaccaa gggccccagc gtgttccccc tggccccccag cagcaagagc     420
accagcggcg gcacagccgc cctgggctgc ctggtgaagg actacttccc cgagcccgtg     480
accgtgagct ggaacagcgg cgccttgacc agcggcgtgc acaccttccc cgccgtgctg     540
cagagcagcg gcctgtacag cctgagcagc gtggtgaccg tgcccagcag cagcctgggc     600
acccagacct acatctgcaa cgtgaaccac aagcccagca acaccaaggt ggacaaacgc     660
gtggagccca agagctgcga caagacccac acctgccccc cctgccctgc ccccgagctg     720
ctgggcggac cctccgtgtt cctgttcccc cccaagccca aggacaccct catgatcagc     780
cggacccccg aggtgacctg cgtggtggtg gacgtgagcc acgaggaccc cgaggtgaag     840
ttcaactggt acgtggacgg cgtggaggtg cacaacgcca agaccaagcc ccgggaggag     900
cagtacaaca gcacctaccg ggtggtgagc gtgctcaccg tgctgcacca ggactggctg     960
aacggcaagg agtacaagtg caaggtgagc aacaaggccc tgcctgcccc catcgagaag    1020
accatcagca aggccaaggg ccagccccgg gagccccagg tgtacaccct gccccccagc    1080
cgggaggaga tgaccaagaa ccaggtgtcc ctcacctgtc tggtgaaggg cttctacccc    1140
agcgacatcg ccgtggagtg ggagagcaac ggccagcccg agaacaacta caagaccacc    1200
cccctgtgc tggacagcga cggcagcttc ttcctgtaca gcaagctcac cgtggacaag    1260
agccggtggc agcagggcaa cgtgttcagc tgcagcgtga tgcacgaggc cctgcacaac    1320
cactacaccc agaagagcct gagcctgagc cccggcaag                           1359
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[595] CR6344 Heavy Chain amino acid sequence (SEQ ID NO: 564)

QVQLVQSGAEVKKPGSSVRVSCKASGSIFRNYAMSWVRQAPGQGLEWMGGIIAIFGTPKYA
QKFQGRVTITADESTSTVYMELSGLRSEDTAMYYCARIPHYNFGSGSYFDYWGQGTLVTVSS
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY
SLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFP
PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV

LTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM
HEALHNHYTQKSLSLSPGK

[596] CR6344 VH amino acid sequence (SEQ ID NO: 562)

QVQLVQSGAEVKKPGSSVRVSCKASGSIFRNYAMSWVRQAPGQGLEWMGGIIAIFGTPKYA
QKFQGRVTITADESTSTVYMELSGLRSEDTAMYYCARIPHYNFGSGSYFDYWGQGTLVTVSS

[597] CR6344 Light Chain nucleotide sequence (SEQ ID NO: 566)

```
actgtgttga cacagccgcc ctcagtgtct ggggccccag ggcagagggt caccatctcc     60
tgcactggga gcagctccaa catcggggca ggttatgatg tacactggta ccagcagctt    120
ccaggaacag cccccaaact cctcatctat ggtaacagca atcggccctc aggggtccct    180
gaccgattct ctggctccaa gtctggcacg tcagccaccc tgggcatcac cggactccag    240
actggggacg aggccgatta ttactgcgga acatgggata gcagcctgag tgcttatgtc    300
ttcggaactg ggaccaaggt caccgtccta ggtgcggccg caggccagcc caaggccgct    360
cccagcgtga ccctgttccc cccctcctcc gaggagctgc aggccaacaa ggccacccta    420
gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc    480
agccccgtga aggccggcgt ggagaccacc accccagca agcagagcaa caacaagtac    540
gccgccagca gctacctgag cctcacccgc gagcagtgga agagccaccg gagctacagc    600
tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggccccac cgagtgcagc     660
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[598] CR6344 Light Chain amino acid sequence (SEQ ID NO: 567)

TVLTQPPSVSGAPGQRVTISCTGSSSNIGAGYDVHWYQQLPGTAPKLLIYGNSNRPSGVPDRF
SGSKSGTSATLGITGLQTGDEADYYCGTWDSSLSAYVFGTGTKVTVLGAAAGQPKAAPSVT
LFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLS
LTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

[599] CR6344 VL amino acid sequence (SEQ ID NO: 565)

TVLTQPPSVSGAPGQRVTISCTGSSSNIGAGYDVHWYQQLPGTAPKLLIYGNSNRPSGVPDRF
SGSKSGTSATLGITGLQTGDEADYYCGTWDSSLSAYVFGTGTKVTVLG

HA antibody epitopes

[600] The invention relates to an isolated human HA antibody that is able to recognize and bind to an epitope in the HA2 subunit of the influenza haemagglutinin protein (HA) (also known as hemagglutinin(HA)), characterized in that the HA antibody has neutralizing activity against an influenza virus 5 including HA of the H5 subtype. Examples of influenza strains that contain such a HA of the H5 subtype and that are important strains in view of pandemic threats are H5N1, H5N2, H5N8, and H5N9. Particularly preferred are HA antibodies that at least neutralize the H5N1 influenza strain. Preferably, an HA antibody of the invention does not depend on an epitope in the HA1 subunit of the HA protein for binding to said HA protein.

[601] A number of the antibodies of the invention (such as CR6307 and CR6323) do not depend on conformational epitopes and recognize the HA2 epitope even in a reduced form (when used in western-blotting). This is an advantage over the antibodies from the art

because when a conformational change is induced in the HA protein due to whatever mutation in another part of the protein, such conformational change will not most likely hamper the binding of the antibodies of the present invention to the HA2 epitope, whereas antibodies that do depend on conformation might very well be unable to bind when such mutations occur.

[602] In another preferred embodiment, an HA antibody of the invention also has neutralizing activity against an influenza virus comprising HA of the H1 subtype, and preferably wherein the HA antibody also has neutralizing activity against influenza virus comprising HA of the H2, H6 and/or H9 subtype. The HA antibodies of the invention interact with an epitope present in the HA2 epitopes present in the H5, HI, H2, H6, and H9 subtypes (see, International Patent Application PCT/EP2007/059356, published as WO 2008/028946, the contents of which are incorporated by reference in their entirety), and it has been shown that the HA antibodies of the invention cross-neutralize between influenza subtypes because of this epitope-sharing.

[603] In another preferred aspect of the invention an HA antibody of the invention binds to an epitope that is selected from the group consisting of the amino acid sequence: GVTNKVNSIIDK (SEQ ID NO: 198), GVTNKVNSIINK (SEQ ID NO: 283), GVTNKENSIIDK (SEQ ID NO: 202), GVTNKVNRIIDK (SEQ ID NO: 201), GITNKVNSVIEK (SEQ ID NO: 281), GITNKENSVIEK (SEQ ID NO: 257), GITNKVNSIIDK (SEQ ID NO: 225), and KITSKVNNIVDK (SEQ ID NO: 216). Certain HA antibodies of the invention, CR6261, CR6325, and CR6329 interact with the GVTNKVNSIIDK (SEQ ID NO: 198) epitope present in H5N1, and are not hampered by a mutation in the TGLRN (SEQ ID NO: 200) epitope in HA1 that do influence the binding of C179. Moreover, some HA antibodies, such as CR6307 and CR6323 are not even hampered by a escape mutant, as disclosed in Okuno et al. (1993) with a valine -> glutamic acid mutation at position 6 (exemplified by GVTNKENSIIDK (SEQ ID NO: 202)). This epitope is part of an extended alpha helix in the HA2 region. The residues in this putative epitope that are predicted to be most solvent exposed are underlined in bold: GV-TNKENSIIDK (SEQ ID NO: 202). These amino acids would be most accessible to an HA antibody and thus may form the most important region of the epitope. Consistent with this notion the highlighted (bolded) amino acids are absolutely conserved in identity and position in all the sequences presented. This knowledge could be used to predict binding epitopes in influenza subtypes that do not carry the same sequence as above (i.e. H3, H7 and B strains).

HA Antibodies II

[604] The invention provides neutralizing human monoclonal antibodies that bind influenza A virus and inhibit the influenza A virus from infecting a cell. Although neutralizing human monoclonal antibodies of the invention bind epitopes within proteins that are exposed on the surface of an influenza virus, the invention focuses on the relatively invariant Influenza hemagglutinin (HA) protein. A neutralizing MAb raised against an Influenza HA protein, which is maintained in its native conformation, provides a superior therapy for all Influenza A strains because it is not dependent upon small changes to the amino acid sequence.

[605] The Influenza hemagglutinin (HA) protein is responsible for allowing the virus to recognize target cells through binding the monosaccharide sialic acid-containing receptors on the surface of the target cell prior to infection. Moreover, the Influenza HA protein is responsible for allowing entry of the viral genome into the target cell by fusing the host endosomal membrane with the viral membrane.

[606] The Influenza hemagglutinin (HA) protein is a homotrimeric integral membrane glycoprotein found on the surface of the Influenza virus. Using the host cell's protein synthesis machinery, the Influenza HA protein is first synthesized as a single-chain precursor polypeptide (HA0) in the endoplasmic reticulum, where it is also assembled as a homotrimer. The resulting HA homotrimer is subsequently exported to the cell surface via the Golgi network. HA homotrimers located on a cell surface are cleaved by a host-produced protease into two smaller peptide subunits: HA1 and HA2. The HA2 subunit forms a long helical chain anchored to the viral membrane whereas the HA1 subunit tops the HA2 subunit to form a large globule. The cleavage step, which converts the HA0 precursor into the mature HA protein containing HA1 and HA2 subunits, is essential for the viral pathogenicity of Influenza. Structurally, the mature HA protein contains a central α-helix coil resulting in an overall cylindrical shape with three spherical heads. The HA protein, and specifically, the HA1 subunit of the mature HA protein, binds receptors containing glycans with terminal sialic acids on host cells. The way in which sialic acid is connected to galactose, for example, α2-3 linkages as in avian serotypes versus α2-6 linkages as in human serotypes, not only determine species specificity of an Influenza virus, but also prevents cross-species infection. However, within certain serotypes of HA, such as H1 and H3, only two amino acid mutations in the framework sequence are required to convert species specificity from avian to human.

[607] To mediate infection, the Influenza HA protein first binds sialic acid-containing receptors present on the surface of the target cell. Consequently, the target cell membrane endocytoses or engulfs the Influenza virus. Once inside the endosome, and upon the host cell's acidification of that compartment, the Influenza HA protein partially unfolds revealing a very hydrophobic fusion peptide that inserts itself into the endosomal membrane. As the rest of the Influenza HA protein refolds, the fusion protein retracts and fuses the endosomal membrane with the viral membrane. Upon fusion of the cellular and viral membranes, the contents of the virus, including the viral genome, are released in the cytoplasm of the target cell.

[608] At least 16 different Influenza A hemagglutinin serotypes or antigens have been identified: H1-H16. Only HA serotypes H1-H3 normally mediate human Influenza infection. However, Influenza strains thought to infect only certain avian or mammalian species can mutate to infect humans. As described above, only a few amino acids need to change along the length of the entire protein to enable Influenza to cross a species barrier. For instance, a single amino acid change in the sequence of the H5 subtype allowed an avian-specific Influenza strain to become infectious in humans (H5N1). A pandemic arose when an Influenza strain common to swine species, became lethal to humans (H1N1). In contrast to Influenza A, Influenza B and C viruses each contain only one form of HA protein.

[609] Specifically, the invention provides an isolated fully human monoclonal antibody, wherein said monoclonal antibody has the following characteristics: a) binds to an influenza A virus; b) binds to a cell contacted with influenza A; c) binds to an epitope of an influenza A viral protein; and, optionally, d) neutralizes influenza A virus infection. An antibody that does not neutralize influenza A virus infection may be used, for instance, for a conjugate therapy. In certain aspects, this antibody binds to a eukaryotic cell. Moreover, the cell is optionally a human cell.

[610] In another aspect, this antibody is isolated from a B-cell from a human donor. Isolation of a fully human monoclonal antibody of the invention from a B-cell is performed using recombinant methods. Alternatively, or in addition, the isolated fully human monoclonal antibody of the invention is isolated from the supernatant of a plasma cell cultured either in vitro or ex vivo. Plasma cells also known as a differentiated B-cells, plasma B-cells, plasmacytes, or effector B-cells. The fully human monoclonal antibody isolated from either a B-cell or a plasma cell demonstrates neutralizing activity.

[611] Antibodies of the invention bind to an epitope of influenza A viral hemagglutinin (HA) protein. Exemplary HA epitopes to which the antibodies of the invention bind include a hemagglutinin precursor peptide (HA0), a HA1 subunit, a HA2 subunit, a mature protein containing HA1 and HA2, and a recombinant HA polypeptide. Alternatively, antibodies of the invention bind to an epitope within a hemagglutinin precursor peptide (HA0), a HA1 subunit, a HA2 subunit, a mature protein containing HA1 and HA2, or a recombinant HA polypeptide. Recombinant HA polypeptides are encoded, for example, by the sequence of SEQ ID NO: 727, 728, 729, 730, 731, 732, 733, 734, 735, 736, 737, 738, 739, 740, 741, 742, 743, or 744.

[612] Antibodies of the invention bind to an epitope that is linear or non-linear. In certain aspects of the invention, a non-linear epitope is a discontinuous epitope.

[613] An antibody of the invention is TCN-522 (3212_I12), TCN-521 (3280_D18), TCN-523 (5248_A17), TCN-563 (5237_B21), TCN-526 (5084_C17), TCN-527 (5086_C06), TCN-528 (5087_P17), TCN-529 (5297_H01), TCN-530 (5248_H10a), TCN-531 (5091_H13), TCN-532 (5262_H18), TCN-533 (5256_A17), TCN-534 (5249_B02), TCN-535 (5246_P19), TCN-536 (5095_N01), TCN-537 (3194_D21), TCN-538 (3206_O17), TCN-539 (5056_A08), TCN-540 (5060_F05), TCN-541 (5062_M11), TCN-542 (5079_A16), TCN-543 (5081_G23), TCN-544 (5082_A19), TCN-545 (5082_I15), TCN-546 (5089_L08), TCN-547 (5092_F11), TCN-548 (5092_P01), TCN-549 (5092_P04), TCN-550 (5096_F06), TCN-551 (5243_D01), TCN-552 (5249_I23), TCN-553 (5261_C18), TCN-554 (5277_M05), TCN-555 (5246_L16), TCN-556 (5089_K12), TCN-557 (5081_A04), TCN-558 (5248_H10b), TCN-559 (5097_G08), TCN-560 (5084_P10), or TCN-504 (3251_K17).

[614] The invention further encompasses an antibody that binds the same epitope as TCN-522 (3212_I12), TCN-521 (3280_D18), TCN-523 (5248_A17), TCN-563 (5237_B21), TCN-526 (5084_C17), TCN-527 (5086_C06), TCN-528 (5087_P17), TCN-529 (5297_H01), TCN-530 (5248_H10a), TCN-531 (5091_H13), TCN-532 (5262_H18), TCN-533 (5256_A17), TCN-534 (5249_B02), TCN-535 (5246_P19), TCN-536 (5095_N01), TCN-537 (3194_D21), TCN-538 (3206_O17), TCN-539 (5056_A08), TCN-540 (5060_F05), TCN-541 (5062_M11), TCN-542 (5079_A16), TCN-543 (5081_G23), TCN-544 (5082_A19), TCN-545 (5082_I15), TCN-546 (5089_L08), TCN-547 (5092_F11), TCN-548 (5092_P01), TCN-549 (5092_P04), TCN-550 (5096_F06), TCN-551 (5243_D01), TCN-552 (5249_I23), TCN-553 (5261_C18), TCN-554 (5277_M05), TCN-555 (5246_L16), TCN-556 (5089_K12),

TCN-557 (5081_A04), TCN-558 (5248_H10b), TCN-559 (5097_G08), TCN-560 (5084_P10), or TCN-504 (3251_K17).

[615] The invention provides an isolated fully human monoclonal anti-HA antibody or fragment thereof, wherein said antibody includes a variable heavy chain (V_H) region comprising CDR1 and CDR2, wherein the V_H region is encoded by a human IGHV1 (or specifically, IGHV1-18, IGHV1-2, IGHV1-69, IGHV1-8), IGHV2 (or specifically, IGHV2-5) , IGHV3 (or specifically, IGHV3-30, IGHV3-33, IGHV3-49, IGHV3-53, 66, IGHV3-7), IGHV4 (or specifically, IGHV4-31, IGHV4-34, IGHV4-39, IGHV4-59, IGHV4-61), or IGHV5 (or specifically, IGHV5-51) V_H germline sequence or an allele thereof, or a nucleic acid sequence that is homologous to the IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 V_H germline gene sequence or an allele thereof. In one aspect, the nucleic acid sequence that is homologous to the IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 V_H germline sequence is at least 75% homologous to the IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 V_H germline sequence or an allele thereof. Exemplary alleles include, but are not limited to, IGHV1-18*01, IGHV1-2*02, IGHV1-2*04, IGHV1-69*01, IGHV1-69*05, IGHV1-69*06, IGHV1-69*12, IGHV1-8*01, IGHV2-5*10, IGHV3-30-3*01, IGHV3-30*03, IGHV3-30*18, IGHV3-33*05, IGHV3-49*04, IGHV3-53*01, IGHV3-66*03, IGHV3-7*01, IGHV4-31*03, IGHV4-31*06, IGHV4-34*01, IGHV4-34*02, IGHV4-34*03, IGHV4-34*12, IGHV4-39*01, IGHV4-59*01, IGHV4-59*03, IGHV4-61*01, IGHV4-61*08, and IGHV5-51*01.

[616] An antibody of the invention, or specifically, any antibody described herein, may be operably-linked to a therapeutic agent or a detectable label.

[617] The invention further provides a pharmaceutical composition including an antibody described herein and a pharmaceutical carrier. This composition optionally includes an anti-viral drug, a viral entry inhibitor or a viral attachment inhibitor. Exemplary anti-viral drugs include, but are not limited to, a neuraminidase inhibitor, a HA inhibitor, a sialic acid inhibitor and an M2 ion channel inhibitor. In one embodiment of the composition, the M2 ion channel inhibitor is amantadine or rimantadine. Alternatively, or in addition, the neuraminidase inhibitor zanamivir or oseltamivir phosphate. The composition may also include a second anti-Influenza A antibody. The second anti-Influenza A antibody is optionally an antibody described herein.

[618] The invention provides a method for stimulating an immune response in a subject, including administering to the subject the pharmaceutical composition described herein.

[619] Moreover, the invention provides a method for the treatment of an Influenza virus infection in a subject, including administering to the subject the pharmaceutical composition described herein. This method further includes administering an anti-viral drug, a viral entry inhibitor or a viral attachment inhibitor.

[620] The invention also provides a method for the prevention of an Influenza virus infection in a subject, including administering to the subject the pharmaceutical composition described herein prior to exposure of the subject to Influenza virus or infection. This method further includes administering an anti-viral drug, a viral entry inhibitor or a viral attachment inhibitor. This method may be a method of vaccination.

[621] The subject of these methods may have an Influenza infection or is predisposed to developing an Influenza virus infection. Subjects predisposed to developing an Influenza infection, or who may be at elevated risk for contracting an infection, are those subjects with compromised immune systems because of autoimmune disease, those persons receiving immunosuppressive therapy (for example, following organ transplant), those persons afflicted with human immunodeficiency syndrome (HIV) or acquired immune deficiency syndrome (AIDS), certain forms of anemia that deplete or destroy white blood cells, those persons receiving radiation or chemotherapy, or those persons afflicted with an inflammatory disorder. Additionally, subject of extreme young or old age are at increased risk. Any person who comes into physical contact or close physical proximity with an infected individual has an increased risk of developing an Influenza virus infection. Moreover, a subject is at risk of contracting an influenza infection due to proximity to an outbreak of the disease, e.g. subject resides in a densely-populated city or in close proximity to subjects having confirmed or suspected infections of Influenza virus, or choice of employment, *e.g.* hospital worker, pharmaceutical researcher, traveler to infected area, or frequent flier.

[622] According to the methods described herein, exemplary anti-viral drugs include, but are not limited to, a neuraminidase inhibitor, a HA inhibitor, a sialic acid inhibitor and an M2 ion channel. In one aspect of these methods, the M2 ion channel inhibitor is amantadine or rimantadine. Alternatively, or in addition, the neuraminidase inhibitor is zanamivir or oseltamivir phosphate.

[623] These methods optionally include administering a second anti-Influenza A antibody. For example, the antibody is administered prior to or after exposure to Influenza virus. In certain aspects of these methods, the antibody is administered at a dose sufficient to promote

viral clearance or to eliminate Influenza A infected cells. The second antibody is optionally an antibody described herein

[624] The invention further provides a method for determining the presence of a Influenza virus infection in a subject, including the steps of: (a) contacting a biological sample obtained from the subject with an antibody described herein or the pharmaceutical composition described herein; (b) detecting an amount of the antibody that binds to the biological sample; and (c) comparing the amount of antibody that binds to the biological sample to a control value, and therefrom determining the presence of the Influenza virus in the subject.

[625] The invention provides a vaccine composition including an antibody described herein. This composition optionally contains a pharmaceutical carrier.

[626] Alternatively, the invention provides a vaccine composition including an epitope of an antibody described herein. This composition optionally contains a pharmaceutical carrier.

[627] Vaccines of the invention are multivalent vaccines. The term "multivalent vaccine" is meant to describe a single vaccine that elicits an immune response either to more than one infectious agent, *e.g.* recombinant homotrimeric HA0 proteins or fragments thereof derived from multiple strains of Influenza A (see, Table 9), or to several different epitopes of a molecule, *e.g.* a linear and a discontinuous epitope of the same recombinant homotrimeric HA0 protein or fragment thereof derived from a single strain of Influenza A. Alternatively, or in addition, the term multivalent vaccine is meant to describe the administration of a combination of human antibodies raised against more than one infectious agent, *e.g.* a combination of HuMHA antibodies raised against recombinant homotrimeric HA0 proteins or fragments thereof derived from multiple strains of Influenza A (see, Table 9).

[628] The invention provides a diagnostic kit including an antibody described herein.

[629] The invention provides a prophylactic kit including an antibody described herein or an epitope of an antibody described herein. Alternatively, or in addition, the invention provides a prophylactic kit including a vaccine composition described herein.

[630] In a preferred embodiment, the present invention provides fully human monoclonal antibodies specifically directed against the Influenza hemagglutinin glycoprotein, which neutralize influenza infection. Optionally, the antibody is isolated from a B-cell from a mammalian donor, and preferably, a human donor. In certain embodiments of the invention, the antibody is identified for its ability to bind an intact or whole Influenza virus. Alternatively, or in addition, the antibody is identified isolated for its ability to bind to an epitope of a recombinant homotrimeric Influenza HA0 protein or HA protein(s) isolated from

multiple Influenza strains, or made as recombinant proteins such as those influenza A virus strains provided in Table 9. Alternatively, or in addition, the antibody is identified for its ability to inhibit or neutralize virus infection of susceptible eukaryotic cells. Exemplary neutralizing antibodies of this profile include, but are not limited to, those antibodies listed in Table 10. Alternatively, the monoclonal antibody is an antibody that binds to the same epitope as the antibodies provided in Table 10. In certain embodiments, neutralizing human monoclonal antibodies of the invention are anti-HA antibodies. A monoclonal anti-HA antibody of the invention has one or more of the following characteristics: a) binds to an epitope in an HA1 subunit of an Influenza hemagglutinin (HA) protein; b) binds to an epitope in the HA2 subunit of Influenza hemagglutinin (HA) protein; c) binds to an epitope in the extracellular domain of an Influenza hemagglutinin (HA) protein, consisting of an HA1 subunit and an HA2 subunit; d) binds to an epitope of a recombinant homotrimeric Influenza HA0 protein; e) binds to an epitope of an Influenza HA protein expressed on an infected cell; f) binds to an epitope of an Influenza HA protein expressed on a modified cell; g) binds to an Influenza virus; or h) inhibits virus infection of susceptible eukaryotic cells.

[631] Modified cells of the invention are transfected or transformed with a polynucleotide that encodes an Influenza HA protein, or any fragment thereof. The term "Influenza HA protein fragment" is meant to describe any portion of the protein that is smaller or less than the entire protein. Polynucleotides and polypeptides of the invention do not always encode a functional Influenza HA protein.

[632] Infected cells of the invention are mammalian, and preferably human in origin. Specifically, mammalian cells are infected with Influenza A virus in vivo, in vitro, in situ, ex vivo, in culture, and any combination thereof. Cells are infected with active or inactive virions. Exemplary inactive virions display the HA protein on their surfaces, however, they are replication-defective, and therefore, unable to propagate within the cell or subject.

[633] Epitopes of the human monoclonal antibodies of the invention include a transmembrane or integral membrane Influenza A protein. Specifically, epitopes of the human monoclonal antibodies of the invention comprise Influenza hemagglutinin (HA) protein.

[634] Epitopes of the human monoclonal antibodies of the invention include one or more subunits of an influenza hemagglutinin (HA) protein. HA proteins of the invention include hemagglutinin precursor proteins (HA0), the HA1 subunit, the HA2 subunit, the mature protein containing the HA1 and HA2 subunits, and a recombinant HA protein. Recombinant

HA proteins contain SEQ ID NO: 726. Exemplary recombinant proteins include but, are not limited to, those proteins described by SEQ ID NO: 727-744.

[635] Epitopes of the human monoclonal antibodies of the invention are linear or non-linear. For instance, a non-linear epitope is discontinuous. Discontinuous epitopes are available for antibody binding only when the Influenza HA protein is maintained in its native homotrimeric conformation. When an antibody binds to a discontinuous epitope, the antibody binds to a three-dimensional surface of the target protein, *i.e.* the Influenza HA protein, upon which juxtaposed amino acids are alternatively exposed or masked.

[636] Recombinant homotrimeric HA0 proteins of the invention are encoded by, for instance, sequences described by any one of SEQ ID NO: 727-744. In certain embodiments of the invention, the human monoclonal antibodies, or monoclonal anti-HA antibodies, described herein bind membrane-bound *or* soluble recombinant homotrimeric Influenza HA proteins. Alternatively, the monoclonal anti-HA antibodies described herein bind membrane-bound *and* soluble recombinant homotrimeric Influenza HA proteins. In certain embodiments of the invention, the monoclonal anti-HA antibodies described herein bind and neutralize Influenza virus subtypes H1, H2, and H3. In other embodiments of the invention, the monoclonal anti-HA antibodies bind Influenza virus subtypes H1, H2, and H3, and neutralize one of these subtypes, such as H1, H2, or H3. In a specific embodiment, the monoclonal anti-HA antibodies bind Influenza subtypes H1N1, H2N2, and H3N2, and neutralize H1N1.

[637] In one aspect, the HA precursor polypeptide (HA0) of the soluble and recombinant homotrimeric Influenza HA protein contains a trimerization domain (foldon) encoded in the phage T4 fibritin. An exemplary trimerization domain isolated from the phage T4 fibritin has the following sequence wherein a thrombin cleavage site is italicized and bolded, a T4 trimerization domain or sequence is underlined, a V5 tag is boxed, and a hexa-histidine (His) tag is bolded:

SGR***LVPRGS***PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLGLDSTG**HHH HHH** (SEQ ID NO: 726).

[638] As used herein, the term "neutralizing antibody" is meant to describe an antibody that inhibits or prevents influenza A infection, inhibits or prevents Influenza A viral entry into a cell, inhibits or prevents influenza replication, inhibits or prevents influenza egress from a host cell, or reduces the Influenza A titer in a cell, biological sample, or subject. In a preferred embodiment, neutralizing antibodies of the invention prevent viral entry into the cytoplasmic compartment of host cells.

[639] The present invention provides fully human monoclonal antibodies that bind influenza virus and neutralize infection. In certain embodiments, the present invention provides fully human monoclonal neutralizing antibodies specific against the Influenza hemagglutinin protein. The antibodies are respectively referred to herein is human monoclonal anti-HA (huMHA) antibodies.

[640] The Influenza hemagglutinin (HA) protein is a homotrimeric integral membrane glycoprotein found on the surface of the Influenza virus. To mimic the native conformation of this homotrimeric protein, the methods of the invention provide an isolated HA protein precursor that is operably-linked to a trimerization or foldon domain from the phage T4 fibritin protein

(SGR***LVPRGS***PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLGLDSTG**HHH HHH** (SEQ ID NO: 726)).

[641] The resultant recombinant homotrimeric foldon HA protein not only retains the native Influenza hemagglutinin homotrimeric conformation, but also becomes soluble, *i.e.* the protein is no longer bound to a viral or cellular membrane. Specifically, these recombinant HA homotrimeric proteins lack an integral membrane or transmembrane domain. In certain embodiments, these recombinant HA homotrimeric proteins include HA1 and HA2 subunits as well as a trimerization domain, the resultant recombinant HA homotrimeric protein containing between 1-50, 50-100, 100-150, 150-200, 200-250, 250-300, 300-350, 350-400, 400-450, 450-500,500-550, 550-600 amino acids (aa) or any length of amino acids in between. Preferably, these recombinant HA homotrimeric proteins contain between 565-575 amino acids (aa). Recombinant HA homotrimeric proteins further include a signal cleavage site at the N-terminus containing between 15-25 aa. Alternatively, or in addition, recombinant HA homotrimeric proteins further include a transmembrane domain positioned between amino acids 525-535 of HA depending on the influenza A virus subtype. In a preferred embodiment, the HA protein is derived from one or more strains of an Influenza A virus. Recombinant HA homotrimeric proteins of the invention retain the native signal sequence to enable secretion. Moreover, recombinant HA homotrimeric proteins of the invention contain a same signal sequence, which is not derived from HA. Futhermore, signal sequences used with recombinant HA homotrimeric proteins of the invention include those signal sequences known in the art that allow efficient secretion of proteins, such as the signal sequence of the immunoglobulin light kappa chain. Alternatively, recombinant HA homotrimeric proteins, or the HA0 precursors thereof, may have the native signal sequences in the expression

constructs used by Immune Technology Corp. (http://www.immune-tech.com/). Signal sequences are retained or manipultated to allow efficient secretion from, for instance, art-recognized cell lines maintained in vitro, *e.g.* 293 HEK cells.

[642] Recombinant HA homotrimeric proteins may retain a native HA1/HA2 protease cleavage site, which is critical for viral pathogenicity. In one aspect of the invention, recombinant HA homotrimeric proteins contain a substituted HA1/HA2 protease cleavage site. For example, the recombinant HA protein encoded by SEQ ID NO: 737 does not have a native cleavage site, but rather a cleavage site substituted from another HA protein. Furthermore, these proteins optionally retain sialic acid-containing receptor binding sites within the HA1 subunit.

[643] According to the methods of the invention, human antibodies obtained from blood, serum, plasma, or cerebral spinal fluid, are contacted to recombinant and soluble HA homotrimers of the invention *in vitro*, wherein the recombinant and soluble HA homotrimers act as targets for human antibody binding to confirm specificity of the isolated human antibody for an Influenza HA homotrimer in its native conformation. In general, the methods include obtaining serum or plasma samples from subjects or patients that have been infected with or vaccinated against an infectious agent. These serum or plasma samples are then screened to identify those that contain antibodies specific for a particular polypeptide associated with the infectious agent, such as, *e.g.* a polypeptide specifically expressed on the surface of cells infected with the infectious agent, but not uninfected cells. In particular embodiments, the serum or plasma samples are screened by contacting the samples with a cell that has been transfected with an expression vector that expresses the polypeptide expressed on the surface of infected cells. In particular embodiments the serum or plasma samples are screened by contacting the samples with a recombinant protein which represents a particular protein of the infectious agent such as, *e.g.* hemagglutinin of the influenza A virus. In particular embodiments the serum or plasma samples are screened by contacting the samples with a purified form of the infectious agent such as, *e.g.* intact whole virions of the influenza A virus. In particular embodiments, the serum or plasma samples are screened by contacting the samples with a live form of the infectious agent such as, *e.g.* intact whole virions of the influenza A virus to determine the presence of serum antibodies that inhibit or neutralize infection of susceptible cells. Exemplary susceptible cells are eukaryotic or mammalian cells, such as MDCK cells.

[644] Once a subject or patient is identified as having serum or plasma containing an antibody specific for the infectious agent polypeptide or virus of interest, mononuclear and/or B cells obtained from the same subject or patient are used to identify a cell or clone thereof that produces the antibody, using any of the methods described herein or available in the art. Once a B cell that produces the antibody is identified, cDNAs encoding the variable regions or fragments thereof of the antibody may be cloned using standard RT-PCR vectors and primers specific for conserved antibody sequences, and subcloned into expression vectors used for the recombinant production of monoclonal antibodies specific for the infectious agent polypeptide of interest.

[645] More specifically, B cells are collected from a particular donor, *i.e.* a subject or patient is identified as having serum or plasma containing an antibody specific for HA, cultured, and antibody is secreted from these B cells into the culture medium. The culture medium is separated from these B cells, the B cells are lysed, and then frozen for storage. The culture medium is then screened for antibody binding to various HA targets and/or inhibition/neutralization of infection *in vitro*. When a culture well is identified as having an antibody of the desired specificity, reverse-transcriptase polymerase chain reaction (RT-PCR) is applied to the B-cell lysate to amplify the antibody variable regions and subsequently clone, express, and test for binding and function of the recombinant antibody,

[646] Human antibodies, such as the MAbs listed in Table 10, which bind the recombinant and soluble HA homotrimer and/or bind whole virions, and optionally inhibit or neutralize infection of live virus are recombinantly reproduced and formulated into a pharmaceutical composition for administration to a subject at risk of contacting an Influenza virus. Furthermore, recombinant and soluble HA homotrimers are derived from multiple strains of Influenza viruses, including multiple strains of influenza A virus. Exemplary human antibodies specifically bind Influenza A, and may be selected for an inability to bind influenza B and C virus strains.

[647] The invention further provides a novel process whereby full-length HA is expressed in mammalian cell lines, which allows for the identification of human antibodies that bind this cell-expressed HA. The huMHA antibodies have been shown to bind conformational determinants on the HA-transfected cells, as well as native HA, which can be isolated, or contacted to huMHA antibodies when presented either on Influenza infected cells or on Influenza A virus. Alternatively, or in addition, huMHA antibodies bind native HA, recombinant homotrimeric HA, purified virus, infected cells, linear peptide, synthetic HA

peptide, HA transfected mammalian cells, and HA expressed on the surface of genetically altered bacteriophage virus, which are used for gene fragment display assays. Thus, this invention has allowed for the identification and production of human monoclonal antibodies that exhibit novel specificity for a very broad range of Influenza A virus strains. These antibodies may be used prophylactically to prevent Influenza A infection, diagnostically to identify Influenza A infection and therapeutically to treat Influenza A infection. Moreover, the epitopes to which huMHA antibodies of the invention bind are used as vaccines to prevent influenza A infection.

[648] The huMHA antibodies of the invention has one or more of the following characteristics: a) binds to an epitope in an HA1 subunit of an Influenza hemagglutinin (HA) protein; b) binds to an epitope in the HA2 subunit of Influenza hemagglutinin (HA) protein; c) binds to an epitope in the extracellular domain of an Influenza hemagglutinin (HA) protein, consisting of an HA1 subunit and an HA2 subunit; d) binds to an epitope of a recombinant homotrimeric Influenza HA0 protein; e) binds to an epitope of an Influenza HA protein expressed on an infected cell; f) binds to an epitope of an Influenza HA protein expressed on a modified cell; g) binds to an Influenza virus; or h) inhibits virus infection of susceptible eukaryotic cells. The huMHA antibodies of the invention eliminate Influenza infected cells through immune effector mechanisms such as ADCC and/or CDC and promote direct viral clearance by binding to Influenza virions.

[649] Exemplary Influenza A strains used for screening human plasma samples, B Cell Culture supernatants (BCC SN), and monoclonal transfection supernatants (MN are shown in Table 8 below). Live strains were used for the neutralization assays described herein. Inactivated strains were used for the virus binding assays described herein. Recombinant homotrimeric HA protein was used in the trimeric HA binding assay.

[650] Table 8

Virus	Subtype	Neutralization	Virus binding	Trimeric HA binding
A/California/4/09	H1			+
A/Solomon Islands/3/06	H1	+	+	+
A/South Carolina/1/18	H1			+
A/Japan/305/57	H2		+	+
A/Wisconsin/67/05	H3	+	+	+
A/swine/Ontario/01911-2/99	H4			+
A/Vietnam/1203/04	H5			+
A/Indonesia/5/05	H5			+
A/Egypt/3300-NAMRU3/08	H5			+
A/common magpie/Hong Kong/5052/07	H5			+
A/Anhui/1/05	H5			+
A/chicken/Vietnam/NCVD-016/08	H5			+
A/Hong Kong/156/97	H5			+
A/northern shoveler/California/HKWF115/07	H6			+
A/Netherlands/219/03	H7			+
A/duck/Yangzhou/02/05	H8			+
A/Hong Kong/2108/03	H9			+
A/Hong Kong/1073/99	H9			+

[651] Exemplary HA sequences include those sequences listed on Table 9 below.

[652] Table 9

Type	GenBank Accession No.	Subtype	HA Sequence from Strain	SEQ ID NO:
A	ACP41105	H1	A/California/04/2009(H1N1)	SEQ ID NO: 727
A	ABU99109	H1	A/Solomon Islands/3/2006(H1N1)	SEQ ID NO: 728
A	AF117241	H1	A/South Carolina/1/18 (H1N1)	SEQ ID NO: 729
A	AAA43185	H2	A/Japan/305/1957(H2N2)	SEQ ID NO: 730
A	ACF54576	H3	A/Wisconsin/67/2005(H3N2)	SEQ ID NO: 731
A	AAG17427	H4	A/Swine/Ontario/01911-2/99 (H4N6)	SEQ ID NO: 732
A	AF028709	H5	A/Hong Kong/156/97 (H5N1)	SEQ ID NO: 733
A	AAT73274	H5	A/VietNam/1203/2004(H5N1)	SEQ ID NO: 734
A	ABW06108	H5	A/Indonesia/5/2005(H5N1)	SEQ ID NO: 735
A	ACI06185	H5	A/Egypt/3300-NAMRU3/2008(H5N1)	SEQ ID NO: 736
A	ACJ26242	H5	A/common magpie/Hong Kong/5052/2007(H5N1)	SEQ ID NO: 737
A	ABD28180	H5	A/Anhui/1/2005(H5N1)	SEQ ID NO: 738
A	ACO07033	H5	A/chicken/Vietnam/NCVD-016/2008(H5N1)	SEQ ID NO: 739
A	ACF21692	H6	A/northern shoveler/California/HKWF115/2007(H6N1)	SEQ ID NO: 740
A	AAR02640	H7	A/Netherlands/219/03(H7N7)	SEQ ID NO: 741
A	ABK32094	H8	A/duck/Yangzhou/02/2005(H8N4)	SEQ ID NO: 742
A	ABB58945	H15	A/HK/2108/2003(H9N2)	SEQ ID NO: 743
A	NC_004908	H9	A/Hong Kong/1073/99 (H9N2)	SEQ ID NO: 744

[653] In one embodiment, the huMHA antibodies of the invention bind to an HA that wholly or partially includes the amino acid residues from position 1 to position 525 of Influenza hemagglutinin when numbered in accordance with SEQ ID NO: 727-744. Alternatively, the monoclonal antibody is an antibody that binds to the same epitope as the mAbs listed in Table 10.

[654] Table 10

BCC well ID	Theraclone ID	BCC well ID	Theraclone ID	BCC well ID	Theraclone ID	BCC well ID	Theraclone ID
3251_K17	TCN-504	5091_H13	TCN-531	5062_M11	TCN-541	5243_D01	TCN-551
3280_D18	TCN-521	5262_H18	TCN-532	5079_A16	TCN-542	5249_I23	TCN-552
3212_I12	TCN-522	5256_A17	TCN-533	5081_G23	TCN-543	5261_C18	TCN-553
5248_A17	TCN-523	5249_B02	TCN-534	5082_A19	TCN-544	5277_M05	TCN-554
5237_B21	TCN-524	5246_P19	TCN-535	5082_I15	TCN-545	5246_L16	TCN-555
5084_C17	TCN-526	5095_N01	TCN-536	5089_L08	TCN-546	5089_K12	TCN-556
5086_C06	TCN-527	3194_D21	TCN-537	5092_F11	TCN-547	5081_A04	TCN-557
5087_P17	TCN-528	3206_O17	TCN-538	5092_P01	TCN-548	5248_H10b	TCN-558
5297_H01	TCN-529	5056_A08	TCN-539	5092_P04	TCN-549	5097_G08	TCN-559
5248_H10a	TCN-530	5060_F05	TCN-540	5096_F06	TCN-550	5084_P10	TCN-560

[655] The antibodies of the invention are able to neutralize Influenza A. Monoclonal antibodies can be produced by known procedures, e.g., as described by R. Kennet et al. in "Monoclonal Antibodies and Functional Cell Lines; Progress and Applications". Plenum

Press (New York), 1984. Further materials and methods applied are based on known procedures, e.g., such as described in J. Virol. 67:6642-6647, 1993.

[656] These antibodies can be used as prophylactic or therapeutic agents upon appropriate formulation, or as a diagnostic tool.

[657] A "neutralizing antibody" is one that can neutralize the ability of that pathogen to initiate and/or perpetuate an infection in a host and/or in target cells *in vitro*. The invention provides a neutralizing monoclonal human antibody, wherein the antibody recognizes an antigen from an Influenza virus, which is preferably derived from the HA protein. Preferably an antibody according to the invention is a novel monoclonal antibody referred to herein as TCN-522 (corresponding to BCC plate and well location 3212_I12), TCN-521 (3280_D18), TCN-523 (5248_A17), TCN-563 (5237_B21), TCN-526 (5084_C17), TCN-527 (5086_C06), TCN-528 (5087_P17), TCN-529 (5297_H01), TCN-530 (5248_H10a), TCN-531 (5091_H13), TCN-532 (5262_H18), TCN-533 (5256_A17), TCN-534 (5249_B02), TCN-535 (5246_P19), TCN-536 (5095_N01), TCN-537 (3194_D21), TCN-538 (3206_O17), TCN-539 (5056_A08), TCN-540 (5060_F05), TCN-541 (5062_M11), TCN-542 (5079_A16), TCN-543 (5081_G23), TCN-544 (5082_A19), TCN-545 (5082_I15), TCN-546 (5089_L08), TCN-547 (5092_F11), TCN-548 (5092_P01), TCN-549 (5092_P04), TCN-550 (5096_F06), TCN-551 (5243_D01), TCN-552 (5249_I23), TCN-553 (5261_C18), TCN-554 (5277_M05), TCN-555 (5246_L16), TCN-556 (5089_K12), TCN-557 (5081_A04), TCN-558 (5248_H10b), TCN-559 (5097_G08), TCN-560 (5084_P10), and TCN-504 (3251_K17). These antibodies were initially isolated from human samples and are produced by the B cell cultures referred to as 3212_I12, 3280_D18, 5248_A17, 5237_B21, 5084_C17, 5086_C06, 5087_P17, 5297_H01, 5248_H10a, 5091_H13, 5262_H18, 5256_A17, 5249_B02, 5246_P19, 5095_N01, 3194_D21, 3206_O17, 5056_A08, 5060_F05, 5062_M11, 5079_A16, 5081_G23, 5082_A19, 5082_I15, 5089_L08, 5092_F11, 5092_P01, 5092_P04, 5096_F06, 5243_D01, 5249_I23, 5261_C18, 5277_M05, 5246_L16, 5089_K12, 5081_A04, 5248_H10b, 5097_G08, 5084_P10, and 3251_K17. These antibodies have broad neutralizing activity or broad binding activity for Influenza A *in vitro*.

[658] The CDRs of the antibody heavy chains are referred to as CDRH1, CDRH2 and CDRH3, respectively. Similarly, the CDRs of the antibody light chains are referred to as CDRL1, CDRL2 and CDRL3, respectively. The position of the CDR amino acids is defined according to the IMGT numbering system as: CDR1--IMGT positions 27 to 38, CDR2--IMGT positions 56 to 65 and CDR3--IMGT positions 105 to 117. (Lefranc, M P. et al. 2003

IMGT unique numbering for immunoglobulin and T cell receptor variable regions and Ig superfamily V-like domains. Dev Comp Immunol. 27(1):55-77; Lefranc, M P. 1997. Unique database numbering system for immunogenetic analysis. Immunology Today, 18:509; Lefranc, M P. 1999. The IMGT unique numbering for Immunoglobulins, T cell receptors and Ig-like domains. The Immunologist, 7:132-136.)

[659] The sequences of the antibodies were determined, including the sequences of the variable regions of the Gamma heavy and Kappa or Lambda light chains of the antibodies designated. In addition, the sequence of each of the polynucleotides and polypeptides encoding the antibody sequences was determined for TCN-522 (3212_I12), TCN-521 (3280_D18), TCN-523 (5248_A17), TCN-563 (5237_B21), TCN-526 (5084_C17), TCN-527 (5086_C06), TCN-528 (5087_P17), TCN-529 (5297_H01), TCN-530 (5248_H10a), TCN-531 (5091_H13), TCN-532 (5262_H18), TCN-533 (5256_A17), TCN-534 (5249_B02), TCN-535 (5246_P19), TCN-536 (5095_N01), TCN-537 (3194_D21), TCN-538 (3206_O17), TCN-539 (5056_A08), TCN-540 (5060_F05), TCN-541 (5062_M11), TCN-542 (5079_A16), TCN-543 (5081_G23), TCN-544 (5082_A19), TCN-545 (5082_I15), TCN-546 (5089_L08), TCN-547 (5092_F11), TCN-548 (5092_P01), TCN-549 (5092_P04), TCN-550 (5096_F06), TCN-551 (5243_D01), TCN-552 (5249_I23), TCN-553 (5261_C18), TCN-554 (5277_M05), TCN-555 (5246_L16), TCN-556 (5089_K12), TCN-557 (5081_A04), TCN-558 (5248_H10b), TCN-559 (5097_G08), TCN-560 (5084_P10), and TCN-504 (3251_K17).

[660] Shown below are the polypeptide and polynucleotide sequences of the heavy and light chains, with the signal peptides at the N-terminus (or 5' end) and the constant regions at the C-terminus (or 3' end) of the variable regions, which are shown in bolded text.

[661] TCN-504 (3251_K17) heavy chain variable region nucleotide sequence:

CAGGTGCAACTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCCTCGGAGACCCTGTCCCTCACTTGCGCTGTCTCT
GGTGTCTCCATCAGCAATATTGATTTCTACTGGGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTAGAATGGATT
GGCAATATCTATTATACGGGGATCACCTTCTACAACCCGTCCCTCAGCAGTCGAGTCGCCATATCCATTGACACC
TCCAAGAACCAGTTCTCCCTGACTCTGACTTCTGTGACCGCCGCAGACACGGCTATGTATTACTGTGCGAGACAT
TACGGTGACTCCGAGGCAATAAACGATGCCTTTGACATCTGGGGCCAAGGGACAATGCTCACCGTCTCGAGC
(SEQ ID NO: 745)

[662] TCN-504 (3251_K17) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQESGPGLVKPSETLSLTCAVSGVSISNIDFYWGWIRQPPGKGLEWIGNIYYTGITFYNPSLSSRV
AISIDTSKNQFSLTLTSVTAADTAMYYCARHYGDSEAINDAFDIWGQGTMLTVSS (SEQ ID NO: 746)

[663] TCN-504 (3251_K17) gamma heavy chain Kabat CDRs:
CDR 1: NIDFYWG (SEQ ID NO: 747)
CDR 2: NIYYTGITFYNPSLSS (SEQ ID NO: 748)
CDR 3: HYGDSEAINDAFDI (SEQ ID NO: 749)

[664] TCN-504 (3251_K17) gamma heavy chain Chothia CDRs
CDR 1: GVSISN (SEQ ID NO: 750)
CDR 2: NIYYTGITF (SEQ ID NO: 751)
CDR 3: HYGDSEAINDAFDI (SEQ ID NO: 749)

[665] TCN-504 (3251_K17) light chain variable region nucleotide sequence:
GAGATAGTGATGACGCAGTCTCCAGCCACCCTGTCTGTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC
AGTCAGAGTGTTGGCAATAGTTTAGCCTGGTACCAGCAGAGACCTGGCCAGGCTCCCAGGCTCCTCATCTACGGT
GCATCCACCAGGGCCACTGGTATCCCACCCAGGTTCAGTGGCAGTGGGTCTGGGACAGAATTCACTCTCACCATC
AGCAGCCTGCAGACTGAAGATTTTGCAGTTTATTACTGTCAACAATATATTAACTGGCGTCCGCTCAGTTTTGGC
GGAGGGACCAAGGTGGAGATCAAA (SEQ ID NO: 752)

[666] TCN-504 (3251_K17) light chain variable region amino acid sequence (KabatCDRs in bold, Chothia CDRs underlined)

EIVMTQSPATLSVSPGERATLSC**RASQSVGNSLA**WYQQRPGQAPRLLIY**GASTRAT**GIPPRFSGSGSGT
EFTLTISSLQTEDFAVYYC**QQYINWRPLS**FGGGTKVEIK (SEQ ID NO: 753)

[667] TCN-504 (3251_K17) light chain Kabat CDRs:
CDR 1: RASQSVGNSLA (SEQ ID NO: 754)
CDR 2: GASTRAT (SEQ ID NO: 755)
CDR 3: QQYINWRPLS (SEQ ID NO: 756)

[668] TCN-504 (3251_K17) light chain Chothia CDRs:
CDR 1: RASQSVGNSLA (SEQ ID NO: 754)
CDR 2: GASTRAT (SEQ ID NO: 755)
CDR 3: QQYINWRPLS (SEQ ID NO: 756)

[669] TCN-521 (3280_D18) heavy chain variable region nucleotide sequence:
GAAGTGCAGTTGGTGCAGTCTGGAGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCGCCTGTGTAGTCTCT
GGGTTCACCGTCACCAGCAATTATATAACTTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGTT
ATTTATAGTCATGGTCGCGCATATTATTCAGCCTCCGTGAATGGCCGATTCACCATCTCCAGACACACTTCCAAG
AACACAGTTTATCTTGAAATGAACAGCCTGAGACCTGAGGACACGGCCGTCTATTACTGTGCGGGCGGGGGCCTA
GTCGGTGGCTACGACGAATATTTCTTTGACTATTGGGGCCAGGGAACCCTGGCCACCGTCTCCTCA (SEQ ID
NO: 758)

[670] TCN-521 (3280_D18) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

EVQLVQSGGGLVQPGGSLRLACVVS<u>GFTVTS</u>**NYIT**WVRQAPGKGLEWVS**VIYSHGRAYYSASVNGRF**
TISRHTSKNTVYLEMNSLRPEDTAVYYCAG<u>**GGLVGGYDEYFFDY**</u>WGQGTLATVSS (SEQ ID NO: 759)

[671] TCN-521 (3280_D18) gamma heavy chain Kabat CDRs:
CDR 1: SNYIT (SEQ ID NO: 760)
CDR 2: VIYSHGRAYYSASVNG (SEQ ID NO: 761)
CDR 3: GGLVGGYDEYFFDY (SEQ ID NO: 762)

[672] TCN-521 (3280_D18) gamma heavy chain Chothia CDRs:
CDR 1: GFTVTS (SEQ ID NO: 763)
CDR 2: VIYSHGRAY (SEQ ID NO: 764)
CDR 3: GGLVGGYDEYFFDY (SEQ ID NO: 762)

[673] TCN-521 (3280_D18) light chain variable region nucleotide sequence:
GAAACTGTCTTGACGCAATCTCCAGGCACCTTGTCTTTGACTCCAGGGGAAAGAGCCACCCTCTCCTGCAGAGTC
GGTCAGAGTGTTAGCGGCAGCCACTTAGCCTGGTACCAACAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTAT
GGTGCATCCAGCAGGGCCACTGGCATCCCAGACAGGTTCGGTGGCAGTGTGTCTGGGACAGACTTCACTCTCACC
ATCAGCAGACTGGAGCCTGAAGATTCTGCAGTTTATTACTGTCAGCAGTATGGTGACTCACGATACACTTTTGGC
CAGGGGACCAAGCTGGAGATCAAA (SEQ ID NO: 765)

[674] TCN-521 (3280_D18) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

ETVLTQSPGTLSLTPGERATLSC**RVGQSVSGSHLA**WYQQKPGQAPRLLIY**GASSRAT**GIPDRFGGSVSG
TDFTLTISRLEPEDSAVYYC**QQYGDSRYT**FGQGTKLEIK (SEQ ID NO: 766)

[675] TCN-521 (3280_D18) Light chain Kabat CDRs:
CDR 1: RVGQSVSGSHLA (SEQ ID NO: 767)
CDR 2: GASSRAT (SEQ ID NO: 768)
CDR 3: QQYGDSRYT (SEQ ID NO: 769)

[676] TCN-521 (3280_D18) Light chain Chothia CDRs:
CDR 1: RVGQSVSGSHLA (SEQ ID NO: 767)
CDR 2: GASSRAT (SEQ ID NO: 768)
CDR 3: QQYGDSRYT (SEQ ID NO: 769)

[677] TCN-522 (3212_I12) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTTTTGAAACCTTCGGAGACCCTGTCCCTCACCTGCACTGTGTCT
GGGGGGTCCCTCACTGATTACTCTTGGAACTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATCGGTGAC
ACCCTTCATAATGGCTACACCAACTACAACCCGTCCCTCAGGGGTCGAGTTTCCATCTCAATAGACACGTCCAAG
AACCAGGTCTCACTCAGGCTGACCTCTGTGACCGCCGCGGACACGGCTCTTTATTACTGTGCGAGAGGCTCAGGT
GGATATGGTGGCTTCGATTATTTTGGCAAGCTCCGGACATGGGACTTCTGGGGCCAGGGAACGCTGGTCACCGTC
TCCTCA (SEQ ID NO: 770)

[678] TCN-522 (3212_I12) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQQWGAGLLKPSETLSLTCTVS**GGSLTD**YSWNWIRQPPGKGLEWIG**DTLHNGYTN**YNPSLRGR
VSISIDTSKNQVSLRLTSVTAADTALYYCAR**GSGGYGGFDYFGKLRTWDF**WGQGTLVTVSS (SEQ ID NO: 771)

[679] TCN-522 (3212_I12) gamma heavy chain Kabat CDRs:
CDR 1: DYSWN (SEQ ID NO: 772)
CDR 2: DTLHNGYTNYNPSLRG (SEQ ID NO: 773)
CDR 3: GSGGYGGFDYFGKLRTWDF (SEQ ID NO: 774)

[680] TCN-522 (3212_I12) gamma heavy chain Chothia CDRs:
CDR 1: GGSLTD (SEQ ID NO: 775)
CDR 2: DTLHNGYTN (SEQ ID NO: 776)
CDR 3: GSGGYGGFDYFGKLRTWDF (SEQ ID NO: 774)

[681] TCN-522 (3212_I12) light chain variable region nucleotide sequence:
GACATTCAGTTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTGGGAGACAGAGTCACCATCACTTGCCGGGCA
AGTCAGGGCATTAGAAATGATTTAGGCTGGTATCAGCAAAAACCAGGGAACGCCCCTAAGCGCCTGATCTTTGGT
GCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAGTTCACTCTCACAATC
AGCAGCCTGCAGCCTGAGGACTTTGCAACTTATTACTGTCTACAGCATAATAGTTACCCGTACACTTTTGGCCAG
GGGACCAAGCTGGAGATCAAG (SEQ ID NO: 777)

[682] TCN-522 (3212_I12) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIQLTQSPSSLSASVGDRVTITC**RASQGIRNDLG**WYQQKPGNAPKRLIF**GASSLQS**GVPSRFSGSGSGT
EFTLTISSLQPEDFATYYC**LQHNSYPYT**FGQGTKLEIK (SEQ ID NO: 778)

[683] TCN-522 (3212_I12) Light chain Kabat CDRs:
CDR 1: RASQGIRNDLG (SEQ ID NO: 779)
CDR 2: GASSLQS (SEQ ID NO: 780)
CDR 3: LQHNSYPYT (SEQ ID NO: 781)

[684] TCN-522 (3212_I12)Light chain Chothia CDRs
CDR 1: RASQGIRNDLG (SEQ ID NO: 779)
CDR 2: GASSLQS (SEQ ID NO: 780)
CDR 3: LQHNSYPYT (SEQ ID NO: 781)

[685] TCN-523 (5248_A17) heavy chain variable region nucleotide sequence:
CAGGTGCAACTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCAAGGCTTCT
GGAGGCAGCTTCAGCAACTATGCCTTCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG
ACCATCCCTCTACTTGGTACAACAAACTACGCACAGAAGTTCCAGGGCAGAGTCACGATTTCCGCGGACCAATTC
ACGAGCACAGCCTACATGGAGCTGGGCAGCCTGAGATCTGAAGACACGGCCGTGTATTACTGTACGAGACGGAAA
ATGACTACGGCTTTTGACTCCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCA (SEQ ID NO: 782)

[686] TCN-523 (5248_A17) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGAEVKKPGSSVKVSCKAS**GGSFSN**YAFSWVRQAPGQGLEWMG**GTIPLLGTTN**YAQKFQ
GRVTISADQFTSTAYMELGSLRSEDTAVYYCTR**RKMTTAFDS**WGQGTLVTVSS (SEQ ID NO: 783)

[687] TCN-523 (5248_A17) gamma heavy chain Kabat CDRs:
CDR 1: NYAFS (SEQ ID NO: 784)
CDR 2: GTIPLLGTTNYAQKFQG (SEQ ID NO: 785)
CDR 3: RKMTTAFDS (SEQ ID NO: 786)

[688] TCN-523 (5248_A17)gamma heavy chain Chothia CDRs:
CDR 1: GGSFSN (SEQ ID NO: 787)
CDR 2: GTIPLLGTTN (SEQ ID NO: 788)
CDR 3: RKMTTAFDS (SEQ ID NO: 786)

[689] TCN-523 (5248_A17)light chain variable region nucleotide sequence:
CAGCCTGTTCTGACTCAGCCACCTTCTGCATCAGCCTCCCTGGGAGCCTCGGTCACACTCACCTGCACCCTGAGC
AGCGCCTACAGTAATTATAAAGTGGACTGGTACCAGCAGAGACCAGGGAAGGGCCCCCGCTTTGTGATGCGAGTG
GGCACTGGTGGGATTGTGGGATCCAAGGGGGATGGCATCCCTGATCGCTTCTCAGTCTTGGGCTCAGGCCTGAAT
CGGTACCTGACCATCAAGAACATCCAGGAAGAGGATGAGAGTGACTACCACTGTGGGGCAGACCATGGCAGTGGG
AGCAACTTCGTGTCCCCTTACGTATTCGGCGGAGGGACCAAGCTGACCGTTCTA (SEQ ID NO: 789)

[690] TCN-523 (5248_A17)light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QPVLTQPPSASASLGASVTLTC**TLSSAYSNYKVD**WYQQRPGKGPRFVMR**VGTGGIVGSKGD**GIPDRF SVLGSGLNRYLTIKNIQEEDESDYHC**GADHGSGSNFVSPYV**FGGGTKLTVL (SEQ ID NO: 790)

[691] TCN-523 (5248_A17)Light chain Kabat CDRs:
CDR 1: TLSSAYSNYKVD (SEQ ID NO: 791)
CDR 2: VGTGGIVGSKGD (SEQ ID NO: 792)
CDR 3: GADHGSGSNFVSPYV (SEQ ID NO: 793)

[692] TCN-523 (5248_A17)Light chain Chothia CDRs:
CDR 1: TLSSAYSNYKVD (SEQ ID NO: 791)
CDR 2: VGTGGIVGSKGD (SEQ ID NO: 792)
CDR 3: GADHGSGSNFVSPYV (SEQ ID NO: 793)

[693] TCN-563 (5237_B21) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGGCGCAGTCTGGGGCTGAGGTGAAGAGGCCTGGGTCCTCGGTGAAAGTCTCATGCACGGCTTCT GGAGGCATCTTCAGGAAGAATGCAATCAGCTGGGTGCGACAGGCCCCTGGACAAGGCCTTGAGTGGATGGGAGGG ATCATCGCAGTCTTTAACACAGCAAATTACGCGCAGAAGTTTCAGGGCAGAGTCAAAATTACCGCAGACGAATCC GGGAATACAGCCTACATGGAGCTGAGCAGCCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGTCACCCA AAATATTTCTATGGTTCGGGGAGTTATCCGGACTTCTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ ID NO: 794)

[694] TCN-563 (5237_B21) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLAQSGAEVKRPGSSVKVSCTAS**GGIFRK**NAISWVRQAPGQGLEWMG**GIIAVFNTAN**YAQKFQG RVKITADESGNTAYMELSSLRSDDTAVYYCAS**HPKYFYGSGSYPDF**WGQGTLVTVSS (SEQ ID NO: 795)

[695] TCN-563 (5237_B21)gamma heavy chain Kabat CDRs:
CDR 1: KNAIS (SEQ ID NO: 796)
CDR 2: GIIAVFNTANYAQKFQG (SEQ ID NO: 797)
CDR 3: HPKYFYGSGSYPDF (SEQ ID NO: 798)

[696] TCN-563 (5237_B21)gamma heavy chain Chothia CDRs:
CDR 1: GGIFRK (SEQ ID NO: 799)
CDR 2: GIIAVFNTAN (SEQ ID NO: 800)
CDR 3: HPKYFYGSGSYPDF (SEQ ID NO: 798)

[697] TCN-563 (5237_B21)light chain variable region nucleotide sequence:
CAATCTGCCCTGACTCAGCCTCGCTCAGTGTCCGGGTCTCCTGGACAGTCAGTCACCATCTCCTGCACTGGAAGC AGCAGTGATGTTGGTGCTTCTAACTCTGTCTCCTGGTACCAACAACACCCAGGCAAAGCCCCCAAACTCGTTATT TATGATGTCACTGAGCGACCCTCAGGGGTCCCTCATCGCTTCTCTGGCTCCAAGTCTGGCAACACGGCCTCCCTG ACCGTCTCTGGGCTCCAGCCTGAGGACGAGGCTGATTATTTCTGCTGCGCATATGGAGGCAAATATCTTGTGGTC TTCGGCGGAGGGACCAAGGTGACCGTCCTC (SEQ ID NO: 801)

[698] TCN-563 (5237_B21)light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QSALTQPRSVSGSPGQSVTISC**TGSSSDVGASNSVS**WYQQHPGKAPKLVIY**DVTERPS**GVPHRFSGSKS
GNTASLTVSGLQPEDEADYFC**CAYGGKYLVV**FGGGTKVTVL (SEQ ID NO: 802)

[699] TCN-563 (5237_B21)light chain Kabat CDRs:
CDR 1: TGSSSDVGASNSVS (SEQ ID NO: 803)
CDR 2: DVTERPS (SEQ ID NO: 804)
CDR 3: CAYGGKYLVV (SEQ ID NO: 805)

[700] TCN-563 (5237_B21)light chain Chothia CDRs:
CDR 1: TGSSSDVGASNSVS (SEQ ID NO: 803)
CDR 2: DVTERPS (SEQ ID NO: 804)
CDR 3: CAYGGKYLVV (SEQ ID NO: 805)

[701] TCN-526 (5084_C17)heavy chain variable region nucleotide sequence:
GAGGTGCTGATGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCGTGAGACTCTCCTGTGTAGCCTCT
GGATTCAGTTTCAGTAGTCATTGGATGACCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTGGCCAAC
ATAGAGGACGATGGAGGTGACAAGTACTATGTGGACTCTGTGAAGGGCCGATTCATTATCTCCAGAGACAACGCC
AAGAATTCAGTGTATCTGCAAATGAACAGCCTAAGAGCCGAGGACACGGCTGTGTATTTCTGTGCGAGAGGTTCG
GGGAGCTCTGATAGAAGTGATTATGACCCCCACTACTACTACTACTTGGACGTCTGGGGCAAAGGGGCCACGGTC
ACCGTCTCCTCA (SEQ ID NO: 806)

[702] TCN-526 (5084_C17) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

EVLMVESGGGLVQPGGSVRLSCVAS**GFSFSS**HWMTWVRQAPGKGLEWVA**NIEDDGGDKYYVDSVK**
GRFIISRDNAKNSVYLQMNSLRAEDTAVYFCAR**GSGSSDRSDYDPHYYYYLDV**WGKGATVTVSS
(SEQ ID NO: 807)

[703] TCN-526 (5084_C17) gamma heavy chain Kabat CDRs:
CDR 1: SHWMT (SEQ ID NO: 808)
CDR 2: NIEDDGGDKYYVDSVKG (SEQ ID NO: 809)
CDR 3: GSGSSDRSDYDPHYYYYLDV (SEQ ID NO: 810)

[704] TCN-526 (5084_C17) gamma heavy chain Chothia CDRs:
CDR 1: GFSFSS (SEQ ID NO: 811)
CDR 2: NIEDDGGDKY (SEQ ID NO: 812)
CDR 3: GSGSSDRSDYDPHYYYYLDV (SEQ ID NO: 810)

[705] TCN-526 (5084_C17) light chain variable region nucleotide sequence:
GACATCCAGCTGACCCAGTCTCCATCTTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCA
AGTCAGAGCATTAGTAGGTATTTAAATTGGTATCAGCAAAAACCAGGGAAAGCCCCTAAGCTCCTGCTGTTTGCT
GCTTCTACTTTGCTAGATGGGGTCCCATCAAGATTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATC
AGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACGGAATCACAGTCCCTCGTGGACGTTCGGCCAA
GGGACCAGGGTGGAAATCAAA (SEQ ID NO: 813)

[706] TCN-526 (5084_C17) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIQLTQSPSSLSASVGDRVTITC**RASQSISRYLN**WYQQKPGKAPKLLLF**AASTLLD**GVPSRFSGSGSGT
DFTLTISSLQPEDFATYYC**QRNHSPSWT**FGQGTRVEIK (SEQ ID NO: 814)

[707] TCN-526 (5084_C17) Light chain Kabat CDRs:
CDR 1: RASQSISRYLN (SEQ ID NO: 815)
CDR 2: AASTLLD (SEQ ID NO: 816)
CDR 3: QRNHSPSWT (SEQ ID NO: 817)

[708] TCN-526 (5084_C17) Light chain Chothia CDRs:
CDR 1: RASQSISRYLN (SEQ ID NO: 815)
CDR 2: AASTLLD (SEQ ID NO: 816)
CDR 3: QRNHSPSWT (SEQ ID NO: 817)

[709] TCN-527 (5086_C06) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGCAAGAGTCGGGCCCGGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCAACTGCGCTGTCTCT
GGAGGCTCCATCAGTAATTACTACTGGAGCTGGATCCGGCAGCCCCCCGGGAAGGGACTGGAGTGGATTGGCTAT
ATCTCTTACAATGGGAGGCCCAAGTACAACCCCTCCCTCACGAGTCGAGTCACCATATCCGTCGACACGTCCAAG
GACCAGTTCTCCCTGGAGCTGCGCTCTGTGACCGCTGCGGACACGGCCCTTTATTACTGTGCGAGAGAAACGCGG
TTCGGGGAGTTATTATCTCCCTATGATGCTTTTGAAATCTGGGGCCAAGGGACAATGGTCACCGTCTCCTCA
(SEQ ID NO: 818)

[710] TCN-527 (5086_C06) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQESGPGLVKPSETLSLNCAVS**GGSISN**YYWSWIRQPPGKGLEWIG**YISYNGRPK**YNPSLTSRVTI
SVDTSKDQFSLELRSVTAADTALYYCAR**ETRFGELLSPYDAFEI**WGQGTMVTVSS (SEQ ID NO: 819)

[711] TCN-527 (5086_C06) gamma heavy chain Kabat CDRs:
CDR 1: NYYWS (SEQ ID NO: 820)
CDR 2: YISYNGRPKYNPSLTS (SEQ ID NO: 821)
CDR 3: ETRFGELLSPYDAFEI (SEQ ID NO: 822)

[712] TCN-527 (5086_C06) gamma heavy chain Chothia CDRs:
CDR 1: GGSISN (SEQ ID NO: 824)
CDR 2: YISYNGRPK (SEQ ID NO: 823)
CDR 3: ETRFGELLSPYDAFEI (SEQ ID NO: 822)

[713] TCN-527 (5086_C06) light chain variable region nucleotide sequence:
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATGACTTGCCGGGCA
AGTCAGAACATTAGAAGCTATTTAAATTGGTATCAGCAGAGACCAGGGACAGCCCCTAAACTCCTGATCTATGCT
GCATCCACTTTACACAGTGGGGTCCCATCAAGGTTCAGTGGCGGTGGGTCTGGGACAGATTTCACTCTCACCATC
AATAATCTGCAACCTGAAGATTTTGCATCTTACTACTGTCAACAGAGTTACGATAACCCTCAGACGTTCGGCCAA
GGGACCAAGGTGGAAATCAAA (SEQ ID NO: 825)

[714] TCN-527 (5086_C06) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIQMTQSPSSLSASVGDRVTMTC**RASQNIRSYLN**WYQQRPGTAPKLLIY**AASTLHS**GVPSRFSGGGSG
TDFTLTINNLQPEDFASYYC**QQSYDNPQT**FGQGTKVEIK (SEQ ID NO: 826)

[715] TCN-527 (5086_C06) Light chain Kabat CDRs:
CDR 1: RASQNIRSYLN (SEQ ID NO: 827)
CDR 2: AASTLHS (SEQ ID NO: 828)
CDR 3: QQSYDNPQT (SEQ ID NO: 829)

[716] TCN-527 (5086_C06) Light chain Chothia CDRs:
CDR 1: RASQNIRSYLN (SEQ ID NO: 827)
CDR 2: AASTLHS (SEQ ID NO: 828)
CDR 3: QQSYDNPQT (SEQ ID NO: 829)

[717] TCN-528 (5087_P17) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGGTGCAGTCTGGGTCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
GGATACACCTTCACCAATTATGACATCAACTGGATTCGACAGGCCCCTGGTCAAGGACTTGAGTGGATGGGCTGG
ATAAATCCCAACAGTGGAACCACGGGCTCTGCACAGAGGTTCCAGGGCAGAGTCACCATAACCGTGGACACCTCC
ATAACCACAGTCTACATGGAACTGAGCAGCCTGAGATCTGACGACACGGCCATTTACTACTGCGCGAGAGGCCGT
GAGCTCCTCCGGCTTCAACATTTTTTGACTGACTCCCAGTCCGAGAGGAGGGACTGCTTCGACCCCTGGGGCCAG
GGAACCCTGGTCACCGTCTCCTCA (SEQ ID NO: 830)

[718] TCN-528 (5087_P17) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGSEVKKPGASVKVSCKAS<u>GYTFTN</u>**YDIN**WIRQAPGQGLEWMG**<u>WINPNSGTTG</u>**SAQRFQG
RVTITVDTSITTVYMELSSLRSDDTAIYYCAR**<u>GRELLRLQHFLTDSQSERRDCFDP</u>**WGQGTLVTVSS
(SEQ ID NO: 831)

[719] TCN-528 (5087_P17) gamma heavy chain Kabat CDRs:
CDR 1: NYDIN (SEQ ID NO: 832)
CDR 2: WINPNSGTTGSAQRFQG (SEQ ID NO: 833)
CDR 3: GRELLRLQHFLTDSQSERRDCFDP (SEQ ID NO: 834)

[720] TCN-528 (5087_P17) gamma heavy chain Chothia CDRs:
CDR 1: GYTFTN (SEQ ID NO: 835)
CDR 2: WINPNSGTTG (SEQ ID NO: 836)
CDR 3: GRELLRLQHFLTDSQSERRDCFDP (SEQ ID NO: 834)

[721] TCN-528 (5087_P17) light chain variable region nucleotide sequence:
GATATCCAGATGACCCAGTCTCCTTCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCA
AATCAAGACATTGGCATTTATTTAAATTGGTATCAACAGAATCCAGGGAAAGTCCCTAAACTCCTGCTCCATGGT
GCGTCCAGTTTGCAGGGCGGGGTCCCATCAAGGTTCAGTGCCAGTGGATCTGGGACAGATTTCACTCTCACCATT
CACAGTCTACAACCTGAAGATTTAGCAACCTACTACTGTCAACAGAGTCGCCGTCTACCGTACACTTTTGGCCAG
GGGACCAGGGTGGAACTCAAA (SEQ ID NO: 837)

[722] TCN-528 (5087_P17) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIQMTQSPSSLSASVGDRVTITC**<u>RANQDIGIYLN</u>**WYQQNPGKVPKLLLH**<u>GASSLQG</u>**GVPSRFSASGSG
TDFTLTIHSLQPEDLATYYC**<u>QQSRRLPYT</u>**FGQGTRVELK (SEQ ID NO: 838)

[723] TCN-528 (5087_P17) Light chain Kabat CDRs:
CDR 1: RANQDIGIYLN (SEQ ID NO: 839)
CDR 2: GASSLQG (SEQ ID NO: 840)
CDR 3: QQSRRLPYT (SEQ ID NO: 841)

[724] TCN-528 (5087_P17) Light chain Chothia CDRs:
CDR 1: RANQDIGIYLN (SEQ ID NO: 839)
CDR 2: GASSLQG (SEQ ID NO: 840)
CDR 3: QQSRRLPYT (SEQ ID NO: 841)

[725] TCN-529 (5297_H01) heavy chain variable region nucleotide sequence:
CAGATCACCTTGAGGGAGTCTGGTCCTACGCTGGTGAAACCCACACAGACCCTCACGCTGACCTGCACCTTCTCT
GGGTTTTCACTCAGCACTAATGGAGTGAATGTGGGCTGGATCCGTCAGCCCCCAGGAAAGGCCCTGGAGTGGCTT
GCACTCATTTACTGGGATGATGATAAGCGCTACAGTCCGTCTCTGAAGAGAAGGCTCACCATCACCAAGGACACC
TCCAAAAACCAAGTGGTCCTTACACTGACCAACATGGACCCTGTAGATACAGCCACATATTACTGTGCACACAGA
CCCGACTTCTATGGTGACTTCGAGTACTGGGGCCCGGGAACCCTGGTCACCGTCTCCTCA (SEQ ID NO:
842)

[726] TCN-529 (5297_H01) gamma heavy chain variable region amino acid sequence:
(Kabat CDRs in bold, Chothia CDRs underlined)

QITLRESGPTLVKPTQTLTLTCTFS<u>GFSLSTNG</u>VNVGWIRQPPGKALEWLA<u>**LIYWDDDKRYSPSLKR**</u>R
LTITKDTSKNQVVLTLTNMDPVDTATYYCAH<u>**RPDFYGDFEY**</u>WGPGTLVTVSS (SEQ ID NO: 843)

[727] TCN-529 (5297_H01) gamma heavy chain Kabat CDRs:
CDR 1: TNGVNVG (SEQ ID NO: 844)
CDR 2: LIYWDDDKRYSPSLKR (SEQ ID NO: 845)
CDR 3: RPDFYGDFEY (SEQ ID NO: 846)

[728] TCN-529 (5297_H01)gamma heavy chain Chothia CDRs:
CDR 1: GFSLSTNG (SEQ ID NO: 847)
CDR 2: LIYWDDDKR (SEQ ID NO: 848)
CDR 3: RPDFYGDFEY (SEQ ID NO: 846)

[729] TCN-529 (5297_H01) light chain variable region nucleotide sequence:
CAGTCTGCACTGACTCAGCCTGCCTCCGTGTCTGGGTCTCCCGGACAGTCGATCACCATCTCCTGCACTGGAAGC
AGCAGTGACATTGGTGGTTATAACTATGTCTCCTGGTACCAACAACACCCAGGCAAGGCCCCCAAACTCATGATT
TACGATGTCAATAATCGGCCCTCAGGGGTTTCTAATCGCTTCTCTGGCTCCAAGTCTGGCAACACGGCCTCCCTG
ACTATCTCTGGGCTCCAGACTGACGACGAGGCTGATTATTACTGCGGCTCATATACAGGCAGTCCTCATTATGTC
TTCGGAACTGGGACCAAGGTCACCGTCCTA (SEQ ID NO: 849)

[730] TCN-529 (5297_H01) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QSALTQPASVSGSPGQSITISC<u>**TGSSSDIGGYNYVS**</u>WYQQHPGKAPKLMIY<u>**DVNNRPS**</u>GVSNRFSGSKS
GNTASLTISGLQTDDEADYYC<u>**GSYTGSPHYV**</u>FGTGTKVTVL (SEQ ID NO: 850)

[731] TCN-529 (5297_H01) Light chain Kabat CDRs:
CDR 1: TGSSSDIGGYNYVS (SEQ ID NO: 851)
CDR 2: DVNNRPS (SEQ ID NO: 852)
CDR 3: GSYTGSPHYV (SEQ ID NO: 853)

[732] TCN-529 (5297_H01)Light chain Chothia CDRs:
CDR 1: TGSSSDIGGYNYVS (SEQ ID NO: 851)
CDR 2: DVNNRPS (SEQ ID NO: 852)
CDR 3: GSYTGSPHYV (SEQ ID NO: 853)

[733] TCN-530 (5248_H10a) heavy chain variable region nucleotide sequence:
CAGGTCCAACTGGTGCAATCTGGGGCTGAGGTGAGGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCAAGGCTTCT
GGAGGCCCCTTCATGAGTTATGCTATCGGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG
ATCAACCCTGTGTTTGGTAGACCGCACTACGCACAGAAGTTCCAGGGCAGAGTCACCATCGCCACGGACGACTCC
ACGAAGACATCGTACATGGAACTGAGTAGCCTGACGTCTGAGGACACGGGCATGTATTACTGTGCGAGTAGGTAT
AGTAGGTCGTCCCCAGGGACCTTTGAGTCCTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ ID NO:
854)

[734] TCN-530 (5248_H10a) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGAEVRKPGSSVKVSCKAS<u>GGPFMS</u>**YAIG**WVRQAPGQGLEWMG<u>GINPVFGRPH</u>**YAQKFQ**
GRVTIATDDSTKTSYMELSSLTSEDTGMYYCAS<u>**RYSRSSPGTFES**</u>WGQGTLVTVSS (SEQ ID NO: 855)

[735] TCN-530 (5248_H10a) gamma heavy chain Kabat CDRs:
CDR 1: SYAIG (SEQ ID NO: 856)
CDR 2: GINPVFGRPHYAQKFQG (SEQ ID NO: 857)
CDR 3: RYSRSSPGTFES (SEQ ID NO: 858)

[736] TCN-530 (5248_H10a) gamma heavy chain Chothia CDRs:
CDR 1: GGPFMS (SEQ ID NO: 859)
CDR 2: GINPVFGRPH (SEQ ID NO: 860)
CDR 3: RYSRSSPGTFES (SEQ ID NO: 858)

[737] TCN-530 (5248_H10a) light chain variable region nucleotide sequence:
GAAATAGTGATGACGCAGTTTCCAGCCACCCTGTCTGTGTCTCCCGGGGAACGAGTCACCCTCTCCTGTAGGGCC
AGTCAGAGTGTTAGCAACAATTTAGCCTGGTACCAGCAAAAACCTGGCCAGCCTCCCAGGCTCCTCATCTATGAT
GCATCTACCAGGGCCACGGGTGTCCCAGCCAAGTTCAGTGGCACTGGGTCTGGCACAGAGTTCACTCTCAGCATC
AGCAGCCTGCAGTCCGAAGATTTTGCAGTTTATTACTGTCAGCAGTATCACAACTGGCCTCCCTCGTACAGTTTT
GGCCTGGGGACCAAGCTGGAGATCAAA (SEQ ID NO: 861)

[738] TCN-530 (5248_H10a) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

EIVMTQFPATLSVSPGERVTLSC<u>**RASQSVSNNLA**</u>WYQQKPGQPPRLLIY<u>**DASTRAT**</u>GVPAKFSGTGSGT
EFTLSISSLQSEDFAVYYC<u>**QQYHNWPPSYS**</u>FGLGTKLEIK (SEQ ID NO: 862)

[739] TCN-530 (5248_H10a) Light chain Kabat CDRs:
CDR 1: RASQSVSNNLA (SEQ ID NO: 863)
CDR 2: DASTRAT (SEQ ID NO: 864)
CDR 3: QQYHNWPPSYS (SEQ ID NO: 865)

[740] TCN-530 (5248_H10a) Light chain Chothia CDRs:
CDR 1: RASQSVSNNLA (SEQ ID NO: 863)
CDR 2: DASTRAT (SEQ ID NO: 864)
CDR 3: QQYHNWPPSYS (SEQ ID NO: 865)

[741] TCN-531 (5091_H13) heavy chain variable region nucleotide sequence:
GAGGTGCAGCTGGTGGAGTCTGGGGGAGACTTGGTACAGCCAGGGCGGTCCCTGAAACTCTCCTGCACAGGTTCT
GGATTCACCTTTGGTGATTATGGTGTGACCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTAGGTTTC
ATTAGAACCAGACCTTGGGGTGGGACAGCAGATACCGCCGCGTCTGTGAAAGGCAGATTCACTATTTCAAGAGAT
GATTCCAAAAGTCTCGCCTATCTGCAAATGAACAGCCTGAAAACCGAGGACACAGCCGTGTATTACTGTTGTAGA
GATGCCCCTCCAAATGTGGAAGTGGCTTCTATGACCAACTGGTACTTCGATCTCTGGGGCCGTGGCACCCTGGTC
ACCGTCTCCTCA (SEQ ID NO: 866)

[742] TCN-531 (5091_H13) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

EVQLVESGGDLVQPGRSLKLSCTGSGFTFGDYGVTWVRQAPGKGLEWVGFIRTRPWGGTADTAASV
KGRFTISRDDSKSLAYLQMNSLKTEDTAVYYCCRDAPPNVEVASMTNWYFDLWGRGTLVTVSS
(SEQ ID NO: 867)

[743] TCN-531 (5091_H13) gamma heavy chain Kabat CDRs:
CDR 1: DYGVT (SEQ ID NO: 868)
CDR 2: FIRTRPWGGTADTAASVKG (SEQ ID NO: 869)
CDR 3: DAPPNVEVASMTNWYFDL (SEQ ID NO: 870)

[744] TCN-531 (5091_H13) gamma heavy chain Chothia CDRs:
CDR 1: GFTFGD (SEQ ID NO: 871)
CDR 2: FIRTRPWGGTAD (SEQ ID NO: 872)
CDR 3: DAPPNVEVASMTNWYFDL (SEQ ID NO: 870)

[745] TCN-531 (5091_H13) light chain variable region nucleotide sequence:
GACATCCAGCTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTGGGAGACAGAGTCACCATCACTTGCCGGGCG
AGTCAGGGCATTCTCAATTGTTTAGCCTGGTATCAGCAGAAACCGGGGAAAGTTCCTAACCTCCTGATGTATGCT
GCATCCACATTGCAGTCAGGGGTCCCATCTCGGTTCAGCGGCAGTGGATTTGGGACAGATTTCACTCTCACCATC
AGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTCAAACGTATGGCGGTGTCTCTACTTTCGGCGGAGGG
ACCAAGGTGGAGATCAGA (SEQ ID NO: 873)

[746] TCN-531 (5091_H13) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIQLTQSPSSLSASVGDRVTITCRASQGILNCLAWYQQKPGKVPNLLMYAASTLQSGVPSRFSGSGFG
TDFTLTISSLQPEDVATYYCQTYGGVSTFGGGTKVEIR (SEQ ID NO: 874)

[747] TCN-531 (5091_H13) Light chain Kabat CDRs:
CDR 1: RASQGILNCLA (SEQ ID NO: 875)
CDR 2: AASTLQS (SEQ ID NO: 876)
CDR 3: QTYGGVST (SEQ ID NO: 877)

[748] TCN-531 (5091_H13) Light chain Chothia CDRs:
CDR 1: RASQGILNCLA (SEQ ID NO: 875)
CDR 2: AASTLQS (SEQ ID NO: 876)
CDR 3: QTYGGVST (SEQ ID NO: 877)

[749] TCN-532 (5262_H18) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCTTGTCCCTCACCTGCACTGTCTCT
GGTGGCTCCGTCAGCAGTGAGACTTACTACTGGAGCTGGATCCGGCAGCCCCCAGGGAAGGGACTAGAGTGGATT
GGATATATCTATTACATTGGGAACACCGACTACAGGCCCTCCCTCAAGAGTCGAGTCACCATATCACTGGACACG
TCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACGGCCGTTTATTACTGTGCGAGAGGC
GCTTATTATGATAGTAGTGGTTACCCGGCTTTTTATATCTGGGGCCAAGGGACAATGGTCACCGTCTCCTCA
(SEQ ID NO: 878)

[750] TCN-532 (5262_H18) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQESGPGLVKPSETLSLTCTVS<u>GGSVSSET</u>**YYWS**WIRQPPGKGLEWIG**<u>YIYYIGNTD</u>YRPSLKS**R
VTISLDTSKNQFSLKLSSVTAADTAVYYCAR<u>GAYYDSSGYPAFYI</u>**WGQGTMVTVSS (SEQ ID NO: 879)

[751] TCN-532 (5262_H18) gamma heavy chain Kabat CDRs:
CDR 1: SETYYWS (SEQ ID NO: 880)
CDR 2: YIYYIGNTDYRPSLKS (SEQ ID NO: 881)
CDR 3: GAYYDSSGYPAFYI (SEQ ID NO: 882)

[752] TCN-532 (5262_H18) gamma heavy chain Chothia CDRs:
CDR 1: GGSVSSET (SEQ ID NO: 883)
CDR 2: YIYYIGNTD (SEQ ID NO: 884)
CDR 3: GAYYDSSGYPAFYI (SEQ ID NO: 882)

[753] TCN-532 (5262_H18) light chain variable region nucleotide sequence:
CAGTCTGTGCTGACGCAGCCGCCCTCAGTGTCTGGGGCCCCAGGGCAGAGGGTCACCATCTCCTGCACTGGGAGC
AGCTCCAACATCGGGTCAGATTATGATGTGCACTGGTACAAGCAACTTCCAGGAACAGCCCCCAAACTCCTCATC
TTTGGTAACAGCAATCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCTG
GCCATCACTGGGCTCCAGGCTGAGGATGAGGCTGATTATTACTGCCAATCCTATGACAGCAGCCTGAGTGGTTTT
CATGTCTTCGGAAGTGGGACCAAGGTCACCGTCCTA (SEQ ID NO: 885)

[754] TCN-532 (5262_H18) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QSVLTQPPSVSGAPGQRVTISC<u>TGSSSNIGSDYDVH</u>WYKQLPGTAPKLLIF<u>GNSNRPS</u>GVPDRFSGSKS
GTSASLAITGLQAEDEADYYC<u>QSYDSSLSGFHV</u>FGSGTKVTVL (SEQ ID NO: 886)

[755] TCN-532 (5262_H18) Light chain Kabat CDRs:
CDR 1: TGSSSNIGSDYDVH (SEQ ID NO: 887)
CDR 2: GNSNRPS (SEQ ID NO: 888)
CDR 3: QSYDSSLSGFHV (SEQ ID NO: 889)

[756] TCN-532 (5262_H18) Light chain Chothia CDRs:
CDR 1: TGSSSNIGSDYDVH (SEQ ID NO: 887)
CDR 2: GNSNRPS (SEQ ID NO: 888)
CDR 3: QSYDSSLSGFHV (SEQ ID NO: 889)

[757] TCN-533 (5256_A17) heavy chain variable region nucleotide sequence:

CAGGTGCAGCTGGTGCAGTCTGGGGCTGACGTGAAGAAGCCTGGGTCCTCGGTGACGGTCTCCTGCAAGGCTTCT
GGAGGCAGCTTCAGCAACTATGGAATCAACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGGGGA
ATCATCCCTCTCATTAATGCACCGAACTACGCACCGAAGTTCCAGGGCAGAGTGACGATTACCGCGGACATGTTC
TCGAATATAGTCTCCTTGCAGTTGACCAGCCTGAGAACTGACGACACGGCCGTGTATTATTGTGCGAGACGAAAA
ATGACTACGGCTATTGACTATTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCA (SEQ ID NO: 890)

[758] TCN-533 (5256_A17) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGADVKKPGSSVTVSCKAS<u>GGSFSN</u>**YGIN**WVRQAPGQGLEWMG**<u>GIIPLINAPN</u>YAPKFQG**
RVTITADMFSNIVSLQLTSLRTDDTAVYYCAR**<u>RKMTTAIDY</u>**WGQGTLVTVSS (SEQ ID NO: 891)

[759] TCN-533 (5256_A17) gamma heavy chain Kabat CDRs:
CDR 1: NYGIN (SEQ ID NO: 892)
CDR 2: GIIPLINAPNYAPKFQG (SEQ ID NO: 893)
CDR 3: RKMTTAIDY (SEQ ID NO: 894)

[760] TCN-533 (5256_A17) gamma heavy chain Chothia CDRs:
CDR 1: GGSFSN (SEQ ID NO: 787)
CDR 2: GIIPLINAPN (SEQ ID NO: 895)
CDR 3: RKMTTAIDY (SEQ ID NO: 894)

[761] TCN-533 (5256_A17) light chain variable region nucleotide sequence:
CAGCCTGTGTTGAGTCAGCCACCTTCTGCATCGGCCTCCCTGGGAGCCTCCGTCACACTCACCTGCAC
CCTGAGTAGCGGCTTCGATAATTATCAAGTGGCCTGGTACCAGCAGAGACCAGGGAAGGGCCCCCGCT
TTGTGATGCGGGTGGGCAATGGTGGGAATGTGGCTTCCAAGGGGGATGGCATTCCTGATCGTTTCTCA
GTCTCGGGCTCAGGCCTGAATCGGTACCTGACCATCAAGAACATCCAGGAAGACGATGAGAGTGACTA
TTATTGTGGGGCAGACCATGGCAGTGGGAACAACTTCGTGTCCCCTTATGTGTTTGGCGGAGGGACCA
AGCTGACCGTTCTA (SEQ ID NO: 896)

[762] TCN-533 (5256_A17) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QPVLSQPPSASASLGASVTLTC**<u>TLSSGFDNYQVA</u>**WYQQRPGKGPRFVMR**<u>VGNGGNVASKG</u>
<u>D</u>GIPDRFSVSGSGLNRYLTIKNIQEDDESDYYC<u>GADHGSGNNFVSPYV</u>**FGGGTKLTVL (SEQ
ID NO: 897)

[763] TCN-533 (5256_A17) Light chain Kabat CDRs:
CDR 1: TLSSGFDNYQVA (SEQ ID NO: 898)
CDR 2: VGNGGNVASKGD (SEQ ID NO: 899)
CDR 3: GADHGSGNNFVSPYV (SEQ ID NO: 900)

[764] TCN-533 (5256_A17) Light chain Chothia CDRs:
CDR 1: TLSSGFDNYQVA (SEQ ID NO: 898)
CDR 2: VGNGGNVASKGD (SEQ ID NO: 899)
CDR 3: GADHGSGNNFVSPYV (SEQ ID NO: 900)

[765] TCN-534 (5249_B02) heavy chain variable region nucleotide sequence:
CAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCAGGGTCCTCGGTGAAGGTCTCCTGCAGGGAATCT
GGAGGCACCTTCAACGGCTACACTATCACCTGGGTGCGACAGGCCCCTGGGCAAGGCCTTGAGTGGATGGGAGGG
ATCATCCCTATGATGGGGACAGTCAACTACGCACAGAAGTTGCAGGGCAGAGTCACCATTACCACGGACTATTTC
ACGAAAACAGCCTACATGGATCTGAACAATTTAAGATCTGAAGACACGGCCATGTATTATTGTGTGAAAATCAGA
TATACTGGGCAGCAGCTGCTCTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCA (SEQ ID NO: 901)

[766] TCN-534 (5249_B02) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGAEVKKPGSSVKVSCRES<u>GGTFNG</u>**YTIT**WVRQAPGQGLEWMG**<u>GIIPMMGTVN</u>YAQKLQ**
GRVTITTDYFTKTAYMDLNNLRSEDTAMYYCVK**<u>IRYTGQQLL</u>**WGQGTLVTVSS (SEQ ID NO: 902)

[767] TCN-534 (5249_B02) gamma heavy chain Kabat CDRs:
CDR 1: GYTIT (SEQ ID NO: 903)
CDR 2: GIIPMMGTVNYAQKLQG (SEQ ID NO: 904)
CDR 3: IRYTGQQLL (SEQ ID NO: 905)

[768] TCN-534 (5249_B02) gamma heavy chain Chothia CDRs:
CDR 1: GGTFNG (SEQ ID NO: 906)
CDR 2: GIIPMMGTVN (SEQ ID NO: 907)
CDR 3: IRYTGQQLL (SEQ ID NO: 905)

[769] TCN-534 (5249_B02) light chain variable region nucleotide sequence:
GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCGGCATCTATAGGAGACAGAGTCACCATCACTTGCCGGGCC
AGTCAGAGTATTGCAAGTTGGTTGGCCTGGTATCAGCAAAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGAG
GCAGTTAATTTAGAAAGTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATC
AGCAGCCTGCAGCCCGATGATTTTGCAACTTATTTCTGCCAACATTATGGTACTATTTCTCAGACCTTCGGCGGA
GGGACCAAGGTGGAGATCAAA (SEQ ID NO: 908)

[770] TCN-534 (5249_B02) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIQMTQSPSTLSASIGDRVTITC<u>**RASQSIASWLA**</u>WYQQKPGKAPKLLIY<u>**EAVNLES**</u>GVPSRFSGSGSGT
DFTLTISSLQPDDFATYFC<u>**QHYGTISQT**</u>FGGGTKVEIK (SEQ ID NO: 909)

[771] TCN-534 (5249_B02) Light chain Kabat CDRs:
CDR 1: RASQSIASWLA (SEQ ID NO: 910)
CDR 2: EAVNLES (SEQ ID NO: 911)
CDR 3: QHYGTISQT (SEQ ID NO: 912)

[772] TCN-534 (5249_B02) Light chain Chothia CDRs:
CDR 1: RASQSIASWLA (SEQ ID NO: 910)
CDR 2: EAVNLES (SEQ ID NO: 911)
CDR 3: QHYGTISQT (SEQ ID NO: 912)

[773] TCN-535 (5246_P19) heavy chain variable region nucleotide sequence:
CAGGTCCAGCTGGTGCAATCTGGGAGTGAGGTGAAGAAGCCTGGGACCTCGGTGAAGGTCTCCTGCACGGCCTCT
GGAAGTGTCTTCACCAATTATGGAATTAGTTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG
ATCATCCCTCTCTTTGGCGCAGCCAAGTACGCACAGAAATTCCAGGGCAGAGTCACCATCACAGCGGACGAATCC
ACGAAGACAGTCTACATGGAGCTGAGCAGGCTGACATCTAAAGACACGGCCATATATTTCTGTGCGAAGGCCCCC
CGTGTCTACGAGTACTACTTTGATCAGTGGGGCCAGGGAACCCCAGTCACCGTCTCCTCA (SEQ ID NO: 913)

[774] TCN-535 (5246_P19) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGSEVKKPGTSVKVSCTAS<u>GSVFTN</u>**YGIS**WVRQAPGQGLEWMG**GIIPLFGAAK**<u>**YAQKFQG**</u>
RVTITADESTKTVYMELSRLTSKDTAIYFCAK<u>**APRVYEYYFDQ**</u>WGQGTPVTVSS (SEQ ID NO: 914)

[775] TCN-535 (5246_P19) gamma heavy chain Kabat CDRs:
CDR 1: NYGIS (SEQ ID NO: 915)
CDR 2: GIIPLFGAAKYAQKFQG (SEQ ID NO: 916)
CDR 3: APRVYEYYFDQ (SEQ ID NO: 917)

[776] TCN-535 (5246_P19) gamma heavy chain Chothia CDRs:
CDR 1: GSVFTN (SEQ ID NO: 918)
CDR 2: GIIPLFGAAK (SEQ ID NO: 919)
CDR 3: APRVYEYYFDQ (SEQ ID NO: 917)

[777] TCN-535 (5246_P19) light chain variable region nucleotide sequence:
GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC
AGTCAGAGTGTTAGCAGCAGTCAATTAGCCTGGTACCAGCAAAAACCTGGCCAGGCTCCCAGGCTCATCATCTAT
GGTGCGTCCACCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGAAGTGGGTCTGGGACAGACTTCACTCTCACC
ATCGGCAGACTGGAGCCTGAAGATTTTGCAGTGTTTTTCTGTCAGCAGTATAGTACCTCACCTCCGACGTTCGGC
CAAGGGACCAAGGTGGATTTCAAA (SEQ ID NO: 920)

[778] TCN-535 (5246_P19) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

EIVLTQSPGTLSLSPGERATLSC<u>**RASQSVSSSQLA**</u>WYQQKPGQAPRLIIY<u>**GASTRAT**</u>GIPDRFSGSGSGT
DFTLTIGRLEPEDFAVFFC<u>**QQYSTSPPT**</u>FGQGTKVDFK (SEQ ID NO: 921)

[779] TCN-535 (5246_P19) Light chain Kabat CDRs:
CDR 1: RASQSVSSSQLA (SEQ ID NO: 922)
CDR 2: GASTRAT (SEQ ID NO: 755)
CDR 3: QQYSTSPPT (SEQ ID NO: 923)

[780] TCN-535 (5246_P19) Light chain Chothia CDRs:
CDR 1: RASQSVSSSQLA (SEQ ID NO: 922)
CDR 2: GASTRAT (SEQ ID NO: 755)
CDR 3: QQYSTSPPT (SEQ ID NO: 923)

[781] TCN-536 (5095_N01) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGCAGCAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCGCTGTCTAT
GGTGGGTCCTTCAGTGTCAGTGGTTACTACTGGAGCTGGATCCGCCAGCCCCCAGGGAGGGGGCTGGAGTGGATT
GGGGAAATCAGTCATGGTGGAAGCACCAACTACAACCCGTCCCTCAAGAGTCGAGTCACCATATCAGTGGACACG
ACCAAGAACCAGTTCTCCCTGAGACTGAGCTCTGTGACCGCCGCGGACACGGCCGTCTATTACTGTGCGAGAGGG
ACAGACCCTGACACGGAAGTATATTGTCGTGTTGGTAACTGCGCGGCCTTTGACTACTGGGGCCAGGGAAGCCTG
GTCACCGTCTCCTCA (SEQ ID NO: 924)

[782] TCN-536 (5095_N01) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQQWGAGLLKPSETLSLTCAVY<u>GGSFSVSG</u>**YYWS**WIRQPPGRGLEWIG**<u>EISHGGSTN</u>YNPSLKS**
RVTISVDTTKNQFSLRLSSVTAADTAVYYCAR**<u>GTDPDTEVYCRVGNCAAFDY</u>**WGQGSLVTVSS (SEQ ID NO: 925)

[783] TCN-536 (5095_N01) gamma heavy chain Kabat CDRs:
CDR 1: VSGYYWS (SEQ ID NO: 926)
CDR 2: EISHGGSTNYNPSLKS (SEQ ID NO: 927)
CDR 3: GTDPDTEVYCRVGNCAAFDY (SEQ ID NO: 928)

[784] TCN-536 (5095_N01) gamma heavy chain Chothia CDRs:
CDR 1: GGSFSVSG (SEQ ID NO: 929)
CDR 2: EISHGGSTN (SEQ ID NO: 930)
CDR 3: GTDPDTEVYCRVGNCAAFDY (SEQ ID NO: 928)

[785] TCN-536 (5095_N01) light chain variable region nucleotide sequence:
GAAATTATATTGGCGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAGAGAGCCACCCTCTCCTGCAGGGCC
AGCCAGTTTGTTAGCACCAGATCCCTGGCCTGGTACCAGCAGAGACCTGGCCAGGCTCCCAGACTCCTCATCTAT
GGTGCATCCAGCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACGCTCACC
ATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTCAGCACTATGGTTACTCACCTAGGTACGCTTTT
GGCCAGGGGTCCAAGGTTGAGATCAAA (SEQ ID NO: 931)

[786] TCN-536 (5095_N01) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

EIILAQSPGTLSLSPGERATLSC**<u>RASQFVSTRSLA</u>**WYQQRPGQAPRLLIY**<u>GASSRAT</u>**GIPDRFSGSGSGT
DFTLTISRLEPEDFAVYYC**<u>QHYGYSPRYA</u>**FGQGSKVEIK (SEQ ID NO: 932)

[787] TCN-536 (5095_N01) Light chain Kabat CDRs:
CDR 1: RASQFVSTRSLA (SEQ ID NO: 933)
CDR 2: GASSRAT (SEQ ID NO: 768)
CDR 3: QHYGYSPRYA (SEQ ID NO: 934)

[788] TCN-536 (5095_N01) Light chain Chothia CDRs:
CDR 1: RASQFVSTRSLA (SEQ ID NO: 933)
CDR 2: GASSRAT (SEQ ID NO: 768)
CDR 3: QHYGYSPRYA (SEQ ID NO: 934)

[789] TCN-537 (3194_D21) heavy chain variable region nucleotide sequence:

CAGGTGCAGCTCCAACAGTGGGGCTCAGGACTGTTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCGCTGTCTAT
GGTGGGTCCTTCAGAGATGACTACTGGACCTGGATTCGCCAGCCCCCAGGCAAGGGGCTGGAGTGGATTGGGGAA
ATCAATCATAGTGGAAGAACCAACTACAACCCGTCCCTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCCTG
AAACAGTTCTCCTTGAAGGTGATTTCTGTGACCGCCGCGGACACGGCTGTTTATTACTGTGCGAGAGGGACGAGC
CATGTTTCCCGGTATTTTGATTGGTTACCACCCACCAACTGGTTCGACCCCTGGGGCCAGGGAACCCAGGTCACC
GTCTCGAGC (SEQ ID NO: 935)

[790] TCN-537 (3194_D21) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQQWGSGLLKPSETLSLTCAVY<u>GGSFRD</u>**DYWT**WIRQPPGKGLEWIG**<u>EINHSGRTN</u>YNPSLKS**RV
TISVDTSLKQFSLKVISVTAADTAVYYCAR<u>**GTSHVSRYFDWLPPTNWFDP**</u>WGQGTQVTVSS (SEQ ID NO: 936)

[791] TCN-537 (3194_D21) gamma heavy chain Kabat CDRs:
CDR 1: DDYWT (SEQ ID NO: 937)
CDR 2: EINHSGRTNYNPSLKS (SEQ ID NO: 938)
CDR 3: GTSHVSRYFDWLPPTNWFDP (SEQ ID NO: 939)

[792] TCN-537 (3194_D21) gamma heavy chain Chothia CDRs:
CDR 1: GGSFRD (SEQ ID NO: 940)
CDR 2: EINHSGRTN (SEQ ID NO: 941)
CDR 3: GTSHVSRYFDWLPPTNWFDP (SEQ ID NO: 939)

[793] TCN-537 (3194_D21) light chain variable region nucleotide sequence:
GACATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC
AGTCAGAGTGTTAGCAGCAGCTACTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCGTCATGTAT
GGTGCAGCCACCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGCCAGACTTCACTCTCACC
ATCAGCAGACTGGAGCCTGAAGATTTTGCAATGTATTACTGTCAGCAGTATGGTAACTCACCGATCACCTTCGGC
CAAGGGACACGACTGGAGATCAAA (SEQ ID NO: 942)

[794] TCN-537 (3194_D21) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIVLTQSPGTLSLSPGERATLSC**<u>RASQSVSSSYLA</u>**WYQQKPGQAPRLVMY**<u>GAATRAT</u>**GIPDRFSGSGS
GPDFTLTISRLEPEDFAMYYC**<u>QQYGNSPIT</u>**FGQGTRLEIK (SEQ ID NO: 943)

[795] TCN-537 (3194_D21) Light chain Kabat CDRs:
CDR 1: RASQSVSSSYLA (SEQ ID NO: 944)
CDR 2: GAATRAT (SEQ ID NO: 945)
CDR 3: QQYGNSPIT (SEQ ID NO: 946)

[796] TCN-537 (3194_D21) Light chain Chothia CDRs:
CDR 1: RASQSVSSSYLA (SEQ ID NO: 944)
CDR 2: GAATRAT (SEQ ID NO: 945)
CDR 3: QQYGNSPIT (SEQ ID NO: 946)

[797] TCN-538 (3206_O17) heavy chain variable region nucleotide sequence:
CAGATCACCTTGAAGGAGTCTGGTCCTACACTGGTGAAACCCACACAGACCCTCACACTGACCTGCGTCTTCTCT
GGGTTCTCACTCAGCATTACTGGAGTGCGTGTGGGCTGGATCCGTCAGCCCCCAGGAAAGGCCCTGGAGTGGCTT
GCACTCATTTCTTGGGATGATGAAAAGCACTACAGCCCATCTCTGCAGAGTAGGCTCACCATCACCAAGGACACC
TCCAAAAACCAGGTGGTCCTTACAATGACCAACCTGGACCCTGTCGACACAGCCACATATTACTGTGCACGGTCA
ACCGACAGGGGCCACGTCTTACGATATTTTGGCTGGATGTTACCGGGTGATGCATTTGATGTCTGGGGCCAAGGG
ACAATGGTCACCGTCTCGAGC (SEQ ID NO: 947)

[798] TCN-538 (3206_O17) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QITLKESGPTLVKPTQTLTLTCVFSGFSLSITGVRVGWIRQPPGKALEWLALISWDDEKHYSPSLQSRL
TITKDTSKNQVVLTMTNLDPVDTATYYCARSTDRGHVLRYFGWMLPGDAFDVWGQGTMVTVSS
(SEQ ID NO: 948)

[799] TCN-538 (3206_O17) gamma heavy chain Kabat CDRs:
CDR 1: ITGVRVG (SEQ ID NO: 949)
CDR 2: LISWDDEKHYSPSLQS (SEQ ID NO: 950)
CDR 3: STDRGHVLRYFGWMLPGDAFDV (SEQ ID NO: 951)

[800] TCN-538 (3206_O17) gamma heavy chain Chothia CDRs:
CDR 1: GFSLSITG (SEQ ID NO: 952)
CDR 2: LISWDDEKH (SEQ ID NO: 953)
CDR 3: STDRGHVLRYFGWMLPGDAFDV (SEQ ID NO: 951)

[801] TCN-538 (3206_O17) light chain variable region nucleotide sequence:
GACATCGTGATGACCCAGTCTCCAGACTTCCTGCCTGTGTCTCTGGGCGAGAGGGCCACCATCAACTGCAAGTCC
AGCCAGAGAGTTTTATACAGCTCCAACAATAAAAACTACTTAGCTTGGTACCAGCTGAAACCAGGGCAGCCTCCT
AAGTTGATCATTTATTGGGCATCTACCCGGGAATCCGGGGTCCCTGACCGATTCAGTGGCAGCGGGTCTGGGACA
GAATTCACTCTCACCATCAGCAGCCTGCAGGCTGAAGATGTGGCAGTTTATTACTGTCAACAATATTATAGTCGT
CCGTACACTTTTGGCCAGGGGACCAAGCTCGAGATCAAA (SEQ ID NO: 954)

[802] TCN-538 (3206_O17) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIVMTQSPDFLPVSLGERATINCKSSQRVLYSSNNKNYLAWYQLKPGQPPKLIIYWASTRESGVPDRFS
GSGSGTEFTLTISSLQAEDVAVYYCQQYYSRPYTFGQGTKLEIK (SEQ ID NO: 955)

[803] TCN-538 (3206_O17) Light chain Kabat CDRs:
CDR 1: KSSQRVLYSSNNKNYLA (SEQ ID NO: 956)
CDR 2: WASTRES (SEQ ID NO: 957)
CDR 3: QQYYSRPYT (SEQ ID NO: 958)

[804] TCN-538 (3206_O17) Light chain Chothia CDRs:
CDR 1: KSSQRVLYSSNNKNYLA (SEQ ID NO: 956)
CDR 2: WASTRES (SEQ ID NO: 957)
CDR 3: QQYYSRPYT (SEQ ID NO: 958)

[805] TCN-539 (5056_A08) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCT
GAAATCACCTTCATTACCTATGCTATGCACTGGGTCCGCCAGGCCCCAGGCAAGGGGCTGGAGTGGGTGGCACTT
ATATCAGATGATGGAAGCAATAAATTCTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCC
AAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGCTTATTACTGTGCGAGAGAAGGG
GTTTACTTTGATTCGGGGACTTATAGGGGCTACTTTGACTACTGGGGCCAGGAAACCCTGGTCACCGTCTCGAGC
(SEQ ID NO: 959)

[806] TCN-539 (5056_A08) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVESGGGVVQPGRSLRLSCAASEITFIT**YAMH**WVRQAPGKGLEWVA**LISDDGSNKF**YADSVKG
RFTISRDNSKNTLYLQMNSLRAEDTAAYYCAR**EGVYFDSGTYRGYFDY**WGQETLVTVSS (SEQ ID NO: 960)

[807] TCN-539 (5056_A08) gamma heavy chain Kabat CDRs:
CDR 1: TYAMH (SEQ ID NO: 961)
CDR 2: LISDDGSNKFYADSVKG (SEQ ID NO: 962)
CDR 3: EGVYFDSGTYRGYFDY (SEQ ID NO: 963)

[808] TCN-539 (5056_A08) gamma heavy chain Chothia CDRs:
CDR 1: EITFIT (SEQ ID NO: 964)
CDR 2: LISDDGSNKF (SEQ ID NO: 965)
CDR 3: EGVYFDSGTYRGYFDY (SEQ ID NO: 963)

[809] TCN-539 (5056_A08) light chain variable region nucleotide sequence:
GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC
AGTCAGAGTGTTAGCAGCTACTTAGCCTGGTACCAACAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGAT
GCATCCAACAGGGCCACTGGCATCCCAGCCAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATC
AGCAGCCTAGAGCCTGAAGATTTTGCAGTTTATTACTGTCAGCAGCGTAGCCACTGGCCTCCGATCACCTTCGGC
CAAGGGACACGACTGGAGATCAAA (SEQ ID NO: 966)

[810] TCN-539 (5056_A08) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

EIVLTQSPATLSLSPGERATLSC**RASQSVSSYLA**WYQQKPGQAPRLLIY**DASNRAT**GIPARFSGSGSGTD
FTLTISSLEPEDFAVYYC**QQRSHWPPIT**FGQGTRLEIK (SEQ ID NO: 967)

[811] TCN-539 (5056_A08) Light chain Kabat CDRs:
CDR 1: RASQSVSSYLA (SEQ ID NO: 968)
CDR 2: DASNRAT (SEQ ID NO: 969)
CDR 3: QQRSHWPPIT (SEQ ID NO: 970)

[812] TCN-539 (5056_A08) Light chain Chothia CDRs:
CDR 1: RASQSVSSYLA (SEQ ID NO: 968)
CDR 2: DASNRAT (SEQ ID NO: 969)
CDR 3: QQRSHWPPIT (SEQ ID NO: 970)

[813] TCN-540 (5060_F05) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGGTACAATCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCT
GGATTCACCTTCAGTAGCTACGCCATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCTATT
ATATCATACGACGGAAATGATCAATACTATACAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAGCTCC
AAAGTGTATCTCCAAATGCACAGGCTGAGACCTGAGGACACGGCTGTTTATTACTGTGCGAAAGAATTTGAAACT
AGTGGTTATTTTCATGGGAGTTTTGACTACTGGGGCCAGGGAATCCTGGTCACCGTCTCGAGC (SEQ ID NO: 971)

[814] TCN-540 (5060_F05) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGGGVVQPGRSLRLSCAASGFTFSS**YAMH**WVRQAPGKGLEWVA**IISYDGNDQY**YTDSVKG
RFTISRDSSKVYLQMHRLRPEDTAVYYCAK**EFETSGYFHGSFDY**WGQGILVTVSS (SEQ ID NO: 972)

[815] TCN-540 (5060_F05) gamma heavy chain Kabat CDRs:
CDR 1: SYAMH (SEQ ID NO: 973)
CDR 2: IISYDGNDQYYTDSVKG (SEQ ID NO: 974)
CDR 3: EFETSGYFHGSFDY (SEQ ID NO: 975)

[816] TCN-540 (5060_F05) gamma heavy chain Chothia CDRs:
CDR 1: GFTFSS (SEQ ID NO: 976)
CDR 2: IISYDGNDQY (SEQ ID NO: 977)
CDR 3: EFETSGYFHGSFDY (SEQ ID NO: 975)

[817] TCN-540 (5060_F05) light chain variable region nucleotide sequence:
CAGTCTGCCCTGACTCAGCCTGCCTCCGTGTCTGGGTCTCCTGGACAGTCGATCACCATCTCCTGCACTGGAACC
AGCAGTGACGTTGGTGGTTATAACTATGTCTCCTGGTACCAACAACACCCAGGCAAAGCCCCCAAACTCTTGATT
TATGAGGTCACTAATTGGCCCTCAGGGGTTTCTAATCGCTTCTCTGGCTCCAAGTCTGGCAACACGGCCTCCCTG
ACAATCTCTGGGCTCCAGGCTGAGGACGAGGCTGACTATTACTGCAGCTCATATGCGGGCAGCAGCACTTGGGTG
TTCGGCGGAGGGACCAGGGTGACCGTTCTA (SEQ ID NO: 978)

[818] TCN-540 (5060_F05) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QSALTQPASVSGSPGQSITISC**TGTSSDVGGYNYVS**WYQQHPGKAPKLLIY**EVTNWPS**GVSNRFSGSK
SGNTASLTISGLQAEDEADYYC**SSYAGSSTWV**FGGGTRVTVL (SEQ ID NO: 979)

[819] TCN-540 (5060_F05) Light chain Kabat CDRs:
CDR 1: TGTSSDVGGYNYVS (SEQ ID NO: 980)
CDR 2: EVTNWPS (SEQ ID NO: 981)
CDR 3: SSYAGSSTWV (SEQ ID NO: 982)

[820] TCN-540 (5060_F05) Light chain Chothia CDRs:
CDR 1: TGTSSDVGGYNYVS (SEQ ID NO: 980)
CDR 2: EVTNWPS (SEQ ID NO: 981)
CDR 3: SSYAGSSTWV (SEQ ID NO: 982)

[821] TCN-541 (5062_M11) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCACTGTCTCT
GGTGGCTCCATCAATAGTTACTACTGGAACTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGCTAT
ATCTATCACAGTGGGAGCACCAACTACAACCCCTCCCTCAAGAGTCGAGTCACCATTTCGGTAGACACGTCCAAG
AACCAGTTCTCCCTGCAGCTGAGCTCTGTGACCGCCGCAGACACGGCCGTGTATTACTGTGCGAGACTCCGGACG
GACTACGGTGACCCCGACTCGGTATACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCG
AGC (SEQ ID NO: 983)

[822] TCN-541 (5062_M11) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQESGPGLVKPSETLSLTCTVSGGSINSYYWNWIRQPPGKGLEWIG**YIYHSGSTN**YNPSLKSRVTI
SVDTSKNQFSLQLSSVTAADTAVYYCAR**LRTDYGDPDSVYYYGMDV**WGQGTTVTVSS (SEQ ID NO: 984)

[823] TCN-541 (5062_M11) gamma heavy chain Kabat CDRs:
CDR 1: SYYWN (SEQ ID NO: 985)
CDR 2: YIYHSGSTNYNPSLKS (SEQ ID NO: 986)
CDR 3: LRTDYGDPDSVYYYGMDV (SEQ ID NO: 987)

[824] TCN-541 (5062_M11) gamma heavy chain Chothia CDRs:
CDR 1: GGSINS (SEQ ID NO: 988)
CDR 2: YIYHSGSTN (SEQ ID NO: 989)
CDR 3: LRTDYGDPDSVYYYGMDV (SEQ ID NO: 987)

[825] TCN-541 (5062_M11) light chain variable region nucleotide sequence:
TCCTATGAGCTGACACAGCCACCCTCGGTGTCAGTGTCCCCAGGACAGACGGCCAGGATCACCTGCTCTGGAGAT
GCATTGCCAAAGCAAAATGCTTATTGGTACCAGCAGAAGCCAGGCCAGGCCCCTGTGCTGCTGATATATAAAGAC
AGTGAGAGGCCCTCAGGGATCCCTGAGCGATTCTCTGGCTCCAGCTCAGGGACAACAGTCACGTTGACCATCAGT
GGAGTCCAGGCAGAGGACGAGGCTGACTATTACTGTCAATCAGCAGACAGCAGTGGTACTTCTTGGGTGTTCGGC
GGAGGGACCAAACTGACCGTTCTA (SEQ ID NO: 990)

[826] TCN-541 (5062_M11) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

SYELTQPPSVSVSPGQTARITC**SGDALPKQNAY**WYQQKPGQAPVLLIY**KDSERPS**GIPERFSGSSSGTT
VTLTISGVQAEDEADYYC**QSADSSGTSWV**FGGGTKLTVL (SEQ ID NO: 991)

[827] TCN-541 (5062_M11) Light chain Kabat CDRs:
CDR 1: SGDALPKQNAY (SEQ ID NO: 994)
CDR 2: KDSERPS (SEQ ID NO: 995)
CDR 3: QSADSSGTSWV (SEQ ID NO: 996)

[828] TCN-541 (5062_M11) Light chain Chothia CDRs:
CDR 1: SGDALPKQNAY (SEQ ID NO: 994)
CDR 2: KDSERPS (SEQ ID NO: 995)
CDR 3: QSADSSGTSWV (SEQ ID NO: 996)

[829] TCN-542 (5079_A16) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCACAGACCCTGTCCCTCACCTGCACTGTCTCT
GGTGGCTCCATCAGCAGTGGTAATTACTACTGGAACTGGGTCCGCCAGCACCCAGGGAAGGGCCTGGAGTGGATT
GGGTACATCTATTACAGAGGGAGCACCTTCTACAACCCGTCCCTCAAGAGTCGAGTGACCATATCAATAGACACG
TCTAAGAACCAGTTCTCCCTGAGGCTGAGCTCTGTGACGGCCGCGGACACGGCCGTGTATTACTGTGCGAAGGAT
ACAAGGTCGAGCCTAGACAATTACCAGTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC
(SEQ ID NO: 992)

[830] TCN-542 (5079_A16) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQESGPGLVKPSQTLSLTCTVS<u>GGSISSGNYYWN</u>WVRQHPGKGLEWIG<u>YIYYRGSTFYNPSLKS</u>R
VTISIDTSKNQFSLRLSSVTAADTAVYYCAK<u>DTRSSLDNYQYGMDV</u>WGQGTTVTVSS (SEQ ID NO: 993)

[831] TCN-542 (5079_A16) gamma heavy chain Kabat CDRs:
CDR 1: SGNYYWN (SEQ ID NO: 997)
CDR 2: YIYYRGSTFYNPSLKS (SEQ ID NO: 998)
CDR 3: DTRSSLDNYQYGMDV (SEQ ID NO: 999)

[832] TCN-542 (5079_A16) gamma heavy chain Chothia CDRs:
CDR 1: GGSISSGN (SEQ ID NO: 1000)
CDR 2: YIYYRGSTF (SEQ ID NO: 1001)
CDR 3: DTRSSLDNYQYGMDV (SEQ ID NO: 999)

[833] TCN-542 (5079_A16) light chain variable region nucleotide sequence:
CAGACTGTGGTGACTCAGGAGCCCTCACTGACTGTGTCCCCAGGAGGGACAGTCACTCTCACCTGTGCTTCCAGC
ACTGGAGCAGTCACCAGTAGTTACTTTCCAAACTGGTTCCAGCAGAAACCTGGACAAGCGCCCAGGCCACTGATT
TATAGTACAACTATCAGACACTCCTGGACCCCGGCCCGATTCTCAGGCTCCCTCCTTGGGGGCAAAGCTGCCCTG
ACACTGTCAGGTGTGCAGCCTGAGGACGAGGCTGACTATTACTGCCTGCTCTACTCTGGTGGTGATCCAGTGGCT
TTCGGCGGAGGGACCAAACTGACCGTTCTA (SEQ ID NO: 1002)

[834] TCN-542 (5079_A16) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QTVVTQEPSLTVSPGGTVTLTC<u>ASSTGAVTSSYFPN</u>WFQQKPGQAPRPLIY<u>STTIRHS</u>WTPARFSGSLL
GGKAALTLSGVQPEDEADYYC<u>LLYSGGDPVA</u>FGGGTKLTVL (SEQ ID NO: 1003)

[835] TCN-542 (5079_A16) Light chain Kabat CDRs:
CDR 1: ASSTGAVTSSYFPN (SEQ ID NO: 1004)
CDR 2: STTIRHS (SEQ ID NO: 1005)
CDR 3: LLYSGGDPVA (SEQ ID NO: 1006)

[836] TCN-542 (5079_A16) Light chain Chothia CDRs:
CDR 1: ASSTGAVTSSYFPN (SEQ ID NO: 1004)
CDR 2: STTIRHS (SEQ ID NO: 1005)
CDR 3: LLYSGGDPVA (SEQ ID NO: 1006)

[837] TCN-543 (5081_G23) heavy chain variable region nucleotide sequence:
CAGGTTCATCTGGTGCAGTCTGGAGCTGAGGTGAGGAAGCCTGGGGACTCAGTGAAGGTCTCCTGTAAGACTTCT
GGTTACACCTTTTCCACCTATCCTGTCGCCTGGGTGCGACAGGTCCCCGGACAAGGGCTTGAGTGGATGGGATGG
ATCAGCACTTACAATGGAAACACAAACTTTGCACAGAACTTCCAGGGCAGAGTCACCCTGACCACAGACACAACC
ACGAACACAGCCTACATGGAAGTGAGGAGCCTGAAATTTGACGACACGGCCGTCTATTACTGTGCGAGAGTGGAA
GGCTCGTACAGGGATTTTTGGAATAATCAAAACAGATTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCG
AGC (SEQ ID NO: 1007)

[838] TCN-543 (5081_G23) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVHLVQSGAEVRKPGDSVKVSCKTS<u>GYTFST</u>**<u>YPVA</u>**WVRQVPGQGLEWMG**<u>WISTYNGNTN</u>**<u>FAQNFQ</u>
GRVTLTTDTTTNTAYMEVRSLKFDDTAVYYCAR**<u>VEGSYRDFWNNQNRFDP</u>**WGQGTLVTVSS (SEQ ID NO: 1008)

[839] TCN-543 (5081_G23) gamma heavy chain Kabat CDRs:
CDR 1: TYPVA (SEQ ID NO: 1009)
CDR 2: WISTYNGNTNFAQNFQG (SEQ ID NO: 1010)
CDR 3: VEGSYRDFWNNQNRFDP (SEQ ID NO: 1011)

[840] TCN-543 (5081_G23) gamma heavy chain Chothia CDRs:
CDR 1: GYTFST (SEQ ID NO: 1012)
CDR 2: WISTYNGNTN (SEQ ID NO: 1013)
CDR 3: VEGSYRDFWNNQNRFDP (SEQ ID NO: 1011)

[841] TCN-543 (5081_G23) light chain variable region nucleotide sequence:
TCCTATGTACTGACTCAGCCACCCTCGGTGTCAGTGGCCCCAGGACAGACGGCCAGGATTTCCTGTGGGGGAAGC
AACATTGGAGGGAAAAGTGTGCACTGGTACCAGCAGAAGCCAGGCCAGGCCCCTGTGCTGGTCGTCTATGATGAT
AGCGGCCGGCCCTCAGGGATCCCTGAGCGATTCTCTGGCTCCAACTCTGGGGACACGGCCACCCTGACCATCAGC
AGGGTCGAAGCCGGGGATGAGGCCGACTATTTCTGTCAGGTGTGGGATAATTTCGGGGGAGTCTTCGGAACTGGG
ACCAAGGTCACCGTTCTA (SEQ ID NO: 1014)

[842] TCN-543 (5081_G23) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

SYVLTQPPSVSVAPGQTARISC**<u>GGSNIGGKSVH</u>**WYQQKPGQAPVLVVY**<u>DDSGRPS</u>**GIPERFSGSNSGD
TATLTISRVEAGDEADYFC**<u>QVWDNFGGV</u>**FGTGTKVTVL (SEQ ID NO: 1015)

[843] TCN-543 (5081_G23) Light chain Kabat CDRs:
CDR 1: GGSNIGGKSVH (SEQ ID NO: 1016)
CDR 2: DDSGRPS (SEQ ID NO: 1017)
CDR 3: QVWDNFGGV (SEQ ID NO: 1018)

[844] TCN-543 (5081_G23) Light chain Chothia CDRs:
CDR 1: GGSNIGGKSVH (SEQ ID NO: 1016)
CDR 2: DDSGRPS (SEQ ID NO: 1017)
CDR 3: QVWDNFGGV (SEQ ID NO: 1018)

[845] TCN-544 (5082_A19) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGGCTGGTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCACTGTCTCT
CGTGGCTCCATCGGTCATTACTTCTGGAGCTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGTTAT
ATCTCTTACAGTGGGAGCACCAAGTACAACCCCTCCCTCAGGAGTCGAGTCACCATATCAGTAGACACGTCCAAG

AACCAGTTCTCCCTGAATCTGAACTCTGTCACCGCTACGGACACGGCCCTATATTACTGTGCGAGAGAGGATTAC
GATATTTTGACTGGGGCGGGACCCGGTATGGAGGTCTGGGGCCAAGGGACCACGGTCACCGTCTCGAGC (SEQ
ID NO: 1019)

[846] TCN-544 (5082_A19) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQESGPGLVKPSETLSLTCTVSRGSIGHYFWSWIRQPPGKGLEWIGYISYSGSTKYNPSLRSRVTIS
VDTSKNQFSLNLNSVTATDTALYYCAREDYDILTGAGPGMEVWGQGTTVTVSS (SEQ ID NO: 1020)

[847] TCN-544 (5082_A19) gamma heavy chain Kabat CDRs:
CDR 1: HYFWS (SEQ ID NO: 1021)
CDR 2: YISYSGSTKYNPSLRS (SEQ ID NO: 1022)
CDR 3: EDYDILTGAGPGMEV (SEQ ID NO: 1023)

[848] TCN-544 (5082_A19) gamma heavy chain Chothia CDRs:
CDR 1: RGSIGH (SEQ ID NO: 1024)
CDR 2: YISYSGSTK (SEQ ID NO: 1025)
CDR 3: EDYDILTGAGPGMEV (SEQ ID NO: 1023)

[849] TCN-544 (5082_A19) light chain variable region nucleotide sequence:
CAGTCTATGTTGACTCAGCCACCCTCAGCGTCTGGGACCCCCGGGCAGAGGGTCACCATCTCTTGTTCTGGGAGC
AGCTCCAACATCGGAAGTAATACTGTCAACTGGTTCAAACATCTCCCAGGAACGGCCCCCAAACTCCTCATCTAC
AGAAATGATCTGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCTGGCC
ATCAGTGGGCTCCAGTCTGAGGATGAGGCTGATTATTACTGTGCAACATGGGATGACAGCCTGAATGGTTTTTAT
GTCTTCGGAACTGGGACCAAAGTCACCGTTCTA (SEQ ID NO: 1026)

[850] TCN-544 (5082_A19) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QSMLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWFKHLPGTAPKLLIYRNDLRPSGVPDRFSGSKSGT
SASLAISGLQSEDEADYYCATWDDSLNGFYVFGTGTKVTVL (SEQ ID NO: 1027)

[851] TCN-544 (5082_A19) Light chain Kabat CDRs:
CDR 1: SGSSSNIGSNTVN (SEQ ID NO: 1028)
CDR 2: RNDLRPS (SEQ ID NO: 1029)
CDR 3: ATWDDSLNGFYV (SEQ ID NO: 1030)

[852] TCN-544 (5082_A19) Light chain Chothia CDRs:
CDR 1: SGSSSNIGSNTVN (SEQ ID NO: 1028)
CDR 2: RNDLRPS (SEQ ID NO: 1029)
CDR 3: ATWDDSLNGFYV (SEQ ID NO: 1030)

[853] TCN-545 (5082_I15) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCTGTCCCTCTCCTGCGCTGTCTTT
GGTGGGTCCTTCAGTGATTACTACTGGACCTGGATACGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGCGAA
ATCAAACATAGTGGAAGAACCAACTACAACCCGTCCCTTGAGAGTCGAGTCACCATATCAGTGGACACGTCCAAG
AACCAGTTTTCCCTGAAACTGAGTTCTGTGACCGCCGCGGACACGGCTATATATTATTGTGCGAGAGGGACAGAC
CCTGACACGGAGGGATATTGTCGTAGTGGTAGCTGCTCGGCCTTTGACTTCTGGGGCCAGGGAACCCTGGTCACC
GTCTCGAGC (SEQ ID NO: 1031)

[854] TCN-545 (5082_I15) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQQWGAGLLKPSETLSLSCAVF**GGSFSD**YYWTWIRQPPGKGLEWIG**EIKHSGRTNYNPSLES**RV TISVDTSKNQFSLKLSSVTAADTAIYYCAR**GTDPDTEGYCRSGSCSAFDF**WGQGTLVTVSS (SEQ ID NO: 1032)

[855] TCN-545 (5082_I15) gamma heavy chain Kabat CDRs:
CDR 1: DYYWT (SEQ ID NO: 1033)
CDR 2: EIKHSGRTNYNPSLES (SEQ ID NO: 1034)
CDR 3: GTDPDTEGYCRSGSCSAFDF (SEQ ID NO: 1035)

[856] TCN-545 (5082_I15) gamma heavy chain Chothia CDRs:
CDR 1: GGSFSD (SEQ ID NO: 1036)
CDR 2: EIKHSGRTN (SEQ ID NO: 1037)
CDR 3: GTDPDTEGYCRSGSCSAFDF (SEQ ID NO: 1035)

[857] TCN-545 (5082_I15) light chain variable region nucleotide sequence:
GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC AGTCACTTTGTGAACTACAGGTCCTTAGCCTGGTACCAGCAGACACCTGGCCAGGTTCCCAGGCTCCTCATCTAT GGTGCGTCCACCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACC ATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTTCTGTCAGCAGTATGGTGGCTCACCTAGGTACACTTTT GGCCAGGGGACCAGGCTGGAGATCAAA (SEQ ID NO: 1038)

[858] TCN-545 (5082_I15) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

EIVLTQSPGTLSLSPGERATLSC**RASHFVNYRSLA**WYQQTPGQVPRLLIY**GASTRAT**GIPDRFSGSGSGT DFTLTISRLEPEDFAVYFC**QQYGGSPRYT**FGQGTRLEIK (SEQ ID NO: 1039)

[859] TCN-545 (5082_I15) Light chain Kabat CDRs:
CDR 1: RASHFVNYRSLA (SEQ ID NO: 1040)
CDR 2: GASTRAT (SEQ ID NO: 755)
CDR 3: QQYGGSPRYT (SEQ ID NO: 1041)

[860] TCN-545 (5082_I15) Light chain Chothia CDRs:
CDR 1: RASHFVNYRSLA (SEQ ID NO: 1040)
CDR 2: GASTRAT (SEQ ID NO: 755)
CDR 3: QQYGGSPRYT (SEQ ID NO: 1041)

[861] TCN-546 (5089_L08) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCGGTGTCTAT GGTGGGTCCCTCAGTGATTACTACTGGAGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGAGAA ATCAATCATAGTGGAGGCACCAACTACAATCCGTCCCTCAAGAGACGAGTCACCATATCAGTAGACACGTCAAAG AAGCAATTCTCCCTGAAGATGAACTCTGTGACCGCCGCGGACACGGCTGTATATTACTGTGCGAGAGGGACAGAC CCTGACACGGAAGTATATTGTCGTGCTGGTAACTGCGCGGCCTTTGACTTCTGGGGCCAGGGAACCCTGGTCACC GTCTCGAGC (SEQ ID NO: 1042)

[862] TCN-546 (5089_L08) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQQWGAGLLKPSETLSLTCGVY**GGSLSDYYWS**WIRQPPGKGLEWIG**EINHSGGTNYNPSLKR**RV TISVDTSKKQFSLKMNSVTAADTAVYYCAR**GTDPDTEVYCRAGNCAAFDF**WGQGTLVTVSS (SEQ ID NO: 1043)

[863] TCN-546 (5089_L08) gamma heavy chain Kabat CDRs:
CDR 1: DYYWS (SEQ ID NO: 1044)
CDR 2: EINHSGGTNYNPSLKR (SEQ ID NO: 1045)
CDR 3: GTDPDTEVYCRAGNCAAFDF (SEQ ID NO: 1046)

[864] TCN-546 (5089_L08) gamma heavy chain Chothia CDRs:
CDR 1: GGSLSD (SEQ ID NO: 1047)
CDR 2: EINHSGGTN (SEQ ID NO: 1048)
CDR 3: GTDPDTEVYCRAGNCAAFDF (SEQ ID NO: 1046)

[865] TCN-546 (5089_L08) light chain variable region nucleotide sequence:
GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAGAGAGCCACCCTCTCCTGCCGGGCC
AGTCACTTTGTTATAGGCAGGGCTGTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTAC
GGTGCATCCAGCAGGGCCACTGGCATCCCGGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACC
ATCAGCAGACTGGAGACTGAAGATTTTGCTGTGTTTTACTGTCAGCACTATGGTAGCTCACCTAGGTACGCTTTT
GGCCAGGGGACCAAGCTGGAGATCAAA (SEQ ID NO: 1049)

[866] TCN-546 (5089_L08) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

EIVLTQSPGTLSLSPGERATLSC**RASHFVIGRAVA**WYQQKPGQAPRLLIY**GASSRAT**GIPDRFSGSGSGT DFTLTISRLETEDFAVFYC**QHYGSSPRYAF**GQGTKLEIK (SEQ ID NO: 1050)

[867] TCN-546 (5089_L08) Light chain Kabat CDRs:
CDR 1: RASHFVIGRAVA (SEQ ID NO: 1051)
CDR 2: GASSRAT (SEQ ID NO: 768)
CDR 3: QHYGSSPRYAF (SEQ ID NO: 1052)

[868] TCN-546 (5089_L08) Light chain Chothia CDRs:
CDR 1: RASHFVIGRAVA (SEQ ID NO: 1051)
CDR 2: GASSRAT (SEQ ID NO: 768)
CDR 3: QHYGSSPRYAF (SEQ ID NO: 1052)

[869] TCN-547 (5092_F11) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCACAGACCCTGTCCCTCACCTGCACTGTCTCT
GGTGACTCCATTAGTAGTGTTGATCACTACTGGAGCTGGATCCGCCAACACCCAGTGAAGGGCCTGGAGTGGATT
GGGTTCATGTATTACAGTGCGAGCACCTATTACAACCCGTCCCTCAAGAGTCGAGTTACCATATCAACGGACACG
TCTAAGAACCAGTTCTCCCTGAGGCTGAGTTCTGTGACTGCCGCGGACACGGCCGTATATTACTGTGCGAGAGGC
ACTTGTGCTGGTGACTGCTCCCTTCACTACTACTACGGTTTGGACGTCTGGGGCCAAGGGAGGACGGTCACC
GTCTCGAGC (SEQ ID NO: 1053)

[870] TCN-547 (5092_F11) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQESGPGLVKPSQTLSLTCTVSGDSISSVDHYWSWIRQHPVKGLEWIGFMYYSASTYYNPSLKSR VTISTDTSKNQFSLRLSSVTAADTAVYYCARGTCAGDCSLHYYYYGLDVWGQGRTVTVSS (SEQ ID NO: 1054)

[871] TCN-547 (5092_F11) gamma heavy chain Kabat CDRs:
CDR 1: SVDHYWS (SEQ ID NO: 1055)
CDR 2: FMYYSASTYYNPSLKS (SEQ ID NO: 1056)
CDR 3: GTCAGDCSLHYYYYGLDV (SEQ ID NO: 1057)

[872] TCN-547 (5092_F11) gamma heavy chain Chothia CDRs:
CDR 1: GDSISSVD (SEQ ID NO: 1058)
CDR 2: FMYYSASTY (SEQ ID NO: 1059)
CDR 3: GTCAGDCSLHYYYYGLDV (SEQ ID NO: 1057)

[873] TCN-547 (5092_F11) light chain variable region nucleotide sequence:
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCA AGTCAGAGCATTAGCAGCTATTTAAATTGGTATCAGCACAAACCAGGGAAAGCCCCTAAGGTCCTGATGTATGCT GTATCCATTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCTGGGGCAGATTTCACTCTCACCATC AGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTTCCCCGCTCACTTTCGGCGGA GGGACCAAGGTGGAGATCAAA (SEQ ID NO: 1060)

[874] TCN-547 (5092_F11) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQHKPGKAPKVLMYAVSILQSGVPSRFSGSGSGA DFTLTISSLQPEDFATYYCQQSYSSPLTFGGGTKVEIK (SEQ ID NO: 1061)

[875] TCN-547 (5092_F11) Light chain Kabat CDRs:
CDR 1: RASQSISSYLN (SEQ ID NO: 1062)
CDR 2: AVSILQS (SEQ ID NO: 1063)
CDR 3: QQSYSSPLT (SEQ ID NO: 1064)

[876] TCN-547 (5092_F11) Light chain Chothia CDRs:
CDR 1: RASQSISSYLN (SEQ ID NO: 1062)
CDR 2: AVSILQS (SEQ ID NO: 1063)
CDR 3: QQSYSSPLT (SEQ ID NO: 1064)

[877] TCN-548 (5092_P01) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCACTGTCTCT AGTGGCCCCATGAGTGATTATTACTGGAGCTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGCAT GTCTCTGTCTCTCACGGAGGGAGGACCAAATCCAATCCCTCCGTCATGAGTCGAGTCACCATTTCAGTAGAAACG TCCAAGAACCAATTCTCCCTGAAACTGACCTCCGTGACCGCTGCGGACACGGCCGTTTATTACTGTGCGAGATTA AATTACTATGATAGAAGTGGTTATCATTCGCCTGACGGCCCCTCGAACAACTGGTTCGACCCCTGGGGCCAGGGA ACCCTGGTCACCGTCTCGAGC (SEQ ID NO: 1065)

[878] TCN-548 (5092_P01) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQESGPGLVKPSETLSLTCTVSSGPMSDYYWSWIRQPPGKGLEWIGHVSVSHGGRTKSNPSVMS
RVTISVETSKNQFSLKLTSVTAADTAVYYCARLNYYDRSGYHSPDGPSNNWFDPWGQGTLVTVSS
(SEQ ID NO: 1066)

[879] TCN-548 (5092_P01) gamma heavy chain Kabat CDRs:
CDR 1: DYYWS (SEQ ID NO: 1044)
CDR 2: HVSVSHGGRTKSNPSVMS (SEQ ID NO: 1067)
CDR 3: LNYYDRSGYHSPDGPSNNWFDP (SEQ ID NO: 1068)

[880] TCN-548 (5092_P01) gamma heavy chain Chothia CDRs:
CDR 1: SGPMSD (SEQ ID NO: 1069)
CDR 2: HVSVSHGGRTK (SEQ ID NO: 1070)
CDR 3: LNYYDRSGYHSPDGPSNNWFDP (SEQ ID NO: 1068)

[881] TCN-548 (5092_P01) light chain variable region nucleotide sequence:
GACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGGCGAGAGGGCCACCATCAACTGCAAGTCC
AGCCAGAGTGTTTTATACAGCTCCAACAATAAGAACTACTTAGCTTGGTACCAGCAGAAACCAGGACAGCCTCCT
AAGCTGCTCATTTACTGGGCATCTACCCGGGAATCCGGGGTCCCTGACCGAATCAGCGGCAGCGGGTCTGGGGCA
GATTTCACTCTCACCATCAGCAGCCTGCAGGCTGAAGATGTGGCAGTTTATTACTGTCAGCAGTATTTTGCTACT
CCTCGGACGTTCGGCCAAGGGACCAAGGTGGAAATCAAA (SEQ ID NO: 1071)

[882] TCN-548 (5092_P01) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYLAWYQQKPGQPPKLLIYWASTRESGVPDRI
SGSGSGADFTLTISSLQAEDVAVYYCQQYFATPRTFGQGTKVEIK (SEQ ID NO: 1072)

[883] TCN-548 (5092_P01) Light chain Kabat CDRs:
CDR 1: KSSQSVLYSSNNKNYLA (SEQ ID NO: 1073)
CDR 2: WASTRES (SEQ ID NO: 957)
CDR 3: QQYFATPRT (SEQ ID NO: 1074)

[884] TCN-548 (5092_P01) Light chain Chothia CDRs:
CDR 1: KSSQSVLYSSNNKNYLA (SEQ ID NO: 1073)
CDR 2: WASTRES (SEQ ID NO: 957)
CDR 3: QQYFATPRT (SEQ ID NO: 1074)

[885] TCN-549 (5092_P04) heavy chain variable region nucleotide sequence:
CAGGTACAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
GGATACACCTTCACCGGCTACTATATGCACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGG
ATCAACCCTAACAGTGGTGACACAAACTATGCACAGAAGTTTCAGGGCAGGGTCACCATGACCAGGGACACGTCC
ATCACCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGAGATTCC
CCCTATAGCAGCAGCTGGTCCTTCTTTGACTACTGGGGCCAGGGACCCCTGGTCACCGTCTCGAGC (SEQ ID
NO: 1075)

[886] TCN-549 (5092_P04) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGAEVKKPGASVKVSCKAS**GYTFTG**<u>**YYMH**</u>WVRQAPGQGLEWMG<u>**WINPNSGDTN**</u>**YAQKF QG**RVTMTRDTSITTAYMELSSLRSDDTAVYYCAR<u>**DSPYSSSWSFFDY**</u>WGQGPLVTVSS (SEQ ID NO: 1076)

[887] TCN-549 (5092_P04) gamma heavy chain Kabat CDRs:
CDR 1: GYYMH (SEQ ID NO: 1077)
CDR 2: WINPNSGDTNYAQKFQG (SEQ ID NO: 1078)
CDR 3: DSPYSSSWSFFDY (SEQ ID NO: 1079)

[888] TCN-549 (5092_P04) gamma heavy chain Chothia CDRs:
CDR 1: GYTFTG (SEQ ID NO: 1080)
CDR 2: WINPNSGDTN (SEQ ID NO: 1081)
CDR 3: DSPYSSSWSFFDY (SEQ ID NO: 1079)

[889] TCN-549 (5092_P04) light chain variable region nucleotide sequence:
GACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGGCGAGAGGGCCACCATCAACTGCAAGTCC AGCCAGAGTGTTTTATACAGCTCCAACAATAAGAGCCACTTAGCTTGGTACCAGCAGAAACCAGGACAGCCTCCT AAGTTGCTCATTTACTGGGCATCTACCCGGGAATCCGGGGTCCCTGACCGATTCAGTGGCAGCGGGTCTGGGACA GATTTCACCCTCATCATCAGCAGCCTGCAGGCTGAGGATGTGGCAGTTTATTACTGTCAGCAATATTATTTTTCT CCCCTCACTTTCGGCGGAGGGACCAAGGTGGAGATCAAA (SEQ ID NO: 1082)

[890] TCN-549 (5092_P04) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIVMTQSPDSLAVSLGERATINC<u>**KSSQSVLYSSNNKSHLA**</u>WYQQKPGQPPKLLIY<u>**WASTRES**</u>GVPDRF SGSGSGTDFTLIISSLQAEDVAVYYC<u>**QQYYFSPLT**</u>FGGGTKVEIK (SEQ ID NO: 1083)

[891] TCN-549 (5092_P04) Light chain Kabat CDRs:
CDR 1: KSSQSVLYSSNNKSHLA (SEQ ID NO: 1084)
CDR 2: WASTRES (SEQ ID NO: 957)
CDR 3: QQYYFSPLT (SEQ ID NO: 1085)

[892] TCN-549 (5092_P04) Light chain Chothia CDRs:
CDR 1: KSSQSVLYSSNNKSHLA (SEQ ID NO: 1084)
CDR 2: WASTRES (SEQ ID NO: 957)
CDR 3: QQYYFSPLT (SEQ ID NO: 1085)

[893] TCN-550 (5096_F06) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCACTGTCTCT GGTGCCTCCATCAATAGTCACTACTGGAGCTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTAT GTCTATTACAGTGGGAGCACCACCTACAACCCCTCCCTCAAGAGTCGAGTCACCTTATCAGTAGATACGTCCAAG AACCAGTTCTCCCTGAACCTGAGCTCTGTGACCGCCGCAGACACGGCCTTCTATTACTGTGCGAGACATCCCTAC GATGTTTTGACTGGTTCCGGGGACTGGTTCGACCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ ID NO: 1086)

[894] TCN-550 (5096_F06) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLQESGPGLVKPSETLSLTCTVS**GASINSHYWS**WIRQPPGKGLEWIG**YVYYSGSTTYNPSLKS**RVT LSVDTSKNQFSLNLSSVTAADTAFYYCAR**HPYDVLTGSGDWFDP**WGQGTLVTVSS (SEQ ID NO: 1087)

[895] TCN-550 (5096_F06) gamma heavy chain Kabat CDRs:
CDR 1: SHYWS (SEQ ID NO: 1088)
CDR 2: YVYYSGSTTYNPSLKS (SEQ ID NO: 1089)
CDR 3: HPYDVLTGSGDWFDP (SEQ ID NO: 1090)

[896] TCN-550 (5096_F06) gamma heavy chain Chothia CDRs:
CDR 1: GASINSH (SEQ ID NO: 1091)
CDR 2: YVYYSGSTT (SEQ ID NO: 1092)
CDR 3: HPYDVLTGSGDWFDP (SEQ ID NO: 1090)

[897] TCN-550 (5096_F06) light chain variable region nucleotide sequence:
TCCTATGTTCTGACTCAGGCACCCTCGGTGTCAGTGGCCCCAGGACAGACGGCCAGGATTACCTGTGGGGGAAAT GCCATTGGAAGTAAAAAAGTTCACTGGTACCAGCACAAGGCAGGCCAGGCCCCTGTACTCGTCGTCTATGATGAT ACAGACCGGCCCTCAGGGATCCCTGAGCGATTCTCTGGCTCCAACTCTTGGAGCACGGCCACCCTGACCATCAAC AGGGTCGAAGCCGGGGATGAGGCCGACTATTACTGTCAGGTGTGGGATTTTACCATTGATCATGTGGTCTTCGGC GGAGGGACCAAGCTGACCGTTCTA (SEQ ID NO: 1093)

[898] TCN-550 (5096_F06) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

SYVLTQAPSVSVAPGQTARITC**GGNAIGSKKVH**WYQHKAGQAPVLVVY**DDTDRPS**GIPERFSGSNSW STATLTINRVEAGDEADYYC**QVWDFTIDHVV**FGGGTKLTVL (SEQ ID NO: 1094)

[899] TCN-550 (5096_F06) Light chain Kabat CDRs:
CDR 1: GGNAIGSKKVH (SEQ ID NO: 1095)
CDR 2: DDTDRPS (SEQ ID NO: 1096)
CDR 3: QVWDFTIDHVV (SEQ ID NO: 1097)

[900] TCN-550 (5096_F06) Light chain Chothia CDRs:
CDR 1: GGNAIGSKKVH (SEQ ID NO: 1095)
CDR 2: DDTDRPS (SEQ ID NO: 1096)
CDR 3: QVWDFTIDHVV (SEQ ID NO: 1097)

[901] TCN-551 (5243_D01) heavy chain variable region nucleotide sequence:
GAGGTGCAACTGGTTCAGTCTGGATCAGAGGTGAAAAAGCCCGGGGAGTCTCTGAAGATCTCCTGTAAGGGTTCT GGCTACAGCTTTAGCAACTACTGGATCGGCTGGGTGCGCCAGATGCCCGGGAAAGGCCTGGAATGGATGGGGATC ATTTATCCTGGTGACTCTGATACCAGATACAGCCCGTCCTTCCAAGGCCAGGTCACCATGTCAGCCGACAAGTCC AGCAGCACCGTCTACCTGCAGTGGAGCAGCCTGAAGGCCTCGGACACCGCCATTTATTATTGTGCGAGACGGGGC GGACATAGTTTTGGATATGGGTCGGGGGGGGACACGCACAGTGAATTCGACTCCTGGGGCCAGGGAACCCTGGTC ACCGTCTCGAGC (SEQ ID NO: 1098)

[902] TCN-551 (5243_D01) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

EVQLVQSGSEVKKPGESLKISCKGSGYSFSNYWIGWVRHMPGKGLEWMGIIYPGDSDTRYSPSFQGQ VTMSADKSSSTVYLQWSSLKASDTAIYYCARRGGHSFGYGSGGDTHSEFDSWGQGTLVTVSS (SEQ ID NO: 1099)

[903] TCN-551 (5243_D01) gamma heavy chain Kabat CDRs:
CDR 1: NYWIG (SEQ ID NO: 1100)
CDR 2: IIYPGDSDTRYSPSFQG (SEQ ID NO: 1101)
CDR 3: RGGHSFGYGSGGDTHSEFDS (SEQ ID NO: 1102)

[904] TCN-551 (5243_D01) gamma heavy chain Chothia CDRs:
CDR 1: GYSFSN (SEQ ID NO: 1103)
CDR 2: IIYPGDSDTR (SEQ ID NO: 1104)
CDR 3: RGGHSFGYGSGGDTHSEFDS (SEQ ID NO: 1102)

[905] TCN-551 (5243_D01) light chain variable region nucleotide sequence:
CAGTCTGTATTGACGCAGTCGCCCTCAGTGTCTGCGGCCCCAGGACAGAAGGTCACCATCTCCTGCTCTGGAAGC GACTCCAACATTGGTGATTATTTTGTATGTTGGTACCAGCACCTCCCAGGAAAACCCCCCCCAACTCCTCATCTAT GAAAATAATAAGCGACCCTCAGGGATTCCTGACCGATTCTCTGGCTCCAAGTCTGGCACGTCAGCCACCCTGGGC ATCACCGGAATCCAGACCGGGGACGAGGCCGATTACTACTGCGCAACTTGGGATGGCAGCCTGAGTGCTTGGGTG TTCGGCGGAGGGACCAAGCTGACCGTTCTA (SEQ ID NO: 1105)

[906] TCN-551 (5243_D01) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QSVLTQSPSVSAAPGQKVTISCSGSDSNIGDYFVCWYQHLPGKPPQLLIYENNKRPSGIPDRFSGSKSGT SATLGITGIQTGDEADYYCATWDGSLSAWVFGGGTKLTVL (SEQ ID NO: 1106)

[907] TCN-551 (5243_D01) Light chain Kabat CDRs:
CDR 1: SGSDSNIGDYFVC (SEQ ID NO: 1107)
CDR 2: ENNKRPS (SEQ ID NO: 1108)
CDR 3: ATWDGSLSAWV (SEQ ID NO: 1109)

[908] TCN-551 (5243_D01) Light chain Chothia CDRs:
CDR 1: SGSDSNIGDYFVC (SEQ ID NO: 1107)
CDR 2: ENNKRPS (SEQ ID NO: 1108)
CDR 3: ATWDGSLSAWV (SEQ ID NO: 1109)

[909] TCN-552 (5249_I23) heavy chain variable region nucleotide sequence:
CAGGTCCAAGTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAGGGTCTCCTGCCAGGCTTCT GGAGGCACCTTCATGAATTATGCTATCATTTGGGTGCGACGGGCCCCTGGACAAGGCCTTGAGTGGATGGGAGGG ATCATCCCTGTCTTTCCTACACCAAACTACGCACAGATGTTCCAGGGCAGAGTCACGATTTCCACGGACGAATCC AGGAGCACATCCTTCTTGGAACTGACCAACCTGAGATATGAGGACACGGCCGTTTATTACTGTGCGAGGCGAATT TATCACGGTGGTAACTCCGGCTTTGACTTCTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ ID NO: 1110)

[910] TCN-552 (5249_I23) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQVVQSGAEVKKPGSSVRVSCQAS**GGTFMN**<u>**YAII**</u>WVRRAPGQGLEWMG**GIIPVFPTPN**<u>**YAQMFQG**</u>
RVTISTDESRSTSFLELTNLRYEDTAVYYCAR**RIYHGGNSGFDF**WGQGTLVTVSS (SEQ ID NO: 1111)

[911] TCN-552 (5249_I23) gamma heavy chain Kabat CDRs:
CDR 1: NYAII (SEQ ID NO: 1112)
CDR 2: GIIPVFPTPNYAQMFQG (SEQ ID NO: 1113)
CDR 3: RIYHGGNSGFDF (SEQ ID NO: 1114)

[912] TCN-552 (5249_I23) gamma heavy chain Chothia CDRs:
CDR 1: GGTFMN (SEQ ID NO: 1115)
CDR 2: GIIPVFPTPN (SEQ ID NO: 1116)
CDR 3: RIYHGGNSGFDF (SEQ ID NO: 1114)

[913] TCN-552 (5249_I23) light chain variable region nucleotide sequence:
GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC
AGTCAGAGTGTTGGCAACTACTTAGCCTGGTACCAACAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGAT
TCATCCAACAGGGCCCCTGGCATCCCAGCCAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATC
AGCAGCCTCGCGCCTGAAGATTTTGCAGTTTATTACTGTCAGCAGCGTAGCAAGTGGCCTCCCATGTACAGTTTT
GGCCATGGGACCAAGCTGGAGATCAAA (SEQ ID NO: 1117)

[914] TCN-552 (5249_I23) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

EIVLTQSPATLSLSPGERATLSC**RASQSVGNYLA**WYQQKPGQAPRLLIY**DSSNRAP**GIPARFSGSGSGT
DFTLTISSLAPEDFAVYYC**QQRSKWPPMYS**FGHGTKLEIK (SEQ ID NO: 1118)

[915] TCN-552 (5249_I23) Light chain Kabat CDRs:
CDR 1: RASQSVGNYLA (SEQ ID NO: 1119)
CDR 2: DSSNRAP (SEQ ID NO: 1120)
CDR 3: QQRSKWPPMYS (SEQ ID NO: 1121)

[916] TCN-552 (5249_I23) Light chain Chothia CDRs:
CDR 1: RASQSVGNYLA (SEQ ID NO: 1119)
CDR 2: DSSNRAP (SEQ ID NO: 1120)
CDR 3: QQRSKWPPMYS (SEQ ID NO: 1121)

[917] TCN-553 (5261_C18) heavy chain variable region nucleotide sequence:
CAGGTCCAGGTGGTGCAGTCTGGGACTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCCAGACTTCT
GGAGGCAGGTTCATGAGTTATGCTATCACCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGC
ATCGTCCCTGTCTTCGGAACAGCAAACTACGCTCAGAAGTTCCAGGGCAGAGTCACGATCACCACGGACGATTCC
ACGCGCACAGCCTATATGGAGTTGAGCAGCCTGAGAAGTGAGGACACGGCCGTTTATTACTGTGGGTTCCGATAC
GGCTCTGGTTACGGGTTTGACTCCTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ ID NO: 1122)

[918] TCN-553 (5261_C18) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQVVQSGTEVKKPGSSVKVSCQTS**GGRFMS**<u>**YAIT**</u>WVRQAPGQGLEWMG**GIVPVFGTAN**<u>**YAQKFQ**</u>
GRVTITTDDSTRTAYMELSSLRSEDTAVYYCGF**RYGSGYGFDS**WGQGTLVTVSS (SEQ ID NO: 1123)

[919] TCN-553 (5261_C18) gamma heavy chain Kabat CDRs:
CDR 1: SYAIT (SEQ ID NO: 1124)
CDR 2: GIVPVFGTANYAQKFQG (SEQ ID NO: 1125)
CDR 3: RYGSGYGFDS (SEQ ID NO: 1126)

[920] TCN-553 (5261_C18) gamma heavy chain Chothia CDRs:
CDR 1: GGRFMS (SEQ ID NO: 1127)
CDR 2: GIVPVFGTAN (SEQ ID NO: 1128)
CDR 3: RYGSGYGFDS (SEQ ID NO: 1126)

[921] TCN-553 (5261_C18) light chain variable region nucleotide sequence:
GAAATTGTATTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC
AGTCAGAGTGTTAGTAGCAGCTACTTAGCCTGGTATCAGAAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTAT
GGTGCTTCCACTAGGGCCACTGGCATCCCGGACCGGTTCACTGGCAGTGGGTCTGGGACAGACTTCACTCTCAGC
ATCAGTAGACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTCAGCACTTTGGTACCTCAGTCTTCACTTTCGGC
GGAGGGACCAAGGTTGAGATCAAA (SEQ ID NO: 1129)

[922] TCN-553 (5261_C18) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

EIVLTQSPGTLSLSPGERATLSC**RASQSVSSSYLA**WYQKKPGQAPRLLIY**GASTRAT**GIPDRFTGSGSGT
DFTLSISRLEPEDFAVYYC**QHFGTSVFT**FGGGTKVEIK (SEQ ID NO: 1130)

[923] TCN-553 (5261_C18) Light chain Kabat CDRs:
CDR 1: RASQSVSSSYLA (SEQ ID NO: 944)
CDR 2: GASTRAT (SEQ ID NO: 755)
CDR 3: QHFGTSVFT (SEQ ID NO: 1131)

[924] TCN-553 (5261_C18) Light chain Chothia CDRs:
CDR 1: RASQSVSSSYLA (SEQ ID NO: 944)
CDR 2: GASTRAT (SEQ ID NO: 755)
CDR 3: QHFGTSVFT (SEQ ID NO: 1131)

[925] TCN-554 (5277_M05) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGGTGCAGTCTGGGGCTGATCTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
GGATACACCTTCACCGACTACTATATTCACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGG
ATCAACCCTGAAAGTGGTGACACAAAGTATGCACAGAAGTTTCAGGGCAGGGTCACCATGACCAGGGACACGTCC
ATCACCACAGCCTACATGGAGCTGGGTAGGCTGAGATCCGACGACACGGCCGTGTATTACTGTGCGAGAGATGTA
AGTACGACCTGGAGCTGGTTCGCCCCCTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ ID NO: 1132)

[926] TCN-554 (5277_M05) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGADLKKPGASVKVSCKAS**GYTFTDYYIH**WVRQAPGQGLEWMG**WINPESGDTKYAQKFQ**
GRVTMTRDTSITTAYMELGRLRSDDTAVYYCAR**DVSTTWSWFAP**WGQGTLVTVSS (SEQ ID NO: 1133)

[927] TCN-554 (5277_M05) gamma heavy chain Kabat CDRs:
CDR 1: DYYIH (SEQ ID NO: 1134)
CDR 2: WINPESGDTKYAQKFQG (SEQ ID NO: 1135)
CDR 3: DVSTTWSWFAP (SEQ ID NO: 1136)

[928] TCN-554 (5277_M05) gamma heavy chain Chothia CDRs:
CDR 1: GYTFTD (SEQ ID NO: 1137)
CDR 2: WINPESGDTK (SEQ ID NO: 1138)
CDR 3: DVSTTWSWFAP (SEQ ID NO: 1136)

[929] TCN-554 (5277_M05) light chain variable region nucleotide sequence:
GACATCGTGATGACCCAGTCTCCAGACTCCCTGGCAGTGTCTCTGGGCGAGAGGGCCACCATCAACTGCAGGTCC
AGCCAGAGTATTTTCCACAACTCCAACAATGAGAACTACTTAGCTTGGTACCAGCAGAAACCAGGACAGCCTCCT
AAGCTGCTCATTTACTGGGCATCTACCCGGGAATCCGGGGTCCCTGACCGATTCAGTGGCAGCGGGTCTGGGACA
GATTTCACTCTCACCATCAGCAGCCTGCAGGCTGAAGATGTGGCGGTTTATTTCTGTCAGCAATATTATAATGCT
CCGCTCACTTTCGGCGGAGGGACCAAGGTGGAGATCAAA (SEQ ID NO: 1139)

[930] TCN-554 (5277_M05) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIVMTQSPDSLAVSLGERATINC**RSSQSIFHNSNNENYLA**WYQQKPGQPPKLLIY**WASTRES**GVPDRF
SGSGSGTDFTLTISSLQAEDVAVYFC**QQYYNAPLT**FGGGTKVEIK (SEQ ID NO: 1140)

[931] TCN-554 (5277_M05) Light chain Kabat CDRs:
CDR 1: RSSQSIFHNSNNENYLA (SEQ ID NO: 1141)
CDR 2: WASTRES (SEQ ID NO: 957)
CDR 3: QQYYNAPLT (SEQ ID NO: 1142)

[932] TCN-554 (5277_M05) Light chain Chothia CDRs:
CDR 1: RSSQSIFHNSNNENYLA (SEQ ID NO: 1141)
CDR 2: WASTRES (SEQ ID NO: 957)
CDR 3: QQYYNAPLT (SEQ ID NO: 1142)

[933] TCN-555 (5246_L16) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAGGCCTGGGTCCTCGGTGAAGGTCTCATGCACGGCTTCT
GGAGGCATCTTCAGGAAGAATGCAATCAGCTGGGTGCGACAGGCCCCTGGACAAGGCCTTGAGTGGATGGGAGGG
ATCATCGCAGTCTTTAACACAGCAAATTACGCGCAGAAGTTCCAGAACAGAGTCAAAATTACCGCAGACGAGTCA
GGCAATACGGCCTACATGGAGCTGAGCAGCCTGACATCTGACGACACGGCCGTGTATTACTGTGCGAGTCACCCA
AAATATTTCTATGGTTCGGGGAGTTATCCGGACTTCTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ
ID NO: 1143)

[934] TCN-555 (5246_L16) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGAEVKRPGSSVKVSCTAS**GGIFRK**NAISWVRQAPGQGLEWMG**GIIAVFNTAN**YAQKFQN
RVKITADESGNTAYMELSSLTSDDTAVYYCAS**HPKYFYGSGSYPDF**WGQGTLVTVSS (SEQ ID NO:
1144)

[935] TCN-555 (5246_L16) gamma heavy chain Kabat CDRs:
CDR 1: KNAIS (SEQ ID NO: 796)
CDR 2: GIIAVFNTANYAQKFQN (SEQ ID NO: 797)
CDR 3: HPKYFYGSGSYPDF (SEQ ID NO: 798)

[936] TCN-555 (5246_L16) gamma heavy chain Chothia CDRs:
CDR 1: GGIFRK (SEQ ID NO: 799)
CDR 2: GIIAVFNTAN (SEQ ID NO: 800)
CDR 3: HPKYFYGSGSYPDF (SEQ ID NO: 798)

[937] TCN-555 (5246_L16) light chain variable region nucleotide sequence:
CAATCTGCCCTGACTCAGCCTCGCTCAGTGTCCGGGTCTCCTGGACAGTCAATCACCATCTCCTGTACTGGTGGC
AGCAGTGATATTGGTGCTTCTAACTCTGTCTCCTGGTACCAACAACACCCAGGCAAAGCCCCCAAACTCGTTATT
TTTGATGTCACTGAGCGACCCTCAGGGGTCCCGCATCGGTTCTCTGGCTCCAAGTCTGGCAACACGGCCTCCCTG
ACCGTCTCTGGGCTCCAGCCTGACGACGAGGCTGATTATTTCTGCTGCGCATATGGAGGCAAATATCTTGTGGTC
TTCGGCGGAGGGACCAAGGTGACCGTTCTA (SEQ ID NO: 1145)

[938] TCN-555 (5246_L16) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QSALTQPRSVSGSPGQSITISC**TGGSSDIGASNSVS**WYQQHPGKAPKLVIF**DVTERPS**GVPHRFSGSKSG
NTASLTVSGLQPDDEADYFC**CAYGGKYLVV**FGGGTKVTVL (SEQ ID NO: 1146)

[939] TCN-555 (5246_L16) Light chain Kabat CDRs:
CDR 1: TGGSSDIGASNSVS (SEQ ID NO: 1147)
CDR 2: DVTERPS (SEQ ID NO: 804)
CDR 3: CAYGGKYLVV (SEQ ID NO: 805)

[940] TCN-555 (5246_L16) Light chain Chothia CDRs:
CDR 1: TGGSSDIGASNSVS (SEQ ID NO: 1147)
CDR 2: DVTERPS (SEQ ID NO: 804)
CDR 3: CAYGGKYLVV (SEQ ID NO: 805)

[941] TCN-556 (5089_K12) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAACCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
GGATACACCTTCATCGGCTATGATATGCACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGG
ATCAACGCTAAAAGAGGTGGCACAAACTATGCACAAAAGTTTCAGGGCAGGGTCACCATGACCAGGGACACGTCT
ATCAGCACAGCCTACATGGAGCTGAACAGCCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGAGGGGTG
GGGTCACGAACTACGATTTTTGGAGTTCTCAACCCGGAATTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTC
TCGAGC (SEQ ID NO: 1148)

[942] TCN-556 (5089_K12) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGAEVKKPGASVKVSCKAS**GYTFIG**YDMHWVRQAPGQGLEWMG**WINAKRGGTNYAQKF**
QGRVTMTRDTSISTAYMELNSLRSDDTAVYYCAR**GVGSRTTIFGVLNPEFDY**WGQGTLVTVSS (SEQ
ID NO: 1149)

[943] TCN-556 (5089_K12) gamma heavy chain Kabat CDRs:
CDR 1: GYDMH (SEQ ID NO: 1150)
CDR 2: WINAKRGGTNYAQKFQG (SEQ ID NO: 1151)
CDR 3: GVGSRTTIFGVLNPEFDY (SEQ ID NO: 1152)

[944] TCN-556 (5089_K12) gamma heavy chain Chothia CDRs:
CDR 1: GYTFIG (SEQ ID NO: 1153)
CDR 2: WINAKRGGTN (SEQ ID NO: 1154)
CDR 3: GVGSRTTIFGVLNPEFDY (SEQ ID NO: 1152)

[945] TCN-556 (5089_K12) light chain variable region nucleotide sequence:
CAGTCTGCCCTGACTCAGCCTCCCTCCGCGTCCGGGTCTCCTGGACAGTCAGTCACCATCTCCTGCACTGGATCC
AGCAGTGACGTTGGTGGTTATGACTATGTCTCCTGGTACCAACAACACCCAGGCAAAGCCCCCAAACTCCTGATT
TATGAGGTCACTAAGCGGCCCTCAGGGGTCCCTGATCGCTTCTCTGGCTCCAAGTCTGGCAACACGGCCTCCCTG
ACCGTCTCTGGGCTCCAGGCTGAGGATGAGGCTGATTATTACTGCAGCTCATATGCGGGCAACTACAATCATGTC
TTCGGACCTGGGACCAAGGTCACCGTTCTA (SEQ ID NO: 1155)

[946] TCN-556 (5089_K12) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QSALTQPPSASGSPGQSVTISC**TGSSSDVGGYDYVS**WYQQHPGKAPKLLIY**EVTKRPS**GVPDRFSGSKS
GNTASLTVSGLQAEDEADYYC**SSYAGNYNHV**FGPGTKVTVL (SEQ ID NO: 1156)

[947] TCN-556 (5089_K12) Light chain Kabat CDRs:
CDR 1: TGSSSDVGGYDYVS (SEQ ID NO: 1157)
CDR 2: EVTKRPS (SEQ ID NO: 1158)
CDR 3: SSYAGNYNHV (SEQ ID NO: 1159)

[948] TCN-556 (5089_K12) Light chain Chothia CDRs:
CDR 1: TGSSSDVGGYDYVS (SEQ ID NO: 1157)
CDR 2: EVTKRPS (SEQ ID NO: 1158)
CDR 3: SSYAGNYNHV (SEQ ID NO: 1159)

[949] TCN-557 (5081_A04) heavy chain variable region nucleotide sequence:
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
GGACACACCTTCACCGGCTACTACATACACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGG
ATCAACCCTGACAGTGGTGCCACCAGTTCTGCACAGAACTTTCAGGGCAGGGTCACCATGACCGGGGACACGTCC
TCTAGCACAGCCTACATGGAGCTGAGTAGGCTGAGTTTTGACGACACGGCCGTCTATTACTGTGCGAGAGTACTG
TTTACCAGTCCTTTTGACTTCTGGGGTGAGGGAACCCTGGTCACCGTCTCGAGC (SEQ ID NO: 1160)

[950] TCN-557 (5081_A04) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGAEVKKPGASVKVSCKAS**GHTFTG**YYIHWVRQAPGQGLEWMG**WINPDSGATS**SAQNFQ
GRVTMTGDTSSSTAYMELSRLSFDDTAVYYCAR**VLFTSPFDF**WGEGTLVTVSS (SEQ ID NO: 1161)

[951] TCN-557 (5081_A04) gamma heavy chain Kabat CDRs:
CDR 1: GYYIH (SEQ ID NO: 1162)
CDR 2: WINPDSGATSSAQNFQG (SEQ ID NO: 1163)
CDR 3: VLFTSPFDF (SEQ ID NO: 1164)

[952] TCN-557 (5081_A04) gamma heavy chain Chothia CDRs:
CDR 1: GHTFTG (SEQ ID NO: 1165)
CDR 2: WINPDSGATS (SEQ ID NO: 1166)
CDR 3: VLFTSPFDF (SEQ ID NO: 1164)

[953] TCN-557 (5081_A04) light chain variable region nucleotide sequence:
CAGGCTGTGGTGACTCAGGAGCCCTCACTGGCTGTGTCCCCAGGAGGGACAGTCACTCTCACCTGTGGCTCCAGC
ACTGGAGCTGTCACCAGGGGTCATTATCCCTATTGGTTCCAGCAGAAGCCTGGCCAAGCCCCCAGGGCACTCATT
TATGATAGTGCAGGCAACAGACACTCCTGGACTCCCGCCCGATTCTCAGGCTCCCTCCTTGGGGGCAAAGCTGCC

CTGACCCTTTCGGGTGCGCAGCCTGAGGATGAGGCTGAGTATTACTGCTTGCTCTCCTATAGTGGTGTCTGGGTG
TTCGGCGGAGGGACGAAGCTGACCGTTCTA (SEQ ID NO: 1167)

[954] TCN-557 (5081_A04) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QAVVTQEPSLAVSPGGTVTLTC**GSSTGAVTRGHYPY**WFQQKPGQAPRALIY**DSAGNRHS**WTPARFSG
SLLGGKAALTLSGAQPEDEAEYYC**LLSYSGVWV**FGGGTKLTVL (SEQ ID NO: 1168)

[955] TCN-557 (5081_A04) Light chain Kabat CDRs:
CDR 1: GSSTGAVTRGHYPY (SEQ ID NO: 1169)
CDR 2: DSAGNRHS (SEQ ID NO: 1170)
CDR 3: LLSYSGVWV (SEQ ID NO: 1171)

[956] TCN-557 (5081_A04) Light chain Chothia CDRs:
CDR 1: GSSTGAVTRGHYPY (SEQ ID NO: 1169)
CDR 2: DSAGNRHS (SEQ ID NO: 1170)
CDR 3: LLSYSGVWV (SEQ ID NO: 1171)

[957] TCN-558 (5248_H10b) heavy chain variable region nucleotide sequence:
CAGGTCCAGCTGGTGCAATCTGGGAGTGAGGTGAAGAAGCCTGGGACCTCGGTGAAGGTCTCCTGCACGGCCTCT
GGAAGTGTCTTCACCAATTATGGAATTAGTTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG
ATCATCCCTCTCTTTGGCGCAGCCAAGTACGCACAGAAATTCCAGGGCAGAGTCACCATCACAGCGGACGAATCC
ACGAAGACAGTCTACATGGAGCTGAGCAGGCTGACATCTAAAGACACGGCCATATATTTCTGTGCGAAGGCCCCC
CGTGTCTACGAGTACTACTTTGATCAGTGGGGCCAGGGAACCCCAGTCACCGTCTCCTCA (SEQ ID NO:
1172)

[958] TCN-558 (5248_H10b) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QVQLVQSGSEVKKPGTSVKVSCTAS**GSVFTN****YGIS**WVRQAPGQGLEWMG**GIIPLFGAAK****YAQKFQG**
RVTITADESTKTVYMELSRLTSKDTAIYFCAK**APRVYEYYFDQ**WGQGTPVTVSS (SEQ ID NO: 914)

[959] TCN-558 (5248_H10b) gamma heavy chain Kabat CDRs:
CDR 1: NYGIS (SEQ ID NO: 915)
CDR 2: GIIPLFGAAKYAQKFQG (SEQ ID NO: 916)
CDR 3: APRVYEYYFDQ (SEQ ID NO: 917)

[960] TCN-558 (5248_H10b) gamma heavy chain Chothia CDRs:
CDR 1: GSVFTN (SEQ ID NO: 918)
CDR 2: GIIPLFGAAK (SEQ ID NO: 919)
CDR 3: APRVYEYYFDQ (SEQ ID NO: 917)

[961] TCN-558 (5248_H10b) light chain variable region nucleotide sequence:
GAAATAGTGATGACGCAGTTTCCAGCCACCCTGTCTGTGTCTCCCGGGGAACGAGTCACCCTCTCCTGTAGGGCC
AGTCAGAGTGTTAGCAACAATTTAGCCTGGTACCAGCAAAAACCTGGCCAGCCTCCCAGGCTCCTCATCTATGAT
GCATCTACCAGGGCCACGGGTGTCCCAGCCAAGTTCAGTGGCACTGGGTCTGGCACAGAGTTCACTCTCAGCATC
AGCAGCCTGCAGTCCGAAGATTTTGCAGTTTATTACTGTCAGCAGTATCACAACTGGCCTCCCTCGTACAGTTTT
GGCCTGGGGACCAAGCTGGAGATCAAA (SEQ ID NO: 1173)

[962] TCN-558 (5248_H10b) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

EIVMTQFPATLSVSPGERVTLSC**RASQSVSNNLA**WYQQKPGQPPRLLIY**DASTRAT**GVPAKFSGTGSGT
EFTLSISSLQSEDFAVYYC**QQYHNWPPSYS**FGLGTKLEIK (SEQ ID NO: 862)

[963] TCN-558 (5248_H10b) Light chain Kabat CDRs:
CDR 1: RASQSVSNNLA (SEQ ID NO: 863)
CDR 2: DASTRAT (SEQ ID NO: 864)
CDR 3: QQYHNWPPSYS (SEQ ID NO: 865)

[964] TCN-558 (5248_H10b) Light chain Chothia CDRs:
CDR 1: RASQSVSNNLA (SEQ ID NO: 863)
CDR 2: DASTRAT (SEQ ID NO: 864)
CDR 3: QQYHNWPPSYS (SEQ ID NO: 865)

[965] TCN-559 (5097_G08) heavy chain variable region nucleotide sequence:
CAAGAGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
AGAAAGTCCTTCATTGGCTACTATGTACACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGG
ATCAGCCCTGACAGTGATGCCACAAAGTACGCACAGAAGTTTCAGGGCTCCGTCATCATGACCAGGGACACGTCC
GTCAGCACAGTGTACATGGAGCTGAGTAGGCTGACATCTGACGACACGGCCCTTTATTACTGTCTCCTTTTTCGA
GGTGGAAACTCCCTCTCCTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGC (SEQ ID NO: 1174)

[966] TCN-559 (5097_G08) gamma heavy chain variable region amino acid sequence: (Kabat CDRs in bold, Chothia CDRs underlined)

QEQLVQSGAEVKKPGASVKVSCKAS**RKSFIG****YYVH**WVRQAPGQGLEWMG**WISPDSDATK****YAQKFQ**
GSVIMTRDTSVSTVYMELSRLTSDDTALYYCLL**FRGGNSLS**WGQGTLVTVSS (SEQ ID NO: 1175)

[967] TCN-559 (5097_G08) gamma heavy chain Kabat CDRs:
CDR 1: GYYVH (SEQ ID NO: 1176)
CDR 2: WISPDSDATKYAQKFQG (SEQ ID NO: 1177)
CDR 3: FRGGNSLS (SEQ ID NO: 1178)

[968] TCN-559 (5097_G08) gamma heavy chain Chothia CDRs:
CDR 1: RKSFIG (SEQ ID NO: 1179)
CDR 2: WISPDSDATK (SEQ ID NO: 1180)
CDR 3: FRGGNSLS (SEQ ID NO: 1178)

[969] TCN-559 (5097_G08) light chain variable region nucleotide sequence:
CAGGCTGTGGTGACTCAGGAGCCCTCACTGACTGTGTCCCCAGGAGGGACAGTCACCCTCACCTGTGGCTCCAGC
ACTGGACCTGTCACCAGTGGTCATTATCCCTACTGGTTCCAGCAGAAGCCTGGCCAAGCCCCCAGGACATTGATT
TCTGCTACATCCAACACACACTCCTGGACACCTGCCCGCTTCTCAGGCTCCCTCCTTGGGGGCAGAGCTGCCCTG
ACCCTTTCGGGTGCGCAGCCTGAGGATGAGGCTGACTATTATTGCTTTCTCTCCTACAGTGGTGCTTGGGTGTTC
GGCGGAGGGACCACGCTGACCGTTCTA (SEQ ID NO: 1181)

[970] TCN-559 (5097_G08) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

QAVVTQEPSLTVSPGGTVTLTC**GSSTGPVTSGHYPY**WFQQKPGQAPRTLIS**ATSNTHS**WTPARFSGSL
LGGRAALTLSGAQPEDEADYYC**FLSYSGAWV**FGGGTTLTVL (SEQ ID NO: 1182)

[971] TCN-559 (5097_G08) Light chain Kabat CDRs:
CDR 1: GSSTGPVTSGHYPY (SEQ ID NO: 1183)
CDR 2: ATSNTHS (SEQ ID NO: 1184)
CDR 3: FLSYSGAWV (SEQ ID NO: 1185)

[972] TCN-559 (5097_G08) Light chain Chothia CDRs:
CDR 1: GSSTGPVTSGHYPY (SEQ ID NO: 1183)
CDR 2: ATSNTHS (SEQ ID NO: 1184)
CDR 3: FLSYSGAWV (SEQ ID NO: 1185)

[973] TCN-560 (5084_P10) heavy chain variable region nucleotide sequence:
GAGGTGCAGCTGGTGGAATCTGGGGGAGGCTTGGTCCAGCCGGGGGGGTCCCTGAGACTCTCCTGTGCAGCCTCT
GGATTTATCTTTAGAAATTACTGGATGAGCTGGGTCCGGCAGGCTCCAGGGAAGGGGCTGGAGTGGGTGGCCAAC
ATAAAACAAGATGGAAGAGAGAAGTACTATGTGGACTCTCTGAGGGGCCGAGTCAACATCTCCAGAGACAACGCC
GAGAACTCATTGTATCTGCACATGAACAGCCTGAGAGTCGAGGACACGGCTGTTTATTTCTGTGCGAGAGCTCGG
ATGGTGGTGGTTACTGGCGATGGTTTTGATGTCTGGGGCCATGGGACAATGGTCACCGTCTCGAGC (SEQ ID
NO: 1186)

[974] TCN-560 (5084_P10) gamma heavy chain variable region amino acid sequence:
(Kabat CDRs in bold, Chothia CDRs underlined)

EVQLVESGGGLVQPGGSLRLSCAAS<u>GFIFRN</u>**YWMS**WVRQAPGKGLEWVA<u>**NIKQDGREKY**</u>**YVDSLR**
GRVNISRDNAENSLYLHMNSLRVEDTAVYFCAR<u>**ARMVVVTGDGFDV**</u>WGHGTMVTVSS (SEQ ID
NO: 1187)

[975] TCN-560 (5084_P10) gamma heavy chain Kabat CDRs:
CDR 1: NYWMS (SEQ ID NO: 1188)
CDR 2: NIKQDGREKYYVDSLRG (SEQ ID NO: 1189)
CDR 3: ARMVVVTGDGFDV (SEQ ID NO: 1190)

[976] TCN-560 (5084_P10) gamma heavy chain Chothia CDRs:
CDR 1: GFIFRN (SEQ ID NO: 1191)
CDR 2: NIKQDGREKY (SEQ ID NO: 1192)
CDR 3: ARMVVVTGDGFDV (SEQ ID NO: 1190)

[977] TCN-560 (5084_P10) light chain variable region nucleotide sequence:
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTGGGAGACAGAGTCACCATCACTTGCCGGGCA
AGTCAGAATATTAAGAGGTATTTCAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCT
GCATCCAATTTAGAAAATGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATC
AGCAGTCTGCAACCTGAGGATTTTGCGACTTATTACTGTCAGCAGAGTTTCAGTAAATCGTGGACATTCGGCCAA
GGGACCAACGTGGACATCAAA (SEQ ID NO: 1193)

[978] TCN-560 (5084_P10) light chain variable region amino acid sequence (Kabat CDRs in bold, Chothia CDRs underlined)

DIQMTQSPSSLSASVGDRVTITC<u>**RASQNIKRYFN**</u>WYQQKPGKAPKLLIY<u>**AASNLEN**</u>GVPSRFSGSGSGT
DFTLTISSLQPEDFATYYC<u>**QQSFSKSWT**</u>FGQGTNVDIK (SEQ ID NO: 1194)

[979] TCN-560 (5084_P10) Light chain Kabat CDRs:
CDR 1: RASQNIKRYFN (SEQ ID NO: 1195)
CDR 2: AASNLEN (SEQ ID NO: 1196)
CDR 3: QQSFSKSWT (SEQ ID NO: 1197)

[980] TCN-560 (5084_P10) Light chain Chothia CDRs:
CDR 1: RASQNIKRYFN (SEQ ID NO: 1195)
CDR 2: AASNLEN (SEQ ID NO: 1196)
CDR 3: QQSFSKSWT (SEQ ID NO: 1197)

[981] The invention provides an isolated fully human monoclonal anti-HA antibody or fragment thereof, wherein said antibody includes a variable heavy chain (V_H) region comprising CDR1 and CDR2, wherein the V_H region is encoded by a human IGHV1 (or specifically, IGHV1-18, IGHV1-2, IGHV1-69, IGHV1-8), IGHV2 (or specifically, IGHV2-5) , IGHV3 (or specifically, IGHV3-30, IGHV3-33, IGHV3-49, IGHV3-53, 66, IGHV3-7), IGHV4 (or specifically, IGHV4-31, IGHV4-34, IGHV4-39, IGHV4-59, IGHV4-61), or IGHV5 (or specifically, IGHV5-51) V_H germline sequence or an allele thereof, or a nucleic acid sequence that is homologous to the IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 V_H germline gene sequence or an allele thereof. In one aspect, the nucleic acid sequence that is homologous to the IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 V_H germline sequence is at least 75% homologous to the IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 V_H germline sequence or an allele thereof. Exemplary alleles include, but are not limited to, IGHV1-18*01, IGHV1-2*02, IGHV1-2*04, IGHV1-69*01, IGHV1-69*05, IGHV1-69*06, IGHV1-69*12, IGHV1-8*01, IGHV2-5*10, IGHV3-30-3*01, IGHV3-30*03, IGHV3-30*18, IGHV3-33*05, IGHV3-49*04, IGHV3-53*01, IGHV3-66*03, IGHV3-7*01, IGHV4-31*03, IGHV4-31*06, IGHV4-34*01, IGHV4-34*02, IGHV4-34*03, IGHV4-34*12, IGHV4-39*01, IGHV4-59*01, IGHV4-59*03, IGHV4-61*01, IGHV4-61*08, and IGHV5-51*01. Exemplary sequences for each allele are provided below.

[982] IGHV1-18*01 nucleotide sequence (SEQ ID NO: 1198)

CAGGTTCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
GGTTACACCTTTACCAGCTATGGTATCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGG
ATCAGCGCTTACAATGGTAACACAAACTATGCACAGAAGCTCCAGGGCAGAGTCACCATGACCACAGACACATCC
ACGAGCACAGCCTACATGGAGCTGAGGAGCCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGAGA

[983] IGHV1-2*02 nucleotide sequence (SEQ ID NO: 1199)

CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
GGATACACCTTCACCGGCTACTATATGCACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGG
ATCAACCCTAACAGTGGTGGCACAAACTATGCACAGAAGTTTCAGGGCAGGGTCACCATGACCAGGGACACGTCC
ATCAGCACAGCCTACATGGAGCTGAGCAGGCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGAGA

[984] IGHV1-2*04 nucleotide sequence (SEQ ID NO: 1200)

CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
GGATACACCTTCACCGGCTACTATATGCACTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGG
ATCAACCCTAACAGTGGTGGCACAAACTATGCACAGAAGTTTCAGGGCTGGGTCACCATGACCAGGGACACGTCC
ATCAGCACAGCCTACATGGAGCTGAGCAGGCTGAGATCTGACGACACGGCCGTGTATTACTGTGCGAGA

[985] IGHV1-69*01 nucleotide sequence (SEQ ID NO: 1201)
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCAAGGCTTCT
GGAGGCACCTTCAGCAGCTATGCTATCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG
ATCATCCCTATCTTTGGTACAGCAAACTACGCACAGAAGTTCCAGGGCAGAGTCACGATTACCGCGGACGAATCC
ACGAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGA

[986] IGHV1-69*05 nucleotide sequence (SEQ ID NO: 1202)
CAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCAAGGCTTCT
GGAGGCACCTTCAGCAGCTATGCTATCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG
ATCATCCCTATCTTTGGTACAGCAAACTACGCACAGAAGTTCCAGGGCAGAGTCACGATTACCACGGACGAATCC
ACGAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGA

[987] IGHV1-69*06 nucleotide sequence (SEQ ID NO: 1203)
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCAAGGCTTCT
GGAGGCACCTTCAGCAGCTATGCTATCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG
ATCATCCCTATCTTTGGTACAGCAAACTACGCACAGAAGTTCCAGGGCAGAGTCACGATTACCGCGGACAAATCC
ACGAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGA

[988] IGHV1-69*12 nucleotide sequence (SEQ ID NO: 1204)
CAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCAAGGCTTCT
GGAGGCACCTTCAGCAGCTATGCTATCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG
ATCATCCCTATCTTTGGTACAGCAAACTACGCACAGAAGTTCCAGGGCAGAGTCACGATTACCGCGGACGAATCC
ACGAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGA

[989] IGHV1-8*01 nucleotide sequence (SEQ ID NO: 1205)
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
GGATACACCTTCACCAGTTATGATATCAACTGGGTGCGACAGGCCACTGGACAAGGGCTTGAGTGGATGGGATGG
ATGAACCCTAACAGTGGTAACACAGGCTATGCACAGAAGTTCCAGGGCAGAGTCACCATGACCAGGAACACCTCC
ATAAGCACAGCCTACATGGAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGG

[990] IGHV2-5*10 nucleotide sequence (SEQ ID NO: 1206)
CAGATCACCTTGAAGGAGTCTGGTCCTACGCTGGTGAAACCCACACAGACCCTCACGCTGACCTGCACCTTCTCT
GGGTTCTCACTCAGCACTAGTGGAGTGGGTGTGGGCTGGATCCGTCAGCCCCCAGGAAAGGCCCTGGAGTGGCTT
GCACTCATTTATTGGGATGATGATAAGCGCTACAGCCCATCTCTGAAGAGCAGGCTCACCATCACCAAGGACACC
TCCAAAAAACCAGGTGGTCCTTACAATGACCAACATGGACCCTGTGGACACAGCCACATATTACTGTGCACGG

[991] IGHV3-30-3*01 nucleotide sequence (SEQ ID NO: 1207)
CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCT
GGATTCACCTTCAGTAGCTATGCTATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTT
ATATCATATGATGGAAGCAATAAATACTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCC
AAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATTACTGTGCGAGA

[992] IGHV3-30*03 nucleotide sequence (SEQ ID NO: 1208)
CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCT
GGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTT
ATATCATATGATGGAAGTAATAAATACTATGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCC
AAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATTACTGTGCGAGAGA

[993] IGHV3-30*18 nucleotide sequence (SEQ ID NO: 1209)
CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCCTCT
GGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTT
ATATCATATGATGGAAGTAATAAATACTATGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCC
AAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAGGACACGGCTGTGTATTACTGTGCGAAAGA

[994] IGHV3-33*05 nucleotide sequence (SEQ ID NO: 1210)
CAGGTGCAGCTGGTGGAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCCTGAGACTCTCCTGTGCAGCGTCT
GGATTCACCTTCAGTAGCTATGGCATGCACTGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTT
ATATCATATGATGGAAGTAATAAATACTATGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCC
AAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGAGA

[995] IGHV3-49*04 nucleotide sequence (SEQ ID NO: 1211)
GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTACAGCCAGGGCGGTCCCTGAGACTCTCCTGTACAGCTTCT
GGATTCACCTTTGGTGATTATGCTATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTAGGTTTC
ATTAGAAGCAAAGCTTATGGTGGGACAACAGAATACGCCGCGTCTGTGAAAGGCAGATTCACCATCTCAAGAGAT
GATTCCAAAAGCATCGCCTATCTGCAAATGAACAGCCTGAAAACCGAGGACACAGCCGTGTATTACTGTACTAGA
GA

[996] IGHV3-53*01 nucleotide sequence (SEQ ID NO: 1212)
GAGGTGCAGCTGGTGGAGTCTGGAGGAGGCTTGATCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAGCCTCT
GGGTTCACCGTCAGTAGCAACTACATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGTT
ATTTATAGCGGTGGTAGCACATACTACGCAGACTCCGTGAAGGGCCGATTCACCATCTCCAGAGACAATTCCAAG
AACACGCTGTATCTTCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTGTATTACTGTGCGAGAGA

[997] IGHV3-66*03 nucleotide sequence (SEQ ID NO: 1213)
CAGGTGCAGCTGGTGCAGTCTGGCCATGAGGTGAAGCAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
GGTTACAGTTTCACCACCTATGGTATGAATTGGGTGCCACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGG
TTCAACACCTACACTGGGAACCCAACATATGCCCAGGGCTTCACAGGACGGTTTGTCTTCTCCATGGACACCTCT
GCCAGCACAGCATACCTGCAGATCAGCAGCCTAAAGGCTGAGGACATGGCCATGTATTACTGTGCGAGATA

[998] IGHV3-7*01 nucleotide sequence (SEQ ID NO: 1214)
GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAGCCTCT
GGATTCACCTTTAGTAGCTATTGGATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTGGCCAAC
ATAAAGCAAGATGGAAGTGAGAAATACTATGTGGACTCTGTGAAGGGCCGATTCACCATCTCCAGAGACAACGCC
AAGAACTCACTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCTGTGTATTACTGTGCGAGAGA

[999] IGHV4-31*03 nucleotide sequence (SEQ ID NO: 1215)
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCACAGACCCTGTCCCTCACCTGCACTGTCTCT
GGTGGCTCCATCAGCAGTGGTGGTTACTACTGGAGCTGGATCCGCCAGCACCCAGGGAAGGGCCTGGAGTGGATT
GGGTACATCTATTACAGTGGGAGCACCTACTACAACCCGTCCCTCAAGAGTCGAGTTACCATATCAGTAGACACG
TCTAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACTGCCGCGGACACGGCCGTGTATTACTGTGCGAGAGA

[1000] IGHV4-31*06 nucleotide sequence (SEQ ID NO: 1216)
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCACAGACCCTGTCCCTCACCTGCACTGTCTCT
GGTGGCTCCATCAGCAGTGGTAGTTACTACTGGAGCTGGATCCGCCAGCACCCAGGGAAGGGCCTGGAGTGGATT
GGGTACATCTATTACAGTGGGAGCACCTACTACAACCCGTCCCTCAAGAGTCGAGTTACCATATCAGTAGACACG
TCTAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACTGCCGCGGACACGGCCGTGTATTACTG

[1001] IGHV4-34*01 nucleotide sequence (SEQ ID NO: 1217)
CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCACTGTCTCT
GGTGGCTCCATCAGCAGTAGTAGTTACTACTGGGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATT
GGGAGTATCTATTATAGTGGGAGCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATATCCGTAGACACG
TCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCAGACACGGCTGTGTATTACTGTGCGAGACA

[1002] IGHV4-34*02 nucleotide sequence (SEQ ID NO: 1218)
CAGGTGCAGCTACAACAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCGCTGTCTAT
GGTGGGTCCTTCAGTGGTTACTACTGGAGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGGAA
ATCAATCATAGTGGAAGCACCAACTACAACCCGTCCCTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAG
AACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCGGACACGGCTGTGTATTACTGTGCGAGAGG

[1003] IGHV4-34*03 nucleotide sequence (SEQ ID NO: 1219)
CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCGCTGTCTAT
GGTGGGTCCTTCAGTGGTTACTACTGGAGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGGAA
ATCAATCATAGTGGAAGCACCAACTACAACCCGTCCCTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAG
AACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCGGACACGGCCGTGTATTACTG

[1004] IGHV4-34*12 nucleotide sequence (SEQ ID NO: 1220)
CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCGCTGTCTAT
GGTGGGTCCTTCAGTGGTTACTACTGGAGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGGAA
ATCATTCATAGTGGAAGCACCAACTACAACCCGTCCCTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAG
AACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCGGACACGGCTGTGTATTACTGTGCGAGA

[1005] IGHV4-39*01 nucleotide sequence (SEQ ID NO: 1221)
CAGCTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCACTGTCTCT
GGTGGCTCCATCAGCAGTAGTAGTTACTACTGGGGCTGGATCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATT
GGGAGTATCTATTATAGTGGGAGCACCTACTACAACCCGTCCCTCAAGAGTCGAGTCACCATATCCGTAGACACG
TCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCCGCAGACACGGCTGTGTATTACTGTGCGAGACA

[1006] IGHV4-59*01 nucleotide sequence (SEQ ID NO: 1222)
GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTAGTAAAGACTGGAGGGGTCTCTGAGACTCTCCTGTGCAGCCTC
TGGATTCACCTTCAGTAGCTCTGCTATGCACTGGGTCCACCAGGCTCCAGGAAAGGGTTTGGAGTGGGTCTCAGT
TATTAGTACAAGTGGTGATACCGTACTCTACACAGACTCTGTGAAGGGCTGATTCACCATCTCTAGAGACAATGC
CCAGAATTCACTGTATCTGCAAATGAACAGCCTGAGAGCCGACGACATGGCTGTGTATTACTGTGTGAAAGA

[1007] IGHV4-59*03 nucleotide sequence (SEQ ID NO: 1223)
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCACTGTCTCT
GGTGGCTCCATCAGTAGTTACTACTGGAGCTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATTGGGTAT
ATCTATTACAGTGGGAGCACCAACTACAACCCCTCCCTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAG
AACCAATTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACGGCCGTGTATTACTGTGCG

[1008] IGHV4-61*01 nucleotide sequence (SEQ ID NO: 1224)
CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACCTGCACTGTCTCT
GGTGGCTCCGTCAGCAGTGGTAGTTACTACTGGAGCTGGATCCGGCAGCCCCCAGGGAAGGGACTGGAGTGGATT
GGGTATATCTATTACAGTGGGAGCACCAACTACAACCCCTCCCTCAAGAGTCGAGTCACCATATCAGTAGACACG
TCCAAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACGGCCGTGTATTACTGTGCGAGAGA

[1009] IGHV4-61*08 nucleotide sequence (SEQ ID NO: 1225)
CAGGTGCAGCTGGTGCAGTCTGGCCATGAGGTGAAGCAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGGCTTCT
GGTTACAGTTTCACCACCTATGGTATGAATTGGGTGCCACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGG
TTCAACACCTACACTGGGAACCCAACATATGCCCAGGGCTTCACAGGACGGTTTGTCTTCTCCATGGACACCTCT
GCCAGCACAGCATACCTGCAGATCAGCAGCCTAAAGGCTGAGGACATGGCCATGTATTACTGTGCGAGATA

[1010] IGHV5-51*01 nucleotide sequence (SEQ ID NO: 1226)
GAGGTGCAGCTGGTGCAGTCTGGAGCAGAGGTGAAAAAGCCCGGGGAGTCTCTGAAGATCTCCTGTAAGGGTTCT
GGATACAGCTTTACCAGCTACTGGATCGGCTGGGTGCGCCAGATGCCCGGGAAAGGCCTGGAGTGGATGGGGATC
ATCTATCCTGGTGACTCTGATACCAGATACAGCCCGTCCTTCCAAGGCCAGGTCACCATCTCAGCCGACAAGTCC
ATCAGCACCGCCTACCTGCAGTGGAGCAGCCTGAAGGCCTCGGACACCGCCATGTATTACTGTGCGAGACA

[1011] In certain embodiments of the invention, the antibody further includes a variable light chain (VL) region encoded by a human IGKV1 (or specifically, IGKV1-17, IGKV1-27, IGKV1-39, IGKV1D-39, IGKV1-5), IGKV2 (or specifically, IGKV2-30), IGKV3 (or specifically, IGKV3-11, IGKV3-15, IGKV3-20), IGKV4 (or specifically, IGKV4-1, IGKV4-1), IGLV1 (or specifically, IGLV1-40, IGLV1-44, IGLV1-55), IGLV2 (or specifically,

IGLV2-11, IGLV2-14, IGLV2-8), IGLV3 (or specifically, IGLV3-21 or IGLV3-25), IGLV7 (or specifically, IGLV7-43 or IGLV7-46), or IGLV9 (or specifically, IGLV9-49) or an allele thereof. V_L germline gene sequenceIGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 or an allele thereof, or a nucleotide acid sequence that is homologous to the IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 V_L germline gene sequence or an allele thereof. Furthermore, the nucleic acid sequence that is homologous to the IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 V_L germline sequence or an allele thereof is at least 65% homologous to the IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 V_L germline sequence or an allele thereof.

[1012] IGKV1-17*01 nucleotide sequence (SEQ ID NO: 1227)
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCA
AGTCAGGGCATTAGAAATGATTTAGGCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCGCCTGATCTATGCT
GCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAATTCACTCTCACAATC
AGCAGCCTGCAGCCTGAAGATTTTGCAACTTATTACTGTCTACAGCATAATAGTTACCCTCC

[1013] IGKV1-27*01 nucleotide sequence (SEQ ID NO: 1228)
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCG
AGTCAGGGCATTAGCAATTATTTAGCCTGGTATCAGCAGAAACCAGGGAAAGTTCCTAAGCTCCTGATCTATGCT
GCATCCACTTTGCAATCAGGGGTCCCATCTCGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATC
AGCAGCCTGCAGCCTGAAGATGTTGCAACTTATTACTGTCAAAAGTATAACAGTGCCCCTCC

[1014] IGKV1-39*01 nucleotide sequence (SEQ ID NO: 1229)
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCA
AGTCAGAGCATTAGCAGCTATTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCT
GCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATC
AGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTACCCCTCC

[1015] IGKV1D-39*01 nucleotide sequence (SEQ ID NO: 1230)
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCA
AGTCAGAGCATTAGCAGCTATTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCT
GCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATC
AGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTACCCCTCC

[1016] IGKV1-5*03 nucleotide sequence (SEQ ID NO: 1231)
GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCC
AGTCAGAGTATTAGTAGCTGGTTGGCCTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATAAG
GCGTCTAGTTTAGAAAGTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGAATTCACTCTCACCATC
AGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAACAGTATAATAGTTATTCTCC

[1017] IGKV2-30*02 nucleotide sequence (SEQ ID NO: 1232)
GATGTTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACCCTTGGACAGCCGGCCTCCATCTCCTGCAGGTCT
AGTCAAAGCCTCGTACACAGTGATGGAAACACCTACTTGAATTGGTTTCAGCAGAGGCCAGGCCAATCTCCAAGG
CGCCTAATTTATAAGGTTTCTAACCGGGACTCTGGGGTCCCAGACAGATTCAGCGGCAGTGGGTCAGGCACTGAT
TTCACACTGAAAATCAGCAGGGTGGAGGCTGAGGATGTTGGGGTTTATTACTGCATGCAAGGTACACACTGGCCT
CC

[1018] IGKV3-11*01 nucleotide sequence (SEQ ID NO: 1233)
GAAATTGTGTTGACACAGTCTCCAGCCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC
AGTCAGAGTGTTAGCAGCTACTTAGCCTGGTACCAACAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGAT
GCATCCAACAGGGCCACTGGCATCCCAGCCAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATC
AGCAGCCTAGAGCCTGAAGATTTTGCAGTTTATTACTGTCAGCAGCGTAGCAACTGGCCTCC

[1019] IGKV3-15*01 nucleotide sequence (SEQ ID NO: 1234)
GAAATAGTGATGACGCAGTCTCCAGCCACCCTGTCTGTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC
AGTCAGAGTGTTAGCAGCAACTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGGT
GCATCCACCAGGGCCACTGGTATCCCAGCCAGGTTCAGTGGCAGTGGGTCTGGGACAGAGTTCACTCTCACCATC
AGCAGCCTGCAGTCTGAAGATTTTGCAGTTTATTACTGTCAGCAGTATAATAACTGGCCTCC

[1020] IGKV3-20*01 nucleotide sequence (SEQ ID NO: 1235)
GAAATTGTGTTGACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC
AGTCAGAGTGTTAGCAGCAGCTACTTAGCCTGGTACCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTAT
GGTGCATCCAGCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACC
ATCAGCAGACTGGAGCCTGAAGATTTTGCAGTGTATTACTGTCAGCAGTATGGTAGCTCACCTCC

[1021] IGKV4-1*01 nucleotide sequence (SEQ ID NO: 1236)
GACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGGCGAGAGGGCCACCATCAACTGCAAGTCC
AGCCAGAGTGTTTTATACAGCTCCAACAATAAGAACTACTTAGCTTGGTACCAGCAGAAACCAGGACAGCCTCCT
AAGCTGCTCATTTACTGGGCATCTACCCGGGAATCCGGGGTCCCTGACCGATTCAGTGGCAGCGGGTCTGGGACA
GATTTCACTCTCACCATCAGCAGCCTGCAGGCTGAAGATGTGGCAGTTTATTACTGTCAGCAATATTATAGTACT
CCTCC

[1022] IGLV1-40*01 nucleotide sequence (SEQ ID NO: 1237)
CAGTCTGTGCTGACGCAGCCGCCCTCAGTGTCTGGGGCCCCAGGGCAGAGGGTCACCATCTCCTGCACTGGGAGC
AGCTCCAACATCGGGGCAGGTTATGATGTACACTGGTACCAGCAGCTTCCAGGAACAGCCCCCAAACTCCTCATC
TATGGTAACAGCAATCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCTG
GCCATCACTGGGCTCCAGGCTGAGGATGAGGCTGATTATTACTGCCAGTCCTATGACAGCAGCCTGAGTGGTTC

[1023] IGLV1-44*01 nucleotide sequence (SEQ ID NO: 1238)
CAGTCTGTGCTGACTCAGCCACCCTCAGCGTCTGGGACCCCCGGGCAGAGGGTCACCATCTCTTGTTCTGGAAGC
AGCTCCAACATCGGAAGTAATACTGTAAACTGGTACCAGCAGCTCCCAGGAACGGCCCCCAAACTCCTCATCTAT
AGTAATAATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCTGGCC
ATCAGTGGGCTCCAGTCTGAGGATGAGGCTGATTATTACTGTGCAGCATGGGATGACAGCCTGAATGGTCC

[1024] IGLV1-51*02 nucleotide sequence (SEQ ID NO: 1239)
CAGTCTGTGTTGACGCAGCCGCCCTCAGTGTCTGCGGCCCCAGGACAGAAGGTCACCATCTCCTGCTCTGGAAGC
AGCTCCAACATTGGGAATAATTATGTATCCTGGTACCAGCAGCTCCCAGGAACAGCCCCCAAACTCCTCATCTAT
GAAAATAATAAGCGACCCTCAGGGATTCCTGACCGATTCTCTGGCTCCAAGTCTGGCACGTCAGCCACCCTGGGC
ATCACCGGACTCCAGACTGGGGACGAGGCCGATTATTACTGCGGAACATGGGATAGCAGCCTGAGTGCTGG

[1025] IGLV2-11*01 nucleotide sequence (SEQ ID NO: 1240)
CAGTCTGCCCTGACTCAGCCTCGCTCAGTGTCCGGGTCTCCTGGACAGTCAGTCACCATCTCCTGCACTGGAACC
AGCAGTGATGTTGGTGGTTATAACTATGTCTCCTGGTACCAACAGCACCCAGGCAAAGCCCCCAAACTCATGATT
TATGATGTCAGTAAGCGGCCCTCAGGGGTCCCTGATCGCTTCTCTGGCTCCAAGTCTGGCAACACGGCCTCCCTG
ACCATCTCTGGGCTCCAGGCTGAGGATGAGGCTGATTATTACTGCTGCTCATATGCAGGCAGCTACACTTTC

[1026] IGLV2-14*01 nucleotide sequence (SEQ ID NO: 1241)
CAGTCTGCCCTGACTCAGCCTGCCTCCGTGTCTGGGTCTCCTGGACAGTCGATCACCATCTCCTGCACTGGAACC
AGCAGTGACGTTGGTGGTTATAACTATGTCTCCTGGTACCAACAGCACCCAGGCAAAGCCCCCAAACTCATGATT
TATGAGGTCAGTAATCGGCCCTCAGGGGTTTCTAATCGCTTCTCTGGCTCCAAGTCTGGCAACACGGCCTCCCTG
ACCATCTCTGGGCTCCAGGCTGAGGACGAGGCTGATTATTACTGCAGCTCATATACAAGCAGCAGCACTCTC

[1027] IGLV2-8*01 nucleotide sequence (SEQ ID NO: 1242)
CAGTCTGCCCTGACTCAGCCTCCCTCCGCGTCCGGGTCTCCTGGACAGTCAGTCACCATCTCCTGCACTGGAACC
AGCAGTGACGTTGGTGGTTATAACTATGTCTCCTGGTACCAACAGCACCCAGGCAAAGCCCCCAAACTCATGATT
TATGAGGTCAGTAAGCGGCCCTCAGGGGTCCCTGATCGCTTCTCTGGCTCCAAGTCTGGCAACACGGCCTCCCTG
ACCGTCTCTGGGCTCCAGGCTGAGGATGAGGCTGATTATTACTGCAGCTCATATGCAGGCAGCAACAATTTC

[1028] IGLV3-21*02 nucleotide sequence (SEQ ID NO: 1243)
TCCTATGAGCTGACACAGCTACCCTCGGTGTCAGTGTCCCCAGGACAGACAGCCAGGATCACCTGCTCTGGAGAT
GTACTGGGGGAAAATTATGCTGACTGGTACCAGCAGAAGCCAGGCCAGGCCCCTGAGTTGGTGATATACGAAGAT
AGTGAGCGGTACCCTGGAATCCCTGAACGATTCTCTGGGTCCACCTCAGGGAACACGACCACCCTGACCATCAGC
AGGGTCCTGACCGAAGACGAGGCTGACTATTACTGTTTGTCTGGGGATGAGGACAATCC

[1029] IGLV3-25*03 nucleotide sequence (SEQ ID NO: 1244)
TCCTATGAGCTGACACAGCCACCCTCGGTGTCAGTGTCCCCAGGACAGACGGCCAGGATCACCTGCTCTGGAGAT
GCATTGCCAAAGCAATATGCTTATTGGTACCAGCAGAAGCCAGGCCAGGCCCCTGTGCTGGTGATATATAAAGAC
AGTGAGAGGCCCTCAGGGATCCCTGAGCGATTCTCTGGCTCCAGCTCAGGGACAACAGTCACGTTGACCATCAGT
GGAGTCCAGGCAGAAGACGAGGCTGACTATTACTGTCAATCAGCAGACAGCAGTGGT

[1030] IGLV7-43*01 nucleotide sequence (SEQ ID NO: 1245)
CAGACTGTGGTGACTCAGGAGCCCTCACTGACTGTGTCCCCAGGAGGGACAGTCACTCTCACCTGTGCTTCCAGC
ACTGGAGCAGTCACCAGTGGTTACTATCCAAACTGGTTCCAGCAGAAACCTGGACAAGCACCCAGGGCACTGATT
TATAGTACAAGCAACAAACACTCCTGGACCCCTGCCCGGTTCTCAGGCTCCCTCCTTGGGGGCAAAGCTGCCCTG
ACACTGTCAGGTGTGCAGCCTGAGGACGAGGCTGAGTATTACTGCCTGCTCTACTATGGTGGTGCTCAG

[1031] IGLV7-46*01 nucleotide sequence (SEQ ID NO: 1246)
CAGGCTGTGGTGACTCAGGAGCCCTCACTGACTGTGTCCCCAGGAGGGACAGTCACTCTCACCTGTGGCTCCAGC
ACTGGAGCTGTCACCAGTGGTCATTATCCCTACTGGTTCCAGCAGAAGCCTGGCCAAGCCCCCAGGACACTGATT
TATGATACAAGCAACAAACACTCCTGGACACCTGCCCGGTTCTCAGGCTCCCTCCTTGGGGGCAAAGCTGCCCTG
ACCCTTTCGGGTGCGCAGCCTGAGGATGAGGCTGAGTATTACTGCTTGCTCTCCTATAGTGGTGCTCGG

[1032] IGLV7-46*02 nucleotide sequence (SEQ ID NO: 1247)
CAGGCTGTGGTGACTCAGGAGCCCTCACTGACTGTGTCCCCAGGAGGGACAGTCACTCTCACCTGTGGCTCCAGC
ACTGGAGCTGTCACCAGTGGTCATTATCCCTACTGGTTCCAGCAGAAGCCTGGCCAAGCCCCCAGGACACTGATT
TATGATACAAGCAACAAACACTCCTGGACACCTGCCCGGTTCTCAGGCTCCCTCCTTGGGGGCAAAGCTGCCCTG
ACCCTTTTGGGTGCGCAGCCTGAGGATGAGGCTGAGTATTACTGCTTGCTCTCCTATAGTGGTGCTCGG

[1033] IGLV9-49*01 nucleotide sequence (SEQ ID NO: 1248)
CAGCCTGTGCTGACTCAGCCACCTTCTGCATCAGCCTCCCTGGGAGCCTCGGTCACACTCACCTGCACCCTGAGC
AGCGGCTACAGTAATTATAAAGTGGACTGGTACCAGCAGAGACCAGGGAAGGGCCCCCGGTTTGTGATGCGAGTG
GGCACTGGTGGGATTGTGGGATCCAAGGGGGATGGCATCCCTGATCGCTTCTCAGTCTTGGGCTCAGGCCTGAAT
CGGTACCTGACCATCAAGAACATCCAGGAAGAGGATGAGAGTGACTACCACTGTGGGGCAGACCATGGCAGTGGG
AGCAACTTCGTGTAACC

[1034] IGLV9-49*03 nucleotide sequence (SEQ ID NO: 1249)
CAGCCTGTGCTGACTCAGCCACCTTCTGCATCAGCCTCCCTGGGAGCCTCGGTCACACTCACCTGCACCCTGAGC
AGCGGCTACAGTAATTATAAAGTGGACTGGTACCAGCAGAGACCAGGGAAGGGCCCCCGATTTGTGATGCGAGTG
GGCACTGGTGGGATTGTGGGATCCAAGGGGGATGGCATCCCTGATCGCTTCTCAGTCTTGGGCTCAGGCCTGAAT
CGGTACCTGACCATCAAGAACATCCAGGAAGAGGATGAGAGTGACTACCACTGTGGGGCAGACCATGGCAGTGGG
AGCAACTTCGTGTAACC

[1035] The heavy chain of an isolated monoclonal anti-hemagglutinin (HA) antibody (i.e., anti-hemagglutinin antibody of the invention) is derived from a germ line V (variable) gene

such as, for example, the IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 germline gene or an allele thereof.

[1036] The HA antibodies of the invention include a variable heavy chain (V_H) region encoded by a human IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 germline gene sequence or an allele thereof. A IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 germline gene sequence is shown, *e.g.*, in SEQ ID NOs: 457 to 485. The HA antibodies of the invention include a V_H region that is encoded by a nucleic acid sequence that is at least 75% homologous to the IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 germline gene sequence or an allele thereof. Preferably, the nucleic acid sequence is at least 75%, 80%, 85%, 90%, 95%, 96%, 97% homologous to the IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 germline gene sequence or an allele thereof, and more preferably, at least 98%, 99% homologous to the IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 germline gene sequence or an allele thereof. The V_H region of the HA antibody is at least 75% homologous to the amino acid sequence of the V_H region encoded by the IGHV1, IGHV2, IGHV3, IGHV4, or IGHV5 V_H germline gene sequence or an allele thereof. Preferably, the amino acid sequence of V_H region of the HA antibody is at least 75%, 80%, 85%, 90%, 95%, 96%, 97% homologous to the amino acid sequence encoded by the 75%, 80%, 85%, 90%, 95%, 96%, 97% germline gene sequence or an allele thereof, and more preferably, at least 98%, 99% homologous to the sequence encoded by the 75%, 80%, 85%, 90%, 95%, 96%, 97% germline gene sequence or an allele thereof.

[1037] The HA antibodies of the invention also include a variable light chain (V_L) region encoded by a human IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 germline gene sequence or an allele thereof. A human IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 V_L germline gene sequence, or an allele thereof is shown, *e.g.*, at SEQ ID NOs: 486 to 508. Alternatively, the HA antibodies include a IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 V_L region that is encoded by a nucleic acid sequence that is at least 65% homologous to the IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 germline gene sequence or an allele thereof. Preferably, the nucleic acid sequence is at least 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97% homologous to the IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 germline gene sequence or an allele thereof, and more preferably, at least 98%, 99% homologous to the IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 germline gene sequence or an allele thereof. The V_L region of the HA antibody is at least 65% homologous to the amino acid sequence of the

V_L region encoded the IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 germline gene sequence or an allele thereof. Preferably, the amino acid sequence of V_L region of the HA antibody is at least 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97% homologous to the amino acid sequence encoded by the IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 germline gene sequence or an allele thereof, and more preferably, at least 98%, 99% homologous to the sequence encoded by the IGKV1, IGKV2, IGKV3, IGKV4, IGLV1, IGLV2, IGLV3, IGLV7, or IGLV9 germline gene sequence or an allele thereof.

HA Antibodies III

[1038] The present invention relates to an immunogen capable of inducing antibodies against a target peptide of the stem region of hemagglutinn protein of an influenza virus. The immunogen is a peptide or a synthetic peptide. In particular, the immunogen of this invention comprises one or more epitopes or epitope units. Optionally, the immunogen further comprises a general immune stimulator. These immunogens of the present invention are capable of inducing antibodies against influenza A virus to prevent infection by the virus.

[1039] In one aspect the invention provides an immunogen having an epitope or epitope unit recognized by a protective monoclonal antibody having the specificity for the stem region of hemagglutinn protein of an influenza virus.

[1040] The antibody binds both the HAl and HA2 peptide. In some embodiments the epitope is recognized by monoclonal antibody D7, D8, F10, G17, H40, A66, D80, E88, E90, or H98 or a monoclonal antibody that competes with the binding of monoclonal antibody D7, D8, F10, G17, H40, A66, D80, E88, E90, or H98 to the HA protein. Preferably, the epitope is the F10 epitope.

[1041] In some embodiments the hemagglutinin protein is in the neutral pH conformation.

[1042] The immunogen is a peptide or a synthetic peptide.

[1043] In some aspects the immunogen is a conjugate having one or more peptides or peptide fragments that are spatially positioned relative to each other so that they together form a non-linear sequence which mimics the tertiary structure of an F10 epitope. Optionally, the one or more peptides or peptide fragments are linked to a backbone. The conjugate competes with the binding of monoclonal antibody F10 to the HA protein.

[1044] The e conformation of the epitope is defined by amino acid residues 18, 38, 39, 40 and 291 of HAl and 18, 19, 20, 21, 38, 41, 42, 45, 49, 52, 53, and 56 of HA2 when the hemagglutinin in the neutral pH conformation.

[1045] In some embodiments the immunogen is a peptide having one or more of the following amino acid sequences.

[1046] $[Xaa_0]_m$-Xaa_1-Xaa_2- $[Xaa_0]_p$, wherein, preferably, Xaa_1 is S, T, F H or Y and Xaa 2 is H, Y, M, L or Q. Most preferably, Xaa_1 is Y. Most preferably, Xaa_2 is H.

[1047] $[Xaa_0]_m$-Xaa_1-Xaa_2- $[Xaa_0]_p$, wherein, preferably, Xaa_1 is H, Q, Y, S, D, N or T and Xaa_2 of is Q, E, K, I , V, M, E, R or T. Most preferably, Xaa_1 is H. Most preferably, Xaa_2 is Q.

[1048] $[Xaa_0]_m$-Xaa_1-Xaa_2-Xaa_3-Xaa_4- $[Xaa_0]_p$, wherein, preferably, Xaa_1 is I, V, M, or L; Xaa_2 is D, N, H, Y, D, A,S or E, Xaa_3 is G or A, and Xaa_4 is W, R, or G. Most preferably, Xaa_1 is V; Xaa_2 is D, Xaa_3 is G, and Xaa_4 is W.

[1049] $[Xaa_0]_m$-Xaa_1-$[Xaa_0]_q$ Xaa_2-Xaa_3-$[Xaa_0]_q$ Xaa_4-$[Xaa_0]_r$ Xaa_5-$[Xaa_0]_q$-Xaa_6 Xaa_7 - $[Xaa_0]_q$ -Xaa_8 -$[Xaa_0]_p$, and $[Xaa_0]_m$-Xaa_1-$[Xaa_0]_q$ Xaa_2-Xaa_3-$[Xaa_0]_q$ Xaa_4-$[Xaa_0]_r$ Xaa_5-$[Xaa_0]_q$-Xaa_6 Xaa_7 -$[Xaa_0]_s$ –$[Xaa_8]_t$ -$[Xaa_0]_p$, wherein, preferably Xaa_1 is K, Q, R, N, L, G, F, H or Y; Xaa_2 is S or T, Xaa_3 is Q or P; Xaa_4 is F, V, I, M, L, or T; Xaa_5 is I, T, S, N, Q, D, or A; Xaa_6 is I, V, M, or L; Xaa_7 is N, S, T, or D and Xaa_8 is I, F,V, A, or T. Most preferably, Xaa_1 is K; Xaa_2 is T, Xaa_3 is Q; Xaa_4 is I ; Xaa_5 is T ; Xaa_6 is V; Xaa_7 is N, and Xaa_8 is I.

[1050] For all of the preceding sequences, m, and p are independently 0 or 1-100, preferably about 1-90, 1-80, 1-70, 1-60, 1-50, 1-40, 1-30, 1-20 or 1-10; q is 2, r is 3, s is 0 or 2, and t is 0 or 1, and Xaa_0, is independently any amino acid. Preferably s is 2 and t is 1.

[1051] In some aspects of the inventions, one or more amino acids are D- amino acids.

[1052] Optionally, the immunogen further comprises an adjuvant or is conjugated to a carrier.

[1053] In various aspects the invention includes a composition containing the immunogen together with one or more pharmaceutically acceptable excipients, diluents, and/or adjuvants. In some embodiments the composition further comprises an anti-influenza antibody of antigen binding fragment thereof. Preferably, the antibody is monoclonal antibody D7, D8, F10, G17, H40, A66, D80, E88, E90, or H98 or a monoclonal antibody that competes with the binding of monoclonal antibody D7, D8, F10, G17, H40, A66, D80, E88, E90, or H98 to the HA protein. Also provided by the invention are nucleic acids encoding the immunogens of the invention and composition comprising the nucleic acids.

[1054] The invention further comprises a method preventing a disease or disorder caused by an influenza virus by administering to person at risk of suffering from said disease or disorder an immunogen composition described herein. Optionally, the method includes further administering an anti-viral drug, a viral entry inhibitor or a viral attachment inhibitor. The anti-viral drug is a neuraminidase inhibitor, a HA inhibitor, a sialic acid inhibitor or an M2 ion channel. The M2 ion channel inhibitor is amantadine or, rimantadine. The neuraminidase inhibitor zanamivir, or oseltamivir phosphate.

[1055] In another aspect the method includes further administering one or more antibodies specific to a Group I influenza virus and or a Group II influenza virus. The antibody is administered at a dose sufficient to neutralize the influenza virus.

[1056] Administration is prior to or after exposure to influenza virus.

[1057] Also disclosed are methods of treating subjects and methods of screening and producing antibodies. For example, disclosed is a method of treating a subject suffering or at risk of influenza infection, the method comprising administering to the subject one or more of the disclosed antibodies, such as the disclosed HA stem antibodies. For example, disclosed is a method of treating a subject, the method comprising administering to the subject the stem region of influenza hemagglutinin in the neutral pH conformation in isolation from other components of influenza virus, wherein the subject produces an immune response to the stem region. For example, disclosed is a method of treating a subject, the method comprising administering to the subject the stem region of influenza hemagglutinin in the neutral pH conformation in isolation from the head region of hemagglutinin, wherein the subject produces an immune response to the stem region. For example, disclosed is a method of treating a subject, the method comprising administering to the subject influenza hemagglutinin in the neutral pH conformation in isolation from other components of influenza virus, wherein the head region of the hemagglutinin is modified to reduce the antigenicity of the head region, wherein the subject produces an immune response to the stem region. For example, disclosed is a method, the method comprising screening antibodies reactive to hemagglutinin for binding to hemagglutinin immobilized on a surface, thereby identifying antibodies of interest. For example, disclosed is a method comprising screening antibodies reactive to hemagglutinin for binding to the stem region of influenza hemagglutinin in the neutral pH conformation in isolation from the head region of hemagglutinin, thereby identifying antibodies of interest. For example, disclosed is a method comprising screening antibodies reactive to hemagglutinin for binding to influenza

hemagglutinin in the neutral pH conformation in isolation from other components of influenza virus, wherein the head region of the hemagglutinin is modified to reduce the antigenicity of the head region, thereby identifying antibodies of interest.

[1058] In some forms, the head region of the hemagglutinin can be modified by removing or replacing glycosylation sites. In some forms, the head region of the hemagglutinin can be modified by adding glycosylation sites. In some forms, the head region of the hemagglutinin can be modified by removing all or a portion of the head region.

[1059] In some forms, the disclosed antibodies, disclosed hemagglutinins, and disclosed methods can produce an immune reaction in a subject. For example, in some forms, the subject can produce an immune response that prevents or reduces the severity of an influenza infection. In some forms, the immune response can be reactive to influenza viruses within a subtype. In some forms, the immune response can be reactive to influenza viruses in each subtype within a cluster. In some forms, the immune response can be reactive to influenza viruses in each cluster within a group. In some forms, the immune response can be reactive to all influenza viruses in each subtype within a group. In some forms, the immune response can be reactive to influenza viruses within group 1.

[1060] In some forms, the disclosed methods can further comprise screening the antibodies of interest for competing with antibody F10 for binding to hemagglutinin, thereby identifying F10-competing antibodies. In some forms, the hemagglutinin can be hemagglutinin from a group 2 influenza virus. In some forms, the hemagglutinin can be hemagglutinin from a group 1 influenza virus. In some forms, the disclosed methods can further comprising producing the identified antibodies. Also disclosed are antibodies produced by the disclosed methods. Also disclosed are antibodies identified by the disclosed methods.

[1061] The disclosed compositions and methods are based upon the discovery of monoclonal antibodies which neutralize the influenza virus, e.g. influenza A virus. The influenza A virus is a Group I influenza A virus such as a H1 cluster influenza virus. The H1 cluster influenza virus is an Hla cluster or an H lb cluster. The monoclonal antibody is fully human. In some forms, the monoclonal antibody can be a bivalent antibody, a monovalent antibody, a single chain antibody or fragment thereof. Specifically, such monoclonal can bind to an epitope on the stem region of the hemagglutinin protein (HA), such as HAl or HA2 polypeptide. The epitope can be non-linear.

[1062] The epitope can comprise both the HAl and HA2. The epitope can be non-linear. In

some forms the epitope can comprise the amino acid position 18, 38, 40, 291 of the Hal polypeptide and the amino acid at position 18, 19, 20, 21, 38, 41, 42, 45, 49, 52, 53 and 56 of the HA2 polypeptide.

[1063] The disclosed compositions and methods are further based upon the discovery of a protocol for generating broadly neutralizing human antibodies that target a highly conserved epitope in the stem region of HA. Using the trimeric H5 ectodomain expressed in baculovirus which produces shorter N-glycans and uncharged mannoses absorbed on a plastic surface, allowed for the dominant presentation of the stem epitope while masking the normally immunodominat globular head. Accordingly, also disclosed is a method of producing an isolated antibody that specifically binds a pathogenic enveloped virus by exposing a single chain or Fab expression library to a membrane fusion protein of the virus, identifying an antibody in the library that specifically binds said protein; and isolating the antibody from the library. The fusion protein can be immobilized on a solid surface, e.g. plastic. In some forms the fusion protein can have modified glycosylations compared to a wild type fusion protein. For example, the fusion can be produced in a non-mammalian cell, such as an insect cell. The fusion protein can be, for example, a trimeric hemagglutinin (HA) protein.

[1064] Also disclosed is a method of vaccinating a subject against pathogenic enveloped virus such as an influenza virus by administering to the subject, for example, a membrane fusion protein (e.g., a trimeric hemagglutinin (HA) protein coated) or embedded in a biologically compatible matrix. In some forms the fusion protein can have modified glycosylations compared to a wild type fusion protein.

[1065] Also disclosed is a composition comprising a monoclonal antibody as described herein and kits containing the composition in one or more containers and instructions for use. The invention further provides a method of screening a compound for binding to an F10 antibody by contacting said F10 antibody with a compound of interest and detecting a compound-antibody complex. Also included in the invention are the compound identified by the method and their use as immunogens.

[1066] High affinity, cross-subtype, broadly-neutralizing human anti-HA mAbs have been identified. Sepcifically, a human Ab phage display library and H5 hemagglutinin (HA) ectodomain was used to select ten neutralizing mAbs (nAbs) with a remarkably broad range among Group 1 influenza viruses, including the H5N1 "bird flu" and the H1N1 "Spanish flu" and "Swine flu" strains. These nAbs inhibit the post-attachment fusion process by recognizing a novel and highly conserved neutralizing epitope within the stem region at a

point where key elements of the conformational change — the fusion peptide and the exposed surface of helix aA — are brought into close apposition. The crystal structure of one mAb (mAbFlO) bound to H5N1 HA reveals that only the heavy chain inserts into a highly conserved pocket in the HA stem region, inhibiting the conformational changes required for membrane fusion. It has been discovered that nAbs targeting this pocket can provide broad protection against both seasonal and pandemic influenza A infections. The crystal structure further revealed that the epitope to which the F10 mAb is defined by amino acid residues 18, 38, 39, 40 and 291 of HAl and 18, 19, 20, 21, 38, 41, 42, 45, 49, 52, 53, and 56 of HA2. This epitope is referred to herein as the F10 epitope. Structural and sequence analysis of all 16 HA subtypes points to the existence of only two variants of this epitope, corresponding to the two phylogenetic groupings of HA (Groups 1 and 2). This discovery indicates that a small cocktail of nAbs derived from a subset of each group can provide broad protection against both seasonal and pandemic influenza.

[1067] Remarkably, nAbs were isolated that utilize the same VH germline gene, IGHV1-69*01, and encode a CDR3 loop containing a tyrosine at an equivalent position to Y102, from a non-immune library. This indicates that broad anti-HA cross-immunity pre-exists in the H5-naive population, possibly due to previous exposure to H1, and, for library donors born before 1968, H2 subtypes. The recurrent use of this germline VH segment, the commonality of the CDR3 tyrosine introduced through N insertion and/or germline D gene assembly, and the promiscuous use of VL genes by the discovered nAbs discovered indicate that the precursor frequency of rearranged VH segments that could recognize this epitope is significant. This indicates that with suitable exposure to the F10 epitope identified here, these broad-spectrum nAbs can be readily induced in vivo. These discoveries led to the disclosed simple solution to provide universal protection against virus subtypes in both groups.

[1068] Three unique anti-HA-1 scFvs were identified by sequencing analysis of the 58 HA-1 positive clones. These scFvs were designated as 38B and 1C. The VH and VL amino acid sequence of 2A is shown herein. Ten unique anti-HAO scFvs were identified by sequencing analysis of the 97 HAO positive clones. These scFvs were designated as 7, 8, 10, 17, 40, 66, 80, 88, 90, and 98. Six different VH and 10 different VL genes were revealed. Some scFvs shared the same VH gene. Five out of the six different VH genes belonged to the IGHV1-69 gene family. Three out of ten VL genes were kappa chain. 2A scFv is a moderate neutralizing antibody, 38B and 1C are non-neutralizing antibodies. Ten scFvs, 7, 8, 10, 17, 40, 66, 80, 88,

90, and 98 are potent neutralizing antibodies. The nucleic acid and amino acid sequence of the neutralizing influenza antibodies are provided below. Methods of making these antibodies are disclosed in PCT/US2009/054950 (Publication No. WO 2010/027818), the entire contents of which are incorporated herein by reference.

[1069] Antibody 2A: Variable Region nucleic acid sequences

[1070] VH chain of 2A (SEQ ID NO: 1305)

CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCAAGGCTTCT
GGAGGCACCTTCAGTGACAATGCTATCAGCTGGGTGCGACAGGCCCCAGGACAAGGGCTTGAGTGGATGGGGGGC
ATCATTCCTATCTTTGGAAAACCAAACTACGCACAGAAGTTCCAGGGCAGAGTCACGATTACTGCGGACGAATCC
ACGAGCACAGCCTACATGGACCTGAGGAGCCTGAGATCTGAGGACACGGCCGTTTATTACTGTGCGAGAGATTCA
GACGCGTATTACTATGGTTCGGGGGGTATGGACGTCTGGGGCCAAGGCACCCTGGTCACCGTCTCCTCA

[1071] VL chain of 2A (SEQ ID NO: 1306)

CTGCCTGTGCTGACTCAATCATCCTCTGCCTCTGCTTCCCTGGGATCCTCGGTCAAGCTCACCTGCACTCTGAGC
AGTGGGCATAGTAACTACATCATCGCATGGCATCAACAGCAGCCAGGGAAGGCCCCTCGGTACTTGATGAAGGTT
AATAGTGATGGCAGCCACACCAAGGGGGACGGGATCCCTGATCGCTTCTCAGGCTCCAGCTCTGGGGCTGACCGC
TACCTCACCATCTCCAACCTCCAGTCTGAGGATGAGGCTAGTTATTTCTGTGAGACCTGGGACACTAAGATTCAT
GTCTTCGGAACTGGGACCAAGGTCTCCGTCCTCAG

[1072] Antibody 2A: Variable Region amino acid sequences

[1073] VH chain of 2A (SEQ ID NO: 1307)

QVQLVQSGAEVKKPGSSVKVSCKASGGTFSDNAISWVRQAPGQGLEWMGGIIPIFGKPNYAQ
KFQGRVTITADESTSTAYMDLRSLRSEDTAVYYCARDSDAYYYGSGGMDVWGQGTLVTVS
S

[1074] VL chain of 2A (SEQ ID NO: 1308)

LPVLTQSSSASASLGSSVKLTCTLSSGHSNYIIAWHQQQPGKAPRYLMKVNSDGSHTKGDGI
PDRFSGSSSGADRYLT ISNLQSEDEASYFCETWDTK I HVFGTGTKVSVL

[1075] Antibody D7: Variable Region nucleic acid sequences

[1076] VH chain of D7 (SEQ ID NO: 1309)

CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCAAGGCTCCT
GGAGGTATCTTCAACACCAATGCTTTCAGCTGGGTCCGACAGGCCCCTGGACAAGGTCTTGAGTGGGTGGGAGGG
GTCATCCCTTTGTTTCGAACAGCAAGCTACGCACAGAACGTCCAGGGCAGAGTCACCATTACCGCGGACGAATCC
ACGAACACAGCCTACATGGAGCTTACCAGCCTGAGATCTGCGGACACGGCCGTGTATTACTGTGCGAGAAGTAGT
GGTTACCATTTTAGGAGTCACTTTGACTCCTGGGGCCTGGGAACCCTGGTCACCGTCTCCTCA

[1077] VL chain of D7 (SEQ ID NO: 1310)

AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGCGTCTCCGGGGAAGACGGTGACCATCTCCTGCACCGGCAGC
AGTGGCAACATTGCCGCCAACTATGTGCAGTGGTACCAACAACGTCCGGGCAGTGCCCCCACTACTGTGATCTAT
GAGGATGACCGAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGACAGGTCCTCCAACTCTGCCTCC
CTCACCATCTCAGGACTGAAGACTGAGGACGAGGCTGACTACTACTGTCAGACTTATGATACCAACAATCATGCT
GTGTTCGGAGGAGGCACCCACCTGACCGTCCTC

[1078] Antibody H98: Variable Region nucleic acid sequences

[1079] VH chain of H98 (SEQ ID NO: 1311)

CAGGTGCAGCTGGTGCAATCTGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCAAGGCTCCT
GGAGGTATCTTCAACACCAATGCTTTCAGCTGGGTCCGACAGGCCCCTGGACAAGGTCTTGAGTGGGTGGGAGGG
GTCATCCCTTTGTTTCGAACAGCAAGCTACGCACAGAACGTCCAGGGCAGAGTCACCATTACCGCGGACGAATCC
ACGAACACAGCCTACATGGAGCTTACCAGCCTGAGATCTGCGGACACGGCCGTGTATTACTGTGCGAGAAGTAGT
GGTTACCATTTTAGGAGTCACTTTGACTCCTGGGGCCTGGGAACCCTGGTCACCGTCTCCTCA

[1080] VL chain of H98 (SEQ ID NO: 1312)

TCCTATGAGCTGACTCAGCCACCCTCAGCGTCTGGGAAACACGGGCAGAGGGTCACCATCTCTTGTTCTGGAGGC
ACCTCCAACATCGGACGTAATCATGTTAACTGGTACCAGCAACTCCCAGGAACGGCCCCCAAACTCCTCATCTAT
AGTAATGAACAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAATCTGGCACCTCCGCCTCCCTGGCC
GTGAGTGGGCTCCAGTCTGAGGATGAGGCTGATTATTACTGTGCATCATGGGATGACAACTTGAGTGGTTGGGTG
TTCGGCGGAGGGACCAAGCTGACCGTCCTA

[1081] Antibody D7 and H98: Variable Region chain amino acid sequences

[1082] VH chain of D7 and H98 (SEQ ID NO: 1313)

QVQLVQSGAEVKKPGSSVKVSCKAPGGIFNTNAFSWVRQAPGQGLEWVGGVIPLFRTASYA
QNVQGRVT I TADESTNTAYMELTSLRSADTAVYYCARSSGYH FRSHFDSWGLGTLVTVSS

[1083] VL chain of D7 (SEQ ID NO: 1314)

NFMLTQPHSVSASPGKTVTISCTGSSGNIAANYVQWYQQRPGSAPTTVIYEDDRRPSGVPDRF
SGSIDRSSNSASLTISGLKTEDEADYYCQTYDTNNHAVFGGGTHLTVL

[1084] VL chain of H98 (SEQ ID NO: 1315)

SYELTQPPSASGKHGQRVTISCSGGTSNIGRNHVNWYQQLPGTAPKLLIYSNEQRPSGVPDRF
SGSKSGTSASLAVSGLQSEDEADYYCASWDDNLSGWVFGGGTKLTVL

[1085] Antibody D8: Variable Region nucleic acid sequences

[1086] VH chain of D8 (SEQ ID NO: 1316)

CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCAAGGCTTCT
GGAGGCACCTTCAGCGCTTATGCTTTCACCTGGGTGCGGCAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGC
ATCACCGGAATGTTTGGCACAGCAAACTACGCACAGAAGTTCCAGGGCAGAGTCACGATTACCGCGGACGAACTC
ACGAGCACAGCCTACATGGAGTTGAGCTCCCTGACATCTGAAGACACGGCCCTTTATTATTGTGCGAGAGGATTG
TATTACTATGAGAGTAGTCTTGACTATTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAG

[1087] VL chain of D8 (SEQ ID NO: 1317)

CAGTCTGTGCTGACTCAGCCACCCTCCGCGTCCGGGTCTCCTGGACAGTCAGTCACCATCTCCTGCACTGGAACC
AGCAGTGACGTTGGTGGTTATAACTCTGTCTCCTGGTACCAACAGCACCCAGGCAAAGCCCCCAAACTCATGATT
TATGAGGTCACTAAGCGGCCCTCAGGGGTCCCTGATCGCTTCTCTGCCTCCAAGTCTGGCAACACGGCCTCCCTG
ACCGTCTCTGGGCTCCAGGCTGAGGATGAGGCTGATTATTTCTGCTGCTCATATGCAGGCCACAGTGCTTATGTC
TTCGGAACTGGGACCAAGGTCACCGTCCTG

[1088] Antibody D80: Variable Region nucleic acid sequences

[1089] VH chain of D80 (SEQ ID NO: 1318)

CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCAGGGCTTCT
GGAGGCACCTTCAGCGCTTATGCTTTCACCTGGGTGCGGCAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGC

ATCACCGGAATGTTTGGCACAGCAAACTACGCACAGAAGTTCCAGGGCAGAGTCACGATTACCGCGGACGAACTC
ACGAGCACAGCCTACATGGAGTTGAGCTCCCTGACATCTGAAGACACGGCCCTTTATTATTGTGCGAGAGGATTG
TATTACTATGAGAGTAGTCTTGACTATTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAG

[1090] VK chain of D80 (SEQ ID NO: 1319)

GAAATTGTGCTGACTCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC
AGTCAGAGTCTTAGCAGCAAGTACTTAGCCTGGTATCAGCAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTAT
GGTGCATCCAGCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACCCTCACC
ATCAGTAGACTGGAGCCTGAAGATTTTGCAGTGTATTCCTGTCAGCAGTATGATGGCGTACCTCGGACGTTCGGC
CAAGGGACCACGGTGGAAATCAAA

[1091] Antibody D8 and D80: Variable Region chain amino acid sequences

[1092] VH chain of D8 and D80 (SEQ ID NO: 1320)

QVQLVQSGAEVKKPGSSVKVSCKASGGTFSAYAFTWVRQAPGQGLEWMGGITGMFGTANY
AQKFQGRVTITADELTSTAYMELSSLTSEDTALYYCARGLYYYESSLDYWGQGTLVTVSS

[1093] VL chain of D8 (SEQ ID NO: 1321)

QSVLTQPPSASGSPGQSVTISCTGTSSDVGGYNSVSWYQQHPGKAPKLMIYEVTKRPSGVPD
RFSASKSGNTASLTVSGLQAEDEADYFCCSYAGHSAYVFGTGTKVTVL

[1094] VK chain of D80 (SEQ ID NO: 1322)
EIVLTQSPGTLSLSPGERATLSCRASQSLSSKYLAWYQQKPGQAPRLLIYGASSRATG
IPDRFSGSGSGTDFTLTISRLEPEDFAVYSCQQYDGVPRTFGQGTTVEIK

[1095] Antibody F10: Variable Region nucleic acid sequences

[1096] VH chain of F10 (SEQ ID NO: 1323)
CAGGTGCAGCTGGTGCAGTCAGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCACGTCCTCT
GAAGTCACCTTCAGTAGTTTTGCTATCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGCTGGGAGGG
ATCAGCCCTATGTTTGGAACACCTAATTACGCGCAGAAGTTCCAAGGCAGAGTCACCATTACCGCGGACCAGTCC
ACGAGGACAGCCTACATGGACCTGAGGAGCCTGAGATCTGAGGACACGGCCGTGTATTATTGTGCGAGATCTCCT
TCTTACATTTGTTCTGGTGGAACCTGCGTCTTTGACCATTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCA

[1097] VL chain of F10 (SEQ ID NO: 1324)
CAGCCTGGGCTGACTCAGCCACCCTCGGTGTCCAAGGGCTTGAGACAGACCGCCACACTCACCTGCACTGGGAAC
AGCAACAATGTTGGCAACCAAGGAGCAGCTTGGCTGCAGCAGCACCAGGGCCACCCTCCCAAACTCCTATCCTAC
AGGAATAATGACCGGCCCTCAGGGATCTCAGAGAGATTCTCTGCATCCAGGTCAGGAAACACAGCCTCCCTGACC
ATTACTGGACTCCAGCCTGAGGACGAGGCTGACTATTACTGCTCAACATGGGACAGCAGCCTCAGTGCTGTGGTA
TTCGGCGGAGGGACCAAGCTGACCGTCCTA

[1098] Antibody E90: Variable Region nucleic acid sequences

[1099] VH chain of E90 (SEQ ID NO: 1325)
CAGGTACAGCTGCAGCAGTCAGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGGTGAAGGTCTCCTGCACGTCCTCT
GAAGTCACCTTCAGTAGTTTTGCTATCAGCTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGCTGGGAGGG
ATCAGCCCTATGTTTGGAACACCTAATTACGCGCAGAAGTTCCAAGGCAGAGTCACCATTACCGCGGACCAGTCC
ACGAGGACAGCCTACATGGACCTGAGGAGCCTGAGATCTGAGGACACGGCCGTGTATTATTGTGCGAGATCTCCT
TCTTACATTTGTTCTGGTGGAACCTGCGTCTTTGACCATTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCA

[1100] VL chain of E90 (SEQ ID NO: 1326)
GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCA
AGTCAGAGCATTAGCAGCTATTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCT

GCATCCAGTTTGCAAAGAGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCTGGGACAGACTTCACTCTCACCATT
AGCAGCCTGCAGCCTGAAGATTTTGCAGTGTATTACTGTCAGCAGTATGATAGTTCACCGTACACTTTTGGCCAG
GGGACCAAGGTAGAGATCAAA

[1101] Antibody F10 and E90 Variable Region amino acid sequences

[1102] VH chain of F10 and E90 (SEQ ID NO: 1327)
QVQLVQSGAEVKKPGS SVKVSCTSSEVTFSSFAISWVRQAPGQGLEWLGGISPMFGT
PNYAQKFQGRVTITADQSTRTAYMDLRSLRSEDTAVYYCARSPSYICSGGTCVFDHWGQGT
LVTVSS

[1103] VL chain of F10 (SEQ ID NO: 1328)
QPGLTQPPSVSKGLRQTATLTCTGNSNNVGNQGAAWLQQHQGHPPKLLSYRNNDRPSGISER
FSASRSGNTASLTITGLQPEDEADYYCSTWDSSLSAVVFGGGTKLTVL

[1104] VL chain of E90 (SEQ ID NO: 1329)
DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQRGVPSRFSG
SGSGTDFTLTISSLQPEDFAVYYCQQYDSSPYTFGQGTKVEIK

[1105] Antibody G17: Variable Region nucleic acid sequences

[1106] VH chain of G17 (SEQ ID NO: 1330)
CAGGTGCAGCTGGTGCAATCTGGGGCTGAAGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTGCAAGACTTCT
GGAGTCACCTTCAGCAGCTATGCTATCAGTTGGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGAGGG
ATCATCGGTGTCTTTGGTGTACCAAAGTACGCGCAGAACTTCCAGGGCAGAGTCACAATTACCGCGGACAAACCG
ACGAGTACAGTCTACATGGAGCTGAACAGCCTGAGAGCTGAGGACACGGCCGTGTATTACTGTGCGAGAGAGCCC
GGGTACTACGTAGGAAAGAATGGTTTTGATGTCTGGGGCCAAGGGACAATGGTCACCGTCTCTTCA

[1107] VL chain of G17 (SEQ ID NO: 1331)
TCCTATGAGCTGACTCAGCCACCCTCGGTGTCCAAGGGCTTGAGACAGACCGCCATACTCACCTGCACTGGAGAC
AGCAACAATGTTGGCCACCAAGGTACAGCTTGGCTGCAACAACACCAGGGCCACCCTCCCAAACTCCTATCCTAC
AGGAATGGCAACCGGCCCTCAGGGATCTCAGAGAGATTCTCTGCATCCAGGTCAGGAAATACAGCCTCCCTGACC
ATTATTGGACTCCAGCCTGAGGACGAGGCTGACTACTACTGCTCAGTATGGGACAGCAGCCTCAGTGCCTGGGTG
TTCGGCGGAGGGACCAAGCTGACCGTCCTA

[1108] Antibody G17 Variable Region amino acid sequences

[1109] VH chain of G17 (SEQ ID NO: 1332)
QVQLVQSGAEVKKPGASVKVSCKTSGVTFSSYAISWVRQAPGQGLEWMGGIIGVFGVPKYA
QNFQGRVTITADKPTSTVYMELNSLRAEDTAVYYCAREPGYYVGKNGFDVWGQGTMVTVS
S

[1110] VL chain of G17 (SEQ ID NO: 1333)
SYELTQPPSVSKGLRQTAILTCTGDSNNVGHQGTAWLQQHQGHPPKLLSYRNGNRPSGISER
FSASRSGNTASLTIIGLQPEDEADYYCSVWDSSLSAWVFGGGTKLTVL

[1111] Antibody H40: Variable Region nucleic acid sequences

[1112] VH chain of H40 (SEQ ID NO: 1334)
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAGGAAGCCTGGGGCCTCAGTGAAGGTCTCATGTAAGGCTTCT
GGATACACCTTCACCGGTTATTATATTCACTGGGTGCGACAGGCCCCTGGACAAGGACTTGAGTGGATGGGTTGG
ATCAACCCTATGACTGGTGGCACAAACTATGCACAGAAGTTTCAGGTCTGGGTCACCATGACCCGGGACACGTCC
ATCAACACAGCCTACATGGAGGTGAGCAGGCTGACATCTGACGACACGGCCGTGTATTACTGTGCGAGGGGGGCT

TCCGTATTACGATATTTTGACTGGCAGCCCGAGGCTCTTGATATCTGGGGCCTCGGGACCACGGTCACCGTCTCC
TCA

[1113] VL chain of H40 (SEQ ID NO: 1335)
CAGCCTGTGCTGACTCAGCCACCCTCGGTGTCAGTGGCCCCAGGACAGACGGCCAGCATTCCCTGTGGGGGGAAC
AACATTGGAGGCTACAGTGTACACTGGTACCAACAAAAGCCGGGCCAGGCCCCCCTCTTGGTCATTTATGACGAT
AAAGACCGGCCCTCAGGGATCCCTGAGCGATTCTCTGGCGCCAACTCTGGGAGCACGGCCACCCTGACAATCAGC
AGGGTCGAAGCCGGGGATGAGGGCGACTACTACTGTCAGGTGTGGGATAGTGGTAATGATCGTCCGCTGTTCGGC
GGAGGGACCAAGCTGACCGTCCTA

[1114] Antibody H40: Variable Region amino acid sequences

[1115] VH chain of H40 (SEQ ID NO: 1336)
QVQLVQSGAEVRKPGASVKVSCKASGYTFTGYYIHWVRQAPGQGLEWMGWINPMTGGTN
YAQKFQVWVTMTRDTSINTAYMEVSRLTSDDTAVYYCARGASVLRYFDWQPEALDIWGLG
TTVTVSS

[1116] VL chain of H40 (SEQ ID NO: 1337)
QPVLTQPPSVSVAPGQTASIPCGGNNIGGYSVHWYQQKPGQAPLLVIYDDKDRPSGIPERFSG
ANSGSTATLTISRVEAGDEGDYYCQVWDSGNDRPLFGGGTKLTVL

[1117] Antibody A66 Variable Region nucleic acid sequences

[1118] VH chain of A66 (SEQ ID NO: 1338)
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAAGTGAAGAAGCCTGGCTCCTCGGTGAAGGTTTCCTGCAAGGCTTCT
GGAGGCCCCTTCAGCATGACTGCTTTCACCTGGCTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGTGGG
ATCAGCCCTATCTTTCGTACACCGAAGTACGCACAGAAGTTCCAGGGCAGAGTCACGATTACCGCGGACGAATCC
ACGAACACAGCCAACATGGAGCTGACCAGCCTGAAATCTGAGGACACGGCCGTGTATTACTGTGCGAGAACCCTT
TCCTCCTACCAACCGAATAATGATGCTTTTGCTATCTGGGGCCAAGGGACAATGGTCACCGTCTCTTCA

[1119] VK chain of A66 (SEQ ID NO: 1339)
GAAATTGTGTTGACGCAGTCTCCAGCCACCCTGTCTTTGTCTCCAGGGGAAAGAGCCACCCTCTCCTGCAGGGCC
AGTCAGAGTGTTAGCAGCTACTTAGCCTGGTACCAACAGAAACCTGGCCAGGCTCCCAGGCTCCTCATCTATGAT
GCATCCAACAGGGCCACTGGCATCCCAGCCAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATC
AGCAGACTGGAGCCTGAAGATTTTGCAGTCTATTTCTGTCAGCAGTATGGTAGCTCACCTCAATTCGGCCAAGGG
ACACGACTGGAGATTAAA

[1120] Antibody A66 Variable Region amino acid sequences

[1121] VH chain of A66 (SEQ ID NO: 1340)
QVQLVQSGAEVKKPGSSVKVSCKASGGPFSMTAFTWLRQAPGQGLEWMGGISPIFRTPKYA
QKFQGRVTITADESTNTANMELTSLKSEDTAVYYCARTLSSYQPNNDAFAIWGQGTMVTVS
S

[1122] VK chain of A66 (SEQ ID NO: 1341)
EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSG
SGSGTDFTLT I SRLEPEDFAVYFCQQYGSSPQFGQGTRLEIK

[1123] Antibody E88 Variable Region nucleic acid sequences

[1124] VH chain of E88 (SEQ ID NO: 1342)
CAGGTGCAGCTGGTGCAGTCTGGGGCTGAAGTGAAGAAGCCTGGCTCCTCGGTGAAGGTTTCCTGCAAGGCTTCT
GGAGGCCCCTTCAGCATGACTGCTTTCACCTGGCTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGTGGG

ATCAGCCCTATCTTTCGTACACCGAAGTACGCACAGAAGTTCCAGGGCAGAGTCACGATTACCGCGGACGAATCC
ACGAACACAGCCAACATGGAGCTGACCAGCCTGAAATCTGAGGACACGGCCGTGTATTACTGTGCGAGAACCCTT
TCCTCCTACCAACCGAATAATGATGCTTTTGCTATCTGGGGCCAAGGGACAATGGTCACCGTCTCTTCA

[1125] VL chain of E88 (SEQ ID NO: 1343)
CTGCCTGTGCTGACTCAGCCACCCTCAGCGTCTGGGACCCCCGGGCAGAGGGTCACCATCTCTTGTTCTGGAAGC
AGCTCCAACATCGGAAGTAATACTGTAAACTGGTACCAGCAGCTCCCAGGAACGGCCCCCAAACTCCTCATCTAT
AGTAATAATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAGGTCAGGCACCTCAGCCTCCCTGGCC
ATCATTGGACTCCGGCCTGAGGATGAAGCTGATTATTACTGTCAGTCGTATGACAGCAGGCTCAGTGCTTCTCTC
TTCGGAACTGGGACCACGGTCACCGTCCTC

[1126] Antibody E88 Variable Region amino acid sequences

[1127] VH chain of E88 (SEQ ID NO: 1344)
QVQLVQSGAEVKKPGSSVKVSCKASGGPFSMTAFTWLRQAPGQGLEWMGGISPIFRTPKYA
QKFQGRVTITADESTNTANMELTSLKSEDTAVYYCARTLSSYQPNNDAFAIWGQGTMVTVS
S

[1128] VL chain of E88 (SEQ ID NO: 1345)
LPVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFS
GSRSGTSASLAIIGLRPEDEADYYCQSYDSRLSASLFGTGTTVTVL

[1129] The amino acid sequences of the heavy and light chain complementary determining regions of the neutralizing influenza antibodies are shown below in Table 18.

[1130] Table 18

ANTIBODY	CHAIN	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
CONSENSUS	HEAVY	SYAFS	299	GIIPMFGTPNYAQKFQG	1263	SSGYYYGGGFDV	1284
D7/H98	HEAVY	TNAFS	302	GVIPLFRTASYAQNVQN	1264	SSGYHFGRSHFDS	1285
D8/D80	HEAVY	AYAFT	305	GITGMFGTANYAQKFQG	1265	GLYYYESSLDY	1286
F10/E90	HEAVY	SFAIS	600	GISPMFGTPNYAQKFQG	1266	SPSYICSGGTCVFDH	1287
G17	HEAVY	SYAIS	606	GIIGVFGVPKYAQKFQG	1267	EPGYYGKNGFDV	1288
H40	HEAVY	GYYIH	630	WINPMTGGTNYAQKFQV	1268	GASVLRYFDWQPEALDI	1289
A66	HEAVY	MTAFT	641	GISPIFRTPKYAQKFQG	1269	TLSSYQPNNDAFAI	1290
E88	HEAVY	MTAFT	647	GISPIFRTPKYAQKFQG	1270	TLSSYQPNNDAFAI	1291
2A	HEAVY	DNAIS	668	GIIPIFGKPNYAQKFQG	1271	DSDAYYYGSGGMDV	1292
CONSENSUS	LIGHT	TGSSSMNIGNYVA	757	SNSDRPS	1272	QSYDSLSAYV	1293
D7	LIGHT	TGSSSNIAANYVQ	1252	EDDRRPS	1273	QTYDTNNHAV	1294
D8	LIGHT	TGTSSDVGGYNSVS	1253	EVTKRPS	1274	CSYAGHSAYV	1295
F10	LIGHT	TGNSNNVGNQGAA	1254	RNNDRPS	1275	STWDSSLSAVV	1296
G17	LIGHT	TGNSNNVGHQGTA	1255	RNGNRPS	1276	SVWDSSLSAWV	1297
H40	LIGHT	GGNNIGGYSVH	1256	DDKDRPS	1277	QVWDSGNDRPL	1298
A66	LIGHT	RASQSVSSYLA	1257	DASNRAT	1278	QQYGSSPQF	1299
D80	LIGHT	RASQSLSSKYLA	1258	GASSRAT	1279	QQYDGVPRT	1300
E88	LIGHT	SGSSSNIGSNTVN	1259	SNNQRPS	1280	QSYDSRLSASL	1301
E90	LIGHT	RASQSISSYLN	1260	AASSLQR	1281	QQYDSSPYT	1302
H98	LIGHT	SGGTSNIGRNHVN	1261	SNEQRPS	1282	ASWDDNLSGWV	1303
2A	LIGHT	TLSSGHSNYIIA	1262	VNSDGSHTKGD	1283	ETWDTKIHV	1304

Antibodies

[1131] Unless otherwise defined, scientific and technical terms used in connection with the present invention shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. Generally, nomenclatures utilized in connection with, and techniques of, cell and tissue culture, molecular biology, and protein and oligo- or polynucleotide chemistry and hybridization described herein are those well known and commonly used in the art. Standard techniques are used for recombinant DNA,

oligonucleotide synthesis, and tissue culture and transformation (*e.g.*, electroporation, lipofection). Enzymatic reactions and purification techniques are performed according to manufacturer's specifications or as commonly accomplished in the art or as described herein. The practice of the present invention will employ, unless indicated specifically to the contrary, conventional methods of virology, immunology, microbiology, molecular biology and recombinant DNA techniques within the skill of the art, many of which are described below for the purpose of illustration. Such techniques are explained fully in the literature. See, *e.g.*, Sambrook, *et al.* Molecular Cloning: A Laboratory Manual (2nd Edition, 1989); Maniatis *et al.* Molecular Cloning: A Laboratory Manual (1982); DNA Cloning: A Practical Approach, vol. I & II (D. Glover, ed.); Oligonucleotide Synthesis (N. Gait, ed., 1984); Nucleic Acid Hybridization (B. Hames & S. Higgins, eds., 1985); Transcription and Translation (B. Hames & S. Higgins, eds., 1984); Animal Cell Culture (R. Freshney, ed., 1986); Perbal, A Practical Guide to Molecular Cloning (1984).

[1132] The nomenclatures utilized in connection with, and the laboratory procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well known and commonly used in the art. Standard techniques are used for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, and delivery, and treatment of patients.

[1133] The following definitions are useful in understanding the present invention:

[1134] The term "antibody" (Ab) as used herein includes monoclonal antibodies, polyclonal antibodies, multispecific antibodies (*e.g.*, bispecific antibodies), and antibody fragments, so long as they exhibit the desired biological activity. The term "immunoglobulin" (Ig) is used interchangeably with "antibody" herein.

[1135] An "isolated antibody" is one that has been separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody is purified: (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight; (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator; or (3) to homogeneity by SDS-PAGE under reducing or non-reducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody *in situ* within recombinant cells since at least one

component of the antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

[1136] The basic four-chain antibody unit is a heterotetrameric glycoprotein composed of two identical light (L) chains and two identical heavy (H) chains. An IgM antibody consists of 5 of the basic heterotetramer unit along with an additional polypeptide called J chain, and therefore contain 10 antigen binding sites, while secreted IgA antibodies can polymerize to form polyvalent assemblages comprising 2-5 of the basic 4-chain units along with J chain. In the case of IgGs, the 4-chain unit is generally about 150,000 daltons. Each L chain is linked to an H chain by one covalent disulfide bond, while the two H chains are linked to each other by one or more disulfide bonds depending on the H chain isotype. Each H and L chain also has regularly spaced intrachain disulfide bridges. Each H chain has at the N-terminus, a variable domain (V_H) followed by three constant domains (C_H) for each of the α and γ chains and four C_H domains for μ and ε isotypes. Each L chain has at the N-terminus, a variable domain (V_L) followed by a constant domain (C_L) at its other end. The V_L is aligned with the V_H and the C_L is aligned with the first constant domain of the heavy chain (C_H1). Particular amino acid residues are believed to form an interface between the light chain and heavy chain variable domains. The pairing of a V_H and V_L together forms a single antigen-binding site. For the structure and properties of the different classes of antibodies, see, *e.g.*, Basic and Clinical Immunology, 8th edition, Daniel P. Stites, Abba I. Terr and Tristram G. Parslow (eds.), Appleton & Lange, Norwalk, Conn., 1994, page 71, and Chapter 6.

[1137] The L chain from any vertebrate species can be assigned to one of two clearly distinct types, called kappa (κ) and lambda (λ), based on the amino acid sequences of their constant domains (C_L). Depending on the amino acid sequence of the constant domain of their heavy chains (C_H), immunoglobulins can be assigned to different classes or isotypes. There are five classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, having heavy chains designated alpha (α), delta (δ), epsilon (ε), gamma (γ) and mu (μ), respectively. The γ and α classes are further divided into subclasses on the basis of relatively minor differences in C_H sequence and function, *e.g.*, humans express the following subclasses: IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2.

[1138] The term "variable" refers to the fact that certain segments of the V domains differ extensively in sequence among antibodies. The V domain mediates antigen binding and defines specificity of a particular antibody for its particular antigen. However, the variability is not evenly distributed across the 110-amino acid span of the variable domains. Instead, the

V regions consist of relatively invariant stretches called framework regions (FRs) of 15-30 amino acids separated by shorter regions of extreme variability called "hypervariable regions" that are each 9-12 amino acids long. The variable domains of native heavy and light chains each comprise four FRs, largely adopting a β-sheet configuration, connected by three hypervariable regions, which form loops connecting, and in some cases forming part of, the β-sheet structure. The hypervariable regions in each chain are held together in close proximity by the FRs and, with the hypervariable regions from the other chain, contribute to the formation of the antigen-binding site of antibodies (see Kabat *et al.*, Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991)). The constant domains are not involved directly in binding an antibody to an antigen, but exhibit various effector functions, such as participation of the antibody in antibody dependent cellular cytotoxicity (ADCC).

[1139] The term "hypervariable region" when used herein refers to the amino acid residues of an antibody that are responsible for antigen binding. The hypervariable region generally comprises amino acid residues from a "complementarity determining region" or "CDR" (*e.g.*, around about residues 24-34 (L1), 50-56 (L2) and 89-97 (L3) in the V_L, and around about 31-35 (H1), 50-65 (H2) and 95-102 (H3) in the V_H when numbered in accordance with the Kabat numbering system; Kabat *et al.*, Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991)); and/or those residues from a "hypervariable loop" (*e.g.*, residues 24-34 (L1), 50-56 (L2) and 89-97 (L3) in the V_L, and 26-32 (H1), 52-56 (H2) and 95-101 (H3) in the V_H when numbered in accordance with the Chothia numbering system; Chothia and Lesk, J. Mol. Biol. 196:901-917 (1987)); and/or those residues from a "hypervariable loop"/CDR (*e.g.*, residues 27-38 (L1), 56-65 (L2) and 105-120 (L3) in the V_L, and 27-38 (H1), 56-65 (H2) and 105-120 (H3) in the V_H when numbered in accordance with the IMGT numbering system; Lefranc, M.P. et al. Nucl. Acids Res. 27:209-212 (1999), Ruiz, M. e al. Nucl. Acids Res. 28:219-221 (2000)). Optionally the antibody has symmetrical insertions at one or more of the following points 28, 36 (L1), 63, 74-75 (L2) and 123 (L3) in the V_L, and 28, 36 (H1), 63, 74-75 (H2) and 123 (H3) in the V_H when numbered in accordance with AHo; Honneger, A. and Plunkthun, A. J. Mol. Biol. 309:657-670 (2001)).

[1140] By "germline nucleic acid residue" is meant the nucleic acid residue that naturally occurs in a germline gene encoding a constant or variable region. "Germline gene" is the DNA found in a germ cell (*i.e.*, a cell destined to become an egg or in the sperm). A

"germline mutation" refers to a heritable change in a particular DNA that has occurred in a germ cell or the zygote at the single-cell stage, and when transmitted to offspring, such a mutation is incorporated in every cell of the body. A germline mutation is in contrast to a somatic mutation which is acquired in a single body cell. In some cases, nucleotides in a germline DNA sequence encoding for a variable region are mutated (*i.e.*, a somatic mutation) and replaced with a different nucleotide.

[1141] The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, *i.e.*, the individual antibodies comprising the population are identical except for possible naturally occurring mutations that may be present in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic site. Furthermore, in contrast to polyclonal antibody preparations that include different antibodies directed against different determinants (epitopes), each monoclonal antibody is directed against a single determinant on the antigen. In addition to their specificity, the monoclonal antibodies are advantageous in that they may be synthesized uncontaminated by other antibodies. The modifier "monoclonal" is not to be construed as requiring production of the antibody by any particular method. For example, the monoclonal antibodies useful in the present invention may be prepared by the hybridoma methodology first described by Kohler et al., Nature, 256:495 (1975), or may be made using recombinant DNA methods in bacterial, eukaryotic animal or plant cells (see, *e.g.*, U.S. Pat. No. 4,816,567). The "monoclonal antibodies" may also be isolated from phage antibody libraries using the techniques described in Clackson *et al.*, Nature, 352:624-628 (1991) and Marks *et al.*, J. Mol. Biol., 222:581-597 (1991), for example.

[1142] The monoclonal antibodies herein include "chimeric" antibodies in which a portion of the heavy and/or light chain is identical with or homologous to corresponding sequences in antibodies derived from a particular species or belonging to a particular antibody class or subclass, while the remainder of the chain(s) is identical with or homologous to corresponding sequences in antibodies derived from another species or belonging to another antibody class or subclass, as well as fragments of such antibodies, so long as they exhibit the desired biological activity (see U.S. Pat. No. 4,816,567; and Morrison *et al.*, Proc. Natl. Acad. Sci. USA, 81:6851-6855 (1984)). The present invention provides variable domain antigen-binding sequences derived from human antibodies. Accordingly, chimeric antibodies of primary interest herein include antibodies having one or more human antigen binding

sequences (*e.g.*, CDRs) and containing one or more sequences derived from a non-human antibody, *e.g.*, an FR or C region sequence. In addition, chimeric antibodies of primary interest herein include those comprising a human variable domain antigen binding sequence of one antibody class or subclass and another sequence, *e.g.*, FR or C region sequence, derived from another antibody class or subclass. Chimeric antibodies of interest herein also include those containing variable domain antigen-binding sequences related to those described herein or derived from a different species, such as a non-human primate (*e.g.*, Old World Monkey, Ape, etc). Chimeric antibodies also include primatized and humanized antibodies.

[1143] Furthermore, chimeric antibodies may comprise residues that are not found in the recipient antibody or in the donor antibody. These modifications are made to further refine antibody performance. For further details, see Jones *et al.*, Nature 321:522-525 (1986); Riechmann *et al.*, Nature 332:323-329 (1988); and Presta, Curr. Op. Struct. Biol. 2:593-596 (1992).

[1144] A "humanized antibody" is generally considered to be a human antibody that has one or more amino acid residues introduced into it from a source that is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization is traditionally performed following the method of Winter and co-workers (Jones *et al.*, Nature, 321:522-525 (1986); Reichmann *et al.*, Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536 (1988)), by substituting import hypervariable region sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Pat. No. 4,816,567) wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species.

[1145] A "human antibody" is an antibody containing only sequences present in an antibody naturally produced by a human. However, as used herein, human antibodies may comprise residues or modifications not found in a naturally occurring human antibody, including those modifications and variant sequences described herein. These are typically made to further refine or enhance antibody performance.

[1146] An "intact" antibody is one that comprises an antigen-binding site as well as a C_L and at least heavy chain constant domains, C_H 1, C_H 2 and C_H 3. The constant domains may be

native sequence constant domains (*e.g.*, human native sequence constant domains) or amino acid sequence variant thereof. Preferably, the intact antibody has one or more effector functions.

[1147] An "antibody fragment" comprises a portion of an intact antibody, preferably the antigen binding or variable region of the intact antibody. Examples of antibody fragments include Fab, Fab', $F(ab')_2$, and Fv fragments; diabodies; linear antibodies (see U.S. Pat. No. 5,641,870; Zapata *et al.*, Protein Eng. 8(10): 1057-1062 [1995]); single-chain antibody molecules; and multispecific antibodies formed from antibody fragments.

[1148] The phrase "functional fragment or analog" of an antibody is a compound having qualitative biological activity in common with a full-length antibody. For example, a functional fragment or analog of an anti-IgE antibody is one that can bind to an IgE immunoglobulin in such a manner so as to prevent or substantially reduce the ability of such molecule from having the ability to bind to the high affinity receptor, $Fc_{\varepsilon}RI$.

[1149] Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, and a residual "Fc" fragment, a designation reflecting the ability to crystallize readily. The Fab fragment consists of an entire L chain along with the variable region domain of the H chain (V_H), and the first constant domain of one heavy chain (C_H 1). Each Fab fragment is monovalent with respect to antigen binding, *i.e.*, it has a single antigen-binding site. Pepsin treatment of an antibody yields a single large $F(ab')_2$ fragment that roughly corresponds to two disulfide linked Fab fragments having divalent antigen-binding activity and is still capable of cross-linking antigen. Fab' fragments differ from Fab fragments by having additional few residues at the carboxy terminus of the C_H1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. $F(ab')_2$ antibody fragments originally were produced as pairs of Fab' fragments that have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

[1150] The "Fc" fragment comprises the carboxy-terminal portions of both H chains held together by disulfides. The effector functions of antibodies are determined by sequences in the Fc region, which region is also the part recognized by Fc receptors (FcR) found on certain types of cells.

[1151] "Fv" is the minimum antibody fragment that contains a complete antigen-recognition and -binding site. This fragment consists of a dimer of one heavy- and one light-chain variable region domain in tight, non-covalent association. From the folding of these two domains emanate six hypervariable loops (three loops each from the H and L chain) that contribute the amino acid residues for antigen binding and confer antigen binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

[1152] "Single-chain Fv" also abbreviated as "sFv" or "scFv" are antibody fragments that comprise the V_H and V_L antibody domains connected into a single polypeptide chain. Preferably, the sFv polypeptide further comprises a polypeptide linker between the V_H and V_L domains that enables the sFv to form the desired structure for antigen binding. For a review of sFv, see Pluckthun in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994); Borrebaeck 1995, *infra.*

[1153] The term "diabodies" refers to small antibody fragments prepared by constructing sFv fragments (see preceding paragraph) with short linkers (about 5-10 residues) between the V_H and V_L domains such that inter-chain but not intra-chain pairing of the V domains is achieved, resulting in a bivalent fragment, *i.e.*, fragment having two antigen-binding sites. Bispecific diabodies are heterodimers of two "crossover" sFv fragments in which the V_H and V_L domains of the two antibodies are present on different polypeptide chains. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger *et al.*, Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993).

[1154] As used herein, an antibody that "internalizes" is one that is taken up by (*i.e.*, enters) the cell upon binding to an antigen on a mammalian cell (*e.g.*, a cell surface polypeptide or receptor). The internalizing antibody will of course include antibody fragments, human or chimeric antibody, and antibody conjugates. For certain therapeutic applications, internalization *in vivo* is contemplated. The number of antibody molecules internalized will be sufficient or adequate to kill a cell or inhibit its growth, especially an infected cell. Depending on the potency of the antibody or antibody conjugate, in some instances, the uptake of a single antibody molecule into the cell is sufficient to kill the target cell to which

the antibody binds. For example, certain toxins are highly potent in killing such that internalization of one molecule of the toxin conjugated to the antibody is sufficient to kill the infected cell.

[1155] As used herein, an antibody is said to be "immunospecific," "specific for" or to "specifically bind" an antigen if it reacts at a detectable level with the antigen, preferably with an affinity constant, K_a, of greater than or equal to about 10^4 M^{-1}, or greater than or equal to about 10^5 M^{-1}, greater than or equal to about 10^6 M^{-1}, greater than or equal to about 10^7 M^{-1}, or greater than or equal to 10^8 M^{-1}. Affinity of an antibody for its cognate antigen is also commonly expressed as a dissociation constant K_D, and in certain embodiments, HuM2e antibody specifically binds to M2e if it binds with a K_D of less than or equal to 10^{-4} M, less than or equal to about 10^{-5} M, less than or equal to about 10^{-6} M, less than or equal to 10^{-7} M, or less than or equal to 10^{-8} M. Affinities of antibodies can be readily determined using conventional techniques, for example, those described by Scatchard *et al.* (*Ann. N.Y. Acad. Sci. USA* 51:660 (1949)).

[1156] Binding properties of an antibody to antigens, cells or tissues thereof may generally be determined and assessed using immunodetection methods including, for example, immunofluorescence-based assays, such as immuno-histochemistry (IHC) and/or fluorescence-activated cell sorting (FACS).

[1157] An antibody having a "biological characteristic" of a designated antibody is one that possesses one or more of the biological characteristics of that antibody which distinguish it from other antibodies. For example, in certain embodiments, an antibody with a biological characteristic of a designated antibody will bind the same epitope as that bound by the designated antibody and/or have a common effector function as the designated antibody.

[1158] The term "antagonist" antibody is used in the broadest sense, and includes an antibody that partially or fully blocks, inhibits, or neutralizes a biological activity of an epitope, polypeptide, or cell that it specifically binds. Methods for identifying antagonist antibodies may comprise contacting a polypeptide or cell specifically bound by a candidate antagonist antibody with the candidate antagonist antibody and measuring a detectable change in one or more biological activities normally associated with the polypeptide or cell.

[1159] An "antibody that inhibits the growth of infected cells" or a "growth inhibitory" antibody is one that binds to and results in measurable growth inhibition of infected cells

expressing or capable of expressing an M2e epitope bound by an antibody. Preferred growth inhibitory antibodies inhibit growth of infected cells by greater than 20%, preferably from about 20% to about 50%, and even more preferably, by greater than 50% (*e.g.*, from about 50% to about 100%) as compared to the appropriate control, the control typically being infected cells not treated with the antibody being tested. Growth inhibition can be measured at an antibody concentration of about 0.1 to 30 μg/ml or about 0.5 nM to 200 nM in cell culture, where the growth inhibition is determined 1-10 days after exposure of the infected cells to the antibody. Growth inhibition of infected cells *in vivo* can be determined in various ways known in the art. The antibody is growth inhibitory *in vivo* if administration of the antibody at about 1 μg/kg to about 100 mg/kg body weight results in reduction the percent of infected cells or total number of infected cells within about 5 days to 3 months from the first administration of the antibody, preferably within about 5 to 30 days.

[1160] An antibody that "induces apoptosis" is one which induces programmed cell death as determined by binding of annexin V, fragmentation of DNA, cell shrinkage, dilation of endoplasmic reticulum, cell fragmentation, and/or formation of membrane vesicles (called apoptotic bodies). Preferably the cell is an infected cell. Various methods are available for evaluating the cellular events associated with apoptosis. For example, phosphatidyl serine (PS) translocation can be measured by annexin binding; DNA fragmentation can be evaluated through DNA laddering; and nuclear/chromatin condensation along with DNA fragmentation can be evaluated by any increase in hypodiploid cells. Preferably, the antibody that induces apoptosis is one that results in about 2 to 50 fold, preferably about 5 to 50 fold, and most preferably about 10 to 50 fold, induction of annexin binding relative to untreated cell in an annexin binding assay.

[1161] Antibody "effector functions" refer to those biological activities attributable to the Fc region (a native sequence Fc region or amino acid sequence variant Fc region) of an antibody, and vary with the antibody isotype. Examples of antibody effector functions include: C1q binding and complement dependent cytotoxicity; Fc receptor binding; antibody-dependent cell-mediated cytotoxicity (ADCC); phagocytosis; down regulation of cell surface receptors (*e.g.*, B cell receptor); and B cell activation.

[1162] "Antibody-dependent cell-mediated cytotoxicity" or "ADCC" refers to a form of cytotoxicity in which secreted Ig bound to Fc receptors (FcRs) present on certain cytotoxic

cells (*e.g.*, Natural Killer (NK) cells, neutrophils, and macrophages) enable these cytotoxic effector cells to bind specifically to an antigen-bearing target cell and subsequently kill the target cell with cytotoxins. The antibodies "arm" the cytotoxic cells and are required for such killing. The primary cells for mediating ADCC, NK cells, express FcγRIII only, whereas monocytes express FcγRI, FcγRII and FcγRIII. FcR expression on hematopoietic cells is summarized in Table 3 on page 464 of Ravetch and Kinet, Annu. Rev. Immunol 9:457-92 (1991). To assess ADCC activity of a molecule of interest, an *in vitro* ADCC assay, such as that described in U.S. Pat. No. 5,500,362 or U.S. Pat. No. 5,821,337 may be performed. Useful effector cells for such assays include peripheral blood mononuclear cells (PBMC) and Natural Killer (NK) cells. Alternatively, or additionally, ADCC activity of the molecule of interest may be assessed *in vivo, e.g.*, in a animal model such as that disclosed in Clynes *et al.*, PNAS (USA) 95:652-656 (1998).

[1163] "Fc receptor" or "FcR" describes a receptor that binds to the Fc region of an antibody. In certain embodiments, the FcR is a native sequence human FcR. Moreover, a preferred FcR is one that binds an IgG antibody (a gamma receptor) and includes receptors of the FcγRI, FcγRII, and FcγRIII subclasses, including allelic variants and alternatively spliced forms of these receptors. FCγRII receptors include FcγRIIA (an "activating receptor") and FcγRIIB (an "inhibiting receptor"), which have similar amino acid sequences that differ primarily in the cytoplasmic domains thereof. Activating receptor FcγRIIA contains an immunoreceptor tyrosine-based activation motif (ITAM) in its cytoplasmic domain. Inhibiting receptor FcγRIIB contains an immunoreceptor tyrosine-based inhibition motif (ITIM) in its cytoplasmic domain. (*see* review M. in Daeron, Annu. Rev. Immunol. 15:203-234 (1997)). FcRs are reviewed in Ravetch and Kinet, Annu. Rev. Immunol 9:457-92 (1991); Capel *et al.*, Immunomethods 4:25-34 (1994); and de Haas *et al.*, J. Lab. Clin. Med. 126:330-41 (1995). Other FcRs, including those to be identified in the future, are encompassed by the term "FcR" herein. The term also includes the neonatal receptor, FcRn, which is responsible for the transfer of maternal IgGs to the fetus (Guyer *et al.*, J. Immunol. 117:587 (1976) and Kim *et al.*, J. Immunol. 24:249 (1994)).

[1164] "Human effector cells" are leukocytes that express one or more FcRs and perform effector functions. Preferably, the cells express at least FcγRIII and perform ADCC effector function. Examples of human leukocytes that mediate ADCC include PBMC, NK cells,

monocytes, cytotoxic T cells and neutrophils; with PBMCs and NK cells being preferred. The effector cells may be isolated from a native source, *e.g.*, from blood.

[1165] "Complement dependent cytotoxicity" or "CDC" refers to the lysis of a target cell in the presence of complement. Activation of the classical complement pathway is initiated by the binding of the first component of the complement system (C1q) to antibodies (of the appropriate subclass) that are bound to their cognate antigen. To assess complement activation, a CDC assay, *e.g.*, as described in Gazzano-Santoro *et al.*, J. Immunol. Methods 202:163 (1996), may be performed.

[1166] The terms "influenza A" and "Influenzavirus A" refer to a genus of the Orthomyxoviridae family of viruses. Influenzavirus A includes only one species: influenza A virus which cause influenza in birds, humans, pigs, and horses. Strains of all subtypes of influenza A virus have been isolated from wild birds, although disease is uncommon. Some isolates of influenza A virus cause severe disease both in domestic poultry and, rarely, in humans.

[1167] A "mammal" for purposes of treating n infection, refers to any mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as dogs, cats, cattle, horses, sheep, pigs, goats, rabbits, etc. Preferably, the mammal is human.

[1168] "Treating" or "treatment" or "alleviation" refers to both therapeutic treatment and prophylactic or preventative measures; wherein the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those in need of treatment include those already with the disorder as well as those prone to have the disorder or those in whom the disorder is to be prevented. A subject or mammal is successfully "treated" for an infection if, after receiving a therapeutic amount of an antibody according to the methods of the present invention, the patient shows observable and/or measurable reduction in or absence of one or more of the following: reduction in the number of infected cells or absence of the infected cells; reduction in the percent of total cells that are infected; and/or relief to some extent, one or more of the symptoms associated with the specific infection; reduced morbidity and mortality, and improvement in quality of life issues. The above parameters for assessing successful treatment and improvement in the disease are readily measurable by routine procedures familiar to a physician.

[1169] The term "therapeutically effective amount" refers to an amount of an antibody or a drug effective to "treat" a disease or disorder in a subject or mammal. See preceding definition of "treating."

[1170] "Chronic" administration refers to administration of the agent(s) in a continuous mode as opposed to an acute mode, so as to maintain the initial therapeutic effect (activity) for an extended period of time. "Intermittent" administration is treatment that is not consecutively done without interruption, but rather is cyclic in nature.

[1171] Administration "in combination with" one or more further therapeutic agents includes simultaneous (concurrent) and consecutive administration in any order.

[1172] "Carriers" as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers that are nontoxic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEEN™ polyethylene glycol (PEG), and PLURONICS™.

[1173] The term "cytotoxic agent" as used herein refers to a substance that inhibits or prevents the function of cells and/or causes destruction of cells. The term is intended to include radioactive isotopes (*e.g.*, At^{211}, I^{131}, I^{125}, Y^{90}, Re^{186}, Re^{188}, Sm^{153}, Bi^{212}, P^{32} and radioactive isotopes of Lu), chemotherapeutic agents e.g., methotrexate, adriamicin, vinca alkaloids (vincristine, vinblastine, etoposide), doxorubicin, melphalan, mitomycin C, chlorambucil, daunorubicin or other intercalating agents, enzymes and fragments thereof such as nucleolytic enzymes, antibiotics, and toxins such as small molecule toxins or enzymatically active toxins of bacterial, fungal, plant or animal origin, including fragments and/or variants thereof, and the various antitumor or anticancer agents disclosed below. Other cytotoxic agents are described below.

[1174] A "growth inhibitory agent" when used herein refers to a compound or composition which inhibits growth of a cell, either *in vitro* or *in vivo*. Examples of growth inhibitory agents include agents that block cell cycle progression, such as agents that induce G1 arrest and M-phase arrest. Classical M-phase blockers include the vinca alkaloids (vincristine, vinorelbine and vinblastine), taxanes, and topoisomerase II inhibitors such as doxorubicin, epirubicin, daunorubicin, etoposide, and bleomycin. Those agents that arrest G1 also spill over into S-phase arrest, for example, DNA alkylating agents such as tamoxifen, prednisone, dacarbazine, mechlorethamine, cisplatin, methotrexate, 5-fluorouracil, and ara-C. Further information can be found in The Molecular Basis of Cancer, Mendelsohn and Israel, eds., Chapter 1, entitled "Cell cycle regulation, oncogenes, and antineoplastic drugs" by Murakami *et al.* (W B Saunders: Philadelphia, 1995), especially p. 13. The taxanes (paclitaxel and docetaxel) are anticancer drugs both derived from the yew tree. Docetaxel (TAXOTERE™, Rhone-Poulenc Rorer), derived from the European yew, is a semisynthetic analogue of paclitaxel (TAXOL®, Bristol-Myers Squibb). Paclitaxel and docetaxel promote the assembly of microtubules from tubulin dimers and stabilize microtubules by preventing depolymerization, which results in the inhibition of mitosis in cells.

[1175] "Label" as used herein refers to a detectable compound or composition that is conjugated directly or indirectly to the antibody so as to generate a "labeled" antibody. The label may be detectable by itself (*e.g.*, radioisotope labels or fluorescent labels) or, in the case of an enzymatic label, may catalyze chemical alteration of a substrate compound or composition that is detectable.

[1176] The term "epitope tagged" as used herein refers to a chimeric polypeptide comprising a polypeptide fused to a "tag polypeptide." The tag polypeptide has enough residues to provide an epitope against which an antibody can be made, yet is short enough such that it does not interfere with activity of the polypeptide to which it is fused. The tag polypeptide is also preferably fairly unique so that the antibody does not substantially cross-react with other epitopes. Suitable tag polypeptides generally have at least six amino acid residues and usually between about 8 and 50 amino acid residues (preferably, between about 10 and 20 amino acid residues).

[1177] A "small molecule" is defined herein to have a molecular weight below about 500 Daltons.

[1178] The terms "nucleic acid" and "polynucleotide" are used interchangeably herein to refer to single- or double-stranded RNA, DNA, or mixed polymers. Polynucleotides may include genomic sequences, extra-genomic and plasmid sequences, and smaller engineered gene segments that express, or may be adapted to express polypeptides.

[1179] An "isolated nucleic acid" is a nucleic acid that is substantially separated from other genome DNA sequences as well as proteins or complexes such as ribosomes and polymerases, which naturally accompany a native sequence. The term embraces a nucleic acid sequence that has been removed from its naturally occurring environment, and includes recombinant or cloned DNA isolates and chemically synthesized analogues or analogues biologically synthesized by heterologous systems. A substantially pure nucleic acid includes isolated forms of the nucleic acid. Of course, this refers to the nucleic acid as originally isolated and does not exclude genes or sequences later added to the isolated nucleic acid by the hand of man.

[1180] The term "polypeptide" is used in its conventional meaning, *i.e.*, as a sequence of amino acids. The polypeptides are not limited to a specific length of the product. Peptides, oligopeptides, and proteins are included within the definition of polypeptide, and such terms may be used interchangeably herein unless specifically indicated otherwise. This term also does not refer to or exclude post-expression modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like, as well as other modifications known in the art, both naturally occurring and non-naturally occurring. A polypeptide may be an entire protein, or a subsequence thereof. Particular polypeptides of interest in the context of this invention are amino acid subsequences comprising CDRs and being capable of binding an antigen or Influenza A-infected cell.

[1181] An "isolated polypeptide" is one that has been identified and separated and/or recovered from a component of its natural environment. In preferred embodiments, the isolated polypeptide will be purified (1) to greater than 95% by weight of polypeptide as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or non-reducing conditions using Coomassie blue or, preferably, silver stain. Isolated polypeptide includes the polypeptide *in situ* within recombinant cells since at least one

component of the polypeptide's natural environment will not be present. Ordinarily, however, isolated polypeptide will be prepared by at least one purification step.

[1182] A "native sequence" polynucleotide is one that has the same nucleotide sequence as a polynucleotide derived from nature. A "native sequence" polypeptide is one that has the same amino acid sequence as a polypeptide (*e.g.*, antibody) derived from nature (*e.g.*, from any species). Such native sequence polynucleotides and polypeptides can be isolated from nature or can be produced by recombinant or synthetic means.

[1183] A polynucleotide "variant," as the term is used herein, is a polynucleotide that typically differs from a polynucleotide specifically disclosed herein in one or more substitutions, deletions, additions and/or insertions. Such variants may be naturally occurring or may be synthetically generated, for example, by modifying one or more of the polynucleotide sequences of the invention and evaluating one or more biological activities of the encoded polypeptide as described herein and/or using any of a number of techniques well known in the art.

[1184] A polypeptide "variant," as the term is used herein, is a polypeptide that typically differs from a polypeptide specifically disclosed herein in one or more substitutions, deletions, additions and/or insertions. Such variants may be naturally occurring or may be synthetically generated, for example, by modifying one or more of the above polypeptide sequences of the invention and evaluating one or more biological activities of the polypeptide as described herein and/or using any of a number of techniques well known in the art.

[1185] Modifications may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional molecule that encodes a variant or derivative polypeptide with desirable characteristics. When it is desired to alter the amino acid sequence of a polypeptide to create an equivalent, or even an improved, variant or portion of a polypeptide of the invention, one skilled in the art will typically change one or more of the codons of the encoding DNA sequence.

[1186] For example, certain amino acids may be substituted for other amino acids in a protein structure without appreciable loss of its ability to bind other polypeptides (*e.g.*, antigens) or cells. Since it is the binding capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless

obtain a protein with like properties. It is thus contemplated that various changes may be made in the peptide sequences of the disclosed compositions, or corresponding DNA sequences that encode said peptides without appreciable loss of their biological utility or activity.

[1187] In many instances, a polypeptide variant will contain one or more conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged.

[1188] In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982). It is accepted that the relative hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like. Each amino acid has been assigned a hydropathic index on the basis of its hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (–0.4); threonine (–0.7); serine (–0.8); tryptophan (–0.9); tyrosine (–1.3); proline (–1.6); histidine (–3.2); glutamate (–3.5); glutamine (–3.5); aspartate (–3.5); asparagine (–3.5); lysine (–3.9); and arginine (–4.5).

[1189] It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydropathic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose hydropathic indices are within ±2 is preferred, those within ±1 are particularly preferred, and those within ±0.5 are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U. S. Patent 4,554,101 states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of its adjacent amino acids, correlates with a biological property of the protein.

[1190] As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0 ± 1); glutamate (+3.0 ± 1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (–0.4); proline (–0.5 ± 1); alanine (–0.5); histidine (–0.5); cysteine (–1.0); methionine (–1.3); valine (–1.5); leucine (–1.8); isoleucine (–1.8); tyrosine (–2.3); phenylalanine (–2.5); tryptophan (–3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In such changes, the substitution of amino acids whose hydrophilicity values are within ±2 is preferred, those within ±1 are particularly preferred, and those within ±0.5 are even more particularly preferred.

[1191] As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that take various of the foregoing characteristics into consideration are well known to those of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

[1192] Amino acid substitutions may further be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

[1193] Polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

[1194] When comparing polynucleotide and polypeptide sequences, two sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

[1195] Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenes pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS 5*:151-153; Myers, E.W. and Muller W. (1988) *CABIOS 4*:11-17; Robinson, E.D. (1971) *Comb. Theor 11*:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol. 4*:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA 80*:726-730.

[1196] Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the

identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

[1197] One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information.

[1198] In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

[1199] For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

[1200] In one approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window

may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residues occur in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

[1201] "Homology" refers to the percentage of residues in the polynucleotide or polypeptide sequence variant that are identical to the non-variant sequence after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent homology. In particular embodiments, polynucleotide and polypeptide variants have at least 70%, at least 75%, at least 80%, at least 90%, at least 95%, at least 98%, or at least 99% polynucleotide or polypeptide homology with a polynucleotide or polypeptide described herein.

[1202] "Vector" includes shuttle and expression vectors. Typically, the plasmid construct will also include an origin of replication (e.g., the ColE1 origin of replication) and a selectable marker (e.g., ampicillin or tetracycline resistance), for replication and selection, respectively, of the plasmids in bacteria. An "expression vector" refers to a vector that contains the necessary control sequences or regulatory elements for expression of the antibodies including antibody fragment of the invention, in bacterial or eukaryotic cells. Suitable vectors are disclosed below.

[1203] As used in this specification and the appended claims, the singular forms "a," "an" and "the" include plural references unless the content clearly dictates otherwise.

[1204] The present invention includes human monoclonal anti-influenza antibodies comprising a polypeptide of the present invention, as well as fragments and variants thereof. In one embodiment, the antibody is an antibody designated herein as TCN-032 (8I10), 21B15, TCN-031 (23K12), 3241_G23, 3244_I10, 3243_J07, 3259_J21, 3245_O19, 3244_H04, 3136_G05, 3252_C13, 3255_J06, 3420_I23, 3139_P23, 3248_P18, 3253_P10, 3260_D19, 3362_B11, 3242_P05, TCN-522 (3212_I12), TCN-521 (3280_D18), TCN-523 (5248_A17), TCN-563 (5237_B21), TCN-526 (5084_C17), TCN-527 (5086_C06), TCN-528 (5087_P17), TCN-529 (5297_H01), TCN-530 (5248_H10), TCN-531 (5091_H13), TCN-532 (5262_H18), TCN-533 (5256_A17), TCN-534 (5249_B02), TCN-535 (5246_P19), TCN-536 (5095_N01), TCN-537 (3194_D21), TCN-538 (3206_O17), TCN-539 (5056_A08), TCN-

540 (5060_F05), TCN-541 (5062_M11), TCN-542 (5079_A16), TCN-543 (5081_G23), TCN-544 (5082_A19), TCN-545 (5082_I15), TCN-546 (5089_L08), TCN-547 (5092_F11), TCN-548 (5092_P01), TCN-549 (5092_P04), TCN-550 (5096_F06), TCN-551 (5243_D01), TCN-552 (5249_I23), TCN-553 (5261_C18), TCN-554 (5277_M05), TCN-555 (5246_L16), TCN-556 (5089_K12), TCN-557 (5081_A04), TCN 558 (5248_H10b), TCN-559 (5097_G08), TCN-560 (5084_P10), TCN-504 (3251_K17), SC06-141, SC06-255, SC06-257, SC06-260, SC06-261, SC06-262, SC06-268, SC06-272, SC06-296, SC06-301, SC06-307, SC06-310, SC06-314, SC06-323, SC06-325, SC06-327, SC06-328, SC06-329, SC06-331, SC06-332, SC06-334, SC06-336, SC06-339, SC06-342, SC06-343, SC06-344, CR6141, CR6255, CR6257, CR6260, CR6261, CR6262, CR6268, CR6272, CR6296, CR6301, CR6307, CR6310, CR6314, CR6323, CR6325, CR6327, CR6328, CR6329, CR6331, CR6332, CR6334, CR6336, CR6339, CR6342, CR6343, or CR6344. These antibodies preferentially bind to or specifically bind to influenza A infected cells as compared to uninfected control cells of the same cell type.

[1205] In particular embodiments, the antibodies of the present invention bind to the M2 or HA protein. In certain embodiments, the present invention provides human anti-influenza antibodies that bind to epitopes within M2e or HA that are only present in the native conformation, i.e., as expressed in cells. In particular embodiments, these antibodies fail to specifically bind to an isolated M2e polypeptide, e.g., the 23 amino acid residue M2e fragment or an isolated HA polypeptide. It is understood that these antibodies recognize non-linear (i.e. conformational) epitope(s) of the M2 or HA peptide or protein.

[1206] These specific conformational epitopes within the M2 or HA protein, and particularly within M2e, may be used as vaccines to prevent the development of influenza infection within a subject.

[1207] As will be understood by the skilled artisan, general description of antibodies herein and methods of preparing and using the same also apply to individual antibody polypeptide constituents and antibody fragments.

[1208] The antibodies of the present invention may be polyclonal or monoclonal antibodies. However, in preferred embodiments, they are monoclonal. In particular embodiments, antibodies of the present invention are fully human antibodies. Methods of producing polyclonal and monoclonal antibodies are known in the art and described generally, *e.g.*, in U.S. Patent No. 6,824,780. Typically, the antibodies of the present invention are produced

recombinantly, using vectors and methods available in the art, as described further below. Human antibodies may also be generated by in vitro activated B cells (see U.S. Pat. Nos. 5,567,610 and 5,229,275).

[1209] Human antibodies may also be produced in transgenic animals (*e.g.*, mice) that are capable of producing a full repertoire of human antibodies in the absence of endogenous immunoglobulin production. For example, it has been described that the homozygous deletion of the antibody heavy-chain joining region (J_H) gene in chimeric and germ-line mutant mice results in complete inhibition of endogenous antibody production. Transfer of the human germ-line immunoglobulin gene array into such germ-line mutant mice results in the production of human antibodies upon antigen challenge. See, *e.g.*, Jakobovits *et al.*, Proc. Natl. Acad. Sci. USA, 90:2551 (1993); Jakobovits *et al.*, Nature, 362:255-258 (1993); Bruggemann *et al.*, Year in Immuno., 7:33 (1993); U.S. Pat. Nos. 5,545,806, 5,569,825, 5,591,669 (all of GenPharm); U.S. Pat. No. 5,545,807; and WO 97/17852. Such animals may be genetically engineered to produce human antibodies comprising a polypeptide of the present invention.

[1210] In certain embodiments, antibodies of the present invention are chimeric antibodies that comprise sequences derived from both human and non-human sources. In particular embodiments, these chimeric antibodies are humanized or primatized™. In practice, humanized antibodies are typically human antibodies in which some hypervariable region residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

[1211] In the context of the present invention, chimeric antibodies also include fully human antibodies wherein the human hypervariable region or one or more CDRs are retained, but one or more other regions of sequence have been replaced by corresponding sequences from a non-human animal.

[1212] The choice of non-human sequences, both light and heavy, to be used in making the chimeric antibodies is important to reduce antigenicity and human anti-non-human antibody responses when the antibody is intended for human therapeutic use. It is further important that chimeric antibodies retain high binding affinity for the antigen and other favorable biological properties. To achieve this goal, according to a preferred method, chimeric antibodies are prepared by a process of analysis of the parental sequences and various

conceptual chimeric products using three-dimensional models of the parental human and non-human sequences. Three-dimensional immunoglobulin models are commonly available and are familiar to those skilled in the art. Computer programs are available which illustrate and display probable three-dimensional conformational structures of selected candidate immunoglobulin sequences. Inspection of these displays permits analysis of the likely role of the residues in the functioning of the candidate immunoglobulin sequence, *i.e.*, the analysis of residues that influence the ability of the candidate immunoglobulin to bind its antigen. In this way, FR residues can be selected and combined from the recipient and import sequences so that the desired antibody characteristic, such as increased affinity for the target antigen(s), is achieved. In general, the hypervariable region residues are directly and most substantially involved in influencing antigen binding.

[1213] As noted above, antibodies (or immunoglobulins) can be divided into five different classes, based on differences in the amino acid sequences in the constant region of the heavy chains. All immunoglobulins within a given class have very similar heavy chain constant regions. These differences can be detected by sequence studies or more commonly by serological means (*i.e.* by the use of antibodies directed to these differences). Antibodies, or fragments thereof, of the present invention may be any class, and may, therefore, have a gamma, mu, alpha, delta, or epsilon heavy chain. A gamma chain may be gamma 1, gamma 2, gamma 3, or gamma 4; and an alpha chain may be alpha 1 or alpha 2.

[1214] In a preferred embodiment, an antibody of the present invention, or fragment thereof, is an IgG. IgG is considered the most versatile immunoglobulin, because it is capable of carrying out all of the functions of immunoglobulin molecules. IgG is the major Ig in serum, and the only class of Ig that crosses the placenta. IgG also fixes complement, although the IgG4 subclass does not. Macrophages, monocytes, PMN's and some lymphocytes have Fc receptors for the Fc region of IgG. Not all subclasses bind equally well; IgG2 and IgG4 do not bind to Fc receptors. A consequence of binding to the Fc receptors on PMN's, monocytes and macrophages is that the cell can now internalize the antigen better. IgG is an opsonin that enhances phagocytosis. Binding of IgG to Fc receptors on other types of cells results in the activation of other functions. Antibodies of the present invention may be of any IgG subclass.

[1215] In another preferred embodiment, an antibody, or fragment thereof, of the present invention is an IgE. IgE is the least common serum Ig since it binds very tightly to Fc receptors on basophils and mast cells even before interacting with antigen. As a consequence of its binding to basophils an mast cells, IgE is involved in allergic reactions. Binding of the allergen to the IgE on the cells results in the release of various pharmacological mediators that result in allergic symptoms. IgE also plays a role in parasitic helminth diseases. Eosinophils have Fc receptors for IgE and binding of eosinophils to IgE-coated helminths results in killing of the parasite. IgE does not fix complement.

[1216] In various embodiments, antibodies of the present invention, and fragments thereof, comprise a variable light chain that is either kappa or lambda. The lamba chain may be any of subtype, including, *e.g.*, lambda 1, lambda 2, lambda 3, and lambda 4.

[1217] As noted above, the present invention further provides antibody fragments comprising a polypeptide of the present invention. In certain circumstances there are advantages of using antibody fragments, rather than whole antibodies. For example, the smaller size of the fragments allows for rapid clearance, and may lead to improved access to certain tissues, such as solid tumors. Examples of antibody fragments include: Fab, Fab', $F(ab')_2$ and Fv fragments; diabodies; linear antibodies; single-chain antibodies; and multispecific antibodies formed from antibody fragments.

[1218] Various techniques have been developed for the production of antibody fragments. Traditionally, these fragments were derived via proteolytic digestion of intact antibodies (*see, e.g.*, Morimoto et al., Journal of Biochemical and Biophysical Methods 24:107-117 (1992); and Brennan *et al.*, Science, 229:81 (1985)). However, these fragments can now be produced directly by recombinant host cells. Fab, Fv and ScFv antibody fragments can all be expressed in and secreted from E. coli, thus allowing the facile production of large amounts of these fragments. Fab'-SH fragments can be directly recovered from E. coli and chemically coupled to form $F(ab')_2$ fragments (Carter *et al.*, Bio/Technology 10:163-167 (1992)). According to another approach, $F(ab')_2$ fragments can be isolated directly from recombinant host cell culture. Fab and $F(ab')_2$ fragment with increased *in vivo* half-life comprising a salvage receptor binding epitope residues are described in U.S. Pat. No. 5,869,046. Other techniques for the production of antibody fragments will be apparent to the skilled practitioner.

[1219] In other embodiments, the antibody of choice is a single chain Fv fragment (scFv). See WO 93/16185; U.S. Pat. Nos. 5,571,894; and 5,587,458. Fv and sFv are the only species with intact combining sites that are devoid of constant regions. Thus, they are suitable for reduced nonspecific binding during *in vivo* use. sFv fusion proteins may be constructed to yield fusion of an effector protein at either the amino or the carboxy terminus of an sFv. See Antibody Engineering, ed. Borrebaeck, *supra*. The antibody fragment may also be a "linear antibody", *e.g.*, as described in U.S. Pat. No. 5,641,870 for example. Such linear antibody fragments may be monospecific or bispecific.

[1220] In certain embodiments, antibodies of the present invention are bispecific or multi-specific. Bispecific antibodies are antibodies that have binding specificities for at least two different epitopes. Exemplary bispecific antibodies may bind to two different epitopes of a single antigen. Other such antibodies may combine a first antigen binding site with a binding site for a second antigen. Alternatively, an anti-M2e arm may be combined with an arm that binds to a triggering molecule on a leukocyte, such as a T-cell receptor molecule (*e.g.*, CD3), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16), so as to focus and localize cellular defense mechanisms to the infected cell. Bispecific antibodies may also be used to localize cytotoxic agents to infected cells. These antibodies possess an M2e-binding arm and an arm that binds the cytotoxic agent (*e.g.*, saporin, anti-interferon-α, vinca alkaloid, ricin A chain, methotrexate or radioactive isotope hapten). Bispecific antibodies can be prepared as full length antibodies or antibody fragments (*e.g.*, $F(ab')_2$ bispecific antibodies). WO 96/16673 describes a bispecific anti-ErbB2/anti-FcγRIII antibody and U.S. Pat. No. 5,837,234 discloses a bispecific anti-ErbB2/anti-FcγRI antibody. A bispecific anti-ErbB2/Fcα antibody is shown in WO98/02463. U.S. Pat. No. 5,821,337 teaches a bispecific anti-ErbB2/anti-CD3 antibody.

[1221] Methods for making bispecific antibodies are known in the art. Traditional production of full length bispecific antibodies is based on the co-expression of two immunoglobulin heavy chain-light chain pairs, where the two chains have different specificities (Millstein *et al.*, Nature, 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. Purification of the correct molecule, which is usually done by affinity chromatography steps,

is rather cumbersome, and the product yields are low. Similar procedures are disclosed in WO 93/08829, and in Traunecker *et al.*, EMBO J., 10:3655-3659 (1991).

[1222] According to a different approach, antibody variable domains with the desired binding specificities (antibody-antigen combining sites) are fused to immunoglobulin constant domain sequences. Preferably, the fusion is with an Ig heavy chain constant domain, comprising at least part of the hinge, C_H2, and C_H3 regions. It is preferred to have the first heavy-chain constant region (C_H1) containing the site necessary for light chain bonding, present in at least one of the fusions. DNAs encoding the immunoglobulin heavy chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host cell. This provides for greater flexibility in adjusting the mutual proportions of the three polypeptide fragments in embodiments when unequal ratios of the three polypeptide chains used in the construction provide the optimum yield of the desired bispecific antibody. It is, however, possible to insert the coding sequences for two or all three polypeptide chains into a single expression vector when the expression of at least two polypeptide chains in equal ratios results in high yields or when the ratios have no significant affect on the yield of the desired chain combination.

[1223] In a preferred embodiment of this approach, the bispecific antibodies are composed of a hybrid immunoglobulin heavy chain with a first binding specificity in one arm, and a hybrid immunoglobulin heavy chain-light chain pair (providing a second binding specificity) in the other arm. It was found that this asymmetric structure facilitates the separation of the desired bispecific compound from unwanted immunoglobulin chain combinations, as the presence of an immunoglobulin light chain in only one half of the bispecific molecule provides for a facile way of separation. This approach is disclosed in WO 94/04690. For further details of generating bispecific antibodies see, for example, Suresh *et al.*, Methods in Enzymology, 121:210 (1986).

[1224] According to another approach described in U.S. Pat. No. 5,731,168, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers that are recovered from recombinant cell culture. The preferred interface comprises at least a part of the C_H3 domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (*e.g.*, tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to

the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (*e.g.*, alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

[1225] Bispecific antibodies include cross-linked or "heteroconjugate" antibodies. For example, one of the antibodies in the heteroconjugate can be coupled to avidin, the other to biotin. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells (U.S. Pat. No. 4,676,980), and for treatment of HIV infection (WO 91/00360, WO 92/200373, and EP 03089). Heteroconjugate antibodies may be made using any convenient cross-linking methods. Suitable cross-linking agents are well known in the art, and are disclosed in U.S. Pat. No. 4,676,980, along with a number of cross-linking techniques.

[1226] Techniques for generating bispecific antibodies from antibody fragments have also been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan *et al.*, Science, 229: 81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate $F(ab')_2$ fragments. These fragments are reduced in the presence of the dithiol complexing agent, sodium arsenite, to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

[1227] Recent progress has facilitated the direct recovery of Fab'-SH fragments from *E. coli*, which can be chemically coupled to form bispecific antibodies. Shalaby et al., J. Exp. Med., 175: 217-225 (1992) describe the production of a fully humanized bispecific antibody $F(ab')_2$ molecule. Each Fab' fragment was separately secreted from E. coli and subjected to directed chemical coupling *in vitro* to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

[1228] Various techniques for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny *et al.*, J. Immunol., 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger *et al.*, Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a V_H connected to a V_L by a linker that is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See Gruber *et al.*, J. Immunol., 152:5368 (1994).

[1229] Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt *et al.*, J. Immunol. 147: 60 (1991). A multivalent antibody may be internalized (and/or catabolized) faster than a bivalent antibody by a cell expressing an antigen to which the antibodies bind. The antibodies of the present invention can be multivalent antibodies with three or more antigen binding sites (*e.g.*, tetravalent antibodies), which can be readily produced by recombinant expression of nucleic acid encoding the polypeptide chains of the antibody. The multivalent antibody can comprise a dimerization domain and three or more antigen binding sites. The preferred dimerization domain comprises (or consists of) an Fc region or a hinge region. In this scenario, the antibody will comprise an Fc region and three or more antigen binding sites amino-terminal to the Fc region. The preferred multivalent antibody herein comprises (or consists of) three to about eight, but preferably four, antigen binding sites. The multivalent antibody comprises at least one polypeptide chain (and preferably two polypeptide chains), wherein the polypeptide chain(s) comprise two or more variable domains. For instance, the polypeptide chain(s) may comprise VD1-$(X1)_n$-VD2-$(X2)_n$-Fc, wherein VD1 is a first variable domain, VD2 is a second variable domain, Fc is one polypeptide chain of an Fc region, X1 and X2 represent an

amino acid or polypeptide, and n is 0 or 1. For instance, the polypeptide chain(s) may comprise: VH-CH1-flexible linker-VH-CH1-Fc region chain; or VH-CH1-VH-CH1-Fc region chain. The multivalent antibody herein preferably further comprises at least two (and preferably four) light chain variable domain polypeptides. The multivalent antibody herein may, for instance, comprise from about two to about eight light chain variable domain polypeptides. The light chain variable domain polypeptides contemplated here comprise a light chain variable domain and, optionally, further comprise a C_L domain.

[1230] Antibodies of the present invention further include single chain antibodies.

[1231] In particular embodiments, antibodies of the present invention are internalizing antibodies.

[1232] Amino acid sequence modification(s) of the antibodies described herein are contemplated. For example, it may be desirable to improve the binding affinity and/or other biological properties of the antibody. Amino acid sequence variants of the antibody may be prepared by introducing appropriate nucleotide changes into a polynucleotide that encodes the antibody, or a chain thereof, or by peptide synthesis. Such modifications include, for example, deletions from, and/or insertions into and/or substitutions of, residues within the amino acid sequences of the antibody. Any combination of deletion, insertion, and substitution may be made to arrive at the final antibody, provided that the final construct possesses the desired characteristics. The amino acid changes also may alter post-translational processes of the antibody, such as changing the number or position of glycosylation sites. Any of the variations and modifications described above for polypeptides of the present invention may be included in antibodies of the present invention.

[1233] A useful method for identification of certain residues or regions of an antibody that are preferred locations for mutagenesis is called "alanine scanning mutagenesis" as described by Cunningham and Wells in Science, 244:1081-1085 (1989). Here, a residue or group of target residues are identified (*e.g.*, charged residues such as arg, asp, his, lys, and glu) and replaced by a neutral or negatively charged amino acid (most preferably alanine or polyalanine) to affect the interaction of the amino acids with PSCA antigen. Those amino acid locations demonstrating functional sensitivity to the substitutions then are refined by introducing further or other variants at, or for, the sites of substitution. Thus, while the site for introducing an amino acid sequence variation is predetermined, the nature of the mutation *per*

se need not be predetermined. For example, to analyze the performance of a mutation at a given site, ala scanning or random mutagenesis is conducted at the target codon or region and the expressed anti- antibody variants are screened for the desired activity.

[1234] Amino acid sequence insertions include amino- and/or carboxyl-terminal fusions ranging in length from one residue to polypeptides containing a hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Examples of terminal insertions include an antibody with an N-terminal methionyl residue or the antibody fused to a cytotoxic polypeptide. Other insertional variants of an antibody include the fusion to the N- or C-terminus of the antibody to an enzyme (*e.g.*, for ADEPT) or a polypeptide that increases the serum half-life of the antibody.

[1235] Another type of variant is an amino acid substitution variant. These variants have at least one amino acid residue in the antibody molecule replaced by a different residue. The sites of greatest interest for substitutional mutagenesis include the hypervariable regions, but FR alterations are also contemplated. Conservative and non-conservative substitutions are contemplated.

[1236] Substantial modifications in the biological properties of the antibody are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain.

[1237] Any cysteine residue not involved in maintaining the proper conformation of the antibody also may be substituted, generally with serine, to improve the oxidative stability of the molecule and prevent aberrant crosslinking. Conversely, cysteine bond(s) may be added to the antibody to improve its stability (particularly where the antibody is an antibody fragment such as an Fv fragment).

[1238] One type of substitutional variant involves substituting one or more hypervariable region residues of a parent antibody. Generally, the resulting variant(s) selected for further development will have improved biological properties relative to the parent antibody from which they are generated. A convenient way for generating such substitutional variants involves affinity maturation using phage display. Briefly, several hypervariable region sites (*e.g.*, 6-7 sites) are mutated to generate all possible amino substitutions at each site. The

antibody variants thus generated are displayed in a monovalent fashion from filamentous phage particles as fusions to the gene III product of M13 packaged within each particle. The phage-displayed variants are then screened for their biological activity (*e.g.*, binding affinity) as herein disclosed. In order to identify candidate hypervariable region sites for modification, alanine scanning mutagenesis can be performed to identify hypervariable region residues contributing significantly to antigen binding. Alternatively, or additionally, it may be beneficial to analyze a crystal structure of the antigen-antibody complex to identify contact points between the antibody and an antigen or infected cell. Such contact residues and neighboring residues are candidates for substitution according to the techniques elaborated herein. Once such variants are generated, the panel of variants is subjected to screening as described herein and antibodies with superior properties in one or more relevant assays may be selected for further development.

[1239] Another type of amino acid variant of the antibody alters the original glycosylation pattern of the antibody. By altering is meant deleting one or more carbohydrate moieties found in the antibody, and/or adding one or more glycosylation sites that are not present in the antibody.

[1240] Glycosylation of antibodies is typically either N-linked or O-linked. N-linked refers to the attachment of the carbohydrate moiety to the side chain of an asparagine residue. The tripeptide sequences asparagine-X-serine and asparagine-X-threonine, where X is any amino acid except proline, are the recognition sequences for enzymatic attachment of the carbohydrate moiety to the asparagine side chain. Thus, the presence of either of these tripeptide sequences in a polypeptide creates a potential glycosylation site. O-linked glycosylation refers to the attachment of one of the sugars N-aceylgalactosamine, galactose, or xylose to a hydroxyamino acid, most commonly serine or threonine, although 5-hydroxyproline or 5-hydroxylysine may also be used.

[1241] Addition of glycosylation sites to the antibody is conveniently accomplished by altering the amino acid sequence such that it contains one or more of the above-described tripeptide sequences (for N-linked glycosylation sites). The alteration may also be made by the addition of, or substitution by, one or more serine or threonine residues to the sequence of the original antibody (for O-linked glycosylation sites).

[1242] The antibody of the invention is modified with respect to effector function, *e.g.*, so as to enhance antigen-dependent cell-mediated cyotoxicity (ADCC) and/or complement dependent cytotoxicity (CDC) of the antibody. This may be achieved by introducing one or more amino acid substitutions in an Fc region of the antibody. Alternatively or additionally, cysteine residue(s) may be introduced in the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated may have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron *et al.*, J. Exp Med. 176:1191-1195 (1992) and Shopes, B. J. Immunol. 148:2918-2922 (1992). Homodimeric antibodies with enhanced anti-infection activity may also be prepared using heterobifunctional cross-linkers as described in Wolff *et al.*, Cancer Research 53:2560-2565 (1993). Alternatively, an antibody can be engineered which has dual Fc regions and may thereby have enhanced complement lysis and ADCC capabilities. See Stevenson *et al.*, Anti-Cancer Drug Design 3:219-230 (1989).

[1243] To increase the serum half-life of the antibody, one may incorporate a salvage receptor binding epitope into the antibody (especially an antibody fragment) as described in U.S. Pat. No. 5,739,277, for example. As used herein, the term "salvage receptor binding epitope" refers to an epitope of the Fc region of an IgG molecule (*e.g.*, IgG_1, IgG_2, IgG_3, or IgG_4) that is responsible for increasing the in vivo serum half-life of the IgG molecule.

[1244] Antibodies of the present invention may also be modified to include an epitope tag or label, *e.g.*, for use in purification or diagnostic applications. The invention also pertains to therapy with immunoconjugates comprising an antibody conjugated to an anti-cancer agent such as a cytotoxic agent or a growth inhibitory agent. Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above.

[1245] Conjugates of an antibody and one or more small molecule toxins, such as a calicheamicin, maytansinoids, a trichothene, and CC1065, and the derivatives of these toxins that have toxin activity, are also contemplated herein.

[1246] In one preferred embodiment, an antibody (full length or fragments) of the invention is conjugated to one or more maytansinoid molecules. Maytansinoids are mitototic inhibitors that act by inhibiting tubulin polymerization. Maytansine was first isolated from the east African shrub Maytenus serrata (U.S. Pat. No. 3,896,111). Subsequently, it was discovered

that certain microbes also produce maytansinoids, such as maytansinol and C-3 maytansinol esters (U.S. Pat. No. 4,151,042). Synthetic maytansinol and derivatives and analogues thereof are disclosed, for example, in U.S. Pat. Nos. 4,137,230; 4,248,870; 4,256,746; 4,260,608; 4,265,814; 4,294,757; 4,307,016; 4,308,268; 4,308,269; 4,309,428; 4,313,946; 4,315,929; 4,317,821; 4,322,348; 4,331,598; 4,361,650; 4,364,866; 4,424,219; 4,450,254; 4,362,663; and 4,371,533.

[1247] In an attempt to improve their therapeutic index, maytansine and maytansinoids have been conjugated to antibodies specifically binding to tumor cell antigens. Immunoconjugates containing maytansinoids and their therapeutic use are disclosed, for example, in U.S. Pat. Nos. 5,208,020, 5,416,064 and European Patent EP 0 425 235 B1. Liu *et al.*, Proc. Natl. Acad. Sci. USA 93:8618-8623 (1996) described immunoconjugates comprising a maytansinoid designated DM1 linked to the monoclonal antibody C242 directed against human colorectal cancer. The conjugate was found to be highly cytotoxic towards cultured colon cancer cells, and showed antitumor activity in an in vivo tumor growth assay.

[1248] Antibody-maytansinoid conjugates are prepared by chemically linking an antibody to a maytansinoid molecule without significantly diminishing the biological activity of either the antibody or the maytansinoid molecule. An average of 3-4 maytansinoid molecules conjugated per antibody molecule has shown efficacy in enhancing cytotoxicity of target cells without negatively affecting the function or solubility of the antibody, although even one molecule of toxin/antibody would be expected to enhance cytotoxicity over the use of naked antibody. Maytansinoids are well known in the art and can be synthesized by known techniques or isolated from natural sources. Suitable maytansinoids are disclosed, for example, in U.S. Pat. No. 5,208,020 and in the other patents and nonpatent publications referred to hereinabove. Preferred maytansinoids are maytansinol and maytansinol analogues modified in the aromatic ring or at other positions of the maytansinol molecule, such as various maytansinol esters.

[1249] There are many linking groups known in the art for making antibody conjugates, including, for example, those disclosed in U.S. Pat. No. 5,208,020 or EP Patent 0 425 235 B1, and Chari *et al.*, Cancer Research 52: 127-131 (1992). The linking groups include disufide groups, thioether groups, acid labile groups, photolabile groups, peptidase labile

groups, or esterase labile groups, as disclosed in the above-identified patents, disulfide and thioether groups being preferred.

[1250] Immunoconjugates may be made using a variety of bifunctional protein coupling agents such as N-succinimidyl-3-(2-pyridyldithio)propionate (SPDP), succinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate, iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutareldehyde), bis-azido compounds (such as bis (p-azidobenzoyl)hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as toluene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). Particularly preferred coupling agents include N-succinimidyl-3-(2-pyridyldithio)propionate (SPDP) (Carlsson *et al.*, Biochem. J. 173:723-737 [1978]) and N-succinimidyl-4-(2-pyridylthio)pentanoate (SPP) to provide for a disulfide linkage. For example, a ricin immunotoxin can be prepared as described in Vitetta *et al.*, Science 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldicthylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026. The linker may be a "cleavable linker" facilitating release of the cytotoxic drug in the cell. For example, an acid-labile linker, Cancer Research 52: 127-131 (1992); U.S. Pat. No. 5,208,020) may be used.

[1251] Another immunoconjugate of interest comprises an antibody conjugated to one or more calicheamicin molecules. The calicheamicin family of antibiotics are capable of producing double-stranded DNA breaks at sub-picomolar concentrations. For the preparation of conjugates of the calicheamicin family, see U.S. Pat. Nos. 5,712,374, 5,714,586, 5,739,116, 5,767,285, 5,770,701, 5,770,710, 5,773,001, 5,877,296 (all to American Cyanamid Company). Another drug that the antibody can be conjugated is QFA which is an antifolate. Both calicheamicin and QFA have intracellular sites of action and do not readily cross the plasma membrane. Therefore, cellular uptake of these agents through antibody mediated internalization greatly enhances their cytotoxic effects.

[1252] Examples of other agents that can be conjugated to the antibodies of the invention include BCNU, streptozoicin, vincristine and 5-fluorouracil, the family of agents known collectively LL-E33288 complex described in U.S. Pat. Nos. 5,053,394, 5,770,710, as well as esperamicins (U.S. Pat. No. 5,877,296).

[1253] Enzymatically active toxins and fragments thereof that can be used include, *e.g.*, diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from Pseudomonas aeruginosa), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Phytolaca americana proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin and the tricothecenes. See, for example, WO 93/21232.

[1254] The present invention further includes an immunoconjugate formed between an antibody and a compound with nucleolytic activity (*e.g.*, a ribonuclease or a DNA endonuclease such as a deoxyribonuclease; DNase).

[1255] For selective destruction of infected cells, the antibody includes a highly radioactive atom. A variety of radioactive isotopes are available for the production of radioconjugated anti-PSCA antibodies. Examples include At^{211}, I^{131}, I^{125}, Y^{90}, Re^{186}, Rc^{188}, Sm^{153}, Bi^{212}, P^{32}, Pb^{212} and radioactive isotopes of Lu. When the conjugate is used for diagnosis, it may comprise a radioactive atom for scintigraphic studies, for example tc^{99m} or I^{123}, or a spin label for nuclear magnetic resonance (NMR) imaging (also known as magnetic resonance imaging, mri), such as iodine-123, iodine-131, indium-111, fluorine-19, carbon-13, nitrogen-15, oxygen-17, gadolinium, manganese or iron.

[1256] The radio- or other label is incorporated in the conjugate in known ways. For example, the peptide may be biosynthesized or may be synthesized by chemical amino acid synthesis using suitable amino acid precursors involving, for example, fluorine-19 in place of hydrogen. Labels such as tc^{99m} or I^{123}, Re^{186}, Re^{188} and In^{111} can be attached via a cysteine residue in the peptide. Yttrium-90 can be attached via a lysine residue. The IODOGEN method (Fraker *et al.* (1978) Biochem. Biophys. Res. Commun. 80: 49-57 can be used to incorporate iodine-123. "Monoclonal Antibodies in Immunoscintigraphy" (Chatal,CRC Press 1989) describes other methods in detail.

[1257] Alternatively, a fusion protein comprising the antibody and cytotoxic agent is made, *e.g.*, by recombinant techniques or peptide synthesis. The length of DNA may comprise respective regions encoding the two portions of the conjugate either adjacent one another or separated by a region encoding a linker peptide which does not destroy the desired properties of the conjugate.

[1258] The antibodies of the present invention are also used in antibody dependent enzyme mediated prodrug therapy (ADET) by conjugating the antibody to a prodrug-activating enzyme which converts a prodrug (*e.g.*, a peptidyl chemotherapeutic agent, see WO81/01145) to an active anti-cancer drug (*see, e.g.*, WO 88/07378 and U.S. Pat. No. 4,975,278).

[1259] The enzyme component of the immunoconjugate useful for ADEPT includes any enzyme capable of acting on a prodrug in such a way so as to covert it into its more active, cytotoxic form. Enzymes that are useful in the method of this invention include, but are not limited to, alkaline phosphatase useful for converting phosphate-containing prodrugs into free drugs; arylsulfatase useful for converting sulfate-containing prodrugs into free drugs; cytosine deaminase useful for converting non-toxic 5-fluorocytosine into the anti-cancer drug, 5-fluorouracil; proteases, such as serratia protease, thermolysin, subtilisin, carboxypeptidases and cathepsins (such as cathepsins B and L), that are useful for converting peptide-containing prodrugs into free drugs; D-alanylcarboxypeptidases, useful for converting prodrugs that contain D-amino acid substituents; carbohydrate-cleaving enzymes such as β-galactosidase and neuraminidase useful for converting glycosylated prodrugs into free drugs; β-lactamase useful for converting drugs derivatized with β-lactams into free drugs; and penicillin amidases, such as penicillin V amidase or penicillin G amidase, useful for converting drugs derivatized at their amine nitrogens with phenoxyacetyl or phenylacetyl groups, respectively, into free drugs. Alternatively, antibodies with enzymatic activity, also known in the art as "abzymes", can be used to convert the prodrugs of the invention into free active drugs (see, *e.g.*, Massey, Nature 328: 457-458 (1987)). Antibody-abzyme conjugates can be prepared as described herein for delivery of the abzyme to a infected cell population.

[1260] The enzymes of this invention can be covalently bound to the antibodies by techniques well known in the art such as the use of the heterobifunctional crosslinking reagents discussed above. Alternatively, fusion proteins comprising at least the antigen binding region of an antibody of the invention linked to at least a functionally active portion of an enzyme of the invention can be constructed using recombinant DNA techniques well known in the art (*see, e.g.*, Neuberger *et al.*, Nature, 312: 604-608 (1984).

[1261] Other modifications of the antibody are contemplated herein. For example, the antibody may be linked to one of a variety of nonproteinaceous polymers, *e.g.*, polyethylene

glycol, polypropylene glycol, polyoxyalkylenes, or copolymers of polyethylene glycol and polypropylene glycol. The antibody also may be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization (for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacylate) microcapsules, respectively), in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules), or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences, 16th edition, Oslo, A., Ed., (1980).

[1262] The antibodies disclosed herein are also formulated as immunoliposomes. A "liposome" is a small vesicle composed of various types of lipids, phospholipids and/or surfactant that is useful for delivery of a drug to a mammal. The components of the liposome are commonly arranged in a bilayer formation, similar to the lipid arrangement of biological membranes. Liposomes containing the antibody are prepared by methods known in the art, such as described in Epstein *et al.*, Proc. Natl. Acad. Sci. USA, 82:3688 (1985); Hwang *et al.*, Proc. Natl Acad. Sci. USA, 77:4030 (1980); U.S. Pat. Nos. 4,485,045 and 4,544,545; and WO97/38731 published Oct. 23, 1997. Liposomes with enhanced circulation time are disclosed in U.S. Pat. No. 5,013,556.

[1263] Particularly useful liposomes can be generated by the reverse phase evaporation method with a lipid composition comprising phosphatidylcholine, cholesterol and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired a diameter. Fab' fragments of the antibody of the present invention can be conjugated to the liposomes as described in Martin *et al.*, J. Biol. Chem. 257: 286-288 (1982) via a disulfide interchange reaction. A chemotherapeutic agent is optionally contained within the liposome. See Gabizon *et al.*, J. National Cancer Inst. 81(19)1484 (1989).

[1264] Antibodies of the present invention, or fragments thereof, may possess any of a variety of biological or functional characteristics. In certain embodiments, these antibodies are Influenza A specific or M2 protein specific antibodies, indicating that they specifically bind to or preferentially bind to Influenza A or the M2 protein thereof, respectively, as compared to a normal control cell. In particular embodiments, the antibodies are HuM2e antibodies, indicating that they specifically bind to a M2e protein, preferably to an epitope of

the M2e domain that is only present when the M2 protein is expressed in cells or present on a virus, as compared to a normal control cell.

[1265] In particular embodiments, an antibody of the present invention is an antagonist antibody, which partially or fully blocks or inhibits a biological activity of a polypeptide or cell to which it specifically or preferentially binds. In other embodiments, an antibody of the present invention is a growth inhibitory antibody, which partially or fully blocks or inhibits the growth of an infected cell to which it binds. In another embodiment, an antibody of the present invention induces apoptosis. In yet another embodiment, an antibody of the present invention induces or promotes antibody-dependent cell-mediated cytotoxicity or complement dependent cytotoxicity.

Methods of Identifying and Producing Antibodies Specific for Influenza Virus

[1266] The present invention provides novel methods for the identification of human anti-influenza antibodies raised against the M2e protein, as exemplified in Example 4, and for the identification of human anti-influenza antibodies raised against the HA protein, as exemplified in Example 13. These methods may be readily adapted to identify antibodies specific for other polypeptides expressed on the cell surface by infectious agents, or even polypeptides expressed on the surface of an infectious agent itself.

[1267] In general, the methods include obtaining serum samples from patients that have been infected with or vaccinated against an infectious agent. These serum samples are then screened to identify those that contain antibodies specific for a particular polypeptide associated with the infectious agent, such as, e.g., a polypeptide or protein specifically expressed on the surface of cells infected with the infectious agent, but not uninfected cells. In particular embodiments, the serum samples are screened by contacting the samples with a cell that has been transfected with an expression vector that expresses the polypeptide expressed on the surface of infected cells.

[1268] Once a patient is identified as having serum containing an antibody specific for the infectious agent polypeptide of interest is identified, mononuclear and/or B cells obtained from the same patient are used to identify a cell or clone thereof that produces the antibody, using any of the methods described herein or available in the art. Once a B cell that produces the antibody is identified, cDNAs encoding the variable regions or fragments thereof of the antibody may be cloned using standard RT-PCR vectors and primers specific for conserved antibody sequences, and subcloned in to expression vectors used for the recombinant production of monoclonal antibodies specific for the infectious agent polypeptide of interest.

[1269] In one embodiment, the present invention provides a method of identifying an antibody that specifically binds influenza A-infected cells, comprising: contacting an Influenza A virus or a cell expressing the M2 protein with a biological sample obtained from a patient having been infected by Influenza A; determining an amount of antibody in the biological sample that binds to the cell; and comparing the amount determined with a control value, wherein if the value determined is at least two-fold greater than the control value, an antibody that specifically binds influenza A-infected cells is indicated.

[1270] In various embodiments, the cells expressing an M2 or HA protein are cells infected with an Influenza A virus or cells that have been transfected with a polynucleotide that expressed the M2 or HA protein. Alternatively, the cells may express a portion of the M2 protein that includes the M2e domain and enough additional M2 sequence that the protein remains associated with the cell and the M2e domain is presented on the cell surface in the same manner as when present within full length M2 protein. Methods of preparing an M2 or HA expression vector and transfecting an appropriate cell, including those described herein, may be readily accomplished, in view of the M2 and HA sequences being publicly available. See, for example, the Influenza Sequence Database (ISD) (flu.lanl.gov on the World Wide Web, described in Macken et al., 2001, "The value of a database in surveillance and vaccine selection" in Options for the Control of Influenza IV. A.D.M.E., Osterhaus & Hampson (Eds.), Elsevier Science, Amsterdam, pp. 103-106) and the Microbial Sequencing Center (MSC) at The Institute for Genomic Research (TIGR) (tigr.org/msc/infl_a_virus.shtml on the World Wide Web).

[1271] The M2e- or HA-expressing cells or virus described above are used to screen the biological sample obtained from a patient infected with influenza A for the presence of antibodies that preferentially bind to the cell expressing the M2 or HA polypeptide using standard biological techniques. For example, in certain embodiments, the antibodies may be labeled, and the presence of label associated with the cell detected, e.g., using FMAT or FACs analysis. In particular embodiments, the biological sample is blood, serum, plasma, bronchial lavage, or saliva. Methods of the present invention may be practiced using high throughput techniques.

[1272] Identified human antibodies may then be characterized further. For example the particular conformational epitopes with in the M2e or HA protein that are necessary or sufficient for binding of the antibody may be determined, e.g., using site-directed mutagenesis of expressed M2e or HA polypeptides. These methods may be readily adapted

to identify human antibodies that bind any protein expressed on a cell surface. Furthermore, these methods may be adapted to determine binding of the antibody to the virus itself, as opposed to a cell expressing recombinant M2e or HA, or infected with the virus.

[1273] Polynucleotide sequences encoding the antibodies, variable regions thereof, or antigen-binding fragments thereof may be subcloned into expression vectors for the recombinant production of human monoclonal anti-M2e or anti-HA antibodies. In one embodiment, this is accomplished by obtaining mononuclear cells from the patient from the serum containing the identified human monoclonal anti-M2e or anti-HA antibody was obtained; producing B cell clones from the mononuclear cells; inducing the B cells to become antibody-producing plasma cells; and screening the supernatants produced by the plasma cells to determine if it contains the human monoclonal anti-M2e or anti-HA antibody. Once a B cell clone that produces a human monoclonal anti-M2e or anti-HA antibody is identified, reverse-transcription polymerase chain reaction (RT-PCR) is performed to clone the DNAs encoding the variable regions or portions thereof of the human monoclonal anti-M2e or anti-HA antibody. These sequences are then subcloned into expression vectors suitable for the recombinant production of human monoclonal anti-M2e or anti-HA antibodies. The binding specificity may be confirmed by determining the recombinant antibody's ability to bind cells expressing M2e or HA polypeptide or protein.

[1274] In particular embodiments of the methods described herein, B cells isolated from peripheral blood or lymph nodes are sorted, *e.g.*, based on their being CD19 positive, and plated, *e.g.*, as low as a single cell specificity per well, *e.g.*, in 96, 384, or 1536 well configurations. The cells are induced to differentiate into antibody-producing cells, *e.g.*, plasma cells, and the culture supernatants are harvested and tested for binding to cells expressing the infectious agent polypeptide on their surface using, *e.g.*, FMAT or FACS analysis. Positive wells are then subjected to whole well RT-PCR to amplify heavy and light chain variable regions of the IgG molecule expressed by the clonal daughter plasma cells. The resulting PCR products encoding the heavy and light chain variable regions, or portions thereof, are subcloned into human antibody expression vectors for recombinant expression. The resulting recombinant antibodies are then tested to confirm their original binding specificity and may be further tested for pan-specificity across various strains of isolates of the infectious agent.

[1275] Thus, in one embodiment, a method of identifying human monoclonal anti-M2e or anti-HA antibodies is practiced as follows. First, full length or approximately full length M2

or HA cDNAs are transfected into a cell line for expression of M2 or HA protein. Secondly, individual human plasma or sera samples are tested for antibodies that bind the cell-expressed M2 or HA. And lastly, MAbs derived from plasma- or serum-positive individuals are characterized for binding to the same cell-expressed M2 or HA. Further definition of the fine specificities of the MAbs can be performed at this point.

[1276] These methods may be practiced to identify a variety of different HuM2e antibodies, including antibodies specific for (a) epitopes in a linear M2e peptide, (b) common epitopes in multiple variants of M2e, (c) conformational determinants of an M2 homotetramer, and (d) common conformational determinants of multiple variants of the M2 homotetramer. The last category is particularly desirable, as this specificity is perhaps specific for all A strains of influenza.

[1277] These methods may be practiced to identify a variety of different human monoclonal anti-HA antibodies, including antibodies specific for (a) epitopes in a linear HA peptide, (b) common epitopes in multiple variants of HA, (c) conformational determinants of an HA protein or homotrimer, and (d) common conformational determinants of multiple variants of the HA protein or homotrimer. The last category is particularly desirable, as this specificity is perhaps specific for all A strains of influenza.

[1278] Polynucleotides that encode the human monoclonal anti-M2e or anti-HA antibodies or portions thereof of the present invention may be isolated from cells expressing human monoclonal anti-M2e or anti-HA antibodies, according to methods available in the art and described herein, including amplification by polymerase chain reaction using primers specific for conserved regions of human antibody polypeptides. For example, light chain and heavy chain variable regions may be cloned from the B cell according to molecular biology techniques described in WO 92/02551; U.S. Patent No. 5,627,052; or Babcook et al., *Proc. Natl. Acad. Sci. USA* 93:7843-48 (1996). In certain embodiments, polynucleotides encoding all or a region of both the heavy and light chain variable regions of the IgG molecule expressed by the clonal daughter plasma cells expressing the human monoclonal anti-M2e or anti-HA antibody are subcloned and sequenced. The sequence of the encoded polypeptide may be readily determined from the polynucleotide sequence.

[1279] Isolated polynucleotides encoding a polypeptide of the present invention may be subcloned into an expression vector to recombinantly produce antibodies and polypeptides of the present invention, using procedures known in the art and described herein.

[1280] Binding properties of an antibody (or fragment thereof) to M2e or infected cells or tissues may generally be determined and assessed using immunodetection methods including, for example, immunofluorescence-based assays, such as immuno-histochemistry (IHC) and/or fluorescence-activated cell sorting (FACS). Immunoassay methods may include controls and procedures to determine whether antibodies bind specifically to M2e from one or more specific strains of Influenza A, and do not recognize or cross-react with normal control cells.

[1281] Following pre-screening of serum to identify patients that produce antibodies to an infectious agent or polypeptide thereof, e.g., M2 or HA, the methods of the present invention typically include the isolation or purification of B cells from a biological sample previously obtained from a patient or subject. The patient or subject may be currently or previously diagnosed with or suspect or having a particular disease or infection, or the patient or subject may be considered free or a particular disease or infection. Typically, the patient or subject is a mammal and, in particular embodiments, a human. The biological sample may be any sample that contains B cells, including but not limited to, lymph node or lymph node tissue, pleural effusions, peripheral blood, ascites, tumor tissue, or cerebrospinal fluid (CSF). In various embodiments, B cells are isolated from different types of biological samples, such as a biological sample affected by a particular disease or infection. However, it is understood that any biological sample comprising B cells may be used for any of the embodiments of the present invention.

[1282] Once isolated, the B cells are induced to produce antibodies, *e.g.*, by culturing the B cells under conditions that support B cell proliferation or development into a plasmacyte, plasmablast, or plasma cell. The antibodies are then screened, typically using high throughput techniques, to identify an antibody that specifically binds to a target antigen, *e.g.*, a particular tissue, cell, infectious agent, or polypeptide. In certain embodiments, the specific antigen, *e.g.*, cell surface polypeptide bound by the antibody is not known, while in other embodiments, the antigen specifically bound by the antibody is known.

[1283] According to the present invention, B cells may be isolated from a biological sample, *e.g.*, a tumor, tissue, peripheral blood or lymph node sample, by any means known and available in the art. B cells are typically sorted by FACS based on the presence on their surface of a B cell-specific marker, *e.g.*, CD19, CD138, and/or surface IgG. However, other methods known in the art may be employed, such as, *e.g.*, column purification using CD19 magnetic beads or IgG-specific magnetic beads, followed by elution from the column.

However, magnetic isolation of B cells utilizing any marker may result in loss of certain B cells. Therefore, in certain embodiments, the isolated cells are not sorted but, instead, phicol-purified mononuclear cells isolated from tumor are directly plated to the appropriate or desired number of specificities per well.

[1284] In order to identify B cells that produce an infectious agent-specific antibody, the B cells are typically plated at low density (*e.g.*, a single cell specificity per well, 1-10 cells per well, 10-100 cells per well, 1-100 cells per well, less than 10 cells per well, or less than 100 cells per well) in multi-well or microtitre plates, *e.g.*, in 96, 384, or 1536 well configurations. When the B cells are initially plated at a density greater than one cell per well, then the methods of the present invention may include the step of subsequently diluting cells in a well identified as producing an antigen-specific antibody, until a single cell specificity per well is achieved, thereby facilitating the identification of the B cell that produces the antigen-specific antibody. Cell supernatants or a portion thereof and/or cells may be frozen and stored for future testing and later recovery of antibody polynucleotides.

[1285] In certain embodiments, the B cells are cultured under conditions that favor the production of antibodies by the B cells. For example, the B cells may be cultured under conditions favorable for B cell proliferation and differentiation to yield antibody-producing plasmablast, plasmacytes, or plasma cells. In particular embodiments, the B cells are cultured in the presence of a B cell mitogen, such as lipopolysaccharide (LPS) or CD40 ligand. In one specific embodiment, B cells are differentiated to antibody-producing cells by culturing them with feed cells and/or other B cell activators, such as CD40 ligand.

[1286] Cell culture supernatants or antibodies obtained therefrom may be tested for their ability to bind to a target antigen, using routine methods available in the art, including those described herein. In particular embodiments, culture supernatants are tested for the presence of antibodies that bind to a target antigen using high- throughput methods. For example, B cells may be cultured in multi-well microtitre dishes, such that robotic plate handlers may be used to simultaneously sample multiple cell supernatants and test for the presence of antibodies that bind to a target antigen. In particular embodiments, antigens are bound to beads, *e.g.*, paramagnetic or latex beads) to facilitate the capture of antibody/antigen complexes. In other embodiments, antigens and antibodies are fluorescently labeled (with different labels) and FACS analysis is performed to identify the presence of antibodies that bind to target antigen. In one embodiment, antibody binding is determined using FMAT™ analysis and instrumentation (Applied Biosystems, Foster City, CA). FMAT™ is a

fluorescence macro-confocal platform for high-throughput screening, which mix-and-read, non-radioactive assays using live cells or beads.

[1287] In the context of comparing the binding of an antibody to a particular target antigen (*e.g.*, a biological sample such as infected tissue or cells, or infectious agents) as compared to a control sample (*e.g.*, a biological sample such as uninfected cells, or a different infectious agent), in various embodiments, the antibody is considered to preferentially bind a particular target antigen if at least two-fold, at least three-fold, at least five-fold, or at least ten-fold more antibody binds to the particular target antigen as compared to the amount that binds a control sample.

[1288] Polynucleotides encoding antibody chains, variable regions thereof, or fragments thereof, may be isolated from cells utilizing any means available in the art. In one embodiment, polynucleotides are isolated using polymerase chain reaction (PCR), *e.g.*, reverse transcription-PCR (RT-PCR) using oligonucleotide primers that specifically bind to heavy or light chain encoding polynucleotide sequences or complements thereof using routine procedures available in the art. In one embodiment, positive wells are subjected to whole well RT-PCR to amplify the heavy and light chain variable regions of the IgG molecule expressed by the clonal daughter plasma cells. These PCR products may be sequenced.

[1289] The resulting PCR products encoding the heavy and light chain variable regions or portions thereof are then subcloned into human antibody expression vectors and recombinantly expressed according to routine procedures in the art (*see, e.g.*, US Patent No. 7,112,439). The nucleic acid molecules encoding a tumor-specific antibody or fragment thereof, as described herein, may be propagated and expressed according to any of a variety of well-known procedures for nucleic acid excision, ligation, transformation, and transfection. Thus, in certain embodiments expression of an antibody fragment may be preferred in a prokaryotic host cell, such as *Escherichia coli* (*see, e.g.*, Pluckthun et al., *Methods Enzymol.* 178:497-515 (1989)). In certain other embodiments, expression of the antibody or an antigen-binding fragment thereof may be preferred in a eukaryotic host cell, including yeast (*e.g.*, *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, and *Pichia pastoris*); animal cells (including mammalian cells); or plant cells. Examples of suitable animal cells include, but are not limited to, myeloma, COS, CHO, or hybridoma cells. Examples of plant cells include tobacco, corn, soybean, and rice cells. By methods known to those having ordinary skill in the art and based on the present disclosure, a nucleic acid

vector may be designed for expressing foreign sequences in a particular host system, and then polynucleotide sequences encoding the tumor-specific antibody (or fragment thereof) may be inserted. The regulatory elements will vary according to the particular host.

[1290] One or more replicable expression vectors containing a polynucleotide encoding a variable and/or constant region may be prepared and used to transform an appropriate cell line, for example, a non-producing myeloma cell line, such as a mouse NSO line or a bacterium, such as *E.coli*, in which production of the antibody will occur. In order to obtain efficient transcription and translation, the polynucleotide sequence in each vector should include appropriate regulatory sequences, particularly a promoter and leader sequence operatively linked to the variable domain sequence. Particular methods for producing antibodies in this way are generally well known and routinely used. For example, molecular biology procedures are described by Sambrook *et al.* (*Molecular Cloning, A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory, New York, 1989; *see also* Sambrook et al., 3rd ed., Cold Spring Harbor Laboratory, New York, (2001)). While not required, in certain embodiments, regions of polynucleotides encoding the recombinant antibodies may be sequenced. DNA sequencing can be performed as described in Sanger *et al.* (*Proc. Natl. Acad. Sci. USA* 74:5463 (1977)) and the Amersham International plc sequencing handbook and including improvements thereto.

[1291] In particular embodiments, the resulting recombinant antibodies or fragments thereof are then tested to confirm their original specificity and may be further tested for pan-specificity, *e.g.*, with related infectious agents. In particular embodiments, an antibody identified or produced according to methods described herein is tested for cell killing via antibody dependent cellular cytotoxicity (ADCC) or apoptosis, and/or well as its ability to internalize.

Polynucleotides

[1292] The present invention, in other aspects, provides polynucleotide compositions. In preferred embodiments, these polynucleotides encode a polypeptide of the invention, *e.g.*, a region of a variable chain of an antibody that binds to Influenza A, M2, M2e, or HA (soluble or recombinant). Polynucleotides of the invention are single-stranded (coding or antisense) or double-stranded DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include, but are not limited to, HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Alternatively, or in addition, coding or non-coding sequences are present within a

polynucleotide of the present invention. Also alternatively, or in addition, a polynucleotide is linked to other molecules and/or support materials of the invention. Polynucleotides of the invention are used, *e.g.*, in hybridization assays to detect the presence of an Influenza A antibody in a biological sample, and in the recombinant production of polypeptides of the invention.

[1293] Therefore, according to another aspect of the present invention, polynucleotide compositions are provided that include some or all of a polynucleotide sequences set forth herein, complements of these polynucleotide sequences, and degenerate variants of these polynucleotide sequences. In certain preferred embodiments, the polynucleotide sequences set forth herein encode polypeptides capable of preferentially binding a Influenza A-infected cell as compared to a normal control uninfected cell, including a polypeptide having a sequence set forth herein. Furthermore, the invention includes all polynucleotides that encode any polypeptide of the present invention.

[1294] In other related embodiments, the invention provides polynucleotide variants having substantial identity to the sequences set forth herein, for example those comprising at least 70% sequence identity, preferably at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a polynucleotide sequence of this invention, as determined using the methods described herein, (*e.g.*, BLAST analysis using standard parameters). One skilled in this art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning, and the like.

[1295] Typically, polynucleotide variants contain one or more substitutions, additions, deletions and/or insertions, preferably such that the immunogenic binding properties of the polypeptide encoded by the variant polynucleotide is not substantially diminished relative to a polypeptide encoded by a polynucleotide sequence specifically set forth herein.

In additional embodiments, the present invention provides polynucleotide fragments comprising various lengths of contiguous stretches of sequence identical to or complementary to one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at least about 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. As used herein, the term "intermediate lengths" is meant to describe any length between the quoted values, such as 16,

17, 18, 19, *etc.*; 21, 22, 23, *etc.*; 30, 31, 32, *etc.*; 50, 51, 52, 53, *etc.*; 100, 101, 102, 103, *etc.*; 150, 151, 152, 153, *etc.*; including all integers through 200-500; 500-1,000, and the like.

[1296] In another embodiment of the invention, polynucleotide compositions are provided that are capable of hybridizing under moderate to high stringency conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary sequence thereof. Hybridization techniques are well known in the art of molecular biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other polynucleotides include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-60°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. One skilled in the art will understand that the stringency of hybridization can be readily manipulated, such as by altering the salt content of the hybridization solution and/or the temperature at which the hybridization is performed. For example, in another embodiment, suitable highly stringent hybridization conditions include those described above, with the exception that the temperature of hybridization is increased, *e.g.*, to 60-65°C or 65-70°C.

[1297] In preferred embodiments, the polypeptide encoded by the polynucleotide variant or fragment has the same binding specificity (*i.e.*, specifically or preferentially binds to the same epitope or Influenza A strain) as the polypeptide encoded by the native polynucleotide. In certain preferred embodiments, the polynucleotides described above, *e.g.*, polynucleotide variants, fragments and hybridizing sequences, encode polypeptides that have a level of binding activity of at least about 50%, preferably at least about 70%, and more preferably at least about 90% of that for a polypeptide sequence specifically set forth herein.

[1298] The polynucleotides of the present invention, or fragments thereof, regardless of the length of the coding sequence itself, may be combined with other DNA sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length may vary considerably. A nucleic acid fragment of almost any length is employed, with the total length preferably being limited by the ease of preparation and use in the intended recombinant DNA protocol. For example, illustrative polynucleotide segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like, (including all intermediate lengths) are included in many implementations of this invention.

[1299] It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are multiple nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that encode a polypeptide of the present invention but which vary due to differences in codon usage are specifically contemplated by the invention. Further, alleles of the genes including the polynucleotide sequences provided herein are within the scope of the invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

[1300] In certain embodiments of the present invention, mutagenesis of the disclosed polynucleotide sequences is performed in order to alter one or more properties of the encoded polypeptide, such as its binding specificity or binding strength. Techniques for mutagenesis are well-known in the art, and are widely used to create variants of both polypeptides and polynucleotides. A mutagenesis approach, such as site-specific mutagenesis, is employed for the preparation of variants and/or derivatives of the polypeptides described herein. By this approach, specific modifications in a polypeptide sequence are made through mutagenesis of the underlying polynucleotides that encode them. These techniques provides a straightforward approach to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the polynucleotide.

[1301] Site-specific mutagenesis allows the production of mutants through the use of specific oligonucleotide sequences include the nucleotide sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on both sides of the deletion junction being traversed. Mutations are employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

[1302] In other embodiments of the present invention, the polynucleotide sequences provided herein are used as probes or primers for nucleic acid hybridization, *e.g.*, as PCR primers. The ability of such nucleic acid probes to specifically hybridize to a sequence of interest enable

them to detect the presence of complementary sequences in a given sample. However, other uses are also encompassed by the invention, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions. As such, nucleic acid segments of the invention that include a sequence region of at least about 15 nucleotides long contiguous sequence that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence disclosed herein is particularly useful. Longer contiguous identical or complementary sequences, *e.g.*, those of about 20, 30, 40, 50, 100, 200, 500, 1000 (including all intermediate lengths) including full length sequences, and all lengths in between, are also used in certain embodiments.

[1303] Polynucleotide molecules having sequence regions consisting of contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, *e.g.*, Southern and Northern blotting, and/or primers for use in, *e.g.*, polymerase chain reaction (PCR). The total size of fragment, as well as the size of the complementary stretch(es), ultimately depends on the intended use or application of the particular nucleic acid segment. Smaller fragments are generally used in hybridization embodiments, wherein the length of the contiguous complementary region may be varied, such as between about 15 and about 100 nucleotides, but larger contiguous complementarity stretches may be used, according to the length complementary sequences one wishes to detect.

[1304] The use of a hybridization probe of about 15-25 nucleotides in length allows the formation of a duplex molecule that is both stable and selective. Molecules having contiguous complementary sequences over stretches greater than 12 bases in length are generally preferred, though, in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. Nucleic acid molecules having gene-complementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired, are generally preferred.

[1305] Hybridization probes are selected from any portion of any of the sequences disclosed herein. All that is required is to review the sequences set forth herein, or to any continuous portion of the sequences, from about 15-25 nucleotides in length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences is governed by various factors. For example, one may wish to employ primers from towards the termini of the total sequence.

[1306] Polynucleotide of the present invention, or fragments or variants thereof, are readily prepared by, for example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments are obtained by application of nucleic acid reproduction technology, such as the PCR™ technology of U. S. Patent 4,683,202, by introducing selected sequences into recombinant vectors for recombinant production, and by other recombinant DNA techniques generally known to those of skill in the art of molecular biology.

Vectors, Host Cells and Recombinant Methods

[1307] The invention provides vectors and host cells comprising a nucleic acid of the present invention, as well as recombinant techniques for the production of a polypeptide of the present invention. Vectors of the invention include those capable of replication in any type of cell or organism, including, *e.g.*, plasmids, phage, cosmids, and mini chromosomes. In various embodiments, vectors comprising a polynucleotide of the present invention are vectors suitable for propagation or replication of the polynucleotide, or vectors suitable for expressing a polypeptide of the present invention. Such vectors are known in the art and commercially available.

[1308] Polynucleotides of the present invention are synthesized, whole or in parts that are then combined, and inserted into a vector using routine molecular and cell biology techniques, including, *e.g.*, subcloning the polynucleotide into a linearized vector using appropriate restriction sites and restriction enzymes. Polynucleotides of the present invention are amplified by polymerase chain reaction using oligonucleotide primers complementary to each strand of the polynucleotide. These primers also include restriction enzyme cleavage sites to facilitate subcloning into a vector. The replicable vector components generally include, but are not limited to, one or more of the following: a signal sequence, an origin of replication, and one or more marker or selectable genes.

[1309] In order to express a polypeptide of the present invention, the nucleotide sequences encoding the polypeptide, or functional equivalents, are inserted into an appropriate expression vector, *i.e.*, a vector that contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods well known to those skilled in the art are used to construct expression vectors containing sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic

recombination. Such techniques are described, for example, in Sambrook, J., et al. (1989) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. et al. (1989) Current Protocols in Molecular Biology, John Wiley & Sons, New York. N.Y.

[1310] A variety of expression vector/host systems are utilized to contain and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with virus expression vectors (*e.g.*, baculovirus); plant cell systems transformed with virus expression vectors (*e.g.*, cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (*e.g.*, Ti or pBR322 plasmids); or animal cell systems. Within one embodiment, the variable regions of a gene expressing a monoclonal antibody of interest are amplified from a hybridoma cell using nucleotide primers. These primers are synthesized by one of ordinary skill in the art, or may be purchased from commercially available sources (*see, e.g.*, Stratagene (La Jolla, California), which sells primers for amplifying mouse and human variable regions. The primers are used to amplify heavy or light chain variable regions, which are then inserted into vectors such as ImmunoZAP™ H or ImmunoZAP™ L (Stratagene), respectively. These vectors are then introduced into *E. coli*, yeast, or mammalian-based systems for expression. Large amounts of a single-chain protein containing a fusion of the V_H and V_L domains are produced using these methods (*see* Bird *et al.*, *Science* 242:423-426 (1988)).

[1311] The "control elements" or "regulatory sequences" present in an expression vector are those non-translated regions of the vector, *e.g.*, enhancers, promoters, 5' and 3' untranslated regions, that interact with host cellular proteins to carry out transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription and translation elements, including constitutive and inducible promoters, is used.

[1312] Examples of promoters suitable for use with prokaryotic hosts include the phoa promoter, β-lactamase and lactose promoter systems, alkaline phosphatase promoter, a tryptophan (trp) promoter system, and hybrid promoters such as the tac promoter. However, other known bacterial promoters are suitable. Promoters for use in bacterial systems also usually contain a Shine-Dalgarno sequence operably linked to the DNA encoding the polypeptide. Inducible promoters such as the hybrid lacZ promoter of the PBLUESCRIPT

phagemid (Stratagene, La Jolla, Calif.) or PSPORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like are used.

[1313] A variety of promoter sequences are known for eukaryotes and any are used according to the present invention. Virtually all eukaryotic genes have an AT-rich region located approximately 25 to 30 bases upstream from the site where transcription is initiated. Another sequence found 70 to 80 bases upstream from the start of transcription of many genes is a CNCAAT region where N may be any nucleotide. At the 3' end of most eukaryotic genes is an AATAAA sequence that may be the signal for addition of the poly A tail to the 3' end of the coding sequence. All of these sequences are suitably inserted into eukaryotic expression vectors.

[1314] In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are generally preferred. Polypeptide expression from vectors in mammalian host cells aer controlled, for example, by promoters obtained from the genomes of viruses such as polyoma virus, fowlpox virus, adenovirus (*e.g.*, Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus (CMV), a retrovirus, hepatitis-B virus and most preferably Simian Virus 40 (SV40), from heterologous mammalian promoters, *e.g.*, the actin promoter or an immunoglobulin promoter, and from heat-shock promoters, provided such promoters are compatible with the host cell systems. If it is necessary to generate a cell line that contains multiple copies of the sequence encoding a polypeptide, vectors based on SV40 or EBV may be advantageously used with an appropriate selectable marker. One example of a suitable expression vector is pcDNA-3.1 (Invitrogen, Carlsbad, CA), which includes a CMV promoter.

[1315] A number of viral-based expression systems are available for mammalian expression of polypeptides. For example, in cases where an adenovirus is used as an expression vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus that is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) Proc. Natl. Acad. Sci. 81:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

[1316] In bacterial systems, any of a number of expression vectors are selected depending upon the use intended for the expressed polypeptide. For example, when large quantities are

desired, vectors that direct high level expression of fusion proteins that are readily purified are used. Such vectors include, but are not limited to, the multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the sequence encoding the polypeptide of interest may be ligated into the vector in frame with sequences for the amino-terminal Met and the subsequent 7 residues of β-galactosidase, so that a hybrid protein is produced; pIN vectors (Van Heeke, G. and S. M. Schuster (1989) J. Biol. Chem. 264:5503-5509); and the like. pGEX Vectors (Promega, Madison, WI) are also used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems are designed to include heparin, thrombin, or factor XA protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

[1317] In the yeast, *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH are used. Examples of other suitable promoter sequences for use with yeast hosts include the promoters for 3-phosphoglycerate kinase or other glycolytic enzymes, such as enolase, glyceraldehyde-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase. For reviews, see Ausubel *et al.* (*supra*) and Grant *et al.* (1987) Methods Enzymol. 153:516-544. Other yeast promoters that are inducible promoters having the additional advantage of transcription controlled by growth conditions include the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, metallothionein, glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization. Suitable vectors and promoters for use in yeast expression are further described in EP 73,657. Yeast enhancers also are advantageously used with yeast promoters.

[1318] In cases where plant expression vectors are used, the expression of sequences encoding polypeptides are driven by any of a number of promoters. For example, viral promoters such as the 35S and 19S promoters of CaMV are used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) *EMBO J. 6*:307-311. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters are used (Coruzzi, G. et al. (1984) EMBO J. *3*:1671-1680; Broglie, R. *et al.* (1984) Science 224:838-843; and Winter, J., *et al.* (1991) Results Probl. Cell Differ. *17*:85-105).

These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (*see, e.g.*, Hobbs, S. or Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

[1319] An insect system is also used to express a polypeptide of interest. For example, in one such system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The sequences encoding the polypeptide are cloned into a non-essential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence renders the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses are then used to infect, for example, *S. frugiperda* cells or *Trichoplusia* larvae, in which the polypeptide of interest is expressed (Engelhard, E. K. *et al.* (1994) Proc. Natl. Acad. Sci. 91 :3224-3227).

[1320] Specific initiation signals are also used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous translational control signals including the ATG initiation codon are provided. Furthermore, the initiation codon is in the correct reading frame to ensure correct translation of the inserted polynucleotide. Exogenous translational elements and initiation codons are of various origins, both natural and synthetic.

[1321] Transcription of a DNA encoding a polypeptide of the invention is often increased by inserting an enhancer sequence into the vector. Many enhancer sequences are known, including, *e.g.*, those identified in genes encoding globin, elastase, albumin, α-fetoprotein, and insulin. Typically, however, an enhancer from a eukaryotic cell virus is used. Examples include the SV40 enhancer on the late side of the replication origin (bp 100-270), the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and adenovirus enhancers. See also Yaniv, Nature 297:17-18 (1982) on enhancing elements for activation of eukaryotic promoters. The enhancer is spliced into the vector at a position 5' or 3' to the polypeptide-encoding sequence, but is preferably located at a site 5' from the promoter.

[1322] Expression vectors used in eukaryotic host cells (yeast, fungi, insect, plant, animal, human, or nucleated cells from other multicellular organisms) typically also contain sequences necessary for the termination of transcription and for stabilizing the mRNA. Such sequences are commonly available from the 5' and, occasionally 3', untranslated regions of eukaryotic or viral DNAs or cDNAs. These regions contain nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA encoding anti-PSCA antibody. One useful transcription termination component is the bovine growth hormone polyadenylation region. See WO94/11026 and the expression vector disclosed therein.

[1323] Suitable host cells for cloning or expressing the DNA in the vectors herein are the prokaryote, yeast, plant or higher eukaryote cells described above. Examples of suitable prokaryotes for this purpose include eubacteria, such as Gram-negative or Gram-positive organisms, for example, *Enterobacteriaceae* such as *Escherichia, e.g., E. coli, Enterobacter, Erwinia, Klebsiella, Proteus, Salmonella, e.g., Salmonella typhimurium, Serratia, e.g., Serratia marcescans*, and *Shigella*, as well as *Bacilli* such as *B. subtilis* and *B. licheniformis* (*e.g., B. licheniformis* 41P disclosed in DD 266,710 published 12 Apr. 1989), *Pseudomonas* such as *P. aeruginosa*, and *Streptomyces*. One preferred *E. coli* cloning host is *E. coli* 294 (ATCC 31,446), although other strains such as *E. coli* B, *E. coli* X1776 (ATCC 31,537), and *E. coli* W3110 (ATCC 27,325) are suitable. These examples are illustrative rather than limiting.

[1324] *Saccharomyces cerevisiae*, or common baker's yeast, is the most commonly used among lower eukaryotic host microorganisms. However, a number of other genera, species, and strains are commonly available and used herein, such as *Schizosaccharomyces pombe*; *Kluyveromyces* hosts such as, *e.g., K lactis, K. fragilis* (ATCC 12,424), *K. bulgaricus* (ATCC 16,045), *K wickeramii* (ATCC 24,178), *K. waltii* (ATCC 56,500), *K. drosophilarum* (ATCC 36,906), *K. thermotolerans*, and *K. marxianus*; *yarrowia* (EP 402,226); *Pichia pastoris.* (EP 183,070); *Candida*; *Trichoderma reesia* (EP 244,234); *Neurospora crassa*; *Schwanniomyces* such as *Schwanniomyces occidentalis*; and filamentous fungi such as, *e.g., Neurospora, Penicillium, Tolypocladium*, and *Aspergillus* hosts such as *A. nidulans* and *A. niger.*

[1325] In certain embodiments, a host cell strain is chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation. glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing that cleaves a "prepro" form of the protein is also used to facilitate correct

insertion, folding and/or function. Different host cells such as CHO, COS, HeLa, MDCK, HEK293, and WI38, which have specific cellular machinery and characteristic mechanisms for such post-translational activities, are chosen to ensure the correct modification and processing of the foreign protein.

[1326] Methods and reagents specifically adapted for the expression of antibodies or fragments thereof are also known and available in the art, including those described, *e.g.*, in U.S. Patent Nos. 4,816,567 and 6,331,415. In various embodiments, antibody heavy and light chains, or fragments thereof, are expressed from the same or separate expression vectors. In one embodiment, both chains are expressed in the same cell, thereby facilitating the formation of a functional antibody or fragment thereof.

[1327] Full length antibody, antibody fragments, and antibody fusion proteins are produced in bacteria, in particular when glycosylation and Fc effector function are not needed, such as when the therapeutic antibody is conjugated to a cytotoxic agent (*e.g.*, a toxin) and the immunoconjugate by itself shows effectiveness in infected cell destruction. For expression of antibody fragments and polypeptides in bacteria, see, *e.g.*, U.S. Pat. Nos. 5,648,237, 5,789,199, and 5,840,523, which describes translation initiation region (TIR) and signal sequences for optimizing expression and secretion. After expression, the antibody is isolated from the *E. coli* cell paste in a soluble fraction and can be purified through, *e.g.*, a protein A or G column depending on the isotype. Final purification can be carried out using a process similar to that used for purifying antibody expressed *e.g.*, in CHO cells.

[1328] Suitable host cells for the expression of glycosylated polypeptides and antibodies are derived from multicellular organisms. Examples of invertebrate cells include plant and insect cells. Numerous baculoviral strains and variants and corresponding permissive insect host cells from hosts such as *Spodoptera frugiperda* (caterpillar), *Aedes aegypti* (mosquito), *Aedes albopicius* (mosquito), *Drosophila melanogaster* (fruitfly), and *Bombyx mori* have been identified. A variety of viral strains for transfection are publicly available, *e.g.*, the L-1 variant of *Autographa californica* NPV and the Bm-5 strain of *Bombyx mori* NPV, and such viruses are used as the virus herein according to the present invention, particularly for transfection of *Spodoptera frugiperda* cells. Plant cell cultures of cotton, corn, potato, soybean, petunia, tomato, and tobacco are also utilized as hosts.

[1329] Methods of propagation of antibody polypeptides and fragments thereof in vertebrate cells in culture (tissue culture) are encompassed by the invention. Examples of mammalian host cell lines used in the methods of the invention are monkey kidney CV1 line transformed

by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham *et al.*, J. Gen Virol. 36:59 (1977)); baby hamster kidney cells (BHK, ATCC CCL 10); Chinese hamster ovary cells/-DHFR (CHO, Urlaub *et al.*, Proc. Natl. Acad. Sci. USA 77:4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod. 23:243-251 (1980)); monkey kidney cells (CV1 ATCC CCL 70); African green monkey kidney cells (VERO-76, ATCC CRL-1587); human cervical carcinoma cells (HELA, ATCC CCL 2); canine kidney cells (MDCK, ATCC CCL 34); buffalo rat liver cells (BRL 3A, ATCC CRL 1442); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); mouse mammary tumor (MMT 060562, ATCC CCL51); TR1 cells (Mather *et al.*, Annals N.Y. Acad. Sci. 383:44-68 (1982)); MRC 5 cells; FS4 cells; and a human hepatoma line (Hep G2).

[1330] Host cells are transformed with the above-described expression or cloning vectors for polypeptide production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences.

[1331] For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines that stably express a polynucleotide of interest are transformed using expression vectors that contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells are allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells that successfully express the introduced sequences. Resistant clones of stably transformed cells are proliferated using tissue culture techniques appropriate to the cell type.

[1332] A plurality of selection systems are used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler, M. *et al.* (1977) *Cell 11*:223-32) and adenine phosphoribosyltransferase (Lowy, I. *et al.* (1990) *Cell 22*:817-23) genes that are employed in tk$^-$ or aprt$^-$ cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance is used as the basis for selection; for example, dhfr, which confers resistance to methotrexate (Wigler, M. *et al.* (1980) *Proc. Natl. Acad. Sci. 77*:3567-70); npt, which confers resistance to the aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. *et al.*(1981) *J. Mol. Biol. 150*:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional

selectable genes have been described. For example, trpB allows cells to utilize indole in place of tryptophan, and hisD allows cells to utilize histinol in place of histidine (Hartman, S. C. and R. C. Mulligan (1988) *Proc. Natl. Acad. Sci. 85*:8047-51). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. *et al.* (1995) *Methods Mol. Biol. 55*:121-131).

[1333] Although the presence/absence of marker gene expression suggests that the gene of interest is also present, its presence and expression is confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences are identified by the absence of marker gene function. Alternatively, a marker gene is placed in tandem with a polypeptide-encoding sequence under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

[1334] Alternatively, host cells that contain and express a desired polynucleotide sequence are identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations and protein bioassay or immunoassay techniques which include, for example, membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

[1335] A variety of protocols for detecting and measuring the expression of polynucleotide-encoded products, using either polyclonal or monoclonal antibodies specific for the product are known in the art. Nonlimiting examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on a given polypeptide is preferred for some applications, but a competitive binding assay may also be employed. These and other assays are described, among other places, in Hampton, R. *et al.* (1990; Serological Methods, a Laboratory Manual, APS Press, St Paul. Minn.) and Maddox, D. E. *et al.* (1983; J. Exp. Med. *158*:1211-1216).

[1336] Various labels and conjugation techniques are known by those skilled in the art and are used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR amplification using a labeled nucleotide.

Alternatively, the sequences, or any portions thereof are cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and are used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures are conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which are used include, but are not limited to, radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

[1337] The polypeptide produced by a recombinant cell is secreted or contained intracellularly depending on the sequence and/or the vector used. Expression vectors containing polynucleotides of the invention are designed to contain signal sequences that direct secretion of the encoded polypeptide through a prokaryotic or eukaryotic cell membrane.

[1338] In certain embodiments, a polypeptide of the invention is produced as a fusion polypeptide further including a polypeptide domain that facilitates purification of soluble proteins. Such purification-facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Amgen, Seattle, WA). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen. San Diego, CA) between the purification domain and the encoded polypeptide are used to facilitate purification. An exemplary expression vector provides for expression of a fusion protein containing a polypeptide of interest and a nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. *et al.* (1992, Prot. Exp. Purif. *3*:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors used for producing fusion proteins is provided in Kroll, D. J. *et al.* (1993; *DNA Cell Biol. 12*:441-453).

[1339] In certain embodiments, a polypeptide of the present invention is fused with a heterologous polypeptide, which may be a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. The heterologous signal sequence selected preferably is one that is recognized and processed (*i.e.*,

cleaved by a signal peptidase) by the host cell. For prokaryotic host cells, the signal sequence is selected, for example, from the group of the alkaline phosphatase, penicillinase, lpp, or heat-stable enterotoxin II leaders. For yeast secretion, the signal sequence is selected from, *e.g.*, the yeast invertase leader, α factor leader (including *Saccharomyces* and *Kluyveromyces* α factor leaders), or acid phosphatase leader, the *C. albicans* glucoamylase leader, or the signal described in WO 90/13646. In mammalian cell expression, mammalian signal sequences as well as viral secretory leaders, for example, the herpes simplex gD signal, are available.

[1340] When using recombinant techniques, the polypeptide or antibody is produced intracellularly, in the periplasmic space, or directly secreted into the medium. If the polypeptide or antibody is produced intracellularly, as a first step, the particulate debris, either host cells or lysed fragments, are removed, for example, by centrifugation or ultrafiltration. Carter *et al.*, Bio/Technology 10:163-167 (1992) describe a procedure for isolating antibodies that are secreted to the periplasmic space of *E. coli*. Briefly, cell paste is thawed in the presence of sodium acetate (pH 3.5), EDTA, and phenylmethylsulfonylfluoride (PMSF) over about 30 min. Cell debris is removed by centrifugation. Where the polypeptide or antibody is secreted into the medium, supernatants from such expression systems are generally first concentrated using a commercially available protein concentration filter, for example, an Amicon or Millipore Pellicon ultrafiltration unit. Optionally, a protease inhibitor such as PMSF is included in any of the foregoing steps to inhibit proteolysis and antibiotics are included to prevent the growth of adventitious contaminants.

[1341] The polypeptide or antibody composition prepared from the cells are purified using, for example, hydroxylapatite chromatography, gel electrophoresis, dialysis, and affinity chromatography, with affinity chromatography being the preferred purification technique. The suitability of protein A as an affinity ligand depends on the species and isotype of any immunoglobulin Fc domain that is present in the polypeptide or antibody. Protein A is used to purify antibodies or fragments thereof that are based on human γ_1, γ_2, or γ_4 heavy chains (Lindmark *et al.*, J. Immunol. Meth. 62:1-13 (1983)). Protein G is recommended for all mouse isotypes and for human γ_3 (Guss *et al.*, EMBO J. 5:15671575 (1986)). The matrix to which the affinity ligand is attached is most often agarose, but other matrices are available. Mechanically stable matrices such as controlled pore glass or poly(styrenedivinyl)benzene allow for faster flow rates and shorter processing times than can be achieved with agarose. Where the polypeptide or antibody comprises a C_H 3 domain, the Bakerbond ABX™ resin (J.

T. Baker, Phillipsburg, N.J.) is useful for purification. Other techniques for protein purification such as fractionation on an ion-exchange column, ethanol precipitation, Reverse Phase HPLC, chromatography on silica, chromatography on heparin SEPHAROSE™ chromatography on an anion or cation exchange resin (such as a polyaspartic acid column), chromatofocusing, SDS-PAGE, and ammonium sulfate precipitation are also available depending on the polypeptide or antibody to be recovered.

[1342] Following any preliminary purification step(s), the mixture comprising the polypeptide or antibody of interest and contaminants are subjected to low pH hydrophobic interaction chromatography using an elution buffer at a pH between about 2.5-4.5, preferably performed at low salt concentrations (*e.g.*, from about 0-0.25M salt).

Pharmaceutical Compositions

[1343] The invention further includes pharmaceutical formulations including a polypeptide, antibody, or modulator of the present invention, at a desired degree of purity, and a pharmaceutically acceptable carrier, excipient, or stabilizer (Remingion's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980)). In certain embodiments, pharmaceutical formulations are prepared to enhance the stability of the polypeptide or antibody during storage, *e.g.*, in the form of lyophilized formulations or aqueous solutions.

[1344] Acceptable carriers, excipients, or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include, *e.g.*, buffers such as acetate, Tris, phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride, benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; tonicifiers such as trehalose and sodium chloride; sugars such as sucrose, mannitol, trehalose or sorbitol; surfactant such as polysorbate; salt-forming counter-ions such as sodium; metal complexes (e.g. Zn-protein complexes); and/or non-ionic surfactants such as TWEEN™, PLURONICS™ or polyethylene glycol (PEG). In certain embodiments, the therapeutic formulation preferably

comprises the polypeptide or antibody at a concentration of between 5-200 mg/ml, preferably between 10-100 mg/ml.

[1345] The formulations herein also contain one or more additional therapeutic agents suitable for the treatment of the particular indication, e.g., infection being treated, or to prevent undesired side-effects. Preferably, the additional therapeutic agent has an activity complementary to the polypeptide or antibody of the resent invention, and the two do not adversely affect each other. For example, in addition to the polypeptide or antibody of the invention, an additional or second antibody, anti-viral agent, anti-infective agent and/or cardioprotectant is added to the formulation. Such molecules are suitably present in the pharmaceutical formulation in amounts that are effective for the purpose intended.

[1346] The active ingredients, *e.g.*, polypeptides and antibodies of the invention and other therapeutic agents, are also entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and polymethylmethacylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remingion's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980).

[1347] Sustained-release preparations are prepared. Suitable examples of sustained-release preparations include, but are not limited to, semi-permeable matrices of solid hydrophobic polymers containing the antibody, which matrices are in the form of shaped articles, *e.g.*, films, or microcapsules. Nonlimiting examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Pat. No. 3,773,919), copolymers of L-glutamic acid and γ ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOT™ (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxyburyric acid.

[1348] Formulations to be used for *in vivo* administration are preferably sterile. This is readily accomplished by filtration through sterile filtration membranes.

Diagnostic Uses

[1349] Antibodies and fragments thereof, and therapeutic compositions, of the invention specifically bind or preferentially bind to infected cells or tissue, as compared to normal

control cells and tissue. Thus, these influenza A antibodies are used to detect infected cells or tissues in a patient, biological sample, or cell population, using any of a variety of diagnostic and prognostic methods, including those described herein. The ability of an anti-M2e or anti-HA specific antibody to detect infected cells depends upon its binding specificity, which is readily determined by testing its ability to bind to infected cells or tissues obtained from different patients, and/or from patients infected with different strains of Influenza A.

[1350] Diagnostic methods generally involve contacting a biological sample obtained from a patient, such as, *e.g.*, blood, serum, saliva, urine, sputum, a cell swab sample, or a tissue biopsy, with an Influenza A, e.g., human monoclonal anti-M2e or anti-HA antibody, and determining whether the antibody preferentially binds to the sample as compared to a control sample or predetermined cut-off value, thereby indicating the presence of infected cells. In particular embodiments, at least two-fold, three-fold, or five-fold more human monoclonal anti-M2e or anti-HA antibody binds to an infected cell as compared to an appropriate control normal cell or tissue sample. A pre-determined cut-off value is determined, *e.g.*, by averaging the amount of human monoclonal anti-M2e or anti-HA antibody that binds to several different appropriate control samples under the same conditions used to perform the diagnostic assay of the biological sample being tested. Alternatively, or in addition, a hemagglutinin (HA) protein is substituted for an Influenza virus in the above method. The HA protein is presented on the surface of a virus, host cell (e.g. any mammalian cell), or in a recombinant and soluble form. In the HA version of this diagnostic method, the control protein is a denatured HA protein, a linear HA peptide, an unrelated protein of similar size and shape, but dissimilar sequence, or a pre-determined cut-off value.

[1351] Bound antibody is detected using procedures described herein and known in the art. In certain embodiments, diagnostic methods of the invention are practiced using human monoclonal anti-M2e or anti-HA antibodies that are conjugated to a detectable label, *e.g.*, a fluorophore, to facilitate detection of bound antibody. However, they are also practiced using methods of secondary detection of the human monoclonal anti-M2e or anti-HA antibody. These include, for example, RIA, ELISA, precipitation, agglutination, complement fixation and immuno-fluorescence.

[1352] In certain procedures, the human monoclonal anti-M2e or anti-HA antibodies are labeled. The label is detected directly. Exemplary labels that are detected directly include, but are not limited to, radiolabels and fluorochromes. Alaternatively, or in addition, labels are moieties, such as enzymes, that must be reacted or derivatized to be detected. Nonlimiting

examples of isotope labels are ^{99}Tc, ^{14}C, ^{131}I, ^{125}I, ^{3}H, ^{32}P and ^{35}S. Fluorescent materials that are used include, but are not limited to, for example, fluorescein and its derivatives, rhodamine and its derivatives, auramine, dansyl, umbelliferone, luciferia, 2,3-dihydrophthalazinediones, horseradish peroxidase, alkaline phosphatase, lysozyme, and glucose-6-phosphate dehydrogenase.

[1353] An enzyme label is detected by any of the currently utilized colorimetric, spectrophotometric, fluorospectro-photometric or gasometric techniques. Many enzymes which are used in these procedures are known and utilized by the methods of the invention. Nonlimiting examples are peroxidase, alkaline phosphatase, β-glucuronidase, β-D-glucosidase, β-D-galactosidase, urease, glucose oxidase plus peroxidase, galactose oxidase plus peroxidase and acid phosphatase.

[1354] The antibodies are tagged with such labels by known methods. For instance, coupling agents such as aldehydes, carbodiimides, dimaleimide, imidates, succinimides, bid-diazotized benzadine and the like are used to tag the antibodies with the above-described fluorescent, chemiluminescent, and enzyme labels. An enzyme is typically combined with an antibody using bridging molecules such as carbodiimides, periodate, diisocyanates, glutaraldehyde and the like. Various labeling techniques are described in Morrison, Methods in Enzymology 32b, 103 (1974), Syvanen *et al.*, J. Biol. Chem. 284, 3762 (1973) and Bolton and Hunter, Biochem J. 133, 529(1973).

[1355] Human monoclonal anti-M2e or anti-HA antibodies of the present invention are capable of differentiating between patients with and patients without an Influenza A infection, and determining whether or not a patient has an infection, using the representative assays provided herein. According to one method, a biological sample is obtained from a patient suspected of having or known to have an influenza A infection. In preferred embodiments, the biological sample includes cells from the patient. The sample is contacted with a human monoclonal anti-M2e or anti-HA antibody, *e.g.*, for a time and under conditions sufficient to allow the human monoclonal anti-M2e or anti-HA antibody to bind to infected cells present in the sample. For instance, the sample is contacted with a human monoclonal anti-M2e or anti-HA antibody for 10 seconds, 30 seconds, 1 minute, 5 minutes, 10 minutes, 30 minutes, 1 hour, 6 hours, 12 hours, 24 hours, 3 days or any point in between. The amount of bound human monoclonal anti-M2e or anti-HA antibody is determined and compared to a control value, which may be, *e.g.*, a pre-determined value or a value determined from normal tissue sample. An increased amount of antibody bound to the

patient sample as compared to the control sample is indicative of the presence of infected cells in the patient sample.

[1356] In a related method, a biological sample obtained from a patient is contacted with a human monoclonal anti-M2e or anti-HA antibody for a time and under conditions sufficient to allow the antibody to bind to infected cells. Bound antibody is then detected, and the presence of bound antibody indicates that the sample contains infected cells. This embodiment is particularly useful when the human monoclonal anti-M2e or anti-HA antibody does not bind normal cells at a detectable level.

[1357] Different human monoclonal anti-M2e or anti-HA antibodies possess different binding and specificity characteristics. Depending upon these characteristics, particular human monoclonal anti-M2e or anti-HA antibodies are used to detect the presence of one or more strains of Influenza A. For example, certain antibodies bind specifically to only one or several strains of Influenza virus, whereas others bind to all or a majority of different strains of Influenza virus. Antibodies specific for only one strain of Influenza A are used to identify the strain of an infection.

[1358] In certain embodiments, antibodies that bind to an infected cell preferably generate a signal indicating the presence of an infection in at least about 20% of patients with the infection being detected, more preferably at least about 30% of patients. Alternatively, or in addition, the antibody generates a negative signal indicating the absence of the infection in at least about 90% of individuals without the infection being detected. Each antibody satisfies the above criteria; however, antibodies of the present invention are used in combination to improve sensitivity.

[1359] The present invention also includes kits useful in performing diagnostic and prognostic assays using the antibodies of the present invention. Kits of the invention include a suitable container comprising a human monoclonal anti-M2e or anti-HA antibody of the invention in either labeled or unlabeled form. In addition, when the antibody is supplied in a labeled form suitable for an indirect binding assay, the kit further includes reagents for performing the appropriate indirect assay. For example, the kit includes one or more suitable containers including enzyme substrates or derivatizing agents, depending on the nature of the label. Control samples and/or instructions are also included.

Therapeutic/ Prophylactic Uses

[1360] Passive immunization has proven to be an effective and safe strategy for the prevention and treatment of viral diseases. (*See* Keller et al., Clin. Microbiol. Rev. 13:602-14

(2000); Casadevall, Nat. Biotechnol. 20:114 (2002); Shibata et al., Nat. Med. 5:204-10 (1999); and Igarashi et al., Nat. Med. 5:211-16 (1999), each of which are incorporated herein by reference)). Passive immunization using human monoclonal antibodies provide an immediate treatment strategy for emergency prophylaxis and treatment of influenza

[1361] Human monoclonal anti-M2e or anti-HA antibodies and fragments thereof, and therapeutic compositions, of the invention specifically bind or preferentially bind to infected cells, as compared to normal control uninfected cells and tissue. Thus, these human monoclonal anti-M2e or anti-HA antibodies are used to selectively target infected cells or tissues in a patient, biological sample, or cell population. In light of the infection-specific binding properties of these antibodies, the present invention provides methods of regulating (*e.g.*, inhibiting) the growth of infected cells, methods of killing infected cells, and methods of inducing apoptosis of infected cells. These methods include contacting an infected cell with a human monoclonal anti-M2e or anti-HA antibody of the invention. These methods are practiced *in vitro*, *ex vivo*, and *in vivo*.

[1362] In various embodiments, antibodies of the invention are intrinsically therapeutically active. Alternatively, or in addition, antibodies of the invention are conjugated to a cytotoxic agent or growth inhibitory agent, *e.g.*, a radioisotope or toxin, which is used in treating infected cells bound or contacted by the antibody.

[1363] In one embodiment, the invention provides methods of treating or preventing infection in a patient, including the steps of providing a human monoclonal anti-M2e or anti-HA antibody of the invention to a patient diagnosed with, at risk of developing, or suspected of having an Influenza A infection. The methods of the invention are used in the first-line treatment of the infection, follow-on treatment, or in the treatment of a relapsed or refractory infection. Treatment with an antibody of the invention is a stand alone treatment. Alternatively, treatment with an antibody of the invention is one component or phase of a combination therapy regime, in which one or more additional therapeutic agents are also used to treat the patient.

[1364] Subjects at risk for an influenza virus -related diseases or disorders include patients who have come into contact with an infected person or who have been exposed to the influenza virus in some other way. Administration of a prophylactic agent can occur prior to the manifestation of symptoms characteristic of the influenza virus -related disease or disorder, such that a disease or disorder is prevented or, alternatively, delayed in its progression.

[1365] In various aspects, the human monoclonal anti-M2e or anti-HA is administered substantially contemporaneously with or following infection of the subject, i.e., therapeutic treatment. In another aspect, the antibody provides a therapeutic benefit. In various aspects, a therapeutic benefit includes reducing or decreasing progression, severity, frequency, duration or probability of one or more symptoms or complications of influenza infection, virus titer, virus replication or an amount of a viral protein of one or more influenza strains. still another aspect, a therapeutic benefit includes hastening or accelerating a subject's recovery from influenza infection.

[1366] Methods for preventing an increase in influenza virus titer, virus replication, virus proliferation or an amount of an influenza viral protein in a subject are further provided. In one embodiment, a method includes administering to the subject an amount of a human monoclonal anti-M2e or anti-HA antibody effective to prevent an increase in influenza virus titer, virus replication or an amount of an influenza viral protein of one or more influenza strains or isolates in the subject.

[1367] Methods for protecting a subject from infection or decreasing susceptibility of a subject to infection by one or more influenza strains/isolates or subtypes, i.e., prophylactic methods, are additionally provided. In one embodiment, a method includes administering to the subject an amount of human monoclonal anti-M2e or anti-HA antibody that specifically binds influenza M2 or HA, respectively, effective to protect the subject from infection, or effective to decrease susceptibility of the subject to infection, by one or more influenza strains/isolates or subtypes.

[1368] Optionally, the subject is further administered with a second agent such as, but not limited to, an influenza virus antibody, an anti-viral drug such as a neuraminidase inhibitor, a HA inhibitor, a sialic acid inhibitor or an M2 ion channel inhibitor, a viral entry inhibitor or a viral attachment inhibitor. The M2 ion channel inhibitor is for example amantadine or rimantadine. The neuraminidase inhibitor for example zanamivir, or oseltamivir phosphate.

[1369] Symptoms or complications of influenza infection that can be reduced or decreased include, for example, chills, fever, cough, sore throat, nasal congestion, sinus congestion, nasal infection, sinus infection, body ache, head ache, fatigue, pneumonia, bronchitis, ear infection, ear ache or death.

[1370] For *in vivo* treatment of human and non-human patients, the patient is usually administered or provided a pharmaceutical formulation including a human monoclonal anti-M2e or anti-HA antibody of the invention. When used for *in vivo* therapy, the antibodies of

the invention are administered to the patient in therapeutically effective amounts (*i.e.*, amounts that eliminate or reduce the patient's viral burden). The antibodies are administered to a human patient, in accord with known methods, such as intravenous administration, *e.g.*, as a bolus or by continuous infusion over a period of time, by intramuscular, intraperitoneal, intracerobrospinal, subcutaneous, intra-articular, intrasynovial, intrathecal, oral, topical, or inhalation routes. The antibodies may be administered parenterally, when possible, at the target cell site, or intravenously. Intravenous or subcutaneous administration of the antibody is preferred in certain embodiments. Therapeutic compositions of the invention are administered to a patient or subject systemically, parenterally, or locally.

[1371] For parenteral administration, the antibodies are formulated in a unit dosage injectable form (solution, suspension, emulsion) in association with a pharmaceutically acceptable, parenteral vehicle. Examples of such vehicles are water, saline, Ringer's solution, dextrose solution, and 5% human serum albumin. Nonaqueous vehicles such as fixed oils and ethyl oleate are also used. Liposomes are used as carriers. The vehicle contains minor amounts of additives such as substances that enhance isotonicity and chemical stability, *e.g.*, buffers and preservatives. The antibodies are typically formulated in such vehicles at concentrations of about 1 mg/ml to 10 mg/ml.

[1372] The dose and dosage regimen depends upon a variety of factors readily determined by a physician, such as the nature of the infection and the characteristics of the particular cytotoxic agent or growth inhibitory agent conjugated to the antibody (when used), *e.g.*, its therapeutic index, the patient, and the patient's history. Generally, a therapeutically effective amount of an antibody is administered to a patient. In particular embodiments, the amount of antibody administered is in the range of about 0.1 mg/kg to about 50 mg/kg of patient body weight. Depending on the type and severity of the infection, about 0.1 mg/kg to about 50 mg/kg body weight (*e.g.*, about 0.1-15 mg/kg/dose) of antibody is an initial candidate dosage for administration to the patient, whether, for example, by one or more separate administrations, or by continuous infusion. The progress of this therapy is readily monitored by conventional methods and assays and based on criteria known to the physician or other persons of skill in the art.

[1373] In one particular embodiment, an immunoconjugate including the antibody conjugated with a cytotoxic agent is administered to the patient. Preferably, the immunoconjugate is internalized by the cell, resulting in increased therapeutic efficacy of the immunoconjugate in killing the cell to which it binds. In one embodiment, the cytotoxic agent

targets or interferes with the nucleic acid in the infected cell. Examples of such cytotoxic agents are described above and include, but are not limited to, maytansinoids, calicheamicins, ribonucleases and DNA endonucleases.

[1374] Other therapeutic regimens are combined with the administration of the HuM2e antibody of the present invention. The combined administration includes co-administration, using separate formulations or a single pharmaceutical formulation, and consecutive administration in either order, wherein preferably there is a time period while both (or all) active agents simultaneously exert their biological activities. Preferably such combined therapy results in a synergistic therapeutic effect.

[1375] In certain embodiments, it is desirable to combine administration of an antibody of the invention with another antibody directed against another antigen associated with the infectious agent.

[1376] Aside from administration of the antibody protein to the patient, the invention provides methods of administration of the antibody by gene therapy. Such administration of nucleic acid encoding the antibody is encompassed by the expression "administering a therapeutically effective amount of an antibody". See, for example, PCT Patent Application Publication WO96/07321 concerning the use of gene therapy to generate intracellular antibodies.

[1377] In another embodiment, human monoclonal anti-M2e or anti-HA antibodies of the invention are used to determine the structure of bound antigen, e.g., conformational epitopes, the structure of which is then used to develop a vaccine having or mimicking this structure, e.g., through chemical modeling and SAR methods. Such a vaccine could then be used to prevent Influenza A infection.

[1378] All of the above U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification and/or listed in the Application Data Sheetare incorporated herein by reference, in their entirety.

EXAMPLES

Example 1: Screening and Characterization of M2e-specific Antibodies Present in Human Plasma Using Cells Expressing Recombinant M2e Protein

[1379] Fully human monoclonal antibodies specific for M2 and capable of binding to influenza A infected cells and the influenza virus itself were identified in patient serum, as described below.

Expression of M2 in Cell Lines

[1380] An expression construct containing the M2 full length cDNA, corresponding to the derived M2 sequence found in Influenza subtype H3N2, was transfected into 293 cells.

[1381] The M2 cDNA is encoded by the following polynucleotide sequence and SEQ ID NO: 53:

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ATGAGTCTTCTAACCGAGGTCGAAACGCCTATCAGAAACGAATGGGGGTGCAGATGCAACGATTCAAGTGATCCTCTT
GTTGTTGCCGCAAGTATCATTGGGATCCTGCACTTGATATTGTGGATTCTTGATCGTCTTTTTTTCAAATGCATTTAT
CGTCTCTTTAAACACGGTCTGAAAAGAGGGCCTTCTACGGAAGGAGTACCAGAGTCTATGAGGGAAGAATATCGAAAG
GAACAGCAGAGTGCTGTGGATGCTGACGATAGTCATTTTGTCAACATAGAGCTGGAG
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[1382] The cell surface expression of M2 was confirmed using the anti-M2e peptide specific MAb 14C2. Two other variants of M2, from A/Hong Kong/483/1997 (HK483) and A/Vietnam/1203/2004 (VN1203), were used for subsequent analyses, and their expression was determined using M2e-specific monoclonal antibodies of the present invention, since 14C2 binding may be abrogated by the various amino acid substitutions in M2e.

Screening of Antibodies in Peripheral Blood

[1383] Over 120 individual plasma samples were tested for antibodies that bound M2. None of them exhibited specific binding to the M2e peptide. However, 10% of the plasma samples contained antibodies that bound specifically to the 293-M2 H3N2 cell line. This indicates that the antibodies could be categorized as binding to conformational determinants of an M2 homotetramer, and binding to conformational determinants of multiple variants of the M2 homotetramer; they could not be specific for the linear M2e peptide.

Characterization of Anti-M2 MAbs

[1384] The human MAbs identified through this process proved to bind to conformational epitopes on the M2 homotetramer. They bound to the original 293-M2 transfectant, as well as to the two other cell-expressed M2 variants. The 14C2 MAb, in addition to binding the M2e peptide, proved to be more sensitive to the M2 variant sequences. Moreover, 14C2 does not readily bind influenza virions, while the conformation specific anti-M2 MAbs did.

[1385] These results demonstrate that the methods of the invention provide for the identification of M2 MAbs from normal human immune responses to influenza without a need for specific immunization of M2. If used for immunotherapy, these fully human MAbs have the potential to be better tolerated by patients that humanized mouse antibodies. Additionally, and in contrast to 14C2 and the Gemini Biosciences MAbs, which bind to linear M2e peptide, the MAbs of the invention bind to conformational epitopes of M2, and are specific not only for cells infected with A strain influenza, but also for the virus itself. Another advantage of the MAbs of the invention is that they each bind all of the M2 variants yet tested, indicating that they are not restricted to a specific linear amino acid sequence.

Example 2: Identification of M2-Specific Antibodies

[1386] Mononuclear or B cells expressing three of the MAbs identified in human serum as described in Example 1 were diluted into clonal populations and induced to produce antibodies. Antibody containing supernatants were screened for binding to 293 FT cells stably transfected with the full length M2E protein from influenza strain Influenza subtype H3N2. Supernatants which showed positive staining/binding were re-screened again on 293 FT cells stably transfected with the full length M2E protein from influenza strain Influenza subtype H3N2 and on vector alone transfected cells as a control.

[1387] The variable regions of the antibodies were then rescue cloned from the B cell wells whose supernatants showed positive binding. Transient transfections were performed in 293 FT cells to reconstitute and produce these antibodies. Reconstituted antibody supernatants were screened for binding to 293 FT cells stably transfected with the full length M2E protein as detailed above to identify the rescued anti-M2E antibodies. Three different antibodies were identified: 8i10, 21B15 and 23K12. A fourth additional antibody clone was isolated by the rescue screens, 4C2. However, it was not unique and had the exact same sequence as clone 8i10 even though it came from a different donor than clone 8i10.

[1388] The sequences of the kappa and gamma variable regions of these antibodies are provided below.

Clone 8i10 (corresponds to TCN-032):

[1389] The Kappa LC variable region of the anti M2 clone 8i10 was cloned as Hind III to BsiW1 fragment (see below), and is encoded by the following polynucleotide sequences, and SEQ ID NO: 54 (top) and SEQ ID NO: 55 (bottom):

HindIII
AAGCTTCCACCATGGACATGAGGGTCCTCGCTCAGCTCCTGGGGCTCCTGCTACTCTGGCTCCGAGGTG
TTCGAAGGTGGTACCTGTACTCCCAGGAGCGAGTCGAGGACCCCGAGGACGATGAGACCGAGGCTCCAC

CCAGATGTGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCA
GGTCTACACTGTAGGTCTACTGGGTCAGAGGTAGGAGGGACAGACGTAGACATCCTCTGTCTCAGTGGT

TCACTTGCCGGGCGAGTCAGAACATTTACAAGTATTTAAATTGGTATCAGCAGAGACCAGGGAAAGCCC
AGTGAACGGCCCGCTCAGTCTTGTAAATGTTCATAAATTTAACCATAGTCGTCTCTGGTCCCTTTCGGG

CTAAGGGCCTGATCTCTGCTGCATCCGGGTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTGGAT
GATTCCCGGACTAGAGACGACGTAGGCCCAACGTTTCACCCCAGGGTAGTTCCAAGTCACCGTCACCTA

CTGGGACAGATTTCACTCTCACCATCACCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAAC
GACCCTGTCTAAAGTGAGAGTGGTAGTGGTCAGACGTTGGACTTCTAAAACGTTGAATGATGACAGTTG

BsiWI
AGAGTTACAGTCCCCCTCTCACTTTCGGCGGAGGGACCAGGGTGGAGATCAAACGTACG
TCTCAATGTCAGGGGGAGAGTGAAAGCCGCCTCCCTGGTCCCACCTCTAGTTTGCATGC

[1390] The translation of the 8i10 Kappa LC variable region is as follows, polynucleotide sequence (above, SEQ ID NO: 54, top) and amino acid sequence (below, corresponding to residues 1-131 of SEQ ID NO: 56):

HindIII
AAGCTTCCACCATGGACATGAGGGTCCTCGCTCAGCTCCTGGGGCTCCTGCTACTCTGGCTCCGAGGTG
M D M R V L A Q L L G L L L L W L R G

CCAGATGTGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCA
A R C D I Q M T Q S P S S L S A S V G D R V T

TCACTTGCCGGGCGAGTCAGAACATTTACAAGTATTTAAATTGGTATCAGCAGAGACCAGGGAAAGCCC
I T C R A S Q N I Y K Y L N W Y Q Q R P G K A

CTAAGGGCCTGATCTCTGCTGCATCCGGGTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTGGAT
P K G L I S A A S G L Q S G V P S R F S G S G

CTGGGACAGATTTCACTCTCACCATCACCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAAC
S G T D F T L T I T S L Q P E D F A T Y Y C Q

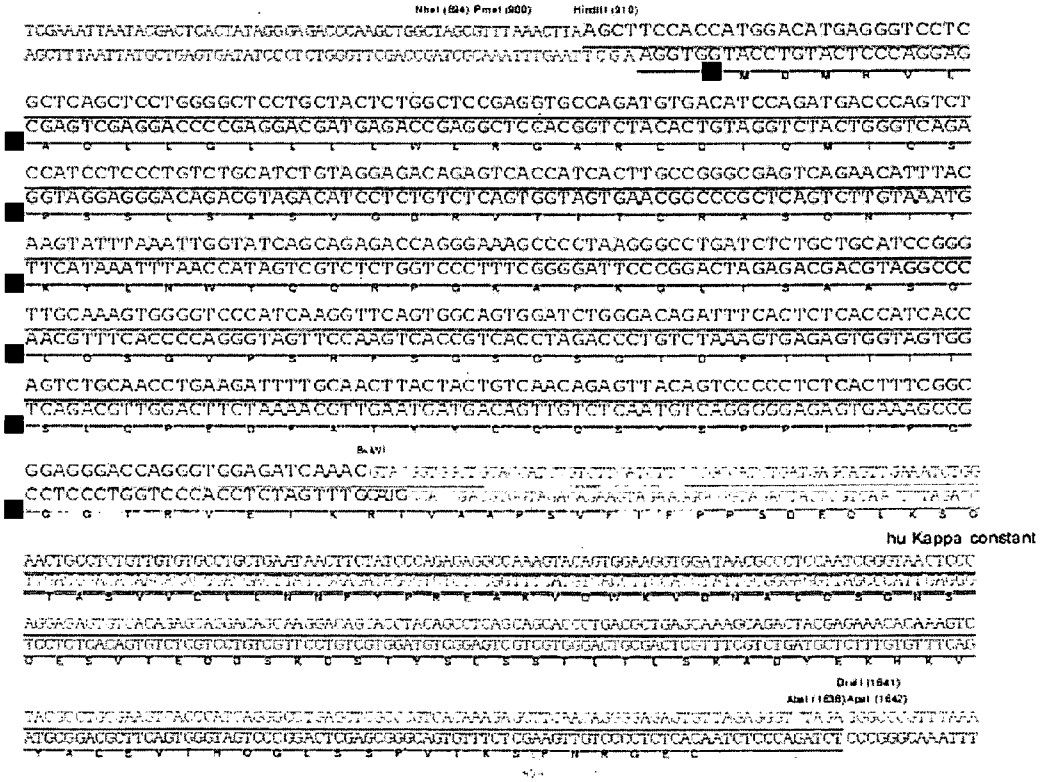
BsiWI
AGAGTTACAGTCCCCCTCTCACTTTCGGCGGAGGGACCAGGGTGGAGATCAAACGTACG
Q S Y S P P L T F G G G T R V E I K R T

[1391] The amino acid sequence of the 8i10 Kappa LC variable region is as follows, with specific domains identified below (CDR sequences defined according to Kabat methods):

M D M R V L A Q L L G L L L L W L R G A R C	VK leader (SEQ ID NO: 57)
D I Q M T Q S P S S L S A S V G D R V T I T C	FR1 (SEQ ID NO: 58)
R A S Q N I Y K Y L N	CDR1(SEQ ID NO: 59)
W Y Q Q R P G K A P K G L I S	FR2 (SEQ ID NO: 60)
A A S G L Q S	CDR2 (SEQ ID NO: 61)

G V P S R F S G S G S G T D F T L T I T S L Q P E D F A T Y Y C	FR3 (SEQ ID NO: 62)
Q Q S Y S P P L T	CDR3 (SEQ ID NO: 63)
F G G G T R V E I K	FR4 (SEQ ID NO: 64)
R T	Start of Kappa constant region

[1392] The following is an example of the Kappa LC variable region of 8i10 cloned into the expression vector pcDNA3.1 which already contained the Kappa LC constant region (upper polynucleotide sequence corresponds to SEQ ID NO: 65, lower polynucleotide sequence corresponds to SEQ ID NO: 66, amino acid sequence corresponds to SEQ ID NO: 56). Bases in black represents pcDNA3.1 vector sequences, underlined bases represent the cloned antibody sequences. The antibodies described herein have also been cloned into the expression vector pCEP4.



[1393] The 8i10 Gamma HC variable region was cloned as a Hind III to Xho 1 fragment, and is encoded the following polynucleotide sequences, and SEQ ID NO: 67 (top) and SEQ ID NO: 68 (bottom).

HindIII

```
AAGCTTCCACCATGAAACACCTGTGGTTCTTCCTTCTCCTGGTGGCAGCTCCCAGCTGGGT
TTCGAAGGTGGTACTTTGTGGACACCAAGAAGGAAGAGGACCACCGTCGAGGGTCGACCCA

CCTGTCCCAGGTGCAATTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTG
GGACAGGGTCCACGTTAACGTCCTCAGCCCGGGTCCTGACCACTTCGGAAGCCTCTGGGAC

TCCCTCACCTGCACTGTCTCTGGTTCGTCCATCAGTAATTACTACTGGAGCTGGATCCGGC
AGGGAGTGGACGTGACAGAGACCAAGCAGGTAGTCATTAATGATGACCTCGACCTAGGCCG

AGTCCCCAGGGAAGGGACTGGAGTGGATTGGGTTTATCTATTACGGTGGAAACACCAAGTA
TCAGGGGTCCCTTCCCTGACCTCACCTAACCCAAATAGATAATGCCACCTTTGTGGTTCAT

CAATCCCTCCCTCAAGAGCCGCGTCACCATATCACAAGACACTTCCAAGAGTCAGGTCTCC
GTTAGGGAGGGAGTTCTCGGCGCAGTGGTATAGTGTTCTGTGAAGGTTCTCAGTCCAGAGG

CTGACGATGAGCTCTGTGACCGCTGCGGAATCGGCCGTCTATTTCTGTGCGAGAGCGTCTT
GACTGCTACTCGAGACACTGGCGACGCCTTAGCCGGCAGATAAAGACACGCTCTCGCAGAA
                                                        XhoI
GTAGTGGTGGTTACTGTATCCTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAG
CATCACCACCAATGACATAGGAACTGATGACCCCGGTCCCTTGGGACCAGTGGCAGAGCTC
```

[1394] The translation of the 8i10 Gamma HC is as follows, polynucleotide sequence (above, SEQ ID NO: 67, top) and amino acid sequence (below, corresponding to residues 1-138 of SEQ ID NO: 69):

HindIII

```
AAGCTTCCACCATGAAACACCTGTGGTTCTTCCTTCTCCTGGTGGCAGCTCCCAGCTGGGTC
              M  K  H  L  W  F  F  L  L  L  V  A  A  P  S  W  V

CTGTCCCAGGTGCAATTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTG
  L  S  Q  V  Q  L  Q  E  S  G  P  G  L  V  K  P  S  E  T  L

TCCCTCACCTGCACTGTCTCTGGTTCGTCCATCAGTAATTACTACTGGAGCTGGATCCGG
  S  L  T  C  T  V  S  G  S  S  I  S  N  Y  Y  W  S  W  I  R

CAGTCCCCAGGGAAGGGACTGGAGTGGATTGGGTTTATCTATTACGGTGGAAACACCAAG
  Q  S  P  G  K  G  L  E  W  I  G  F  I  Y  Y  G  G  N  T  K

TACAATCCCTCCCTCAAGAGCCGCGTCACCATATCACAAGACACTTCCAAGAGTCAGGTC
  Y  N  P  S  L  K  S  R  V  T  I  S  Q  D  T  S  K  S  Q  V

TCCCTGACGATGAGCTCTGTGACCGCTGCGGAATCGGCCGTCTATTTCTGTGCGAGAGCG
  S  L  T  M  S  S  V  T  A  A  E  S  A  V  Y  F  C  A  R  A
                                                        XhoI

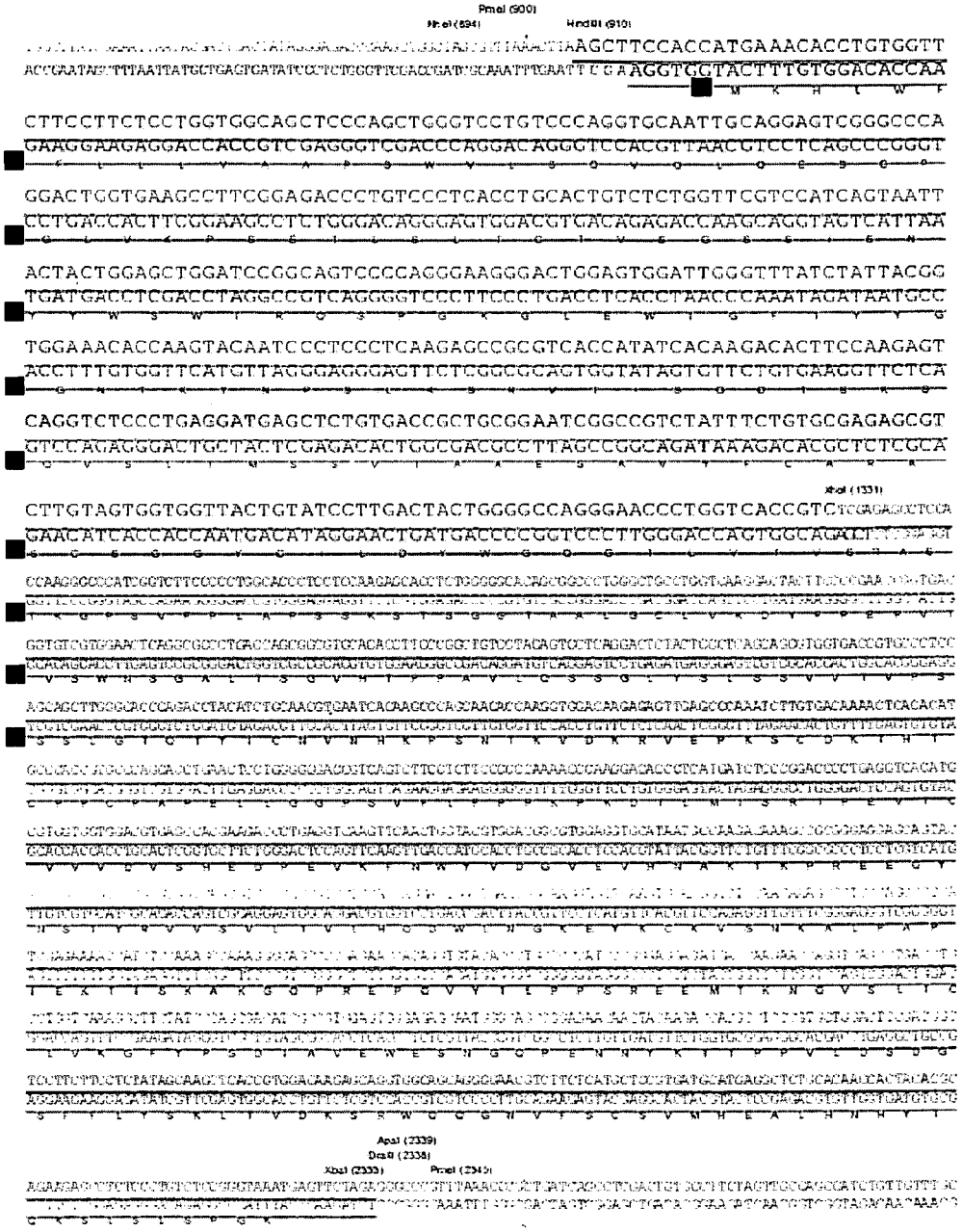
TCTTGTAGTGGTGGTTACTGTATCCTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTC
  S  C  S  G  G  Y  C  I  L  D  Y  W  G  Q  G  T  L  V  T  V

TCGAG
  S
```

[1395] The amino acid sequence of the 8i10 Gamma HC is as follows with specific domains identified below (CDR sequences defined according to Kabat methods):

M K H L W F F L L L V A A P S W V L S	VH leader (SEQ ID NO: 70)
Q V Q L Q E S G P G L V K P S E T L S L T C T V S G S S I S	FR1 (SEQ ID NO: 71)
N Y Y W S	CDR1(SEQ ID NO: 72)
W I R Q S P G K G L E W I G	FR2 (SEQ ID NO: 73)
F I Y Y G G N T K Y N P S L K S	CDR2 (SEQ ID NO: 74)
R V T I S Q D T S K S Q V S L T M S S V T A A E S A V Y F C A R	FR3 (SEQ ID NO: 75)
A S C S G G Y C I L D	CDR3 (SEQ ID NO: 76)
Y W G Q G T L V T V S	FR4 (SEQ ID NO: 77)
YWGQGTLVTVSS	Long FR4 (SEQ ID NO: 266)

[1396] The following is an example of the Gamma HC variable region of 8i10 cloned into the expression vector pcDNA3.1 which already contained the Gamma HC constant region (upper polynucleotide sequence corresponds to SEQ ID NO: 78, lower polynucleotide sequence corresponds to SEQ ID NO: 79, amino acid sequence corresponds to SEQ ID NO: 69). Bases in black represents pcDNA3.1 vector sequences, underlined bases represent the cloned antibody sequences.



[1397] The framework 4 (FR4) region of the Gamma HC normally ends with two serines (SS), so that the full framework 4 region should be WGQGTLVTVSS (SEQ ID NO: 80). The

accepting Xho 1 site and one additional base downstream of the Xho1 site in the vector, in which the Gamma HC constant region that the Gamma HC variable regions are cloned, supplies the last bases, which encode this final amino acid of framework 4. However, the original vector did not adjust for the silent mutation made when the Xho1 site (CTCGAG, SEQ ID NO: 81) was created and contained an "A" nucleotide downstream of the Xho1 site, which caused an amino acid change at the end of framework 4: a serine to arginine (S to R) substitution present in all the working Gamma HC clones. Thus, the full framework 4 region reads WGQGTLVTVSR (SEQ ID NO: 82) . Future constructs are being created wherein the base downstream of the Xho 1 site is a "C" nucleotide. Thus, the creation of the Xho 1 site used for cloning of the Gamma HC variable region sequences in alternative embodiments is a silent mutation and restores the framework 4 amino acid sequence to its proper WGQGTLV TVSS (SEQ ID NO: 80). This is true for all M2 Gamma HC clones described herein.

Clone 21B15:

[1398] The Kappa LC variable region of the anti M2 clone 21B15 was cloned as Hind III to BsiW1 fragment, and is encoded by the following polynucleotide sequences and SEQ ID NO: 83 and SEQ ID NO: 84:

HindIII

```
AAGCTTCCACCATGGACATGAGGGTCCTCGCTCAGCTCCTGGGGCTCCTGCTACTCTGGCTCCGAGGTGC
TTCGAAGGTGGTACCTGTACTCCCAGGAGCGAGTCGAGGACCCCGAGGACGATGAGACCGAGGCTCCACG

CAGATGTGACATCCAGGTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATC
GTCTACACTGTAGGTCCACTGGGTCAGAGGTAGGAGGGACAGACGTAGACATCCTCTGTCTCAGTGGTAG

ACTTGCCGCGCGAGTCAGAACATTTACAAGTATTTAAATTGGTATCAGCAGAGACCAGGGAAAGCCCCTA
TGAACGGCGCGCTCAGTCTTGTAAATGTTCATAAATTTAACCATAGTCGTCTCTGGTCCCTTTCGGGGAT

AGGGCCTGATCTCTGCTGCATCCGGGTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTGGATCTGG
TCCCGGACTAGAGACGACGTAGGCCCAACGTTTCACCCCAGGGTAGTTCCAAGTCACCGTCACCTAGACC

GACAGATTTCACTCTCACCATCACCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGT
CTGTCTAAAGTGAGAGTGGTAGTGGTCAGACGTTGGACTTCTAAAACGTTGAATGATGACAGTTGTCTCA

                                                    BsiWI
TACAGTCCCCCTCTCACTTTCGGCGGAGGGACCAGGGTGGATATCAAACGTACG
ATGTCAGGGGGAGAGTGAAAGCCGCCTCCCTGGTCCCACCTATAGTTTGCATGC
```

[1399] The translation of the 21B15 Kappa LC variable region is as follows, polynucleotide sequence (above, SEQ ID NO: 83, top) and amino acid sequence (below, corresponding to SEQ ID NO: 298):

HindIII
AAGCTTCCACCATGGACATGAGGGTCCTCGCTCAGCTCCTGGGGCTCCTGCTACTCTGGCTCCGAGGT
M D M R V L A Q L L G L L L L W L R G
GCCAGATGTGACATCCAGGTGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACC
A R C D I Q V T Q S P S S L S A S V G D R V T
ATCACTTGCCGCGCGAGTCAGAACATTTACAAGTATTTAAATTGGTATCAGCAGAGACCAGGGAAAGCC
I T C R A S Q N I Y K Y L N W Y Q Q R P G K A
CCTAAGGGCCTGATCTCTGCTGCATCCGGGTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGGCAGTGGA
P K G L I S A A S G L Q S G V P S R F S G S G
TCTGGGACAGATTTCACTCTCACCATCACCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAA
S G T D F T L T I T S L Q P E D F A T Y Y C Q
BsiWI
CAGAGTTACAGTCCCCCTCTCACTTTCGGCGGAGGGACCAGGGTGGATATCAAACGTACG
Q S Y S P P L T F G G G T R V D I K R T

[1400] The amino acid sequence of the 21B15 Kappa LC variable region is as follows, with specific domains identified below (CDR sequences defined according to Kabat methods):

M D M R V L A Q L L G L L L L W L R G A R C	VK leader (SEQ ID NO: 57)
D I Q V T Q S P S S L S A S V G D R V T I T C	FR1 (SEQ ID NO: 58)
R A S Q N I Y K Y L N	CDR1 (SEQ ID NO: 59)
W Y Q Q R P G K A P K G L I S	FR2 (SEQ ID NO: 60)
A A S G L Q S	CDR2 (SEQ ID NO: 61)
G V P S R F S G S G S G T D F T L T I T S L Q P E D F A T Y Y C	FR3 (SEQ ID NO: 62)
Q Q S Y S P P L T	CDR3 (SEQ ID NO: 63)
F G G G T R V D I K	FR4 (SEQ ID NO: 64)
R T	Start of Kappa constant region

[1401] The primer used to clone the Kappa LC variable region extended across a region of diversity and had wobble base position in its design. Thus, in the framework 4 region a D or E amino acid could occur. In some cases, the amino acid in this position in the rescued antibody may not be the original parental amino acid that was produced in the B cell. In most kappa LCs the position is an E. Looking at the clone above (21B15) a D in framework 4 (DIKRT) (SEQ ID NO: 544) was observed. However, looking at the surrounding amino acids, this may have occurred as the result of the primer and may be an artifact. The native antibody from the B cell may have had an E in this position.

[1402] The 21B15 Gamma HC variable region was cloned as a Hind III to Xho 1 fragment, and is encoded by the following polynucleotide sequences and SEQ ID NO: 85 (top), and SEQ ID NO: 86 (bottom):

HindIII
AAGCTTCCACCATGAAACACCTGTGGTTCTTCCTTCTCCTGGTGGCAGCTCCCAGCTGGGTCC
TTCGAAGGTGGTACTTTGTGGACACCAAGAAGGAAGAGGACCACCGTCGAGGGTCGACCCAGG

TGTCCCAGGTGCAATTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCC
ACAGGGTCCACGTTAACGTCCTCAGCCCGGGTCCTGACCACTTCGGAAGCCTCTGGGACAGGG

TCACCTGCACTGTCTCTGGTTCGTCCATCAGTAATTACTACTGGAGCTGGATCCGGCAGTCCC
AGTGGACGTGACAGAGACCAAGCAGGTAGTCATTAATGATGACCTCGACCTAGGCCGTCAGGG

CAGGGAAGGGACTGGAGTGGATTGGGTTTATCTATTACGGTGGAAACACCAAGTACAATCCCT
GTCCCTTCCCTGACCTCACCTAACCCAAATAGATAATGCCACCTTTGTGGTTCATGTTAGGGA

CCCTCAAGAGCCGCGTCACCATATCACAAGACACTTCCAAGAGTCAGGTCTCCCTGACGATGA
GGGAGTTCTCGGCGCAGTGGTATAGTGTTCTGTGAAGGTTCTCAGTCCAGAGGGACTGCTACT

GCTCTGTGACCGCTGCGGAATCGGCCGTCTATTTCTGTGCGAGAGCGTCTTGTAGTGGTGGTT
CGAGACACTGGCGACGCCTTAGCCGGCAGATAAAGACACGCTCTCGCAGAACATCACCACCAA

XhoI
ACTGTATCCTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAG
TGACATAGGAACTGATGACCCCGGTCCCTTGGGACCAGTGGCAGAGCTC

[1403] The translation of the 21B15 Gamma HC is as follows, polynucleotide sequence (above, SEQ ID NO: 87, top) and amino acid sequence (below, corresponding to residues 1-138 of SEQ ID NO: 69):

HindIII
AAGCTTCCACCATGAAACACCTGTGGTTCTTCCTTCTCCTGGTGGCAGCTCCCAGCTGGGTC
M K H L W F F L L L V A A P S W V

CTGTCCCAGGTGCAATTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCC
L S Q V Q L Q E S G P G L V K P S E T L S

CTCACCTGCACTGTCTCTGGTTCGTCCATCAGTAATTACTACTGGAGCTGGATCCGGCAGTCC
L T C T V S G S S I S N Y Y W S W I R Q S

CCAGGGAAGGGACTGGAGTGGATTGGGTTTATCTATTACGGTGGAAACACCAAGTACAATCCC
P G K G L E W I G F I Y Y G G N T K Y N P

TCCCTCAAGAGCCGCGTCACCATATCACAAGACACTTCCAAGAGTCAGGTCTCCCTGACGATG
S L K S R V T I S Q D T S K S Q V S L T M

AGCTCTGTGACCGCTGCGGAATCGGCCGTCTATTTCTGTGCGAGAGCGTCTTGTAGTGGTGGT
S S V T A A E S A V Y F C A R A S C S G G

XhoI
TACTGTATCCTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAG
Y C I L D Y W G Q G T L V T V S

[1404] The amino acid sequence of the 21B15 Gamma HC is as follows, with specific domains identified below (CDR sequences defined according to Kabat methods):

M K H L W F F L L L V A A P S W V L S — VH leader (SEQ ID NO: 70)

Q V Q L Q E S G P G L V K P S E T L S L T C T V S G S S I S — FR1 (SEQ ID NO: 71)

N Y Y W S — CDR1 (SEQ ID NO: 72)

W I R Q S P G K G L E W I G	FR2 (SEQ ID NO: 73)
F I Y Y G G N T K Y N P S L K S	CDR2 (SEQ ID NO: 74)
R V T I S Q D T S K S Q V S L T M S S V T A A E S A V Y F C A R	FR3 (SEQ ID NO: 75)
A S C S G G Y C I L D	CDR3 (SEQ ID NO: 76)
Y W G Q G T L V T V S	FR4 (SEQ ID NO: 77)
YWGQGTLVTVSS	Long FR4 (SEQ ID NO: 266)

Clone 23K12 (corresponds to TCN-031):

[1405] The Kappa LC variable region of the anti M2 clone 23K12 was cloned as Hind III to BsiW1 fragment (see below), and is encoded by the following polynucleotide sequences SEQ ID NO: 88 (top) and SEQ ID NO: 89 (below).

HindIII
AAGCTTCCACCATGGACATGAGGGTCCTCGCTCAGCTCCTGGGGCTCCTGCTACTCTGGCTCCGAGG
TTCGAAGGTGGTACCTGTACTCCCAGGAGCGAGTCGAGGACCCCGAGGACGATGAGACCGAGGCTCC

TGCCAGATGTGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTC
ACGGTCTACACTGTAGGTCTACTGGGTCAGAGGTAGGAGGGACAGACGTAGACATCCTCTGTCTCAG

ACCATCACTTGCCGGACAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATCAGCAGAAACCAGGGA
TGGTAGTGAACGGCCTGTTCAGTCTCGTAATCGTCGATAAATTTAACCATAGTCGTCTTTGGTCCCT

AAGCCCCTAAACTCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGG
TTCGGGGATTTGAGGACTAGATACGACGTAGGTCAAACGTTTCACCCCAGGGTAGTTCCAAGTCACC

CAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCGGTCTGCAACCTGAAGATTTTGCAACCTAC
GTCACCTAGACCCTGTCTAAAGTGAGAGTGGTAGTCGCCAGACGTTGGACTTCTAAAACGTTGGATG

BsiWI
TACTGTCAACAGAGTTACAGTATGCCTGCCTTTGGCCAGGGGACCAAGCTGGAGATCAAACGTACG
ATGACAGTTGTCTCAATGTCATACGGACGGAAACCGGTCCCCTGGTTCGACCTCTAGTTTGCATGC

[1406] The translation of the 23K12 Kappa LC variable region is as follows, polynucleotide sequence (above, SEQ ID NO: 90, top) and amino acid sequence (below, corresponding to SEQ ID NO: 91).

HindIII
AAGCTTCCACCATGGACATGAGGGTCCTCGCTCAGCTCCTGGGGCTCCTGCTACTCTGGCTCCGAGG
M D M R V L A Q L L G L L L L W L R G

TGCCAGATGTGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTC
A R C D I Q M T Q S P S S L S A S V G D R V

ACCATCACTTGCCGGACAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATCAGCAGAAACCAGGGA
T I T C R T S Q S I S S Y L N W Y Q Q K P G

AAGCCCCTAAACTCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGTGG
K A P K L L I Y A A S S L Q S G V P S R F S G

CAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCGGTCTGCAACCTGAAGATTTTGCAACCTAC
S G S G T D F T L T I S G L Q P E D F A T Y

BsiWI
TACTGTCAACAGAGTTACAGTATGCCTGCCTTTGGCCAGGGGACCAAGCTGGAGATCAAACGTACG
Y C Q Q S Y S M P A F G Q G T K L E I K R T

[1407] The amino acid sequence of the 23K12 Kappa LC variable region is as follows, with specific domains identified below (CDR sequences defined according to Kabat methods):

M D M R V L A Q L L G L L L L W L R G A R C	VK leader (SEQ ID NO: 57)
D I Q M T Q S P S S L S A S V G D R V T I T C	FR1 (SEQ ID NO: 58)
R T S Q S I S S Y L N	CDR1 (SEQ ID NO: 92)
W Y Q Q K P G K A P K L L I Y	FR2 (SEQ ID NO: 93)
A A S S L Q S G V P S R F	CDR2 (SEQ ID NO: 94)
S G S G S G T D F T L T I S G L Q P E D F A T Y Y C	FR3 (SEQ ID NO: 95)
Q Q S Y S M P A	CDR3 (SEQ ID NO: 96)
F G Q G T K L E I K	FR4 (SEQ ID NO: 114)
R T	Start of Kappa LC constant region

[1408] The 23K12 Gamma HC variable region was cloned as a Hind III to Xho 1 fragment, and is encoded by the following polynucleotide sequences and SEQ ID NO: 97 (top) and SEQ ID NO: 98 (bottom).

HindIII
AAGCTTCCACCATGGAGTTGGGGCTGTGCTGGGTTTTCCTTGTTGCTATTTTAAAAGGTGTCCAGT
TTCGAAGGTGGTACCTCAACCCCGACACGACCCAAAAGGAACAACGATAAAATTTTCCACAGGTCA

GTGAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTCCAGCCTGGGGGGTCCCTGAGAATCTCCT
CACTCCACGTCGACCACCTCAGACCCCCTCCGAACCAGGTCGGACCCCCCAGGGACTCTTAGAGGA

GTGCAGCCTCTGGATTCACCGTCAGTAGCAACTACATGAGTTGGGTCCGCCAGGCTCCAGGGAAGG
CACGTCGGAGACCTAAGTGGCAGTCATCGTTGATGTACTCAACCCAGGCGGTCCGAGGTCCCTTCC

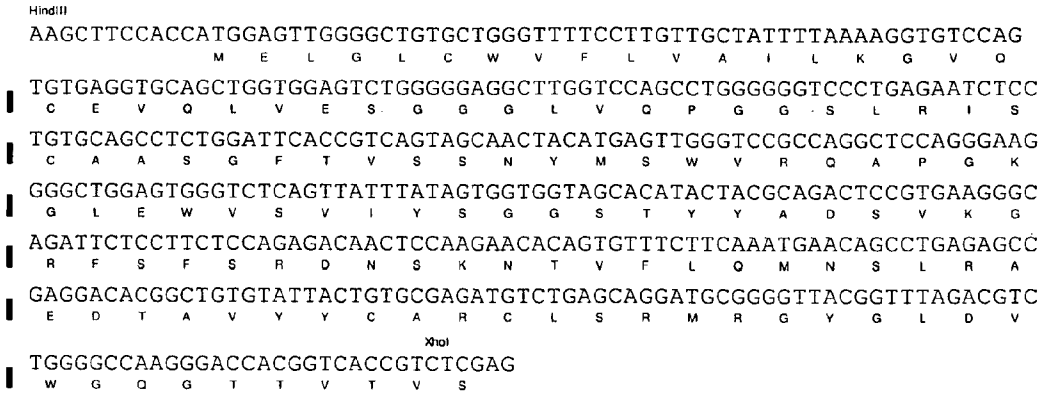
GGCTGGAGTGGGTCTCAGTTATTTATAGTGGTGGTAGCACATACTACGCAGACTCCGTGAAGGGCA
CCGACCTCACCCAGAGTCAATAAATATCACCACCATCGTGTATGATGCGTCTGAGGCACTTCCCGT

GATTCTCCTTCTCCAGAGACAACTCCAAGAACACAGTGTTTCTTCAAATGAACAGCCTGAGAGCCG
CTAAGAGGAAGAGGTCTCTGTTGAGGTTCTTGTGTCACAAAGAAGTTTACTTGTCGGACTCTCGGC

AGGACACGGCTGTGTATTACTGTGCGAGATGTCTGAGCAGGATGCGGGGTTACGGTTTAGACGTCT
TCCTGTGCCGACACATAATGACACGCTCTACAGACTCGTCCTACGCCCCAATGCCAAATCTGCAGA

XhoI
GGGGCCAAGGGACCACGGTCACCGTCTCGAG
CCCCGGTTCCCTGGTGCCAGTGGCAGAGCTC

[1409] The translation of the 23K12 Gamma HC variable region is as follows, polynucleotide sequence (above, SEQ ID NO: 99, top), and amino acid sequence (below, corresponding to SEQ ID NO: 100):



[1410] The amino acid sequence of the 23K12 Gamma HC variable region is as follows, with specific domains identified below (CDR sequences defined according to Kabat methods):

M E L G L C W V F L V A I L K G V Q C	VH leader (SEQ ID NO: 101)
E V Q L V E S G G G L V Q P G G S L R I S C A A S G F T V S	FR1 (SEQ ID NO: 102)
S N Y M S	CDR1 (SEQ ID NO: 103)
W V R Q A P G K G L E W V S	FR2 (SEQ ID NO: 104)
V I Y S G G S T Y Y A D S V K	CDR2 (SEQ ID NO: 105)
G R F S F S R D N S K N T V F L Q M N S L R A E D T A V Y Y C A R	FR3 (SEQ ID NO: 106)
C L S R M R G Y G L D V	CDR3 (SEQ ID NO: 107)
W G Q G T T V T V S	FR4 (SEQ ID NO: 108)
WGQGTTVTVSS	Long FR4 (SEQ ID NO: 111)

Example 3: Identification of Conserved Antibody Variable Regions

[1411] The amino acid sequences of the three antibody Kappa LC and Gamma HC variable regions were aligned to identify conserved regions and residues, as shown below.

[1412] Amino acid sequence alignment of the Kappa LC variable regions of the three clones (SEQ ID NOs 673-675, respectively, in order of appearance):

										10										20									30						
Translation of mp 73 21B15	A	S	T	M	D	M	R	V	L	A	Q	L	L	G	L	L	L	L	W	L	R	G	A	R	C	D	I	Q	V	T	Q	S	P	S	S	L
Translation of mp 147 8I10	A	S	T	M	D	M	R	V	L	A	Q	L	L	G	L	L	L	L	W	L	R	G	A	R	C	D	I	Q	M	T	Q	S	P	S	S	L
Translation of mp 137 23K12	A	S	T	M	D	M	R	V	L	A	Q	L	L	G	L	L	L	L	W	L	R	G	A	R	C	D	I	Q	M	T	Q	S	P	S	S	L
				40										50										60										70		
Translation of mp 73 21B15	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	N	I	Y	K	Y	L	N	W	Y	Q	Q	R	P	G	K	A	P	K	G	L
Translation of mp 147 8I10	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	N	I	Y	K	Y	L	N	W	Y	Q	Q	R	P	G	K	A	P	K	G	L
Translation of mp 137 23K12	S	A	S	V	G	D	R	V	T	I	T	C	R	T	S	Q	S	I	S	S	Y	L	N	W	Y	Q	Q	K	P	G	K	A	P	K	L	L
								80										90										100							
Translation of mp 73 21B15	I	S	A	A	S	G	L	Q	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	T	S	L	Q	P	E	D	F
Translation of mp 147 8I10	I	S	A	A	S	G	L	Q	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	T	S	L	Q	P	E	D	F
Translation of mp 137 23K12	I	Y	A	A	S	S	L	Q	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	G	L	Q	P	E	D	F
		110										120										130													
Translation of mp 73 21B15	A	T	Y	Y	C	Q	Q	S	Y	S	P	P	L	T	F	G	G	G	T	R	V	D	I	K	R	T										
Translation of mp 147 8I10	A	T	Y	Y	C	Q	Q	S	Y	S	P	P	L	T	F	G	G	G	T	R	V	E	I	K	R	T										
Translation of mp 137 23K12	A	T	Y	Y	C	Q	Q	S	Y	S	M	P	-	A	F	G	Q	G	T	K	L	E	I	K	R	T										

[1413] Amino acid sequence alignment of the Gamma HC variable regions of the three clones (SEQ ID NOs 676-678, respectively, in order of appearance):

										10										20								
Translation of mp 81 21B15	A	S	T	M	K	H	L	W	F	F	L	I	L	V	A	A	P	S	W	V	L	S	Q	V	Q	L	Q	E	S
Translation of mp 145 23K12	A	S	T	M	E	L	G	L	C	W	V	F	L	V	A	I	L	K	G	V	Q	C	E	V	Q	L	V	E	S
Translation of mp 153 8I10	A	S	T	M	K	H	L	W	F	F	L	I	L	V	A	A	P	S	W	V	L	S	Q	V	Q	L	Q	E	S
	30										40										50								
Translation of mp 81 21B15	G	P	G	L	V	K	P	S	E	T	L	S	L	T	C	T	V	S	G	S	S	I	S	N	Y	Y	W	S	W
Translation of mp 145 23K12	G	G	G	L	V	Q	P	G	G	S	L	R	I	S	C	A	A	S	G	F	T	V	S	S	N	Y	M	S	W
Translation of mp 153 8I10	G	P	G	L	V	K	P	S	E	T	L	S	L	T	C	T	V	S	G	S	S	I	S	N	Y	Y	W	S	W
		60										70										80							
Translation of mp 81 21B15	I	R	Q	S	P	G	K	G	L	E	W	I	G	F	I	Y	Y	G	G	N	T	K	Y	N	P	S	L	K	S
Translation of mp 145 23K12	V	R	Q	A	P	G	K	G	L	E	W	V	S	V	I	Y	S	G	G	S	T	Y	Y	A	D	S	V	K	G
Translation of mp 153 8I10	I	R	Q	S	P	G	K	G	L	E	W	I	G	F	I	Y	Y	G	G	N	T	K	Y	N	P	S	L	K	S
			90										100										110						
Translation of mp 81 21B15	R	V	T	I	S	Q	D	T	S	K	S	Q	V	S	L	T	M	S	S	V	T	A	A	E	S	A	V	Y	F
Translation of mp 145 23K12	R	F	S	F	S	R	D	N	S	K	N	T	V	F	L	Q	M	N	S	L	R	A	E	D	T	A	V	Y	Y
Translation of mp 153 8I10	R	V	T	I	S	Q	D	T	S	K	S	Q	V	S	L	T	M	S	S	V	T	A	A	E	S	A	V	Y	F
				120										130									140						
Translation of mp 81 21B15	C	A	R	A	S	C	S	G	G	Y	C	I	L	D	Y	W	G	Q	T	L	V	T	V	S					
Translation of mp 145 23K12	C	A	R	C	L	S	R	M	R	G	Y	G	L	D	V	W	G	Q	T	T	V	T	V	S					
Translation of mp 153 8I10	C	A	R	A	S	C	S	G	G	Y	C	I	L	D	Y	W	G	Q	T	L	V	T	V	S					

[1414] Clones 8I10 and 21B15 came from two different donors, yet they have the same exact Gamma HC and differ in the Kappa LC by only one amino acid at position 4 in the framework 1 region (amino acids M versus V, see above), (excluding the D versus E wobble position in framework 4 of the Kappa LC).

[1415] Sequence comparisons of the variable regions of the antibodies revealed that the heavy chain of clone 8i10 was derived from germline sequence IgHV4 and that the light chain was derived from the germline sequence IgKV1.

[1416] Sequence comparisons of the variable regions of the antibodies revealed that the heavy chain of clone 21B15 was derived from germline sequence IgHV4 and that the light chain was derived from the germline sequence IgKV1.

[1417] Sequence comparisons of the variable regions of the antibodies revealed that the heavy chain of clone 23K12 was derived from germline sequence IgHV3 and that the light chain was derived from the germline sequence IgKV1.

Example 4: Production and characterization of M2 Antibodies

[1418] The antibodies described above were produced in milligram quantities by larger scale transient transfections in 293 PEAK cells. Crude un-purified antibody supernatants were used to examine antibody binding to influenza A/Puerto Rico/8/1932 (PR8) virus on ELISA plates, and were compared to the binding of the control antibody 14C2, which was also produced by larger scale transient transfection. The anti-M2 recombinant human monoclonal antibodies bound to influenza while the control antibody did not (Figure 9).

[1419] Binding was also tested on MDCK cells infected with the PR8 virus (Figure 10). The control antibody 14C2 and the three anti M2E clones: 8I10, 21B15 and 23K12, all showed specific binding to the M2 protein expressed on the surface of PR8-infected cells. No binding was observed on uninfected cells.

[1420] The antibodies were purified over protein A columns from the supernatants. FACs analysis was performed using purified antibodies at a concentration of 1 ug per ml to examine the binding of the antibodies to transiently transfected 293 PEAK cells expressing the M2 proteins on the cell surface. Binding was measured testing binding to mock transfected cells and cells transiently transfected with the Influenza subtype H3N2, A/Vietnam/1203/2004 (VN1203), or A/Hong Kong/483/1997 HK483 M2 proteins. As a positive control the antibody 14C2 was

used. Unstained and secondary antibody alone controls helped determined background. Specific staining for cells transfected with the M2 protein was observed for all three clones. Furthermore, all three clones bound to the high path strains A/Vietnam/1203/2004 and A/Hong Kong/483/1997 M2 proteins very well, whereas the positive control 14C2 which bound well to H3N2 M2 protein, bound much weaker to the A/Vietnam/1203/2004 M2 protein and did not bind the A/Hong Kong/483/1997 M2 protein. See Figure 11.

[1421] Antibodies 21B15, 23K12, and 8I10 bound to the surface of 293-HEK cells stably expressing the M2 protein, but not to vector transfected cells (see Figure 1). In addition, binding of these antibodies was not competed by the presence of 5 mg/ml 24-mer M2 peptide, whereas the binding of the control chimeric mouse V-region/human IgG1 kappa 14C2 antibody (hu14C2) generated against the linear M2 peptide was completely inhibited by the M2 peptide (see Figure 1). These data confirm that these antibodies bind to conformational epitopes present in M2e expressed on the cell or virus surface, as opposed to the linear M2e peptide.

Example 5: Viral Binding of human anti-influenza monoclonal antibodies

[1422] UV-inactivated influenza A virus (A/PR/8/34) (Applied Biotechnologies) was plated in 384-well MaxiSorp plates (Nunc) at 1.2 µg/ml in PBS, with 25 µl/well, and was incubated at 4°C overnight. The plates were then washed three times with PBS, and blocked with 1% Nonfat dry milk in PBS, 50 µl/well, and then were incubated at room temp for 1 hr. After a second wash with PBS, MAbs were added at the indicated concentrations in triplicate, and the plates were incubated at room temp for 1 hour. After another wash with PBS, to each well was added 25 µl of a 1/5000 dilution of horseradish peroxidase (HRP) conjugated goat anti-human IgG Fc (Pierce) in PBS/1% Milk, and the plates were left at room temp for 1 hr. After the final PBS wash, the HRP substrate 1-Step™ Ultra-TMB-ELISA (Pierce) was added at 25 µl/well, and the reaction proceeded in the dark at room temp. The assay was stopped with 25 µl/well 1N H_2SO_4, and light absorbance at 450 nm (A450) was read on a SpectroMax Plus plate reader. Data are normalized to the absorbance of MAb 8I10 binding at10 µg/ml. Results are shown in Figures 2A and 2B.

Example 6: Binding of Human Anti-Influenza Monoclonal Antibodies to Full-Length M2 Variants

[1423] M2 variants (including those with a high pathology phenotype in vivo) were selected for analysis. See Figure 3A for sequences.

[1424] M2 cDNA constructs were transiently transfected in HEK293 cells and analyzed as follows: To analyze the transient transfectants by FACS, cells on 10 cm tissue culture plates were treated with 0.5 ml Cell Dissociation Buffer (Invitrogen), and harvested. Cells were washed in PBS containing 1% FBS, 0.2% NaN_3 (FACS buffer), and resuspended in 0.6 ml FACS buffer supplemented with 100 µg/ml rabbit IgG. Each transfectant was mixed with the indicated MAbs at 1 µg/ml in 0.2 ml FACS buffer, with 5 x 10^5 to 10^6 cells per sample. Cells were washed three times with FACS buffer, and each sample was resuspended in 0.1 ml containing 1 µg/ml alexafluor (AF) 647-anti human IgG H&L (Invitrogen). Cells were again washed and flow cytometry was performed on a FACSCanto device (Becton-Dickenson). The data is expressed as a percentage of the mean fluorescence of the M2-D20 transient transfectant. Data for variant binding are representative of 2 experiments. Data for alanine mutants are average readouts from 3 separate experiments with standard error. Results are shown in Figure 3B and 3C.

Example 7: Alanine Scanning Mutagenesis to Evaluate M2 Binding

[1425] To evaluate the antibody binding sites, alanine was substituted at individual amino acid positions as indicated by site-directed mutagenesis.

[1426] M2 cDNA constructs were transiently transfected in HEK293 cells and analyzed as described above in Example 6. Results are shown in Figure 4A and 4B. Figure 8 shows that the epitope is in a highly conserved region of the amino terminus of the M2 polypeptide. As shown in Figures 4A, 4B and Figure 8, the epitope includes the serine at position 2, the threonine at position 5 and the glutamic acid at position 6 of the M2 polypeptide.

Example 8: Epitope Blocking

[1427] To determine whether the MAbs 8I10 and 23K12 bind to the same site, M2 protein representing influenza strain A/HK/483/1997 sequence was stably expressed in the CHO (Chinese Hamster Ovary) cell line DG44. Cells were treated with Cell Dissociation Buffer (Invitrogen), and harvested. Cells were washed in PBS containing 1% FBS, 0.2% NaN_3 (FACS

buffer), and resuspended at 10^7 cells/ml in FACS buffer supplemented with 100 µg/ml rabbit IgG. The cells were pre-bound by either MAb (or the 2N9 control) at 10 µg/ml for 1 hr at 4 °C, and were then washed with FACS buffer. Directly conjugated AF647-8I10 or -23K12 (labeled with the AlexaFluor® 647 Protein Labeling kit (Invitrogen) was then used to stain the three pre-blocked cell samples at 1 µg/ml for 10^6 cells per sample. Flow cytometric analyses proceeded as before with the FACSCanto. Data are average readouts from 3 separate experiments with standard error. Results are shown in Figure 5.

Example 9: Binding of human anti-influenza monoclonal antibodies to M2 Variants and Truncated M2 Peptides

[1428] The cross reactivity of mAbs 8i10 and 23K12 to other M2 peptide variants was assessed by ELISA. Peptide sequences are shown in Figures 6A and 6B. Additionally, a similar ELISA assay was used to determine binding activity to M2 truncated peptides.

[1429] In brief, each peptide was coated at 2 µg/mL to a flat bottom 384 well plate (Nunc) in 25 µL/ well of PBS buffer overnight at 4°C. Plates were washed three times and blocked with 1% Milk/PBS for one hour at room temperature. After washing three times, MAb titers were added and incubated for one hour at room temperature. Diluted HRP conjugated goat anti-human immunoglobulin FC specific (Pierce) was added to each well after washing three times. Plates were incubated for one hour at room temperature and washed three times. 1-Step™ Ultra-TMB-ELISA (Pierce) was added at 25 µl/well, and the reaction proceeded in the dark at room temp. The assay was stopped with 25 µl/well 1N H_2SO_4, and light absorbance at 450 nm (A450) was read on a SpectroMax Plus plate reader. Results are shown in Figures 6A and 6B.

Example 10: In Vivo Evaluation of the Ability of Human Anti-Influenza Monoclonal Antibodies to Protect From Lethal Viral Challenge

[1430] The ability of antibodies, 23K12 and 8I10, to protect mice from lethal viral challenge with a high path avian influenza strain was tested.

[1431] Female BALB/c mice were randomized into 5 groups of 10. One day prior (Day -1 (minus one)) and two days post infection (Day +2 (plus two), 200 ug of antibody was given via 200 ul intra-peritoneal injection. On Day 0 (zero), an approximate LD90 (lethal dose 90) of

A/Vietnam/1203/04 influenza virus, in a volume of 30 µl was given intra-nasally. Survival rate was observed from Day 1 through Day 28 post-infection. Results are shown in Figure 7.

[1432] Example 11: Characterization of M2 Antibodies TCN-032 (8I10), 21B15, TCN-031 (23K12), 3241_G23, 3244_I10, 3243_J07, 3259_J21, 3245_O19, 3244_H04, 3136_G05, 3252_C13, 3255_J06, 3420_I23, 3139_P23, 3248_P18, 3253_P10, 3260_D19, 3362_B11, and 3242_P05.

FACS

[1433] Full length M2 cDNA (A/Hong Kong/483/97) were synthesized (Blue Heron Technology) and cloned into the plasmid vector pcDNA3.1 which was then transfected into CHO cells with Lipofectamine (Invitrogen) to create a stable pool of CHO-HK M2-expressing cells. For the panel of anti-M2 Mabs, 20 µl samples of supernatant from transient transfections from each of the IgG heavy and light chain combinations was used to stain the CHO-HK M2 stable cell line. Bound anti-M2 mabs were visualized on viable cells with Alexafluor 647-conjugated goat anti-Human IgG H&L antibody (Invitrogen). Flow cytometry was performed with a FACSCanto, and analysis on the accompanying FACSDiva software (Becton Dickenson).

ELISA

[1434] Purified Influenza A (A/Puerto Rico/8/34) inactivated by β-propiolactone (Advanced Biotechnologies, Inc.) was biotinylated (EZ-Link Sulfo-NHS-LC-Biotin, Pierce) and adsorbed for 16 hours at 4°C to 384-well plates in 25 µl PBS that were pre-coated with neutravidin (Pierce). Plates were blocked with BSA in PBS, samples of supernatant from transient transfections from each of the IgG heavy and light chain combinations were added at a final dilution of 1:5, followed by HRP-conjugated goat anti-human Fc antibody (Pierce), and developed with TMB substrate (ThermoFisher).

[1435] The results of this analysis are shown below in Table 2.

[1436] Table 2.

Transfection no.	BCC well ID	Sequence ID		FACS M2-HK MFI	Virus ELISA OD A_{450}
		Gamma	Light		
322	3241_G23	G4_005	K1_004	1697	3.02
352	3244_I10	G4_007	K2_006	434	3.01
339	3243_J07	G4_007	K1_007	131	2.94
336	3259_J21	G4_005	K2_005	1673	2.40
348	3245_O19	G3_004	K1_001	919	3.51
345	3244_H04	G3_003	K1_006	963	3.31
346		Pos Cont (HC)	Pos Cont (LC)	754	2.69
347		Neg Cont (HC)	Neg Cont (LC)	11	0.15
374	3136_G05	G4_007	K1_007	109	ND
386	3252_C13	G4_013	K1_002	449	ND
390	3255_J06	G4_013	K2_007	442	ND
400	3420_I23	G4_004	K1_003	112	ND
432	3139_P23	G4_016	K1_007a	110	1.02
412	3248_P18	G4_009	K1_006	967	0.56
413	3253_P10	G4_007	K1_004	43	0.50
434	3260_D19	G3_004a	K2_001	846	2.46
439	3362_B11	G4_010a	K1_007	218	1.83
408	3242_P05	G3_005	K2_004	596	0.50
451		Pos Cont (HC)	Pos Cont (LC)	1083	1.87
452		Neg Cont (HC)	Neg Cont (LC)	6	0.05

Positive control: supernatant from tranisent transfection with the IgG heavy and light chain combination of mAb 8I10
Negative control: supernatant from tranisent transfection with the IgG heavy and light chain combination of mAb 2N9
MFI= mean fluorescence intensity

Example 12: Human Antibodies Reveal a Protective Epitope that is Highly Conserved Among Human and Non-Human Influenza A Viruses

[1437] Influenza remains a serious public health threat throughout the world. Vaccines and antivirals are available that can provide protection from infection. However, new viral strains emerge continuously because of the plasticity of the influenza genome which necessitates annual reformulation of vaccine antigens, and resistance to antivirals can appear rapidly and become entrenched in circulating virus populations. In addition, the spread of new pandemic strains is difficult to contain due to the time required to engineer and manufacture effective vaccines.

Monoclonal antibodies that target highly conserved viral epitopes might offer an alternative protection paradigm. Herein we describe the isolation of a panel of monoclonal antibodies derived from the IgG^+ memory B cells of healthy, human subjects that recognize a previously unknown conformational epitope within the ectodomain of the influenza matrix 2 protein, M2e. This antibody binding region is highly conserved in influenza A viruses, being present in nearly all strains detected to date including highly pathogenic viruses that infect primarily birds and swine, and the current 2009 swine-origin H1N1 pandemic strain (S-OIV). Furthermore, these human anti-M2e monoclonal antibodies protect mice from lethal challenges with either H5N1 or H1N1 influenza viruses. These results suggest that viral M2e can elicit broadly cross-reactive and protective antibodies in humans. Accordingly, recombinant forms of these human antibodies may provide useful therapeutic agents to protect against infection from a broad spectrum of influenza A strains.

Introduction

[1438] Seasonal influenza epidemics hospitalize more than 200,000 people each year in the US and kill an estimated 500,000 worldwide (Thompson, W.W. et al. (2004) JAMA 292:1333-1340). The immune system affords only partial protection from seasonal strains in most individuals because of constantly arising point mutations in the viral genome which lead to structural variability known as antigenic drift. Pandemic strains encounter even less immune resistance due to genomic reassortment events among different viruses which result in more radical shifts in viral antigenic determinants. Consequently, pandemic influenza has the potential to cause widespread illness, death, and economic disruption. Vaccines and antiviral agents are available to counter the threat of influenza epidemics and pandemics. However, the strain composition of influenza vaccines must be determined prior to the influenza season on an annual basis, and predicting in advance which strains will become dominant is challenging. Moreover, the emergence of strains that evade vaccine-induced, protective immune responses is relatively rapid which often results in inadequate protection (Carrat F, Flahault A. (2007) Influenza vaccine: the challenge of antigenic drift. Vaccine 25:6852-6862). Antiviral drugs include oseltamivir and zanamivir which inhibit the function of the viral protein neuraminidase (NA), and adamantanes which inhibit the ion channel function of the

viral M2 protein (Gubareva LV, et al. (2000) Lancet 355:827-835; Wang C, et al. (1993) J Virol 67:5585-5594). Antiviral agents are effective for sensitive virus strains but viral resistance can develop quickly and has the potential to render these drugs ineffective. In the 2008-2009 US influenza season nearly 100% of seasonal H1N1 or H3N2 influenza isolates tested were resistant to oseltamivir or adamantane antivirals, respectively (CDC Influenza Survey: www.cdc.gov/flu/weekly/weeklyarchives2008-2009/weekly23.htm).

[1439] Passive immunotherapy using anti-influenza antibodies represents an alternative paradigm for preventing or treating viral infection. Evidence for the utility of this approach dates back nearly 100 years when passive serum transfer was used during the 1918 influenza pandemic with some success (Luke TC, et al. (2006) Ann Intern Med 145:599- 609). While protection provided by anti-influenza monoclonal antibodies (mAbs) is typically narrow in breadth because of the antigenic heterogeneity of influenza viruses, several groups have recently reported protective mAbs that bind to conserved epitopes within the stem region of viral hemagglutinin (HA) (Okuno Y, et al. (1993) J Virol 67:2552-2558; Throsby M, et al. (2008) PLoS One. 3: e3942; Sui J, et al. (2009) Nat Struct Mol Biol 16:265-273; Corti D, et al. (2010) J Clin Invest doi:10.1172/JCI41902). These epitopes appear to be restricted to a subset of influenza viruses; these anti-HA mAbs would not be expected to provide protection against viruses of the H3 and H7 subtypes. Of these, the former comprises an important component of circulating human strains (Russell CA, et al. (2008) Science 320:340-346) while the latter includes highly pathogenic avian strains which have caused mortality in humans (Fouchier RA, et al. (2004) Proc Natl Acad Sci USA 101:1356-1361; Belser JA, et al. (2009) Emerg Infect Dis 15:859-865).

[1440] Of the three antibody targets present on the surface of the influenza virus, the ectodomain of the viral M2 protein (M2e) is much more highly conserved than either HA or NA, which makes it an attractive target for broadly protective mAbs. Monoclonal antibodies to M2e have been shown to be protective in vivo (Wang R, et al. (2008) Antiviral Res 80:168-177; Liu W, et al. (2004) Immunol Lett 93:131-6; Fu TM, et al. (2008) Virology 385:218-226; Treanor JJ, et al. (1990) J Virol 64:1375-1357; Beerli R, et al. (2009) Virology J 6:224-234), and several groups have demonstrated protection against infection with vaccine strategies based

on M2e (Fu TM, et al. (2009) Vaccine 27:1440-1447; Fan J, et al. (2004) Vaccine 22:2993-3003; Slepushkin VA, et al. (1995) Vaccine 13:1399-1402; Neirynck S, et al. (1999) Nat Med 5:1157-1163; Tompkins SM, et al. (2007) Emerg Infect Dis 13:426-435; Mozdzanowska K, et al. (2003) Vaccine 21:2616-2626). In these cases, purified M2 protein or peptides derived from M2e sequence have been used as immunogens to generate anti-M2e antibodies in animals or as vaccine candidates. In the present study, mAbs were isolated directly from human B cells that bind to the M2 protein displayed on virus particles and on virus-infected cells. Further, we demonstrate that these antibodies protect mice from a lethal influenza A virus challenge and that they can recognize M2 variants derived from a wide range of human and animal influenza A virus isolates. This combination of properties may enhance the utility of these antibodies to prevent and treat influenza A virus infections.

Results and Discussion

[1441] *Isolation of a Family of Anti-M2e mAbs from Human B Cells.* To explore the humoral immune response to natural influenza infection in humans, we have isolated antibodies from IgG^+ memory B cells of M2e-seropositive subjects. Serum samples from 140 healthy adult, United States-sourced donors were tested for reactivity with M2e expressed on the surface of HEK293 cells that were transfected with a viral M2 gene (derived from A/Fort Worth/50 H1N1). IgG^+ memory B cells from 5 of the 23 M2e-seropositive subjects were cultured under conditions where they proliferated and differentiated into IgG-secreting plasma cells. B cell culture wells were screened for IgG reactivity to cell-surface M2e and immunoglobulin heavy and light chain variable region (V_H and V_L) genes were rescued by RT-PCR from 17 positive wells and incorporated into a human IgG1 constant region background for recombinant expression and purification. VH and VL sequences of 15 of the 17 anti-M2e mAbs cluster into two related groups (Table 3) (IMGT®, the International ImMunoGeneTics Information system®, available at www.imgt.org). In group A, assignment of the germline VH gene segment is IGHV4- 59*01 while in the group B, the germline gene segment is IGHV3-66*01. The two more distantly related mAbs 62B11 and 41G23 (group C) utilize the germline V gene segment IGHV4- 31*03 which has only 5 amino acid residue differences from the germline V gene segment IGHV4-59*01 of group A. All of these mAbs

utilize the same light chain V gene, IGKV1-39*01 or its allele IGKV1D-39*01 and show evidence of somatic hypermutation from the germline heavy or kappa chain sequence (Fig. 12). Competitive binding experiments showed that all of these human mAbs appear to bind similar sites on native M2e expressed on the surface of Chinese hamster ovary (CHO) cells (Fig. 13). We selected for further characterization one mAb from each of groups A and B, designated TCN-031 and TCN-032, respectively.

[1442] Table 3. Immunoglobulin gene segment usage of human anti-M2e antibodies.

		Heavy chain germline gene segments			Light chain germline gene segments	
	mAb	Variable	Diversity	Joining	Variable	Joining
Group A	TCN-032	IGHV4-59*01	IGHD2-15*01	IGHJ4*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ4*01
	43J7	IGHV4-59*07	IGHD1-26*01	IGHJ4*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ2*01
	53P10	IGHV4-59*07	IGHD1-26*01	IGHJ4*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ2*01
	44I10	IGHV4-59*07	IGHD1-26*01	IGHJ4*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ2*01
	55J6	IGHV4-59*01	IGHD5-18*01	IGHJ4*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ5*01
	52C13	IGHV4-59*01	IGHD5-18*01	IGHJ4*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ5*01
	39P23	IGHV4-59*01	IGHD4-23*01	IGHJ4*01	IGKV1-39*01, or IGKV1D-39*01	IGKJ1*01
	36G5	IGHV4-59*01	IGHD2-8*01	IGHJ6*04	IGKV1-39*01, or IGKV1D-39*01	IGKJ3*01
	48P18	IGHV4-59*01	IGHD2-15*01	IGHJ6*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ4*01
	59J21	IGHV4-59*01	IGHD2-15*01	IGHJ6*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ4*01
	20I23	IGHV4-59*01	IGHD6-6*01	IGHJ6*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ5*01
Group C	62B11	IGHV4-31*03	IGHD4-23*01	IGHJ6*02 (a)	IGKV1-39*01, or IGKV1D-39*01	IGKJ5*01
	41G23	IGHV4-31*03	IGHD3-16*01	IGHJ6*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ5*01
Group B	TCN-031	IGHV3-66*01	IGHD3-10*01	IGHJ3*01	IGKV1-39*01, or IGKV1D-39*01	IGKJ2*01
	44H4	IGHV3-66*01	Cannot assign	IGHJ6*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ5*01
	45O19	IGHV3-66*01	Cannot assign	IGHJ6*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ5*01
	60D19	IGHV3-66*01	Cannot assign	IGHJ6*02	IGKV1-39*01, or IGKV1D-39*01	IGKJ2*01

Reference sequences for each mAb heavy and light chain were analysed using IMGT/V-QUEST to determine gene usage.

[1443] *High Affinity Binding to the Surface of Influenza Virus.* Both TCN-031 and TCN-032 bound directly to an H1N1 virus (A/Puerto Rico/8/34) with high avidity, with half-maximal

binding at about 100 ng/mL (Fig. 14a). Fab fragments prepared from TCN-031 and TCN-032 bound virus with affinities (KD) of 14 and 3 nM, respectively, as determined by surface plasmon resonance (Table 4). The human mAbs did not bind appreciably to a 23 amino acid synthetic peptide corresponding to the M2e domain of an H1N1 virus (A/Fort Worth /1/50) (Fig. 14b). A chimeric derivative of the murine anti-M2e mAb 14C2 (ch14C2), which was originally generated by immunization with purified M2 (Zebedee SL and Lamb RA. (1988) J Virol 62:2762-2772), exhibited the opposite behavior to that observed with the human mAbs, with little binding to virus but robust binding to the isolated 23mer M2e peptide with half-maximal binding to peptide at 10 ng/mL (Figs. 14a and 14b). Interestingly, both the human mAbs and ch14C2 bound to the surface of Madin-Darby canine kidney (MDCK) cells infected with H1N1 virus (A/Puerto Rico/8/34) with similar avidities (Fig. 14c). It thus appears that viral epitopes recognized by the human anti-M2e mAbs are present and accessible on the surface of both virus and infected cells, while the epitope bound by ch14C2 is accessible only on the surface of infected cells. Our observation that the human anti-M2e mAbs do not bind appreciably to immobilized synthetic peptides derived from M2e, and further that such peptides do not compete for binding of these antibodies to M2e expressed on the surface of mammalian cells (Fig. 14d), supports the idea that secondary structure within the M2e epitope is important for binding by the human antibodies. That ch14C2 binds peptide immobilized on plastic suggests a lesser importance of higher order structure for binding of this mAb.

[1444] Table 4. Affinity of anti-M2e Fab fragments for influenza virus.

Fab	ka ($M^{-1}*s^{-1}$)	kd (s^{-1})	KD
TCN-031	1.0 e6	1.4 e-2	14 nM
TCN-032	7.4 e5	2.3 e-3	3.2 nM
cH14C2	5.0 e2	1.8 e-3	4.0 µM

[1445] *Protection from Lethal Challenges with H5N1 and H1N1 viruses.* We next examined the protective efficacy of the human anti-M2e mAbs TCN-031 and TCN-032 in a lethal challenge model of influenza infection in mice. Animals were challenged intranasally with 5 x LD50 units of a high-pathogenicity H5N1 virus (A/Vietnam/1203/04) and both human mAbs were protective when treatment was initiated one day after viral challenge. In contrast, mice that

were subjected to similar treatment regimens with a subclass-matched, irrelevant control mAb 2N9, which targets the AD2 epitope of the gp116 portion of the human cytomegalovirus gB, or with a vehicle control were protected to a lesser extent, or not at all, resulting in 70-80% survival for mice treated with human mAbs versus 20% survival for control mAb and 0% survival for vehicle (Fig. 15a). The anti-M2e mAb ch14C2 did not confer substantial protection in this model (20% survival; Figure 15a), though this mAb has been shown to reduce the titer of virus in the lungs of mice infected with other strains of influenza virus (Treanor JJ, et al. (1990) J Virol 64:1375-1357). All of the animals, including those in the TCN-031 and TCN-032 treatment groups, exhibited weight loss from days 4 to 8 post infection followed by a gradual increase in weight in the surviving animals through the end of the study on day 14 (Fig. 15b), indicating that the human anti-M2e mAbs afforded protection by reducing the severity or extent of infection rather than by completely preventing infection. Indeed, results of immunohistological and viral load analyses of lung, brain and liver tissue from additional animals in each treatment cohort are consistent with a reduction in the spread of virus beyond the lung to the brain and also possibly liver in animals that were treated with the human anti-M2e mAbs, but not with ch14C2 or the subclass-matched control mAb 2N9. The effect of the human anti-M2e mAbs on viral load in the lung versus the control mAbs was, however, more moderate (Table 5 and Fig 16, respectively).

[1446] To test whether protection conferred by the human anti-M2e mAbs mirrors their broad binding behavior, we performed a similar in vivo challenge study with a mouse-adapted isolate of the relatively divergent H1N1 virus A/Puerto Rico/8/34. One hundred percent of PBS-treated or subclass-matched, control antibody-treated mice were killed by this virus, while a majority of the animals treated with the human anti-M2e mAbs TCN-031 and TCN-032 survived (60%; Fig. 15c). With this virus mice treated with ch14C2 provided a similar survival benefit to that of the human anti-M2e mAbs (Fig. 15c). Weight changes in each treatment group throughout the course of infection and its subsequent resolution followed a pattern that was similar to that of mice infected with the H5N1 virus (Fig. 15d).

[1447] The human anti-M2e mAbs and ch14C2 bound to cell surface-expressed M2e from A/Vietnam/1203/04 and A/Puerto Rico/8/34 viruses (Fig 19b, Table 6) and cells infected with

A/Puerto Rico/8/34 (Fig. 14c). Mechanisms for antibody-mediated protection could include killing of infected host cells by antibody-dependent cell-mediated cytotoxicity or complement-dependent cytotoxicity (Wang R, et al. (2008) Antiviral Res 80:168-177; Jegerlehner A, et al. (2004) J Immunol 172:5598-5605). We found in vitro evidence for both of these mechanisms with the human anti-M2e mAbs and ch14C2 (Fig. 17 and Table 6). An explanation for the enhanced in vivo protection observed with the human anti-M2e mAbs as compared to ch14C2 following challenge by the high-pathogenicity avian virus A/Vietnam/1203/04 as compared with A/Puerto Rico/8/34 could be due to the unique capability of the human mAbs to bind virus directly whereas ch14C2 does not appear to bind influenza virions (Fig 14a). Protective properties of antibodies that bind to virus might be expected to include mechanisms such as antibody-dependent virolysis (Nakamura M, et al. (2000) Hybridoma 19:427-434) and clearance via opsonophagocytosis by host cells (Huber VC, et al. (2001) J Immunol 166:7381- 7388). Some of these mechanisms require efficient interaction between antibodies and host Fc receptors. In our mouse challenge experiments all of the mAbs tested had human constant regions; however other studies have shown that human antibodies can interact productively with murine Fc receptors (Clynes RA, et al. (2000) Nat Med 6:443-446).

[1448] Table 5. Pathological assessment of lung, liver, and brain of mice treated with anti-M2e mAbs TCN-031 and TCN-032 after challenge with H5N1 A/Vietnam/1203/04.

Organs	Mouse	TCN-031	TCN-032	2N9	CH14C2	PBS	UT/C
Lung	1	++/++	++/++	++/++	++/++	++/++	++/+++
	2	++/++	++/++	++/+++	++/++	++/++	++/++
	3	++/++	++/++	++/++	++/++	++/+++	++/++
Brain	1	-/-	-/-	+/+	-/-	+/+++	++/+++
	2	-/-	±/+	+/+++	+/+	-/-	+/+
	3	-/-	-/-	+/+	+/++	+/+++	++/+++
Liver	1	-/-	-/-	+/+	+/-	+/+	+/+
	2	-/-	-/-	+/+	+/-	+/-	+/-
	3	-/-	+/-	+/+	+/+	+/+	+/+

Pathological changes and viral antigens were detected in the lungs of all virus-challenged mice. The mice had similar lung lesions across all groups, although mice in the TCN-031 and TCN-032 groups had a tendency toward less viral antigen expression in the lung. In the brain and liver, lesions were not detected in mice in the TCN-31 group and only one of three mice in the TCN-032 group showed some evidence of viral antigens in the brain. Pathological changes/viral antigens: +++ severe/many, ++ moderate/moderate, + mild/few, ± scant/rare, - not observed/negative.

[1449] Table 6.

		Amino acids 1-23 of the M2 extracellular domain																				
1	A/Brevig Mission/1/1918 H1N1	S	L	L	T	E	V	E	T	P	T	R	N	E	W	G	C	R	C	N	D	S	S	D
2	A/Fort Monmouth/1/1947 H1N1											K				E								
3	A/ Singapore/02/2005 H3N2										I					E								
4	A/Wisconsin/10/1998 H1N1										I			G		E								
5	A/Wisconsin/301/1976.H1N1										I		S											
6	A/Panama/1/1966 H2N2		F		P						I													
7	A/New York/321/1999 H3N2										I													N
8	A/Caracas/1/1971 H3N2										I		K											
9	A/Taiwan/3/1971 H3N2		F								I		S											
10	A/Wuhan/359/1995 H3N2			P							I		S											
11	A/Hong Kong/1144/1999 H3N2				P						I													
12	A/Hong Kong/1180/1999 H3N2				P						I			G										
13	A/Hong Kong/1774/1999 H3N2													G		E				S	G			
14	A/New York/217/2002 H1N2										I					E	Y							
15	A/New York/300/2003 H1N2										I					E	Y			S				
16	A/swine /Spain/54008/2004 H3N2													G		E			Y	S				
17	A/Guangzhou/333/99 H9N2		F							L				G		E				S				
18	A/Hong Kong/1073/1999 H9N2									L				G		E		K		R				
19	A/Hong Kong/1/1968 H3N2										I													
20	A/swine /Hong Kong/126/1982 H3N2										I		S										G	
21	A/New York/703/1995 H3N2										I					E					G			
22	A/swine/Quebec/192/1981 H1N1			P							I													
23	A/Puerto Rico/8/1934 H1N1										I										G			
24	A/ Hong Kong/485/1997 H5N1							D		L				G						S				
25	A/Hong Kong.542/1997 H5N1									L		K		G						S				
26	A/silky chicken/Shantou /1826/2004 H9N2													G		E		K		S				
27	A/chicken/Taiwan/0305/2004 H6N1									H				G		E		K		S				
28	A/Quail/Arkansas/16309-7/1994 H7N3							K						G		E		K		S				
29	A/Hong Kong/486/1997 H5N1									L				G						S				
30	A/chicken/Pennsylvania/13552-1/1998 H7N2												D	G		E		K		S				
31	A/chicken/Heilongjiang/48/2001 H9N2													G						S				
32	A/swine/Korea/S5/2005 H1N2													G		E		K						
33	A/Hong Kong/ 1073/1999 H9N2									L				G		E		K		S				
34	A/Wisconsin/3523/1988 H1N1										I							K						
35	A/X-31 Vaccine strain H3N2		F								I										G			
36	A/Chicken/Rostock/8/1934 H7N1													G		E								
37	A/environment /New York/16326-1/2005 H7N2										I		K	G		E		N		S				
38	A/chicken/Hong Kong/SF1/2003 H9N2					G				H				G				K		S				
39	A/chicken/Hong Kong/ YU427/2003 H9N2				P					H				G						S				
40	A/Indonesia/ 560H/2006 H5N1															E								
HK	A/Hong Kong/483/1997 H5N1									L				G						S				
VN	A/Vietnam/1203/2004 H5N1															E				S				
D20	A/FW/1/1950 H1N1										I													

The M2e sequence at the top is from A/Brevig Mission/1/18 (H1N1) and is used as the reference sequence for alignment of the M2 ectodomain amino acids 1-23 of 43 wild-type variants. Grey boxes denote amino acid identity with the reference sequence and white boxesare amino acid replacement mutations. This list of non-identical sequences, except for HK, VN,and D20, was derived from M2 sequences used in references 11 and 27. Sequence data are from The Influenza Virus Resource at the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/genomes/FLU/FLU.html).

[1450] *Binding to the Highly Conserved N-Terminal Segment of M2e.* To better understand the unique viral binding property of the human anti-M2e mAbs we mapped their binding

sites within the M2e domain. The lack of appreciable binding of the human mAbs to M2e-derived linear peptides precluded a synthetic peptide approach to fine structure mapping of their epitopes. Instead, binding of the mAbs to M2e alanine substitution mutants and naturally occurring M2 variants that were expressed on the surface of cDNA-transfected mammalian cells was quantified by flow cytometry. Binding experiments with a panel of M2 mutant proteins where each position in the 23 amino acid M2 ectodomain was substituted with alanine revealed that the first (S), fourth (T), and fifth (E) positions of the mature (methionine-clipped) M2 polypeptide were critical for binding of both TCN-031 and TCN-032 (Fig. 19a). In contrast, the binding of ch14C2 was selectively diminished when alanine was substituted at position 14 of mature M2 (Fig. 19a). These observations were confirmed in studies with a panel of divergent, naturally occurring M2 variants; substitution with proline at position 4 (Table 6: A/Panama /1/1966 H2N2, A/Hong Kong/1144/1999 H3N2, A/Hong Kong/1180/1999 H3N2, and A/chicken/Hong Kong/YU427/2003 H9N2) and glycine at position 5 (Table 6: A/chicken/Hong Kong/SF1/2003 H9N2) correlated with diminished binding of the human anti-M2e mAbs but not ch14C2 (Fig. 19b, Table 6). These results suggest that both TCN-031 and TCN-032 recognize a core sequence of SLLTE at positions 1-5 of the N-terminus of mature M2e. This is supported by data which show that these mAbs compete effectively with each other for binding to M2e expressed on the surface of CHO cells (Fig. 20). In contrast, our results indicate that ch14C2 binds to a site that is spatially distinct and downstream of the SLLTE core that is recognized by the human anti-M2e mAbs. Indeed, previous studies have shown that 14C2 binds a relatively broad, linear epitope with the sequence EVERTPIRNEW at positions 5-14 of processed M2e (Wang R, et al. (2008) Antiviral Res 80:168-177).

[1451] While the epitopes recognized by TCN-031 and TCN-032 are likely very similar, there were some differences between these human mAbs in their binding to several of the M2e mutants. For instance, TCN-031 appears to have a greater dependence than TCN-032 on residues 2 (L) and 3 (L) of the mature M2e sequence (Fig. 19a). The VH regions of these two human mAbs utilize different variable, diversity, and joining gene segments

which may explain the minor differences in binding observed between these mAbs. Interestingly, despite the differences in their VH make-up these human mAbs utilize the same germline kappa chain V gene segments, albeit with distinct kappa chain joining segments.

[1452] Localization of the binding region of the human anti-M2e mAbs at the N-terminal region of M2e is especially significant in light of the remarkably high sequence conservation in this part of the polypeptide among influenza A viruses. The viral M gene segment that encodes M2 also encodes the internal viral protein M1 via differential splicing. However, the splice site is located downstream of the shared N-terminus of M2 and M1 resulting in two distinct mature polypeptides with an identical 8 amino acid N-terminal sequence (Lamb RA and Choppin PW (1981) Virology 112:729-737). Options for viral escape from host anti-M2e antibodies that bind this region might be limited as escape mutations in the N-terminal region would result in changes to not just M2 but also the M1 protein. Indeed, this N-terminal 8 amino acid segment of M2e shows nearly complete identity in the 1364 unique full-length M2 variants catalogued in the NCBI Influenza Database (www.ncbi.nlm.nih.gov/genomes/FLU/Database/multiple.cgi) while much lower levels of conservation are seen in M2e sequences downstream of this region (Fig. 19c). In fact, the core human anti-M2e antibody epitope SLLTE is present in ~98% of the 1364 unique full-length M2e sequences catalogued in the NCBI Influenza Database, including 97%, 98% and 98% of the human, swine and avian viruses, respectively. This contrasts to the much lower conservation within the linear binding sites of anti-M2e mAbs elicited by immunization with M2e peptides or proteins. For instance, 14C2 and Z3G1 (Wang R, et al. (2008) Antiviral Res 80:168-177) bind sequences that are conserved in less than 40% of influenza A viruses, and conservation within this region is even lower in avian and swine viruses (Table 7).

[1453] The linear M2e epitopes recognized by peptide-elicited antibodies may be more sensitive to escape mutations and natural substitutions that are present in some viral isolates. For example, P10L and P10H escape mutations to mAb 14C2 have been mapped to the central portion of M2e (Zharikova D, et al. (2005). J Virol 79:6644-6654) and those same substitutions also occur in M2e variants from some highly pathogenic H5N1 strains. We have found that the

human mAbs TCN-031 and TCN-032 but not ch14C2 bind to the M2 variant from the H5N1 virus A/Hong Kong/483/97 (HK) which contains the P10L substitution (Fig. 19b, Table 6). Thus, monoclonal antibodies with specificities similar to that of 14C2 are likely to have limited utility as broad spectrum therapeutic agents.

[1454] In the examination of 5 human subjects we found 17 unique anti-M2e antibodies that bind the conserved N-terminal region of M2e, but did not observe IgG-reactivity with M2e-derived peptides that contain the linear epitopes recognized by 14C2 and other peptide-elicited antibodies. In contrast to the apparently uniform antibody response to M2e in naturally infected or vaccinated humans, mice immunized with M2e-derived peptides produced antibodies with a range of specificities within M2e, including the conserved N-terminus and also downstream regions (Fu TM, et al. (2008) Virology 385:218-226). It is tempting to speculate that the human immune system has evolved a humoral response that exclusively targets the highly conserved N-terminal segment of M2e rather than the more divergent, and thus less sustainably protective, downstream sites. Despite the lack of evidence for human antibodies that recognize this internal region of M2e, analysis of the evolution of the M gene suggests that this region of M2e is under strong positive selection in human influenza viruses (Furuse Y, et al. (2009) J Virol 29:67). One explanation for this finding is that selective pressure is being directed at this internal region by immune mechanisms other than antibodies. For instance, human T cell epitopes have been mapped to these internal M2e sites (Jameson J, et al. (1998) J Virol 72:8682-8689).

[1455] Table 7. Conservation of the viral binding site for human anti-M2e mAbs compared with those for mAbs derived from immunized mice, in influenza A.

mAb	Human (n=506)	Swine (n=193)	Avian (n=665)	All (n=1364)
TCN-031, TCN-032 [1-SLLTE-5]	97	98	98	98
Z3G1 [2-LLTEVETPIR-11] (Ref. 11)	79	39	7	38
14C2 [5-EVETPIRNEW-14] (Ref. 11)	75	19	2	31

[1456] *Recognition of 2009 H1N1 S-OIV.* Broadly protective anti-influenza mAbs could be used in passive immunotherapy to protect or treat humans in the event of outbreaks from highly pathogenic, pandemic viral strains. A critical test of the potential for such mAbs as immunotherapeutic agents is whether they are capable of recognizing virus strains that may evolve from future viral reassortment events. As a case in point, the human anti-M2e mAbs TCN-031 and TCN-032 were tested for their ability to recognize the current H1N1 swine-origin pandemic strain (S-OIV). These mAbs were derived from human blood samples taken in 2007 or earlier, prior to the time that this strain is thought to have emerged in humans (Neumann G, et al. (2009) Nature 459:931-939). Both human mAbs bound to MDCK cells infected with A/California/4/2009 (S-OIV H1N1, pandemic) and A/Memphis/14/1996 (H1N1, seasonal) whereas ch14C2 bound only to cells infected with the seasonal virus (Fig. 21). If this broad binding behavior proves to correlate with protection, as was the case with A/Vietnam/1203/2004 and A/Puerto Rico/8/34, then these human mAbs might be useful to

prevent or treat the S-OIV pandemic strain or possibly other pandemic strains that might emerge in the future.

[1457] While it is remarkable that humans have the capability to make antibodies that may confer nearly universal protection against influenza infection, the discovery of this heretofore un-described class of antibodies raises the question of why this virus is able to mount a productive infection in immunocompetent individuals at all. This apparent paradox may be explained by the nature of the protective M2e epitope and its relative immunogenicity. It has been noted by others that M2e appears to exhibit low immunogenicity in humans (Feng J, et al. (2006) Virol J 3:102; Liu W, et al. (2003) FEMS Immunol Med Microbio 35:141-146), especially when compared to the immunodominant virus glycoproteins HA and NA. Therefore, protective anti-M2e antibodies may exist in many individuals but at suboptimal titers. In support of this notion is our observation that most individuals did not display a detectable humoral response to M2e. We observed that fewer than 20% (23/140) of the individuals that we sampled in our cohort of healthy subjects had detectable serum levels of anti-M2e antibodies. The reasons for this phenomenon are not clear but a similar situation exists in HCMV where only a minority of HCMV seropositive subjects has measurable antibodies to the broadly conserved, neutralizing AD2 epitope within the gB complex of HCMV (Meyer H, et al. (1992) J Gen Virol 73:2375-2383; Ayata M, et al. (1994) J Med Virol 43:386-392; Navarro D, et al. (1997) J Med Virol 52:451-459).

[1458] An important requirement for an immunotherapeutic solution to the influenza threat will be the identification of protective epitopes that are conserved in pre-existing and emerging viruses. Using large-scale sampling of the human immune response to native influenza M2 we have identified a naturally immunogenic and protective epitope within the highly conserved N-terminal region of M2e. Human antibodies directed to this epitope, including those described in the present study, may be useful for the prevention and treatment of pandemic and seasonal influenza.

Methods

[1459] *Memory B cell culture.* Whole blood samples were collected from normal donors under IRB approved informed consent and peripheral blood mononuclear cells (PBMC) were purified

by standard techniques. B cell cultures were set up using PBMC, B cells enriched by selection with M2-expressing cells, or IgG^+ memory B cells enriched from PBMC via negative depletion of nonIgG^+ cells with antibodies to CD3, CD14, CD16, IgM, IgA, and IgD on magnetic beads (Miltenyi, Auburn, CA) as previously described (Walker L, et al. (2009) Science 326:289-293). Briefly, to promote B cell activation, proliferation, terminal differentiation and antibody secretion, cells were seeded in 384-well microtiter plates in the presence of feeder cells and conditioned media generated from mitogen-stimulated human T cells from healthy donors. The culture supernatants were collected 8 days later and screened in a high throughput format for binding reactivity to M2 protein expressed on HEK 293 cells stably transfected with influenza virus M2 (A/Fort Worth/50 H1N1) using fluorescent imaging (FMAT system, Applied Biosystems).

[1460] *Reconstitution of recombinant mAbs from B cell cultures.* mRNA was isolated from lysed B-cell cultures using magnetic beads (Ambion). After reverse transcription (RT) with gene-specific primers, variable domain genes were PCR amplified using VH, V , and Vλ family-specific primers with flanking restriction sites (Walker L, et al. (2009) Science 326:289-293). PCR reactions producing an amplicon of the expected size were identified using 96-well E-gels (Invitrogen) and the variable domain amplicons were cloned into the pTT5 expression vector (National Research of Canada, Ottawa, Canada) containing human IgG1, Igκ, or Igλ constant regions. Each VH pool was combined with the corresponding Vκ, or Vλ pools from individual BCC wells and was transiently transfected in 293-6E cells to generate recombinant antibody. Conditioned media was harvested 3-5 days after transfection and assayed for antibody binding to M2 protein expressed on HEK 293 cells. Individual clones were isolated from positive pools and unique VH and VL genes were identified by sequencing. From these, monoclonal antibodies were subsequently expressed and re-assayed for binding activity.

[1461] *ELISA.* To detect viral antigen, either 10.2 μg/mL UV-inactivated H1N1 A/Puerto Rico/8/34 (PR8) virus (Advanced Biotechnologies, Inc.) was passively adsorbed to 384-well plates in 25 μL PBS/ well for 16 hr at 4°C, or PR8 inactivated by β-propiolactone (Advanced Biotechnologies, Inc.) was biotinylated (EZ-Link Sulfo-NHS-LC-Biotin, Pierce) and likewise adsorbed to plates coated with neutravidin (Pierce). Virus-coated and biotinylated virus-coated

plates were blocked with PBS containing 1% milk or BSA, respectively. Binding of mAbs at the indicated concentrations was detected with HRP-conjugated goat anti-human Fc antibody (Pierce) and visualized with TMB substrate (ThermoFisher). The M2e peptide, SLLTEVETPIRNEWGCRCNDSSD (SEQ ID NO: 680) (Genscript) was passively adsorbed at 1 μg/mL and antibody binding to the peptide was detected by the same method.

[1462] *FACS analysis of virally infected cells.* To detect M2e following in vitro infection, MDCK cells were treated with PR8 at multiplicity of infection (MOI) of 60:1 for 1 hr at 37° C after which the culture media was replaced. The infected MDCK cells were further cultured for 16 hr before harvesting for cell staining with the indicated mAbs. Bound anti-M2 mAbs were visualized on viable cells with Alexafluor 647-conjugated goat anti-Human IgG H&L antibody (Invitrogen). Flow cytometry was performed on FACSCanto equipped with the FACSDiva software (Becton Dickenson). For the panel of anti-M2 mAbs, 20 μL samples of supernatant from transient transfections from each of the IgG heavy and light chain combinations was used to stain the 293 stable cell line expressing M2 of A/Hong Kong/483/97 FACS analysis was performed as above.

[1463] *M2 variant analyses.* Individual full length M2 cDNA mutants were synthesized with single ala mutations at each position of the ectodomain representing A/Fort Worth/1/1950 (D20), as well as were the forty-three naturally occurring variants of M2 (Blue Heron Technology). They were cloned into the plasmid vector pcDNA3.1. After transient transfection with Lipofectamine (Invitrogen), HEK293 cells were treated with 1 μg/mL of the indicated mAbs in PBS supplemented with 1% fetal bovine serum and 0.2% NaN3 (FACS buffer). Bound anti-M2 mAbs were visualized on viable cells with Alexafluor 647-conjugated goat anti-Human IgG H&L antibody (Invitrogen). Flow cytometry was performed with FACSCanto equipped with the FACSDiva software (Becton Dickenson). The relative binding to the naturally occurring variants was expressed as the percentage of the respective mAb staining of the D20 transiently transfected cells, using the formula of Normalized MFI (%) 100 x (MFIexperimental-MFImock transfected)/(MFID20-MFImock transfected).

[1464] *Therapeutic efficacy studies in mice.* Animal studies were conducted under Institutional Animal Care and Use Committee protocols. We inoculated 6 groups of 10 mice (female 6-8 week

old BALB/C) intranasally with 5 x $_{LD50}$ of A/Vietnam/1203/04 (Fig 15a and b) or 6 groups of 5 mice intranasally with 5 x $_{LD50}$ A/Puerto Rico/8/34 (Fig 15c and d). At 24, 72, and 120 hours post-infection the mice received intraperitoneal injections of 400 μg/200 μL dose of the anti-M2e mAbs TCN-031 TCN-032, control human mAb 2N9, control chimeric mAb ch14C2, PBS, or were left untreated. Mice were weighed daily for 2 weeks and were euthanized when weight loss exceeded 20% (H5N1 study shown in Fig 15a and 15b and H1N1 study shown in Fig 15c and 15d) of the pre-infection body weight.

[1465] *Antibody reactivity to A/California/4/2009 infected cells.* MDCK cells were infected with media alone or media containing A/California/4/2009 (H1N1) or A/Memphis/14/1996 (H1N1) at an MOI of approximately 1 and were cultured for 24 hours at 37° C. The cells were detached from the tissue culture plates with trypsin, washed extensively, and then fixed in 2% paraformaldehyde for 15 minutes. The cells were incubated with 1 μg/ml of the indicated antibodies and the primary antibody binding was detected with Alexafluor 647-conjugated goat anti-Human IgG H&L antibody (Invitrogen). The cells were analyzed with a Becton Dickinson FACSCalibur and data were processed using FlowJo software.

[1466] *Competition analysis of antibody binding.* Transient transfection supernatant containing antibody was screened for binding to 293 cells stably transfected with M2 from H1N1 (A/Fort Worth/50 H1N1), or mock transfected cells, in the presence or absence of the M2e peptide SLLTEVETPIRNEWGCRCNDSSD (Genscript) at 5 μg/mL. Bound anti-M2 mAbs were detected with anti-huIgG Fc FMAT Blue at 700 ng/ml in DMEM with 10% FCS and visualized by fluorescent imaging (FMAT system, Applied Biosystems).

Example 13: Screening and Characterization of HA-specific Antibodies Present in Human Plasma that bind purified whole inactivated Influenza A Virions, bind recombinant homotrimeric HA proteins, and neutralize infectious influenza A.

[1467] Fully human monoclonal antibodies specific for HA and capable of binding purified whole inactivated Influenza A Virions, binding recombinant homotrimeric HA proteins, and neutralizing live influenza A were identified in patient plasma, as described below.

Expression of recombinant soluble HA

[1468] An expression construct was generated containing a cDNA encoding an HA precursor (HA0) polypeptide corresponding to the derived HA sequence found in the Influenza subtypes,

for example, as listed in Table 9. Recombinant HA0 precursor polypeptides of the invention lack an integral membrane or transmembrane domain, and contain additional amino acids at the C-terminus of the HA0 ectodomain, for instance, corresponding to the sequence: SGR***LVPRGS***PGSGYIPEAPRDGQAYVRKDGEWVLL STFLGKPIPNPLLGLDSTG**HHHHHH** (SEQ ID NO: 726), wherein the thrombin cleavage site is bolded and italicized, the bacteriophage T4 fibritin "foldon" or trimerization domain is underlined, the last amino acid of the trimerization domain, "G", is the start of the boxed "V5" epitope tag, which is followed by the hexa histadine (HIS) epitope tag in bold. The hexa-HIS tag within the preceding C-terminal region is used for purification of recombinant HA proteins of the invention. Thus, recombinant HA0 precursor proteins that contain a trimerization domain are considered recombinant HA homotrimeric proteins of the invention.

[1469] Recombinant HA homotrimeric proteins of the invention retain the native signal sequence to allow efficient secretion from art-recognized cell lines maintained in vitro, e.g. 293 HEK cells as done by Immune Technology Corp. (http://www.immune-tech.com/). Moreover, within these recombinant HA homotrimeric proteins, or the HA0 precursors thereof, the native HA1/HA2 viral protease cleavage site was maintained, for instance, in all of the sequences provided in Table 9, except SEQ ID NO: 737, in which the native cleavage site positioned at amino acids 337-347 and consisting of the sequence "PQREGGRRRKR" (SEQ ID NO: 1250) was substituted with the sequence "PQTETR" (SEQ ID NO: 1251).

[1470] Furthermore, exemplary receptor binding domains of recombinant HA homotrimeric proteins, or the HA0 precursors thereof, include the following structural elements: a 190 α-helix, a 130-loop, and a 220-loop (*see*, sequence of Influenza A strain A/Vietnam/1203/2004) (or equivalent HA structures in other Influenza A strains that the ordinarily skilled artisan could readily obtain by accessing public databases, including GenBank, http://www.ncbi.nlm.nih.gov, and The Influenza Sequence Database, www.flu.lanl.gov, and downloading sequences) (Stevens et al. 2006. Science 312: 404-410). In other embodiments of the invention, in which the recombinant HA homotrimeric protein, or HA0 precursor thereof, encoded by this expression construct is partially or entirely expressed and administered to a subject, these receptor binding domains may be modified. The term "modified" is meant to describe the removal of one or more

structural elements. Alternatively, or in addition, "modified" is meant to describe the addition, deletion, substitution, inversion, or translocation of one or more amino acids within a structural element of a receptor-binding domain of HA. For instance, a linear or discontinuous epitope to which a HuMHA antibody of the invention binds is administered to a subject at risk of contracting an influenza infection to prevent the infection. Alternatively or in addition, a linear or discontinuous epitope to which a HuMHA antibody of the invention binds is administered to a subject prior to exposure to an influenza virus to prevent influenza infection. In other embodiments a structural mimic of the conformational or discontinuous epitope is administered to a subject. When the above proteins are used for prophylactic purposes, for instance, as a vaccine, it may be advantageous to modify one or more receptor binding domains to control the resultant immune response in the subject. Exemplary structural elements of HA that are optionally modified include, but are not limited to, the 190 α-helix, the130-loop, and the 220-loop of HA.

[1471] Recombinant homotrimeric HA proteins of the invention are encoded by the following amino acid sequences, wherein the native sequence is bolded and the sequence of SEQ ID NO: 726 is normal (*see also*, Table 9):

[1472] A/California/4/09 (SEQ ID NO: 727)

DTLCIGYHANNSTDTVDTVLEKNVTVTHSVNLLEDKHNGKLCKLRGVAPLHLGKC
NIAGWILGNPECESLSTASSWSYIVETPSSDNGTCYPGDFIDYEELREQLSSVSSFERF
EIFPKTSSWPNHDSNKGVTAACPHAGAKSFYKNLIWLVKKGNSYPKLSKSYINDKG
KEVLVLWGIHHPSTSADQQSLYQNADTYVFVGSSRYSKKFKPEIAIRPKVRDQEGR
MNYYWTLVEPGDKITFEATGNLVVPRYAFAMERNAGSGIIISDTPVHDCNTTCQTP
KGAINTSLPFQNIHPITIGKCPKYVKSTKLRLATGLRNIPSIQSRGLFGAIAGFIEGG
WTGMVDGWYGYHHQNEQGSGYAADLKSTQNAIDEITNKVNSVIEKMNTQFTAVG
KEFNHLEKRIENLNKKVDDGFLDIWTYNAELLVLLENERTLDYHDSNVKNLYEKV
RSQLKNNAKEIGNGCFEFYHKCDNTCMESVKNGTYDYPKYSEEAKLNREEIDGVK
LESTRIYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLGLDS
TGHHHHHH

[1473] A/Solomon Islands/3/06 - H1N1 (SEQ ID NO: 728)
DTICIGYHANNSTDTVDTVLEKNVTVTHSVNLLEDSHNGKLCLLKGIAPLQLGNCS
VAGWILGNPECELLISRESWSYIVEKPNPENGTCYPGHFADYEELREQLSSVSSFER
FEIFPKESSWPNHTTTGVSASCSHNGESSFYKNLLWLTGKNGLYPNLSKSYANNKE
KEVLVLWGVHHPPNIGDQRALYHKENAYVSVVSSHYSRKFTPEIAKRPKVRDQEG
RINYYWTLLEPGDTIIFEANGNLIAPRYAFALSRGFGSGIINSNAPMDECDAKCQTP

**QGAINSSLPFQNVHPVTIGECPKYVRSAKLRMVTGLRNIPSIQSRGLFGAIAGFIEGG
WTGMVDGWYGYHHQNEQGSGYAADQKSTQNAINGITNKVNSVIEKMNTQFTAVG
KEFNKLERRMENLNKKVDDGFIDIWTYNAELLVLLENERTLDFHDSNVKNLYEKV
KSQLKNNAKEIGNGCFEFYHKCNDECMESVKNGTYDYPKYSEESKLNREKIDGVK
LESMGVYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLGLD
STGHHHHHH**

[1474] A/South Carolina/1/18 – (SEQ ID NO: 729)
**MEARLLVLLCAFAATNADTICIGYHANNSTDTVDTVLEKNVTVTHSVNLLEDSHNGKL
CKLKGIAPLQLGKCNIAGWLLGNPECDLLLTASSWSYIVETSNSENGTCYPGDFIDYEE
LREQLSSVSSFEKFEIFPKTSSWPNHETTKGVTAACSYAGASSFYRNLLWLTKKGSSYP
KLSKSYVNNKGKEVLVLWGVHHPPTGTDQQSLYQNADAYVSVGSSKYNRRFTPEIAA
RPKVRDQAGRMNYYWTLLEPGDTITFEATGNLIAPWYAFALNRGSGSGIITSDAPVHD
CNTKCQTPHGAINSSLPFQNIHPVTIGECPKYVRSTKLRMATGLRNIPSIQSRGLFGAIA
GFIEGGWTGMIDGWYGYHHQNEQGSGYAADQKSTQNAIDGITNKVNSVIEKMNTQFT
AVGKEFNNLERRIENLNKKVDDGFLDIWTYNAELLVLLENERTLDFHDSNVRNLYEKV
KSQLKNNAKEIGNGCFEFYHKCDDACMESVRNGTYDYPKYSEESKLNREEIDGVKLES
MGVYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLGLDSTGHH
HHHH**

[1475] A/Japan/305/57 - H2N2 (SEQ ID NO: 730)
**DQICIGYHANNSTEKVDTNLERNVTVTHAKDILEKTHNGKLCKLNGIPPLELGDCSI
AGWLLGNPECDRLLSVPEWSYIMEKENPRDGLCYPGSFNDYEELKHLLSSVKHFE
KVKILPKDRWTQHTTTGGSRACAVSGNPSFFRNMVWLTKEGSDYPVAKGSYNNTS
GEQMLIIWGVHHPIDETEQRTLYQNVGTYVSVGTSTLNKRSTPEIATRPKVNGQGG
RMEFSWTLLDMWDTINFESTGNLIAPEYGFKISKRGSSGIMKTEGTLENCETKCQT
PLGAINTTLPFHNVHPLTIGECPKYVKSEKLVLATGLRNVPQIESRGLFGAIAGFIEG
GWQGMVDGWYGYHHSNDQGSGYAADKESTQKAFDGITNKVNSVIEKMNTQFEA
VGKEFGNLERRLENLNKRMEDGFLDVWTYNAELLVLMENERTLDFHDSNVKNLY
DKVRMQLRDNVKELGNGCFEFYHKCDDECMNSVKNGTYDYPKYEEESKLNRNEI
KGVKLSSMGVYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPL
LGLDSTGHHHHHH**

[1476] A/Wisconsin/67/05 - H3N2 (SEQ ID NO: 731)
**QKLPGNDNSTATLCLGHHAVPNGTIVKTITNDQIEVTNATELVQSSSTGGICDSPHQ
ILDGENCTLIDALLGDPQCDGFQNKKWDLFVERSKAYSNCYPYDVPDYASLRSLVA
SSGTLEFNDESFNWTGVTQNGTSSSCKRRSNNSFFSRLNWLTQLKFKYPALNVTMP
NNEKFDKLYIWGVHHPVTDNDQIFLYAQASGRITVSTKRSQQTVIPNIGSRPRIRNIP
SRISIYWTIVKPGDILLINSTGNLIAPRGYFKIRSGKSSIMRSDAPIGKCNSECITPNGS
IPNDKPFQNVNRITYGACPRYVKQNTLKLATGMRNVPEKQTRGIFGAIAGFIENGW
EGMVDGWYGFRHQNSEGIGQAADLKSTQAAINQINGKLNRLIGKTNEKFHQIEKE
FSEVEGRIQDLEKYVEDTKIDLWSYNAELLVALENQHTIDLTDSEMNKLFERTKKQ
LRENAEDMGNGCFKIYHKCDNACIGSIRNGTYDHDVYRDEALNNRFQIKGVELKS**

GSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLGLDSTG**HHHH HH**

[1477] A/swine/Ontario/01911-2/99 - H4N6 (SEQ ID NO: 732)
QNYTGNPVICLGHHAVSNGTMVKTLTDDQIEVVTAQELVESQHLPELCPSPLRLVD GQTCDIVNGALGSPGCDHLNGAEWDVFIERPTAVDTCYPFDVPDYQSLRSILANNG KFEFIAEEFQWNTVKQNGKSGACKRANVNDFFNRLNWLTKSDGNAYPLQNLTKV NNGDYARLYIWGVHHPSTDTEQTNLYKNNPGRVTVSTQTSQTSVVPNIGSRPWVR GLSSRISFYWTIVEPGDLIVFNTIGNLIAPRGHYKLNSQKKSTILNTAVPIGSCVSKCH TDKGSISTTKPFQNISRISIGDCPKYVKQGSLKLATGMRSILEKATRGLFGAIAGFIE NGWQGLIDGWYGFRHQNAEGTGTAADLKSTQAAIDQINGKLNRLIGKPNEKYHQI EKEFEQVEGRIQDLEKYVEDTKIDLWSYNAELLVALENQHTIDVTDSEMNKLFERV RHQLRENAEDKGNGCFEIFHQCDNSCIESIRNGTYDHDIYRDEAINNRFQIQGVKLI QGYKDSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLGLDSTG HHHHHH

[1478] A/Hong Kong/156/97 – H5N1 (SEQ ID NO: 733)
MERTVLLLATVSLVKSDQICIGYHANNSTEQVDTIMEKNVTVTHAQDILERTHNGK LCDLNGVKPLILRDCSVAGWLLGNPMCDEFINVPEWSYIVEKASPANDLCYPGNFN DYEELKHLLSRINHFEKIQIIPKSSWSNHDASSGVSSACPYLGRSSFFRNVVWLIKKN SAYPTIKRSYNNTNQEDLLVLWGVHHPNDAAEQTKLYQNPTTYISVGTSTLNQRLV PEIATRPKVNGQSGRMEFFWTILKPNDAINFESNGNFIAPEYAYKIVKKGDSTIMKS ELEYGNCNTKCQTPMGAINSSMPFHNIHPLTIGECPKYVKSNRLVLATGLRNTPQR ERRRKKRGLFGAIAGFIEGGWQGMVDGWYGYHHSNEQGSCYSADKESTQKAIDG VTNKVNSIINKMNTQFEAVGREFNNLERRIENLNKKMEDGFLDVWTYNAELLVLM ENERTLDFHDSNVKNLYDKVRLQLRDNAKELGNGCFEFYHKCDNECMESVKNGT YDYPQYSEEARLNREEISGVKLESMGTYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKD GEWVLLSTFLGKPIPNPLLGLDSTGHHHHHH**

[1479] A/Vietnam/1203/04 - H5N1 (SEQ ID NO: 734)
DQICIGYHANNSTEQVDTIMEKNVTVTHAQDILEKKHNGKLCDLDGVKPLILRDCS VAGWLLGNPMCDEFINVPEWSYIVEKANPVNDLCYPGDFNDYEELKHLLSRINHFE KIQIIPKSSWSSHEASLGVSSACPYQGKSSFFRNVVWLIKKNSTYPTIKRSYNNTNQE DLLVLWGIHHPNDAAEQTKLYQNPTTYISVGTSTLNQRLVPRIATRSKVNGQSGRM EFFWTILKPNDAINFESNGNFIAPEYAYKIVKKGDSTIMKSELEYGNCNTKCQTPMG AINSSMPFHNIHPLTIGECPKYVKSNRLVLATGLRNSPQRERRRKKRGLFGAIAGFI EGGWQGMVDGWYGYHHSNEQGSGYAADKESTQKAIDGVTNKVNSIIDKMNTQFE AVGREFNNLERRIENLNKKMEDGFLDVWTYNAELLVLMENERTLDFHDSNVKNL YDKVRLQLRDNAKELGNGCFEFYHKCDNECMESVRNGTYDYPQYSEEARLKREEI SGVKLESIGIYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLL GLDSTGHHHHHH**

[1480] A/Indonesia/5/05 - H5N1 (SEQ ID NO: 735)
DQICIGYHANNSTEQVDTIMEKNVTVTHAQDILEKTHNGKLCDLDGVKPLILRDCS
VAGWLLGNPMCDEFINVPEWSYIVEKANPTNDLCYPGSFNDYEELKHLLSRINHFE
KIQIIPKSSWSDHEASSGVSSACPYLGSPSFFRNVVWLIKKNSTYPTIKKSYNNTNQE
DLLVLWGIHHPNDAAEQTRLYQNPTTYISIGTSTLNQRLVPKIATRSKVNGQSGRM
EFFWTILKPNDAINFESNGNFIAPEYAYKIVKKGDSAIMKSELEYGNCNTKCQTPM
GAINSSMPFHNIHPLTIGECPKYVKSNRLVLATGLRNSPQRESRRKKRGLFGAIAGF
IEGGWQGMVDGWYGYHHSNEQGSGYAADKESTQKAIDGVTNKVNSIIDKMNTQF
EAVGREFNNLERRIENLNKKMEDGFLDVWTYNAELLVLMENERTLDFHDSNVKNL
YDKVRLQLRDNAKELGNGCFEFYHKCDNECMESIRNGTYNYPQYSEEARLKREEI
SGVKLESIGTYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLL
GLDSTG**HHHHHH**

[1481] A/Egypt/3300-NAMRU3/08 - H5N1 (SEQ ID NO: 736)
DQICIGYHANNSTEQVDTIMEKNVTVTHAQDILEKTHNGKLCDLDGVKPLILRDCS
VAGWLLGNPMCDEFLNVSEWSYIVEKINPANDLCYPGNFNNYEELKHLLSRINRFE
KIQIIPKSSWPDHEASLGVSSACPYQGGPSFYRNVVWLIKKNNTYPTIKKSYHNTNQ
EDLLVLWGIHHPNDEAEQTRIYKNPTTYISVGTSTLNQRLVPKIATRSKVNGQSGR
VEFFWTILKSNDTINFESNGNFIAPENAYKIVKKGDSTIMKSELEYGNCNTKCQTPI
GAINSSMPFHNIHPLTIGECPKYVKSNRLVLATGLRNSPQGERRRKKRGLFGAIAGF
IEGGWQGMVDGWYGYHHSNEQGSGYAADKESTQKAIDGVTNKVNSIIDKMNTQF
EAVGREFNNLERRIENLNKKMEDGFLDVWTYNAELLVLMENERTLDFHDSNVKNL
YDKVRLQLRDNAKELGNGCFEFYHRCDNECMESVRNGTYDYPQYSEEARLKREEI
SGVKLESIGTYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLL
GLDSTG**HHHHHH**

[1482] A/Common magpie/Hong Kong/5052/07 - H5N1 (SEQ ID NO: 737)
DHICIGYHANNSTEQVDTIMEKNVTVTHAQDILEKTHNGKLCDLNGVKPLILKDCS
VAGWLLGNPMCDEFINVPEWSYIVEKANPANDLCYPGNFNDYEELKHLLSRINHFE
KIQIIPKDSWSDHEASLGVSSACPYQGNSSFFRNVVWLIKKGNAYPTIKKSYNNTNQ
EDLLVLWGIHHPNDEAEQTRLYQNPTTYISIGTSTLNQRLVPKIATRSKVNGQSGRI
DFFWTILKPNDAINFESNGNFIAPEYAYKIVKKGDSTIMKSEVEYGNCNTRCQTPM
GAINSSMPFHNIHPLTIGECPKYVKSNKLVLATGLRNSPQRERRRKRGLFGAIAGFI
EGGWQGMVDGWYGYHHSNEQGSGYAADKESTQKAIDGVTNKVNSIIDKMNTQFE
AVGREFNNLERRIENLNKKMEDGFLDVWTYNAELLVLMENERTLDFHDSNVKNL
YDKVRLQLRDNAKELGNGCFEFYHKCDNECMESVRNGTYDYPQYSEEARLKREEI
SGVKLESIGTYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLL
GLDSTG**HHHHHH**

[1483] A/Anhui/1/05 - H5N1 (SEQ ID NO: 738)
DQICIGYHANNSTEQVDTIMEKNVTVTHAQDILEKTHNGKLCDLDGVKPLILRDCS
VAGWLLGNPMCDEFINVPEWSYIVEKANPANDLCYPGNFNDYEELKHLLSRINHFE
KIQIIPKSSWSDHEASSGVSSACPYQGTPSFFRNVVWLIKKNNTYPTIKRSYNNTNQE
DLLILWGIHHSNDAAEQTKLYQNPTTYISVGTSTLNQRLVPKIATRSKVNGQSGRM

**DFFWTILKPNDAINFESNGNFIAPEYAYKIVKKGDSAIVKSEVEYGNCNTKCQTPIG
AINSSMPFHNIHPLTIGECPKYVKSNKLVLATGLRNSPLRERRRKRGLFGAIAGFIE
GGWQGMVDGWYGYHHSNEQGSGYAADKESTQKAIDGVTNKVNSIIDKMNTQFEA
VGREFNNLERRIENLNKKMEDGFLDVWTYNAELLVLMENERTLDFHDSNVKNLY
DKVRLQLRDNAKELGNGCFEFYHKCDNECMESVRNGTYDYPQYSEEARLKREEIS
GVKLESIGTYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLG
LDSTG**HHHHHH**

[1484] A/chicken/Vietnam/NCVD-016/08 - H5N1 (SEQ ID NO: 739)
**DQICIGYHANNSTEQVDTIMEKNVTVTHAQDILEKTHNGKLCNLDGVKPLILKDCS
VAGWLLGNPMCDEFLNVSEWSYIVEKASPANGLCYPGDFNDYEELKHLLSRINHL
KKIKIIPKSYWSNHEASSGVSAACSYLGEPSFFRNVVWLIKKNNTYPPIKVNYTNTN
QEDLLVLWGIHHPNDEKEQIRIYQNPNTSISVGTSTLNQRLVPKIATRPKVNGQSGR
MEFFWTILKPNDSINFDSNGNFIAPEYAYKIAKKGDSVIMKSELEYGNCNTKCQTP
MGAINSSMPFHNIHPLTIGECPKYVKSNRLVLATGLRNAPQTETRGLFGAIAGFIEG
GWQGMVDGWYGYHHSNEQGSGYAADKESTQKAIDGITNKVNSIIDKMNTQFEIVG
REFNNLERRIENLNKKMEDGFLDVWTYNAELLVLMENERTLDFHDSNVKNLYEKV
RLQLRDNAKELGNGCFEFYHKCDNECMESVRNGTYDYPQYSEEARLSREEISGVK
MESMVTYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLGLD
STG**HHHHHH**

[1485] A/northern shoveler/California/HKWF115/2007 - H6N1 (SEQ ID NO: 740)
**DKICIGYHANNSTTQVDTILEKNVTVTHSVELLENQKEERFCKILNKAPLDLRGCTI
EGWILGNPQCDLLLGDQSWSYIVERPTAQNGICYPGALNEVEELKALIGSGERVER
FEMFPKSTWTGVDTSSGVTKACPYNSGSSFYRNLLWIIKTKSAAYPVIKGTYNNTGS
QPILYFWGVHHPPDTNEQNTLYGSGDRYVRMGTESMNFAKSPEIAARPAVNGQRG
RIDYYWSVLKPGETLNVESNGNLIAPWYAYKFVSTNNKGAIFKSNLPIENCDATCQ
TIAGVLRTNKTFQNVSPLWIGECPKYVKSESLRLATGLRNVPQIETRGLFGAIAGFI
EGGWTGMIDGWYGYHHENSQGSGYAADKESTQKAIDGITNKVNSIIDKMNTQFEA
VDHEFSNLERRIDNLNKRMEDGFLDVWTYNAELLVLLENERTLDLHDANVKNLYE
KVKSQLRDNANDLGNGCFEFWHKCDNECIESVKNGTYDYPKYQDESKLNRQEIES
VKLDNLGVYQSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLG
LDSTG**HHHHHH**

[1486] A/Netherlands/219/03 - H7N7 (SEQ ID NO: 741)
**DKICLGHHAVSNGTKVNTLTERGVEVVNATETVERTNVPRICSKGKRTVDLGQCG
LLGTITGPPQCDQFLEFSADLIIERREGSDVCYPGKFVNEEALRQILRESGGIDKET
MGFTYSGIRTNGTTSACRRSGSSFYAEMKWLLSNTDNAAFPQMTKSYKNTRKDPA
LIIWGIHHSGSTTEQTKLYGSGNKLITVGSSNYQQSFVPSPGARPQVNGQSGRIDFH
WLILNPNDTVTFSFNGAFIAPDRASFLRGKSMGIQSEVQVDANCEGDCYHSGGTIIS
NLPFQNINSRAVGKCPRYVKQESLLLATGMKNVPEIPKRRRRGLFGAIAGFIENGW
EGLIDGWYGFRHQNAQGEGTAADYKSTQSAIDQITGKLNRLIEKTNQQFELIDNEF
TEVERQIGNVINWTRDSMTEVWSYNAELLVAMENQHTIDLADSEMNKLYERVKR
QLRENAEEDGTGCFEIFHKCDDDCMASIRNNTYDHSKYREEAIQNRIQIDPVKLSSG**

YKDSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLGLDSTG**HH HHHH**

[1487] H8N4 - A/duck/Yangzhou/02/2005 (SEQ ID NO: 742)
DRICIGYQSNNSTDTVNTLIEQKVPVTQTMELVETEKHPAYCNTDLGAPLELRDCKI EAVIYGNPKCDIHLKDQGWSYIVERPSAPEGMCYPGSVENLEELRFVFSSAASYKRI RLFDYSRWNVTSSGTSKACNASTGGQSFYRSINWLTKKKPDTYDFNEGTYVNNED GDIIFLWGIHHPPDTKEQTTLYKNANTLSSVTTNTINRSFQPNIGPRPLVRGQQGRM DYYWGILKRGETLKIRTNGNLIAPEFGYLLKGESHGRTIQNEDIPIGNCYTKCQTYA GAINSSKPFQNASRHYMGECPKYVKKASLRLAVGLRNTPSVEPRGLFGAIAGFIEG GWSGMIDGWYGFHHSNSEGTGMAADQKSTQEAIDKITNKVNNIVDKMNREFEVV NHEFSEVEKRINMINDKIDDQIEDLWAYNAELLVLLENQKTLDEHDSNVKNLFDEV KRRLSANAIDAGNGCFDILHKCDNECMETIKNGTYDHKEYEEEAKLERSKINGVKL EENTTYKSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLGLDST GHHHHHH

[1488] A/Hong Kong/2108/03 - H9N2 (SEQ ID NO: 743)
DKICIGYQSTNSTETVDTLTKTNVPVTQAKELLHTEHNGMLCATNLGHPLILDTCTI EGLIYGNPSCDLLLGGREWSYIVERPSAVNGMCYPGNVENLEELRLLFSSASSYQR VQIFPDTIWNVTYSGTSSACSNSFYRSMRWLTQKDNTYPVQDAQYTNNRGKSILFM WGINHPPTDTVQTNLYTRTDTTTSVTTEDINRAFKPVIGPRPLVNGLQGRIDYYWS VLKPGQTLRVRSNGNLIAPWYGHILSGESHGRILKSDLNSGNCVVQCQTERGGLNT TLPFHNVSKYAFGNCPKYVGVKSLKLAVGMRNVPARSSRGLFGAIAGFIEGGWPG LVAGWYGFQHSNDQGVGMAADRDSTQKAIDKITSKVNNIVDKMNKQYEIIDHEFS EIETRLNMINNKIDDQIQDIWAYNAELLVLLENQKTLDEHDANVNNLYNKVKRALG SNAMEDGKGCFELYHKCDDRCMETIRNGTYNRGKYKEESRLERQKIEGVKLESEG TYKSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTFLGKPIPNPLLGLDSTGHH HHHH**

[1489] A/Hong Kong/1073/99 – H9N2 (SEQ ID NO: 744)
METISLITILLVVTASNADKICIGHQSTNSTETVDTLTETNVPVTHAKELLHTEHNG MLCATSLGHPLILDTCTIEGLVYGNPSCDLLLGGREWSYIVERSSAVNGTCYPGNV ENLEELRTLFSSASSYQRIQIFPDTTWNVTYTGTSRACSGSFYRSMRWLTQKSGFYP VQDAQYTNNRGKSILFVWGIHHPPTYTEQTNLYIRNDTTTSVTTEDLNRTFKPVIGP RPLVNGLQGRIDYYWSVLKPGQTLRVRSNGNLIAPWYGHVLSGGSHGRILKTDLK GGNCVVQCQTEKGGLNSTLPFHNISKYAFGTCPKYVRVNSLKLAVGLRNVPARSSR GLFGAIAGFIEGGWPGLVAGWYGFQHSNDQGVGMAADRDSTQKAIDKITSKVNNI VDKMNKQYEIIDHEFSEVETRLNMINNKIDDQIQDVWAYNAELLVLLENQKTLDEH DANVNNLYNKVKRALGSNAMEDGKGCFELYHKCDDQCMETIRNGTYNRRKYREE SRLERQKIEGVKLESEGTYKSGR*LVPRGS*PGSGYIPEAPRDGQAYVRKDGEWVLLSTF LGKPIPNPLLGLDSTGHHHHHH**

[1490] The recombinant and soluble HA expression constructs of SEQ ID NO: 727-744 were transfected into 293 HEK cells. Recombinant HA0 protein or HA cleaved into its respective subunits HA1 and HA2 and disulphide linked was purified from culture supernatant by standard procedures using the hexa-HIS tag at the C-terminal. The purified protein was analyzed by size exclusion chromatography and/or denaturing coomasie gel to confirm a recombinant protein of the expected size was present.

Example 14: Screening of Antibodies in Peripheral Blood

[1491] One hundred and twenty-six individual serum or plasma samples were screened for the presence of IgG antibody that bound to recombinant soluble homotrimeric HA proteins (Table 9) using a micro-array scanning system, bind to whole inactivated Influenza A virions (Table 10) using standard ELISA techniques, and inhibits or neutralizes virus infection of MDCK cells with Influenza A H1N1 A/Solomon Islands/3/06 or H3N2 A/Wisconsin/67/05. A portion of the plasma samples contained IgG antibodies that bound specifically to the recombinant soluble HA homotrimeric protein, bound to inactivated virions, and neutralized virus infectivity. This indicates that the antibodies could be binding linear or discontinuous epitopes in the HA homotrimer, as well as binding to conformational determinants of multiple variants of the HA homotrimer. Soluble targets include, but are not limited to, exemplary recombinant HA proteins derived from the influenza virus strains listed in Table 2 and the inactivated virus strains listed in Table 11.

[1492] Table 11. Inactivated whole virions used in ELISA binding assays.

Influenza A Subtype	Strain designation
H1N1	A/Solomon Islands/3/06
H2N2	A/Japan/305/57
H3N2	A/Wisconsin/67/05

Example 15: Identification and rescue of HA-Specific Antibodies

[1493] IgG+ memory B cells purified from a human blood sample were cultured for 9 days in order to activate, proliferate, and differentiate these memory B cells into IgG secreting plasma cells. The B cell culture media containing the IgG was screened for the presence of IgG antibody that bound to recombinant soluble homotrimeric HA proteins (Table 9) using a micro-array

scanning system, bind to whole Influenza A virus (Table 10) using standard ELISA techniques, and inhibits or neutralizes virus infection of MDCK cells with Influenza A H1N1 A/Solomon Islands/3/06 or H3N2 A/Wisconsin/67/05. As shown in Tables 12, 13, and 14, thirty-nine BCC wells were identified that contained an IgG antibody with several virus, HA, or neutralizing profiles and the variable regions of the antibody were then cloned from the corresponding B cell cultures.

[1494] Transient transfections with monoclonal heavy and light chain pairs from each BCC well were performed in 293 6E cells to reconstitute and produce the antibody. Reconstituted antibody supernatants were then screened for IgG that binds to recombinant soluble homotrimeric HA proteins (Table 9) using a micro-array scanning system, bind to whole Influenza A virus (Table 11) using standard ELISA techniques, and inhibits or neutralizes virus infection of MDCK cells with Influenza A H1N1 A/Solomon Islands/3/06, and/or H1N1 A/California/04/09, and/or H3N2 A/Wisconsin/67/05 to identify the rescued anti-HA antibody. Binding and neutralization of the human IgG antibodies to the preceding targets is compared to the binding of the proprietary positive control antibody TCN-032 (specific for the N-terminal of the matrix 2 protein of influenza A, U.S. Patent Application No. 12/795,618) or to the binding of the broadly HA specific, non-neutralzing mAb TCN-504 (also known as 3251K17, and described herein), and the proprietary negative control antibody TCN-202 (specific for the AD2 site I epitope on human cytomegalovirus gB) to these same targets.

[1495] The sequences of the rescued antibodies are determined. In addition, the sequence of each of the polynucleotides encoding the antibody sequences is determined.

Example 16: Binding profiles of IgG in B cell culture supernatant or Monoclonal transfection supernatant using inactivated whole influenza A virions

[1496] To determine whether the human mAbs in BCC SN or monoclonal transfection supernatantbind to purified virus, Enzyme-Linked ImmunoSorbent Assays (ELISAs) were performed according to the following methods. Briefly, various purified Influenza A virus subtype strains were coated directly onto an ELISA plate. A single dilution of BCC supernatant of the mAbs shown in Table 12 or of the monoclonal transfection supernatant shown in Table 15 and various dilutions of a positive control antibody (TCN-032) were then added to the virus

coated wells. Unbound antibody was washed away and the bound antibody was detected with an anti-human antibody conjugated to HRP. The presence of anti-influenza antibodies was detected when the chromogen (TMB) is oxidized by the HRP conjugate, resulting in a bluecolor. The reaction is stopped by the addition of HCl, turning antibody positive wells yellow. The yellow color has a maximal absorbance at 450 nm.

[1497] *Methods:*

Coat Microlon™ plates with 25 ul/well of 3 ug/ml inactivated influenza A virions

Incubate plates overnight at 4°C.

Remove plates from 4°C and wash four times with phosphate buffered saline with Calicum and Magnesium (PBS w/Ca^{2+}, Mg^{2+}), using EL405x (Wash program: ELISA_4x_wash).

Add 20 ul/well of 1% milk/PBS to plates.

Prepare control mAb curves by 1:3 dilutions of 6 ug/ml

5 ul of each BCC SN or monoclonal transient transfection supernatant and control mAb curves are stamped onto the plate according to the plate map.

Incubate 2 hour (hr) at room temperature (RT).

Wash plates four times with PBS w/Ca^{2+}, Mg^{2+}, using EL405x (Wash program: ELISA_4x_wash)

Add 25 ul/well of polyclonal antibody (pAb) goat anti-human (αHuman) IgG Fc horseradish peroxidase (HRP) at a dilution of 1:5000.

Incubate 1 hr at RT.

Wash plates four times with PBS w/Ca^{2+}, Mg^{2+}, using EL405x (Wash program: ELISA_4x_wash)

Add 25 ul/well of Ultra-TMB (3,3′,5,5′-tetramethylbenzidine) at Neat.

Develop 30 minutes (min) at RT.

Stop by adding 25 ul /well of hydrochloric acid (HCl) at a concentration of 0.3M.

Read the plate at 450 nm with the Spectromax.

[1498] One or more of the following control antibodies were used in these experiments: TCN-504 (also known as 3251_K17, and described herein) TCN-032 (also known as 8I10, specific for

the influenza A M2 protein), and TCN-202 (also known as 2N9, specific for the AD2 site I epitope on human cytomegalovirus gB) protein.

[1499] The following purified viruses were used in these experiments: A/Solomon Islands/3/2006(H1N1) (SEQ ID NO: 728), A/Japan/305/1957(H2N2) (SEQ ID NO: 729), A/Wisconsin/67/2005(H3N2) (SEQ ID NO: 730). As shown in Table 15 the human monoclonal antibodies in the transient transfection supernatant bind strongly to one or more of the H1N1, H2N2, and/or H3N2 viruses reproducing the virus binding profile of the IgG antibody in the original BCC SN (Table 12).

Example 17: Binding profiles of IgG in in B cell culture supernatant or Monoclonal transfection supernatant using trimeric HA

[1500] To determine whether the human mAbs in BCC SN or monoclonal transfection supernatant bind to one or more of the recombinant homotrimeric HA proteins, a micro-array scanning system was used according to the following methods. Twenty Nexterion P (Schott) glass slides are incubated overnight in a humid chamber with 3 mg/ml goat anti-human, Fc - specific antibody. Nexterion P slides contain a hydrogel that terminates in an NHS ester reactive group that binds the capture antibody. The reaction is then quenched using 50 mM ethanolamine in 50 mM NaBorate (pH 8.0) buffer for 1 hour with agitation followed by 3 washes with ultrapure water. Transfection supernatants are transferred to 384-well array source plates. Control array source plates are made in 8-point, 3-fold serial dilutions of antibody starting at 3ug/ml and ending 0 ug/ml in BCC or mock transfection media. Both BCC or transfection supernatant array source plates and control plates are loaded onto an Aushon 2470 microarray printer along with the 20 prepared slides.

[1501] Microarrays are printed in 48 subarray blocks with variable number of features and replicates depending on number of transfection supernatants are being printed. Printed microarrays are allowed to sit for at least 1 hour after printing (to overnight) in the printer's humidity controlled chamber (80%). They are then quickly removed from the printer, washed, and spun dry to prepare the slides for sample incubations. A LifterSlip is placed on each slide and 90 uls of sample is added to each. Each slide receives either one of 18 V5-tagged HA trimerics at predetermined concentrations, a horseradish peroxidase goat anti-human H+L

specific antibody at a 1ug/ml, or a blank for a total of 20 slides. The slides are then incubated overnight in a humid chamber at room temperature. After washing, spin drying, and new LifterSlip application, 19 slides, excluding slide incubated with anti-human IgG, are incubated with anti-V5 conjugated to biotin at a 1:1000 dilution for 1 hour. Subsequently the slides are again washed, dried and prepared for an 1-hour incubation with a 1:300 dilution of NeutrAvidin-HRP. After further washing, drying and preparation all 20 slides are incubated for 1 hour with a Tyramide-AlexaFluor reagent according to kit instructions. After final washing and drying the slides are scanned on an Axon Genepix 4300A at an excitation wavelength of 594nm and with an emission band ranging from 619nm to 641nm. Data is recovered using the Axon Genepix software and is then analyzed for binding profiles.

[1502] *Methods:*

1. Dilute goat anti-human, FC -specific antibody (JacksonImmuno, 10mg/ml) to 3mg/ml in PBS 0.05&Tween and apply to 20 Nexterion P Slides (Schott) using 90 uls under lifterslips (Thermo).
2. Incubate in a humid chamber overnight at room temperature
3. Removing the lifterslip quench all slides in 50 mM ethanolamine (Fisher) in 50 mM Sodium tetraborate decahydrate (Fisher, S248-500) at a pH of 8.0
4. Quench for 1 hour with incubation at room temperature
5. Wash all slides (3x 2 min MilliQ water washes with agitation).
6. Load all slides onto Aushon 2470 MicroArray printer.
7. Prepare control plates using by spiking control antibodies into transfection media to form an 8 point 3-fold serial dilution starting at 3 ug/ml and ending in 0 ug/ml. Transfer control dilutions to 4 array source plates (Thermo).
8. Load all array source plates, control and sample, onto Aushon 2470 microarray printer and begin deposition after checking all required fluid levels. Number of replicates is based on number of transfection supernatants being printed. Typically 1 to 10 replicates.
9. Allow slides to sit for at least an hour, to overnight, after deposition.
10. Immediately wash (PBS with 2% tween 20, 5 min; MilliQ water, 2 min, 3x) and spin dry (2000 RPM for 1 minute)

11. Using lifterslips and apply 90 uls of HA at the following concentration:

Homotrimeric HA - strain	[ug/ml]
A/California/4/09 - H1N1	5
A/Solomon Islands/3/06 - H1N1	5
A/Japan/305/57 - H2N2	5
A/Wisconsin/67/05 - H3N2	20
A/swine/Ontario/01911-2/99 - H4N6	5
A/Vietnam/1203/04 - H5N1	20
A/Indonesia/5/05 - H5N1	0.5
A/Egypt/3300-NAMRU3/08 - H5N1	0.5
A/Common magpie/Hong Kong/5052/07 - H5N1	0.5
A/Anhui/1/05 - H5N1	0.5
A/chicken/Vietnam/NCVD-016/08 - H5N1	0.5
A/northern shoveler/California/HKWF115/2007 - H6N1	0.5
A/Netherlands/219/03 - H7N7	0.5
A/duck/Yangzhou/02/2005 - H8N4	5
A/Hong Kong/2108/03 - H9N2	5
A/South Carolina/1/18 - H1N1	20
A/Hong Kong/1073/99	20
A/Hong Kong/156/97 - H5N1	5

Use 1x PBS, 0.05% Tween 20, 10% Blocker Casein (Thermo, #37528) to bring the homotrimeric HA to the desired concentration.

12. Incubate overnight in a humid chamber at room temperature

13. Immediately wash (PBS with 2% tween 20, 5 min; MilliQ water, 2 min, 3x) and spin dry (2000 RPM for 1 minute)

14. Using lifterslips incubate all but slide previously incubated with anti-human IgG(H&L)-HRP with 90uls of anti-V5-biotin (AbD Serotec, MCA1360B) at 1 ug/ml in 1x PBS 0.05% Tween 20 for 1 hour at room temperature in a humid chamber.

15. Immediately wash (PBS with 2% tween 20, 5 min; MilliQ water, 2 min, 3x) and spin dry (2000 RPM for 1 minute)

16. Using lifterslips incubate with 90 uls of horseradish peroxidase conjugated NeutrAvidin (Pierce #31030) for 1 hour at room temperature in a humid chamber.

17. Immediately wash (PBS with 2% tween 20, 5 min; MilliQ water, 2 min, 3x) and spin dry (2000 RPM for 1 minute)

18. Prepare Tyramide Signal Amplification reagent according to kit instructions (TSA Kit #25, Invitrogen, T20935). Briefly dilute 1 ul of hydrogen peroxide solution into 200 uls of amplification buffer. Take 20 uls of hydrogen peroxide/amplification buffer solution and add to 1940 uls of fresh amplification buffer. Then add 40 uls of tyramide-Alexa Fluor resulting in a total of 2 mls of amplification reagent

19. Incubate all 20 slides with amplification reagent for 1 hour at room temperature in a humid chamber.

20. Immediately wash (PBS with 2% tween 20, 5 min; MilliQ water, 2 min, 3x) and spin dry (2000 RPM for 1 minute)

21. Scan all slides on an Axon Genepix 4300A at an excitation wavelength of 594nm and with an emission band ranging from 619nm to 641nm or optical scanner with similar capabilities.

22. Lay templates on each slide using GenePix Pro 7 or similar software to recover feature data.

23. Analyze feature data for binding profiles to each HA trimeric.

[1503] As shown in Table 16, the human monoclonal antibodies in the transient transfection supernatant bind strongly to one or more of the recombinant homotrimeric HA proteins reproducing the virus binding profile of the IgG antibody in the original BCC SN (Table 12).

Example 18: Neutralization profiles of IgG in in B cell culture supernatant or monoclonal transfection supernatant

[1504] MDCK cells were plated at 3 x 10^3 cells/ well in a 384-well plate in complete DMEM media (supplemented with 10% FBS, 1X penicillin/streptomycin, 1X Glutamax™, and 1X Sodium Pyruvate) and incubated at 37°C overnight.

[1505] Influenza A virus was preincubated with either BCC supernatant or monoclonal transfection supernatant or a positive control neutralizing monoclonal antibody (MAb), which was diluted in pooled BCC supernatant or in mock transfection supernatant at the desired concentrations and incubated overnight (~16 hours) at 37°C. Void volumes and dilutions were made in PBS with Mg^{2+}, Ca^{2+}, 200 mM Mannose, and 1% BSA at 37°C with a total volume of 30 µl/well.

[1506] Each sample well contained:

(a) 20 µl/well BCC supernatant; or

(b) 20 ul/well of monoclonal transfection

(c) 3000 IU/well A/Solomon Islands/03/2006 (H1N1) in 10 µl/well; or

(e) 3000 IU/well A/California/04/2009 (H1N1) in 10 ul/well; or

(f) 3000 IU/well A/Wisconsin/67/05 (H3N2) in 10 ul/well

[1507] Prior to infection, the MDCK cells were washed once with a solution containing PBS, Mg^{2+}, and Ca^{2+} at 60 µl/well. After the wash, 25 ul of the virus/mAb mixture was transferred and the infection proceeded for 4 hours at 37°C.

[1508] After 4 hours of infection, the MDCK cells are washed twice with complete DMEM. After the last wash, 25 µl/well of complete DMEM remained, and the plates were incubated overnight at 37°C.

[1509] After the overnight incubation the culture media was removed and 20 µl of BD Cytofix/Cytoperm™ (cat# 51-2090KZ) was added to each well and incubated at room temperature (RT) for 30 minutes. Next, the wells were washed three times using the M384 Atlas plate washer.

[1510] After the final wash, 15 µl/well of 100 µg/ml Rabbit IgG (Sigma) in PBS with Mg^{2+}, Ca^{2+}, and 1% BSA, was added and incubated for at least 5 minutes at RT. Twenty µl/well of anti-M2e mAb TCN-032 at 2 µg/ml in PBS with Mg^{2+}, Ca^{2+}, and 1% BSA, were added to each well and incubated for at least 30 mins at room temperature. The wells are washed one time using the Atlas plate washer with PBS with Mg^{2+}, Ca^{2+} Twenty µl/well of 2 µg/ml Alexa Fluor® 647 anti - Human IgG H+L (Invitrogen™) and 20 µg/ml Hoechst 33342 (Invitrogen™) was added and incubated in the dark for 45 mins at room temperature. Wells were washed three timesusing the Atlas plate washer with PBS with Mg^{2+}, Ca^{2+}. Twenty microliters of PBS with Mg^{2+}, Ca^{2+}, and 1% BSA was added to each well, and plates were sealed with black sealing tape. Plates were analyzed by scanning using an IN Cell analyzer. Specifically, the scan was performed using the IN Cell Developer Software, Protocol "384 GG Hoechst AF647 4x." Analysis of the scan was performed using the Developer Tool Box software, Protocol "Cellular Binding Nuclei GG Density 4."

[1511] The assay was able to detect well supernatants that individually neutralized the Influenza A infection. If an arbitrary cutoff was established at ≤ 150 nucleoprotein (NP)+ cells and the wells with a disrupted cell monolayer were subtracted, a total of 122 wells scored as positive.

[1512] Exemplary influenza neutralizing antibodies that were identified using this method are TCN-522 (3212_I12), TCN-521 (3280_D18), TCN-523 (5248_A17), TCN-563 (5237_B21), TCN-526 (5084_C17), TCN-527 (5086_C06), TCN-528 (5087_P17), TCN-529 (5297_H01), TCN-530 (5248_H10a), TCN-531 (5091_H13), TCN-532 (5262_H18), TCN-533 (5256_A17), TCN-534 (5249_B02), TCN-535 (5246_P19), TCN-536 (5095_N01), TCN-537 (3194_D21), TCN-538 (3206_O17), TCN-539 (5056_A08), TCN-540 (5060_F05), TCN-541 (5062_M11), TCN-542 (5079_A16), TCN-543 (5081_G23), TCN-544 (5082_A19), TCN-545 (5082_I15), TCN-546 (5089_L08), TCN-547 (5092_F11), TCN-548 (5092_P01), TCN-549 (5092_P04), TCN-550 (5096_F06), TCN-551 (5243_D01), TCN-552 (5249_I23), TCN-553 (5261_C18), TCN-554 (5277_M05), TCN-555 (5246_L16), TCN-556 (5089_K12), TCN-557 (5081_A04), TCN-558 (5248_H10b), TCN-559 (5097_G08), TCN-560 (5084_P10), and TCN-504 (3251_K17). The individual neutralization activities of some of these antibodies are provided in Table 17.

[1513] Several antibodies were identified that may be non-neutralizing, including, TCN-504 (3251_K17), TCN-556 (5089_K12), TCN-557 (5081_A04), TCN-559 (5097_G08), and TCN-560 (5084_P10). These antibodies, similar to the neutralizing antibodies of the invention, bind to a broad range of HA proteins, including sequence and conformational variants. In certain embodiments of the invention, non-neutralizing antibodies, including TCN-504 (3251_K17), TCN-556 (5089_K12), TCN-557 (5081_A04), TCN-559 (5097_G08), and TCN-560 (5084_P10) may be used as antibody-drug conjugates.

[1514] Table 12: Summary of BCC SN screening by ELISA for virus binding.

		ELISA: Virus Binding (OD_{450})					ELISA: Virus Binding (OD_{450})		
Theraclone mAb ID	**BCC well ID**	**A/ Solomon Islands/ 3/06 H1N1**	**A/Japan/ 305/57 H2N2**	**A/Wisconsin/ 67/05 H3N2**	**Theraclone mAb ID**	**BCC well ID**	**A/Solomon Islands/ 3/06 H1N1**	**A/Japan/ 305/57 H2N2**	**A/Wisconsin/ 67/05 H3N2**
TCN-521	3280_D18	3.70	3.10	1.10	TCN-542	5079_A16	3.66	0.08	3.13
TCN-522	3212_I12	2.12	ND	0.07	TCN-543	5081_G23	3.63	3.62	0.07
TCN-523	5248_A17	3.47	1.62	0.08	TCN-544	5082_A19	0.32	0.07	2.71
TCN-563	5237_B21	3.62	1.23	0.07	TCN-545	5082_I15	3.32	0.06	0.47
TCN-526	5084_C17	0.06	0.07	3.65	TCN-546	5089_L08	1.95	0.06	3.69
TCN-527	5086_C06	3.03	1.48	0.07	TCN-547	5092_F11	0.06	0.07	3.68
TCN-528	5087_P17	3.62	2.82	0.24	TCN-548	5092_P01	0.09	0.09	3.62
TCN-529	5297_H01	0.07	ND	3.62	TCN-549	5092_P04	0.09	0.08	3.58
TCN-530	5248_H10	3.52	1.73	0.06	TCN-550	5096_F06	0.06	0.06	3.65
TCN-531	5091_H13	3.23	0.67	3.45	TCN-551	5243_D01	3.35	0.19	0.07
TCN-532	5262_H18	0.06	0.07	3.67	TCN-552	5249_I23	3.57	0.71	0.06
TCN-533	5256_A17	3.54	1.10	0.10	TCN-553	5261_C18	3.60	2.54	0.07
TCN-534	5249_B02	3.55	2.56	0.07	TCN-554	5277_M05	0.06	ND	1.09
TCN-535	5246_P19	3.43	1.46	0.08	TCN-555	5246_L16	2.89	0.60	0.06
TCN-536	5095_N01	3.63	0.08	3.66	TCN-556	5089_K12	2.70	2.41	0.06
TCN-537	3194_D21	3.24	ND	0.06	TCN-557	5081_A04	2.32	2.70	0.07
TCN-538	3206_O17	3.47	ND	0.07	TCN-559	5097_G08	3.68	1.25	0.70
TCN-539	5056_A08	0.06	0.06	2.85	TCN-560	5084_P10	3.63	2.07	0.07
TCN-540	5060_F05	0.07	3.62	3.65	TCN-202	2N9	ND	ND	ND
TCN-541	5062_M11	3.44	0.06	0.25	TCN-504	3251_K17	ND	ND	ND
					TCN-032	8I10	3.61	3.61	3.62

[1515] Table 13: Summary of BCC SN screening for virus binding to recombinant homotrimeric HA.

		Trimeric HA Binding: RLU																	
Theraclone mAb ID	BCC well ID	A/ California/4/09 H1N1	A/ Solomon Islands/3/06 H1N1	A/ South Carolina/1/18 H1N1	A/ Japan/305/57 H2N2	A/ Wisconsin/67/05 H3N2	A/ swine/Ontario/01911-2/99 H4N6	A/ Vietnam/1203/04 H5N1	A/ Indonesia/5/05 H5N1	A/ Egypt/3300-NAMRU3/08 H5N1	A/ common magpie/Hong Kong/5052/07 H5N1	A/ Anhui/1/05 H5N1	A/ chicken/Vietnam/NCVD-016/08 H5N1	A/ Hong Kong/156/97 H5N1	A/ northern shoveler/California/HKWF115/07 H6N4	A/ Netherlands/219/03 H7N7	A/ duck/Yangzhou/02/05 H8N4	A/ Hong Kong/2108/03 H9N2	A/ Hong Kong/1073/99 H9N2
TCN-521	3280_D18	25726	39644	ND	6732	2298	210	196	31473	47871	13528	487	32390	ND	47991	2496	11659	93	ND
TCN-522	3212_I12	5019	38914	ND	989	302	156	145	67	ND	ND	ND	ND	ND	ND	ND	502	639	ND
TCN-523	5248_A17	34721	37916	ND	5111	22568	1288	3383	45815	36471	45837	5705	48880	ND	46908	2336	28949	189	ND
TCN-563	5237_B21	45157	30005	ND	6612	40848	4501	4836	39533	27514	27500	9581	40953	ND	27328	7515	46729	225	ND
TCN-526	5084_C17	203	341	ND	246	49312	253	372	46027	ND	ND	20916	179	ND	2100	1338	596	36629	ND
TCN-527	5086_C06	27991	16507	ND	19261	5715	7686	21264	23838	ND	ND	21369	27047	ND	30323	8892	28803	15956	ND
TCN-528	5087_P17	48845	44804	ND	46393	48795	47500	45577	42801	ND	ND	49772	38191	ND	46781	49251	38362	41966	ND
TCN-529	5297_H01	434	179	ND	435	51631	235	101	44085	53394	302	39376	410	ND	533	1165	771	42271	ND
TCN-530	5248_H10	46600	32801	ND	47049	36846	2743	7152	39774	30430	42460	11874	48341	ND	45339	2896	41661	486	ND
TCN-531	5091_H13	22207	51663	ND	410	7094	408	357	37443	ND	ND	3606	20840	ND	43874	1969	3117	745	ND
TCN-532	5262_H18	135	327	ND	176	18046	119	440	27992	24500	134	25219	46	ND	511	327	785	29816	ND
TCN-533	5256_A17	29280	39186	ND	10806	13823	1582	5677	44063	34299	44511	8065	47704	ND	41449	2473	24745	172	ND
TCN-534	5249_B02	30109	44185	ND	50626	7978	683	3435	46352	41381	32514	6861	56642	ND	52429	4340	46537	165	ND
TCN-535	5246_P19	48576	39442	ND	26068	34320	5950	4740	45592	39412	45937	6875	49961	ND	48192	4757	36650	861	ND
TCN-536	5095_N01	151	150	ND	121	34996	79	146	3969	ND	ND	543	287	ND	2210	976	436	1566	ND
TCN-537	3194_D21	21918	44264	ND	44685	549	19	80	14858	38168	18702	335	8617	ND	5206	1052	7826	147	ND
TCN-538	3206_O17	13808	33228	ND	43002	6900	406	60	26421	23553	18746	689	37312	ND	17448	6531	6123	109	ND
TCN-539	5056_A08	1803	239	ND	468	715	1579	545	49	11420	3957	91	100	ND	814	1698	1488	292	ND
TCN-540	5060_F05	57	64	ND	2969	728	178	63	31	1968	113	25	70	ND	131	381	117	22	ND
TCN-541	5062_M11	34	51	ND	83	2923	102	43	30	1162	71	17	40	ND	106	381	131	29	ND

[1516] Table 13 (Con't): Summary of BCC SN screening for virus binding to recombinant homotrimeric HA.

		Trimeric HA Binding: RLU																
Theradone mAb ID	BCC well ID	A/ California /4/09 H1N1	A/ Solomon Islands/ 3/06 H1N1	A/ South Carolina/ 1/18 H1N1	A/ Japan/ 305/57 H2N2	A/ Wisconsin /67/05 H3N2	A/ swine/ Ontario/ 01911-2/ 99 H4N6	A/ Vietnam/ 1203 /04 H5N1	A/ Indonesia /5/05 H5N1	A/ Egypt/ 3300-NAMRU3/ 08 H5N1	A/ common magpie/ Hong Kong/ 5052/07 H5N1	A/ Anhui/1/ 05 H5N1	A/ chicken/ Vietnam/ NCVD-016/08 H5N1	A/ Hong Kong/ 156/97 H5N1	A/ northern shoveler/ California /HKWF11 5/07 H6N4	A/ Netherlan ds/ 219/03 H7N7	A/ duck/ Yangzhou /02/05 H8N4	A/ Hong Kong/ 2108/03 H9N2
TCN-542	5079_A16	3108	132	ND	142	1940	350	306	ND	ND	ND	ND	375	ND	900	909	332	1907
TCN-543	5081_G23	13080	511	ND	197	1358	428	488	ND	ND	ND	325	347	ND	2128	661	737	131
TCN-544	5082_A19	281	179	ND	187	2090	316	349	3052	ND	ND	ND	272	ND	1690	1618	464	296
TCN-545	5082_I15	365	266	ND	157	575	289	235	ND	ND	ND	ND	392	ND	1167	1182	656	227
TCN-546	5089_L08	350	256	ND	520	30209	587	349	18432	ND	ND	2037	421	ND	1354	1451	487	12983
TCN-547	5092_F11	170	155	ND	40	16932	252	308	6986	ND	ND	1476	198	ND	1005	401	278	3986
TCN-548	5092_P01	234	283	ND	416	48600	240	270	17626	ND	ND	5381	254	ND	314	758	184	3424
TCN-549	5092_P04	338	284	ND	387	30912	421	312	11445	ND	ND	1793	498	ND	1103	1134	844	5037
TCN-550	5096_F06	454	204	ND	201	26315	195	277	9100	ND	ND	1206	361	ND	964	939	407	2279
TCN-551	5243_D01	53362	53821	ND	22633	6840	733	4152	53543	47183	45688	4187	42301	ND	52491	786	9817	224
TCN-552	5249_I23	35312	39314	ND	23832	14769	493	2728	43559	39971	42201	4156	46249	ND	38413	1241	13115	171
TCN-553	5261_C18	20281	16271	ND	25509	20043	2583	6560	24406	18828	25979	12610	24158	ND	21732	1838	27998	273
TCN-554	5277_M05	173	115	ND	328	46531	78	113	32348	36126	224	10851	250	ND	296	610	583	28594
TCN-555	5246_L16	44903	26404	ND	2131	9800	1953	876	34539	42676	16060	1497	22302	ND	49507	3399	18390	262
TCN-556	5089_K12	14640	2846	ND	5611	9323	5604	13823	8454	ND	ND	3703	8800	ND	11890	10606	16910	7413
TCN-557	5081_A04	17603	40699	ND	43367	10218	26967	47282	45165	ND	ND	46033	45545	ND	24375	6779	50106	35309
TCN-559	5097_G08	539	7376	ND	16332	2402	1658	21670	18295	ND	ND	11888	12935	ND	7233	1983	10385	2791
TCN-560	5084_P10	49166	38758	ND	46720	49078	41599	43990	35864	ND	ND	49133	45969	ND	42303	48519	44696	49385
TCN-202	2N9	39	46	ND	85	252	75	53	24	1275	162	25	69	ND	105	348	196	50
TCN-504	3251_K17	3326	24140	ND	4091	40516	14669	196	43259	44352	17038	26175	38456	ND	7869	47190	14137	454
TCN-032	8I10	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

[1517] Table 14: Summary of BCC SN screening for virus neutralization.

		% Neutralization				% Neutralization	
Theraclone mAb ID	BCC well ID	A/ Solomon Islands/ 3/06 H1N1	A/ Wisconsin/ 67/05 H3N2	Theraclone mAb ID	BCC well ID	A/ Solomon Islands/ 3/06 H1N1	A/ Wisconsin/ 67/05 H3N2
TCN-522	3212_I12	33	0	TCN-542	5079_A16	98	51
TCN-521	3280_D18	99	ND	TCN-543	5081_G23	100	55
TCN-523	5248_A17	69	21	TCN-544	5082_A19	95	62
TCN-563	5237_B21	78	1	TCN-545	5082_I15	98	72
TCN-526	5084_C17	0	100	TCN-546	5089_L08	0	100
TCN-527	5086_C06	12	0	TCN-547	5092_F11	0	100
TCN-528	5087_P17	0	15	TCN-548	5092_P01	0	97
TCN-529	5297_H01	0	99	TCN-549	5092_P04	0	99
TCN-530	5248_H10	64	4	TCN-550	5096_F06	0	100
TCN-531	5091_H18	65	80	TCN-551	5243_D01	100	19
TCN-532	5262_H18	11	99	TCN-552	5249_I23	57	0
TCN-533	5256_A17	56	0	TCN-553	5261_C18	87	0
TCN-534	5249_B02	86	0	TCN-554	5277_M05	42	100
TCN-535	5246_P19	82	1	TCN-555	5246_L16	48	ND
TCN-536	5095_N01	75	100	TCN-556	5089_K12	0	4
TCN-537	3194_D21	89	5	TCN-557	5081_A04	0	2
TCN-538	3206_O17	35	0	TCN-559	5097_G08	82	ND
TCN-539	5056_A08	97	62	TCN-560	5084_P10	94	ND
TCN-540	5060_F05	100	75	TCN-202	2N9	ND	ND
TCN-541	5062_M11	89	99	TCN-504	3251_K17	ND	ND
				TCN-032	8I10	ND	ND

[1518] Table 15: Summary of monoclonal antibody transfection supernatant screening by ELISA for virus binding.

			ELISA: Virus Binding (OD_{450})		
	Theraclone mAb ID	BCC well ID	A/ Solomon Islands/ 3/06 H1N1	A/Japan/305/57 H2N2	A/ Wisconsin/67/05 H3N2
Monoclonal transfection set 1	TCN-523	5248_A17	3.59	1.69	0.09
	TCN-504	3251_K17	3.65	3.65	3.65
	TCN-202	2N9	0.07	0.07	0.07
Monoclonal transfection set 2	TCN-522	3212_I12	3.48	0.61	0.07
	TCN-526	5084_C17	0.08	0.07	0.31
	TCN-527	5086_C06	3.69	3.63	0.14
	TCN-528	5087_P17	3.66	3.64	0.23
	TCN-563	5237_B21	3.60	0.84	0.09
	TCN-504	3251_K17	3.65	3.62	3.65
	TCN-523	5248_A17	3.67	1.39	0.09
	TCN-202	2N9	0.08	0.07	0.07
Monoclonal transfection set 3	TCN-531	5091_H13	0.10	0.09	3.59
	TCN-530	5248_H10	3.62	3.43	0.21
	TCN-529	5297_H01	0.16	0.10	3.65
	TCN-533	5256_A17	3.61	3.65	0.22
	TCN-532	5262_H18	0.13	0.08	3.43
	TCN-504	3251_K17	3.63	3.64	3.65
	TCN-523	5248_A17	3.59	3.47	0.15
	TCN-202	2N9	0.10	0.08	0.08
Monoclonal transfection set 4	TCN-535	5246_P19	3.52	2.45	0.10
	TCN-534	5249_B02	3.50	2.45	0.08
	TCN-536	5095_N01	3.52	0.06	3.61
	TCN-504	3251_K17	3.52	3.51	3.59
	TCN-523	5248_A17	3.43	1.73	0.09
	TCN-202	2N9	0.10	0.08	0.07

[1519] Table 15 (Con't): Summary of monoclonal antibody transfection supernatant screening by ELISA for virus binding.

			ELISA: Virus Binding (OD_{450})		
	Theraclone mAb ID	BCC well ID	A/ Solomon Islands/ 3/06 H1N1	A/ Japan/305/57 H2N2	A/ Wisconsin/67/05 H3N2
Monoclonal transfection set 5	TCN-537	3194_D21	3.56	3.48	0.11
	TCN-538	3206_O17	3.59	3.37	0.12
	TCN-539	5056_A08	0.07	0.07	0.13
	TCN-540	5060_F05	0.09	3.61	3.62
	TCN-541	5062_M11	3.63	0.07	0.07
	TCN-542	5079_A16	3.60	0.07	0.23
	TCN-543	5081_G23	3.63	3.64	2.23
	TCN-544	5082_A19	0.07	0.07	3.65
	TCN-545	5082_I15	1.36	0.10	3.62
	TCN-546	5089_L08	3.67	0.07	3.67
	TCN-547	5092_F11	0.09	0.09	0.13
	TCN-548	5092_P01	0.13	0.09	3.63
	TCN-549	5092_P04	0.09	0.08	0.46
	TCN-550	5096_F06	0.13	0.08	3.62
	TCN-551	5243_D01	3.65	0.10	0.27
	TCN-552	5249_I23	3.61	2.68	0.27
	TCN-553	5261_C18	3.56	3.28	0.17
	TCN-554	5277_M05	0.18	0.11	3.40
	TCN-555	5246_L16	3.57	2.10	0.13
	TCN-556	5089_K12	3.64	3.64	0.34
	TCN-557	5081_A04	3.58	3.59	3.47
	TCN-558	5248_H10	3.52	3.31	0.20
	TCN-559	5097_G08	1.16	2.29	2.39
	TCN-560	5084_P10	3.52	3.55	0.30
	TCN-504	3251_K17	3.60	3.59	3.60
	TCN-523	5248_A17	3.62	2.56	0.14
	TCN-202	2N9	0.07	0.07	0.07

[1520] **Table 16:** Summary of monoclonal antibody transfection supernatant screening for virus binding to recombinant homotrimeric HA.

			Trimeric HA Binding: RLU																	
	Theraclone mAb ID	BCC well ID	A/ California/4/09 H1N1	A/ Solomon Islands/3/06 H1N1	A/ South Carolina/1/18 H1N1	A/ Japan/305/57 H2N2	A/ Wisconsin/67/05 H3N2	A/ swine/ Ontario/ 01911-2/ 99 H4N6	A/ Vietnam/ 1203/04 H5N1	A/ Indonesia/5/05 H5N1	A/ Egypt/ 3300-NAMRU3/ 08 H5N1	A/ common magpie/ Hong Kong/ 5052/07 H5N1	A/ Anhui/1/ 05 H5N1	A/ chicken/ Vietnam/ NCVD-016/08 H5N1	A/ Hong Kong/ 156/97 H5N1	A/ northern shoveler/ California/HKWF1 15/07 H6N4	A/ Netherlands/ 219/03 H7N7	A/ duck/ Yangzhou /02/05 H8N4	A/ Hong Kong/ 2108/03 H9N2	A/ Hong Kong/ 1073/99 H9N2
Monoclonal transfection set 1	TCN-523	5248_A17	17703	6785	26364	191	1646	49	80	18508	25494	6235	60	10813	ND	9046	28	229	41	21719
	TCN-504	3251_K17	18286	29844	21541	15059	14311	26491	1300	16640	16113	29696	29046	27765	ND	5791	23828	28934	78	25703
	TCN-202	2N9	20	67	32	27	27	29	37	57	76	21	20	14	ND	13	55	26	24	21
Monoclonal transfection set 2	TCN-522	3212_I12	37463	17281	39613	11936	3346	1048	48169	50472	55413	21393	2031	49343	ND	54364	2170	1646	203	11800
	TCN-526	5084_C17	3598	1468	2312	3592	27776	3487	9181	37831	39894	1758	43991	3294	ND	3789	5659	4305	23267	490
	TCN-527	5086_C06	21498	19685	48062	20758	35796	30085	20600	23433	23595	43794	15238	20112	ND	19272	49149	17921	25527	557
	TCN-528	5087_P17	44586	26908	25226	23083	46012	49173	23336	39704	36834	45257	21207	22573	ND	28370	47229	19792	33621	322
	TCN-563	5237_B21	21231	26475	17808	11198	23686	2248	31549	47277	23915	52783	1568	36304	ND	21901	5423	6275	364	49230
	TCN-504	3251_K17	15621	31447	24695	22573	21615	32496	14953	19717	21365	16850	30975	27266	ND	1277	19272	17751	23	25832
	TCN-523	5248_A17	18654	3270	25504	882	2062	82	26227	24527	30672	7214	139	17590	ND	21214	407	383	18	31283
	TCN-202	2N9	52	16	195	32	46	15	121	8	18	11	9	22	ND	30	26	19	7	33
Monoclonal transfection set 3	TCN-531	5091_H13	2830	194	1557	489	4159	296	2411	54	363	37	76	44	ND	96	384	3220	158	370
	TCN-530	5248_H10	21176	13820	17166	5174	3048	123	25172	25546	25523	5576	97	17979	ND	23513	118	227	44	10219
	TCN-529	5297_H01	735	43	158	45	2939	45	415	1353	1673	33	1258	33	ND	110	33	48	1197	46
	TCN-533	5256_A17	6877	15526	16417	18618	16132	180	11677	28339	18587	25210	301	24551	ND	7806	209	711	33	23808
	TCN-532	5262_H18	23601	59	311	441	9967	29	452	2786	2821	20	2402	29	ND	78	42	57	2767	48
	TCN-504	3251_K17	18614	32672	27617	35957	21437	34456	13284	18559	17969	17814	29988	10261	ND	8335	19600	19647	36	27781
	TCN-523	5248_A17	19366	11014	23710	4554	8558	1640	22129	21973	29080	640	546	18903	ND	29404	3144	2017	51	24193
	TCN-202	2N9	205	57	731	42	51	54	967	43	63	16	33	14	ND	73	247	66	30	57
Monoclonal transfection set 4	TCN-535	5246_P19	25157	836	22433	21491	4450	138	25244	18202	25318	477	24	20929	ND	18057	159	428	18	21197
	TCN-534	5249_B02	27035	60	11830	14745	897	264	23675	948	8314	127	20	11352	ND	21287	361	79	27	731
	TCN-536	5095_N01	49	30	39	260	20576	168	182	80	97	27	18	19	ND	95	246	48	24	115
	TCN-504	3251_K17	549	14625	21713	19576	20627	21792	25665	18154	24796	8675	14053	19176	ND	2609	6707	19872	7	18770
	TCN-523	5248_A17	28847	371	22983	3845	9742	850	30898	24534	33351	2131	48	23995	ND	25087	443	463	38	24575
	TCN-202	2N9	94	34	27	334	125	157	67	19	40	21	13	42	ND	117	173	77	22	81

[1521] Table 16 (Con't): Summary of monoclonal antibody transfection supernatant screening for virus binding to recombinant homotrimeric HA.

			Trimeric HA Binding: RLU															
	Theraclone mAb ID	BCC well ID	A/ California/4/09 H1N1	A/ Solomon Islands/3/06 H1N1	A/ South Carolina/1/18 H1N1	A/ Japan/305/57 H2N2	A/ Wisconsin/67/05 H3N2	A/ swine/ Ontario/01911-2/99 H4N6	A/ Vietnam/1203/04 H5N1	A/ Indonesia/5/05 H5N1	A/ Egypt/3300-NAMRU3/08 H5N1	A/ common magpie/ Hong Kong/5052/07 H5N1	A/ Anhui/1/05 H5N1	A/ chicken/ Vietnam/ NCVD-016/08 H5N1	A/ Hong Kong/156/97 H5N1	A/ northern shoveler/ California/HKWF115/07 H6N4	A/ Netherlands/219/03 H7N7	A/ duck/ Yangzhou/02/05 H8N4
Monoclonal transfection set 5	TCN-537	3194_D21	33793	760	46788	16197	1935	3282	50280	2420	33495	2068	2580	4476	10681	2376	3654	25529
	TCN-538	3206_O17	15956	1965	8434	6624	2070	3354	52375	13748	40969	3141	2745	2948	5167	8895	4374	4065
	TCN-539	5056_A08	1053	871	5330	2565	58831	6511	53254	8947	24338	1436	3244	3496	1450	2862	15729	7281
	TCN-540	5060_F05	984	1176	1356	47894	52986	5419	42500	2569	15589	1799	2192	1514	1551	2461	4386	6078
	TCN-541	5062_M11	1557	2277	2583	5382	1238	4724	45517	2959	23234	1936	2998	11039	1975	2684	13649	21203
	TCN-542	5079_A16	667	48021	1116	5184	711	14340	29492	1761	14763	1674	7407	5458	786	2369	8049	11598
	TCN-543	5081_G23	2338	43523	28290	2775	37048	2866	33145	1826	17583	1070	2626	5877	1433	2512	12873	13130
	TCN-544	5082_A19	706	997	1331	1003	38514	2391	38620	4400	19414	1116	3770	3069	1491	2915	4647	9444
	TCN-545	5082_I15	818	951	900	1355	32037	2936	42906	5269	26538	1388	4876	3230	1560	2319	3125	13197
	TCN-546	5089_L08	1085	1140	955	1730	28453	4609	47108	40866	53039	1916	33344	2940	1243	2429	3743	11391
	TCN-547	5092_F11	1474	1082	2016	1354	6968	1602	27666	12041	16784	856	1238	1315	1955	2618	2089	3335
	TCN-548	5092_P01	818	750	1154	1016	34194	1624	23678	29142	37002	813	15578	1059	1555	2104	2131	5735
	TCN-549	5092_P04	622	640	2340	1075	51626	1878	32265	8645	18581	1340	4113	1601	1848	996	8475	9452
	TCN-550	5096_F06	628	758	1014	731	37809	1704	41900	9001	26791	993	7680	1802	955	2305	3248	4713
	TCN-551	5243_D01	46133	43523	4344	25191	936	3120	41915	1289	17368	1123	2643	792	792	1764	4837	3097
	TCN-552	5249_I23	23459	48559	37374	51986	18451	9084	18494	43382	21246	34619	9010	34451	36317	43861	7416	15937
	TCN-553	5261_C18	23323	49581	41300	39848	25248	12230	19214	31183	19470	39224	8548	34718	36337	32461	7532	12545
	TCN-554	5277_M05	4034	992	1261	2621	25329	5402	36582	44935	42395	1734	42805	2708	1441	3352	4522	5808
	TCN-555	5246_L16	20223	44571	48009	16743	14660	4522	19300	33927	20001	33642	12236	35215	36302	28717	12656	8544
	TCN-556	5089_K12	20865	23409	32732	22805	44715	19346	17421	15229	16603	20140	13795	22676	24620	34817	43640	22400
	TCN-557	5081_A04	44419	26960	44865	27282	46082	41525	21320	22246	26351	54874	19980	23323	27061	49611	53747	24015
	TCN-558	5248_H10	20220	36107	40709	34434	26611	10003	23527	24632	21861	49655	9783	33423	47113	29396	5841	19531
	TCN-559	5097_G08	8079	41254	2233	46993	15279	35761	37607	51869	47369	12900	41835	33850	28953	6632	4852	42614
	TCN-560	5084_P10	31134	22427	30462	25855	55383	16751	19475	16971	18730	30485	18628	18174	29287	35866	32120	27927
	TCN-504	3251_K17	17599	30086	31975	23254	38088	54789	21485	18485	20625	37328	37168	34166	26597	39179	30626	35074
	TCN-523	5248_A17	34415	37587	52010	22019	13690	1699	27819	55048	35484	33905	6079	51296	28380	46941	6750	25599
	TCN-202	2N9	733	525	5331	1883	581	2692	30002	1973	13876	1366	10033	2570	945	3036	18026	13796

[1522] Table 17. Summary of monoclonal antibody transfection supernatant screening for virus neutralization.

			% Neutralization						% Neutralization		
	Theraclone mAb ID	BCC well ID	A/ Solomon Islands/ 3/06 H1N1	A/ California/4 /09 H1N1	A/ Wisconsin/6 7/05 H3N2		Theraclone mAb ID	BCC well ID	A/ Solomon Islands/ 3/06 H1N1	A/ California/4 /09 H1N1	A/ Wisconsin/6 7/05 H3N2
Monoclonal transfection set 1	TCN-523	5248_A17	82.71	ND	ND	Monoclonal transfection set 5	TCN-537	3194_D21	0	71	0
	TCN-504	3251_K17	0.00	ND	0.00		TCN-538	3206_O17	21	66	0
	TCN-202	2N9	0.00	ND	0.00		TCN-539	5056_A08	0	0	99
Monoclonal transfection set 2	TCN-522	3212_I12	39.46	ND	0.84		TCN-540	5060_F05	3	0	98
	TCN-526	5084_C17	10.58	ND	94.26		TCN-541	5062_M11	88	0	4
	TCN-527	5086_C06	17.55	ND	0.00		TCN-542	5079_A16	99	15	8
	TCN-528	5087_P17	23.92	ND	0.00		TCN-543	5081_G23	98	0	73
	TCN-563	5237_B21	88.85	ND	0.00		TCN-544	5082_A19	0	0	97
	TCN-504	3251_K17	7.19	ND	0.00		TCN-545	5082_I15	88	0	99
	TCN-523	5248_A17	80.68	ND	0.00		TCN-546	5089_L08	98	0	100
	TCN-202	2N9	7.00	ND	0.00		TCN-547	5092_F11	0	0	88
Monoclonal transfection set 3	TCN-531	5091_H13	0.00	ND	97.30		TCN-548	5092_P01	0	0	96
	TCN-530	5248_H10	96.95	ND	34.54		TCN-549	5092_P04	0	0	100
	TCN-529	5297_H01	0.00	ND	99.59		TCN-550	5096_F06	0	0	100
	TCN-533	5256_A17	96.12	ND	32.51		TCN-551	5243_D01	99	74	6
	TCN-532	5262_H18	0.00	ND	99.73		TCN-552	5249_I23	0	81	14
	TCN-504	3251_K17	0.00	ND	10.74		TCN-553	5261_C18	44	83	5
	TCN-523	5248_A17	62.19	ND	34.00		TCN-554	5277_M05	0	0	100
	TCN-202	2N9	0.00	ND	17.77		TCN-555	5246_L16	49	89	5
Monoclonal transfection set 4	TCN-535	5246_P19	88.60	97.28	0.00		TCN-556	5089_K12	0	0	15
	TCN-534	5249_B02	65.66	96.37	0.00		TCN-557	5081_A04	7	10	0
	TCN-536	5095_N01	81.63	18.76	99.88		TCN-558	5248_H10	84	96	7
	TCN-504	3251_K17	29.68	0.00	0.00		TCN-559	5097_G08	7	10	12
	TCN-523	5248_A17	65.54	93.19	0.00		TCN-560	5084_P10	0	0	4
	TCN-202	2N9	ND	ND	ND		TCN-504	3251_K17	0	0	0
							TCN-523	5248_A17	39	86	7
							TCN-202	2N9	0	0	0

OTHER EMBODIMENTS

[1523] Although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

[1524] While the invention has been described in conjunction with the detailed description thereof, the foregoing description is intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended claims. Other aspects, advantages, and modifications are within the scope of the following claims.

[1525] The patent and scientific literature referred to herein establishes the knowledge that is available to those with skill in the art. All United States patents and published or unpublished United States patent applications cited herein are incorporated by reference. All published foreign patents and patent applications cited herein are hereby incorporated by reference. Genbank and NCBI submissions indicated by accession number cited herein are hereby incorporated by reference. All other published references, documents, manuscripts and scientific literature cited herein are hereby incorporated by reference.

[1526] While this invention has been particularly shown and described with references to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the scope of the invention encompassed by the appended claims.

CLAIMS

What is claimed is:

1. A composition comprising:

(a) an isolated human antibody that specifically binds to an epitope of the hemagglutinin (HA) glycoprotein of an influenza virus; and

(b) an isolated human monoclonal antibody that specifically binds to an epitope in the extracellular domain of the matrix 2 ectodomain (M2e) polypeptide of an influenza virus.

2. The composition of claim 1, wherein said isolated human monoclonal antibody that specifically binds an epitope of the M2e polypeptide is TCN-032 (8I10), 21B15, TCN-031 (23K12), 3241_G23, 3244_I10, 3243_J07, 3259_J21, 3245_O19, 3244_H04, 3136_G05, 3252_C13, 3255_J06, 3420_I23, 3139_P23, 3248_P18, 3253_P10, 3260_D19, 3362_B11, or 3242_P05.

3. The composition of claim 1, wherein said isolated human antibody that specifically binds an epitope of the HA glycoprotein is TCN-522 (3212_I12), TCN-521 (3280_D18), TCN-523 (5248_A17), TCN-563 (5237_B21), TCN-526 (5084_C17), TCN-527 (5086_C06), TCN-528 (5087_P17), TCN-529 (5297_H01), TCN-530 (5248_H10), TCN-531 (5091_H13), TCN-532 (5262_H18), TCN-533 (5256_A17), TCN-534 (5249_B02), TCN-535 (5246_P19), TCN-536 (5095_N01), TCN-537 (3194_D21), TCN-538 (3206_O17), TCN-539 (5056_A08), TCN-540 (5060_F05), TCN-541 (5062_M11), TCN-542 (5079_A16), TCN-543 (5081_G23), TCN-544 (5082_A19), TCN-545 (5082_I15), TCN-546 (5089_L08), TCN-547 (5092_F11), TCN-548 (5092_P01), TCN-549 (5092_P04), TCN-550 (5096_F06), TCN-551 (5243_D01), TCN-552 (5249_I23), TCN-553 (5261_C18), TCN-554 (5277_M05), TCN-555 (5246_L16), TCN-556 (5089_K12), TCN-557 (5081_A04), TCN 558 (5248_H10b), TCN-559 (5097_G08), TCN-560 (5084_P10), TCN-504 (3251_K17), SC06-141, SC06-255, SC06-257, SC06-260, SC06-261, SC06-262, SC06-268, SC06-272, SC06-296, SC06-301, SC06-307, SC06-310, SC06-314, SC06-323, SC06-325, SC06-327, SC06-328, SC06-329, SC06-331, SC06-332, SC06-334, SC06-336, SC06-339, SC06-342, SC06-343, SC06-344, CR6141, CR6255, CR6257, CR6260, CR6261, CR6262, CR6268, CR6272, CR6296, CR6301, CR6307, CR6310, CR6314, CR6323,

CR6325, CR6327, CR6328, CR6329, CR6331, CR6332, CR6334, CR6336, CR6339, CR6342, CR6343, CR6344, 2A, D7, D8, F10, G17, H40, A66, D80, E88, E90, or H98.

4. The composition of claim 1, wherein said epitope of the HA glycoprotein is GVTNKVNSIIDK (SEQ ID NO: 198), GVTNKVNSIINK (SEQ ID NO: 283), GVTNKENSIIDK (SEQ ID NO: 202), GVTNKVNRIIDK (SEQ ID NO: 201), GITNKVNSVIEK (SEQ ID NO: 281), GITNKENSVIEK (SEQ ID NO: 257), GITNKVNSIIDK (SEQ ID NO: 225), and KITSKVNNIVDK (SEQ ID NO: 216).

5. The composition of claim 1, wherein said epitope of the M2e polypeptide is a discontinuous epitope.

6. The composition of claim 1, wherein said epitope of the M2e polypeptide comprises,

a) the amino acid at positions 2, 5, and 6 of MSLLTEVETPTRNEWGCRCNDSSD (SEQ ID NO: 1); or

b) the amino acid at positions 2, 5, and 6 of SLLTEV (SEQ ID NO: 42).

7. A composition comprising:

(a) an isolated human anti-HA antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region (VH) domain and a light chain variable (VL) domain, wherein the VH domain and the VL domain each comprise three complementarity determining regions 1 to 3 (CDR1-3), and wherein each CDR comprises the following amino acid sequences:
VH CDR1: SEQ ID NOs: 247, 571, 586, 597, 603, 609, 615, 627, 633, 637, 643, 649, 658, 664, 670, 303, 251, 242, or 222;
VH CDR2: SEQ ID NOs: 248, 572, 587, 592, 598, 604, 610, 616, 628, 634, 638, 644, 650, 655, 659, 665, 671, 306, 249, 307, or 221;
VH CDR3: SEQ ID NOs: 568, 573, 588, 593, 599, 605, 611, 617, 629, 635, 639, 645, 651, 656, 660, 666, 672, 725, 246, 290, or 220;
VL CDR1: SEQ ID NOs: 569, 574, 577, 580, 583, 589, 594, 612, 618, 621, 624, 640, 646, 652, 661, 667, 285, 289, 245, 224, or 219;

VL CDR2: SEQ ID NOs: 570, 575, 578, 581, 584, 590, 595, 601, 607, 613, 619, 622, 625, 631, 653, 662, 668, 305, 223, or 231;
VL CDR3: SEQ ID NOs: 289, 576, 579, 582, 585, 591, 596, 602, 608, 614, 620, 623, 626, 632, 636, 642, 648, 654, 657, 663, 669, 308, 250, 227, or 280; and

(b) an isolated anti-matrix 2 ectodomain (M2e) antibody, or antigen-binding fragment thereof, comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain and the VL domain each comprise three complementarity determining regions 1 to 3 (CDR1-3), and wherein each CDR comprises the following amino acid sequences:
VH CDR1: SEQ ID NOs: 72, 103, 179, 187, 203, 211, 228, 252, 260, 268, 284, 293, or 301;
VH CDR2: SEQ ID NOs: 74, 105, 180, 188, 204, 212, 229, 237, 253, 261, 269, 285, or 294;
VH CDR3 SEQ ID NOs: 76, 107, 181, 189, 197, 205, 213, 230, 238, 254, 262, 270, 286, or 295;
VL CDR1: SEQ ID NOs: 59, 92, 184, 192, 208, 192, 233, 241, 265, or 273;
VL CDR2: SEQ ID NOs: 61, 94, 185, 193, 209, 217, 226, 234, 258, 274, or 282; and
VL CDR3: SEQ ID NOs: 63, 96, 186, 194, 210, 218, 243, 259, 267, 275, 291, or 300.

8. A composition comprising:

(a) an isolated human anti-HA antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region (VH) domain and a light chain variable (VL) domain, wherein the VH domain and the VL domain each comprise three complementarity determining regions 1 to 3 (CDR1-3), and wherein each CDR comprises the following amino acid sequences:
VH CDR1: SEQ ID NOs: 247, 571, 586, 597, 603, 609, 615, 627, 633, 637, 643, 649, 658, 664, 670, 303, 251, 242, or 222;
VH CDR2: SEQ ID NOs: 248, 572, 587, 592, 598, 604, 610, 616, 628, 634, 638, 644, 650, 655, 659, 665, 671, 306, 249, 307, or 221;
VH CDR3: SEQ ID NOs: 568, 573, 588, 593, 599, 605, 611, 617, 629, 635, 639, 645, 651, 656, 660, 666, 672, 725, 246, 290, or 220;
VL CDR1: SEQ ID NOs: 569, 574, 577, 580, 583, 589, 594, 612, 618, 621, 624, 640, 646, 652, 661, 667, 285, 289, 245, 224, or 219;
VL CDR2: SEQ ID NOs: 570, 575, 578, 581, 584, 590, 595, 601, 607, 613, 619, 622, 625, 631, 653, 662, 668, 305, 223, or 231;

VL CDR3: SEQ ID NOs: 289, 576, 579, 582, 585, 591, 596, 602, 608, 614, 620, 623, 626, 632, 636, 642, 648, 654, 657, 663, 669, 308, 250, 227, or 280; and

(b) an isolated anti-matrix 2 ectodomain (M2e) antibody, or antigen-binding fragment thereof, comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain and the VL domain each comprise three complementarity determining regions 1 to 3 (CDR1-3), and wherein each CDR comprises the following amino acid sequences:
VH CDR1: SEQ ID NOs: 109, 112, 182, 190, 206, 214, 239, 255, 263, 271, 287, 296, or 304;
VH CDR2: SEQ ID NOs: 110, 113, 183, 191, 207, 215, 232, 240, 256, 264, 272, 288, or 297;
VH CDR3 SEQ ID NOs: 76, 107, 181, 189, 197, 205, 213, 230, 238, 254, 262, 270, 286, or 295;
VL CDR1: SEQ ID NOs: 59, 92, 184, 192, 208, 192, 223, 241, 265, or 273;
VL CDR2: SEQ ID NOs: 61, 94, 185, 193, 209, 217, 226, 234, 258, 274, or 282; and
VL CDR3: SEQ ID NOs: 63, 96, 186, 194, 210, 218, 243, 259, 267, 275, 291, or 300.

9. A composition comprising:

(a) an isolated human anti-HA antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable region (VH) domain, wherein the VH domain comprises the following amino acid sequences: SEQ ID NOs 309, 313, 317, 321, 325, 329, 333, 337, 341, 345, 349, 353, 357, 361, 365, 369, 373, 377, 381, 385, 389, 393, 397, 401, 405, 409, 199, 417, 423, 429, 435, 441, 447, 453, 459, 465, 471, 477, 483, 489, 495, 501, 507, 513, 519, 525, 531, 537, 543, 550, 556, or 562, and a light chain variable (VL) domain, wherein the VL domain comprises the following amino acid sequences: SEQ ID NOs 310, 314, 318, 322, 326, 330, 334, 338, 342, 346, 350, 354, 358, 362, 366, 370, 374, 378, 382, 386, 390, 394, 398, 402, 406, 410, 414, 420, 426, 432, 438, 444, 450, 456, 462, 468, 474, 480, 486, 492, 498, 504, 510, 516, 522, 528, 534, 540, 547, 553, 559, or 565; and

(b) an isolated anti-matrix 2 ectodomain (M2e) antibody, or antigen-binding fragment thereof, comprising a heavy chain variable (VH) domain, wherein the VH domain comprises the following amino acid sequences: SEQ ID NOs 44, 277, 276, 50, 236, 235, 116, 120, 124, 128, 132, 136, 140, 144, 148, 152, 156, 160, 164, 168, 172, or 176, and a light chain variable (VL) domain, wherein the VL domain comprises the following amino acid sequences: SEQ ID NOs 46, 292, 52, 118, 122, 126, 130, 134, 138, 142, 146, 150, 154, 158, 162, 166, 170, or 178.

10. A multivalent vaccine composition comprising the composition of claim 7, 8, or 9.

11. A multivalent vaccine composition comprising the composition of claim 1.

12. A pharmaceutical composition comprising the composition of claim 1, 7, 8, or 9 and a pharmaceutical carrier.

13. A method for stimulating an immune response in a subject, comprising administering to the subject the composition of claim 12.

14. A method for the treatment of an influenza virus infection in a subject in need thereof, comprising administering to said subject the composition of claim 12.

15. The method of claim 14, wherein the subject has been exposed to an influenza virus.

16. The method of claim 15, wherein the subject has not be diagnosed with an influenza infection.

17. A method for the prevention of an influenza virus infection in a subject in need thereof, comprising administering to said subject the vaccine of claim 10 or 11, prior to exposure of said subject to an influenza virus.

18. The method of claim 14 or 17, wherein the method further comprises administering an anti-viral drug, a viral entry inhibitor or a viral attachment inhibitor.

19. The method of claim 18, wherein said anti-viral drug is a neuraminidase inhibitor, a HA inhibitor, a sialic acid inhibitor or an M2 ion channel.

20. The method of claim 19, wherein said M2 ion channel inhibitor is amantadine or rimantadine.

21. The method of claim 19, wherein said neuraminidase inhibitor is zanamivir or oseltamivir phosphate.

22. The method of claim 14 or 17, further comprising administering a second anti-Influenza A antibody.

23. The method of claim 22, wherein said antibody is administered prior to or after exposure to Influenza virus.

24. The method of claim 15, wherein the subject is at risk of contracting an influenza infection.

25. The method of claim 14 or 17, wherein said composition is administered at a dose sufficient to promote viral clearance or eliminate influenza infected cells.

26. A method for determining the presence of an Influenza virus infection in a subject, comprising the steps of:
(a) contacting a biological sample obtained from the subject with the antibody according to any one of claims 1, 7-9;
(b) detecting an amount of the antibody that binds to the biological sample; and
(c) comparing the amount of antibody that binds to the biological sample to a control value, and therefrom determining the presence of the Influenza virus in the subject.

27. The method of claim 26, wherein the control value is determined by contacting a control sample obtained from the subject with the antibody according to any one of claims 1, 7-9 and detecting an amount of the antibody that binds to the control sample.

28. A diagnostic kit comprising the composition of claim 1, 7, 8, or 9.

29. A prophylactic kit comprising the vaccine according to claim 10 or 11.

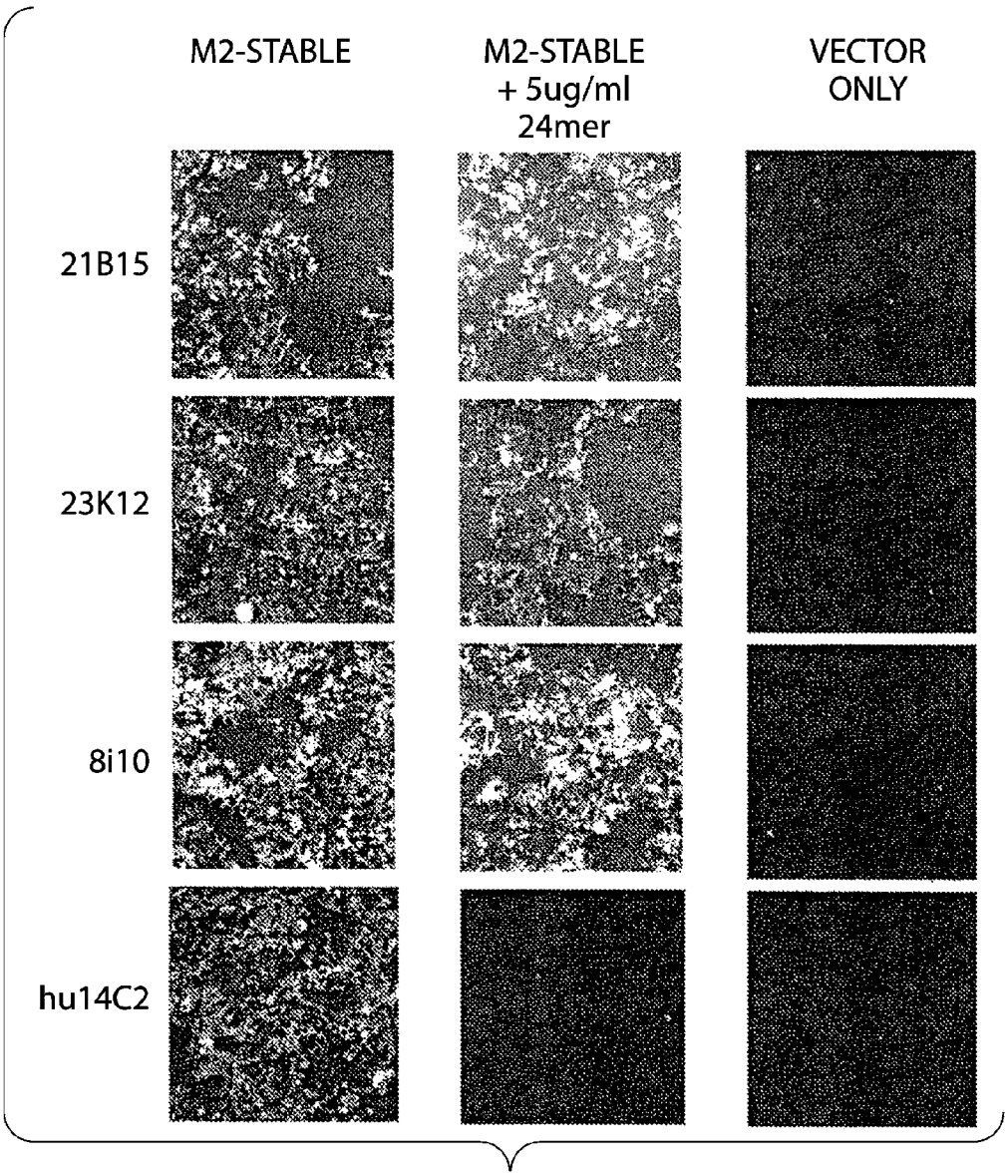

M2-STABLE
M2-STABLE + 5ug/ml 24mer
VECTOR ONLY
21B15
23K12
8i10
hu14C2

FIG. 1

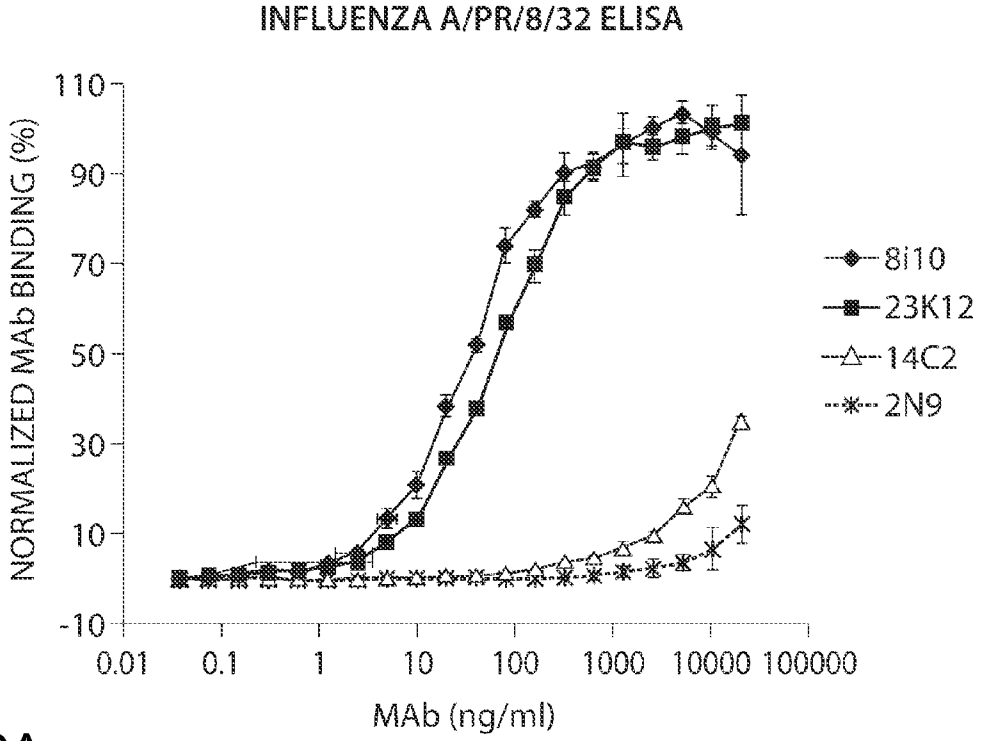

VIRAL BINDING
INFLUENZA A/PR/8/32 ELISA
NORMALIZED MAb BINDING (%)
110
90
70
50
30
10
-10
0.01
0.1
1
10
100
1000
10000
100000
MAb (ng/ml)
8i10
23K12
14C2
2N9

FIG. 2A

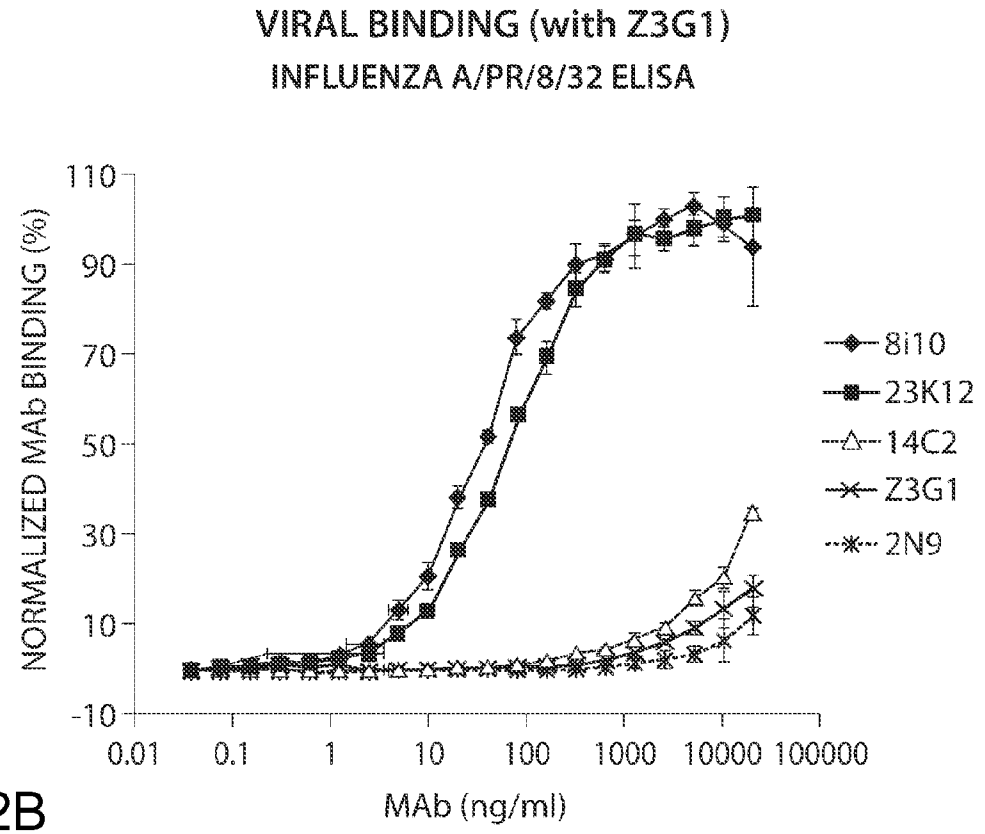

VIRAL BINDING (with Z3G1)
INFLUENZA A/PR/8/32 ELISA
NORMALIZED MAb BINDING (%)
110
90
70
50
30
10
-10
0.01
0.1
1
10
100
1000
10000
100000
MAb (ng/ml)
8i10
23K12
14C2
Z3G1
2N9

FIG. 2B

FIG. 3A

FULL-LENGTH M2 VARIANT BINDING

AMINO ACID SEQUENCES OF EXTRACELLULAR DOMAINS OF M2 VARIANTS.

SEQ ID: No:		10								20							
1	A.Brevig Mission.1.1918.H1N1	M	S	L	L	T	E	V	E	T	P	T	R	N	E	W	G	C	R	C	N	D	S	S	D
2	A.Fort Monmouth.1.1947.H1N1	M	S	L	L	T	E	V	E	T	P	T	K	N	E	W	E	C	R	C	N	D	S	S	D
3	A.Singapore.02.2005.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	E	C	R	C	N	D	S	S	D
679	A.Wisconsin.10.98.H1N1	M	S	L	L	T	E	V	E	T	P	I	K	N	G	W	E	C	K	C	N	D	S	S	D
5	A.Wisconsin.301.1976.H1N1	M	S	L	L	T	E	V	E	T	P	I	R	S	E	W	G	C	R	C	N	D	S	S	D
6	A.Panama.1.66.H2N2	M	S	F	L	P	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	D
7	A.New York.321.1999.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	N
8	A.Caracas.1.71.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	K	E	W	G	C	R	C	N	D	S	S	D
9	A.Taiwan.3.71.H3N2	M	S	F	L	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	D
10	A.Wuhan.359.95.H3N2	M	S	L	P	T	E	V	E	T	P	I	R	S	E	W	G	C	R	C	N	D	S	S	D
11	A.Hong Kong.1144.99.H3N2	M	S	L	L	P	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	D
12	A.Hong Kong.1180.99 H3N2	M	S	L	L	P	E	V	E	T	P	I	R	N	G	W	G	C	R	C	N	D	S	S	D
13	A.Hong Kong.1774.99 H3N2	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	E	C	R	C	S	G	S	S	D
14	A.New York.217.02 H1N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	E	Y	R	C	N	D	S	S	D
15	A.New York.300.2003.H1N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	E	Y	R	C	S	D	S	S	D
16	A.swine.Spain.54008.2004.H3N2	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	E	C	R	Y	S	D	S	S	D
17	A.Guangzhou.333.99.H9N2	M	S	F	L	T	E	V	E	T	L	T	R	N	G	W	E	C	R	C	S	D	S	S	D
18	A.Hong Kong.1073.99.H9N2	M	S	L	L	T	E	V	E	T	L	T	R	N	G	W	E	C	K	C	R	D	S	S	D
19	A.Hong Kong.1.68.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	D
20	A.swine.Hong Kong.126.1982.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	S	E	W	G	C	R	C	N	D	S	G	D
21	A.New York.703.1995.H3N2	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	E	C	R	C	N	G	S	S	D
22	A.swine.Quebec.192.81 H1N1	M	S	L	P	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	D	S	S	D
23	A.Puerto Rico.8.34.H1N1	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	G	S	S	D
24	A.Hong Kong.485.97.H5N1	M	S	L	L	T	E	V	D	T	L	T	R	N	G	W	G	C	R	C	S	D	S	S	D
25	A.Hong Kong.542.97.H5N1	M	S	L	L	T	E	V	E	T	L	T	K	N	G	W	G	C	R	C	S	D	S	S	D
26	A.silky chicken.Shantou.1826.2004.H	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	E	C	K	C	S	D	S	S	D
27	A,chicken.Taiwan.0305.04.H6N1	M	S	L	L	T	E	V	E	T	H	T	R	N	G	W	E	C	K	C	S	D	S	S	D
28	A.Quail.Arkansas.16309-7.94.H7N3	M	S	L	L	T	E	V	K	T	P	T	R	N	G	W	E	C	K	C	S	D	S	S	D
29	A.Hong Kong.486.97.H5N1	M	S	L	L	T	E	V	E	T	L	T	R	N	G	W	G	C	R	C	S	D	S	S	D
30	A.Chicken.Pennsylvania.13552-1.98	M	S	L	L	T	E	V	E	T	P	T	R	D	G	W	E	C	K	C	S	D	S	S	D
31	A.chicken.Heilongjiang.48.01.H9N2	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	G	C	R	C	S	D	S	S	D
32	A.swine.Korea.S5.2005.H1N2	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	E	C	K	C	N	D	S	S	D
33	A.Hong Kong.1073.99.H9N2	M	S	L	L	T	E	V	E	T	L	T	R	N	G	W	E	C	K	C	S	D	S	S	D
34	A.Wisconsin.3523.88.H1N1	M	S	L	L	T	E	V	E	T	P	I	R	N	E	W	G	C	K	C	N	D	S	S	D
35	A.X-31 Vaccine strain H3N2	M	S	F	L	T	E	V	E	T	P	I	R	N	E	W	G	C	R	C	N	G	S	S	D
36	A.Chicken.Rostock.8.1934.H7N1	M	S	L	L	T	E	V	E	T	P	T	R	N	G	W	E	C	R	C	N	D	S	S	D
37	A.environment.New York. 16326-1.2	M	S	L	L	T	E	V	E	T	P	I	R	K	G	W	E	C	N	C	S	D	S	S	D
38	A.Indonesia.560H.2006.H5N1	M	S	L	L	T	E	V	E	T	P	T	R	N	E	W	E	C	R	C	S	D	S	S	D
39	A.Chicken.Hong Kong.SF1.03.H9N2	M	S	L	L	T	G	V	E	T	H	T	R	N	G	W	G	C	K	C	S	D	S	S	D
40	A.chicken.Hong Kong YU427.03.H9N	M	S	L	L	P	E	V	E	T	H	T	R	N	G	W	G	C	R	C	S	D	S	S	D

EXTRACELLULAR SEQUENCE OF D20 IS IDENTICAL TO #19, HK483 TO #29, AND VN1203 TO #38.

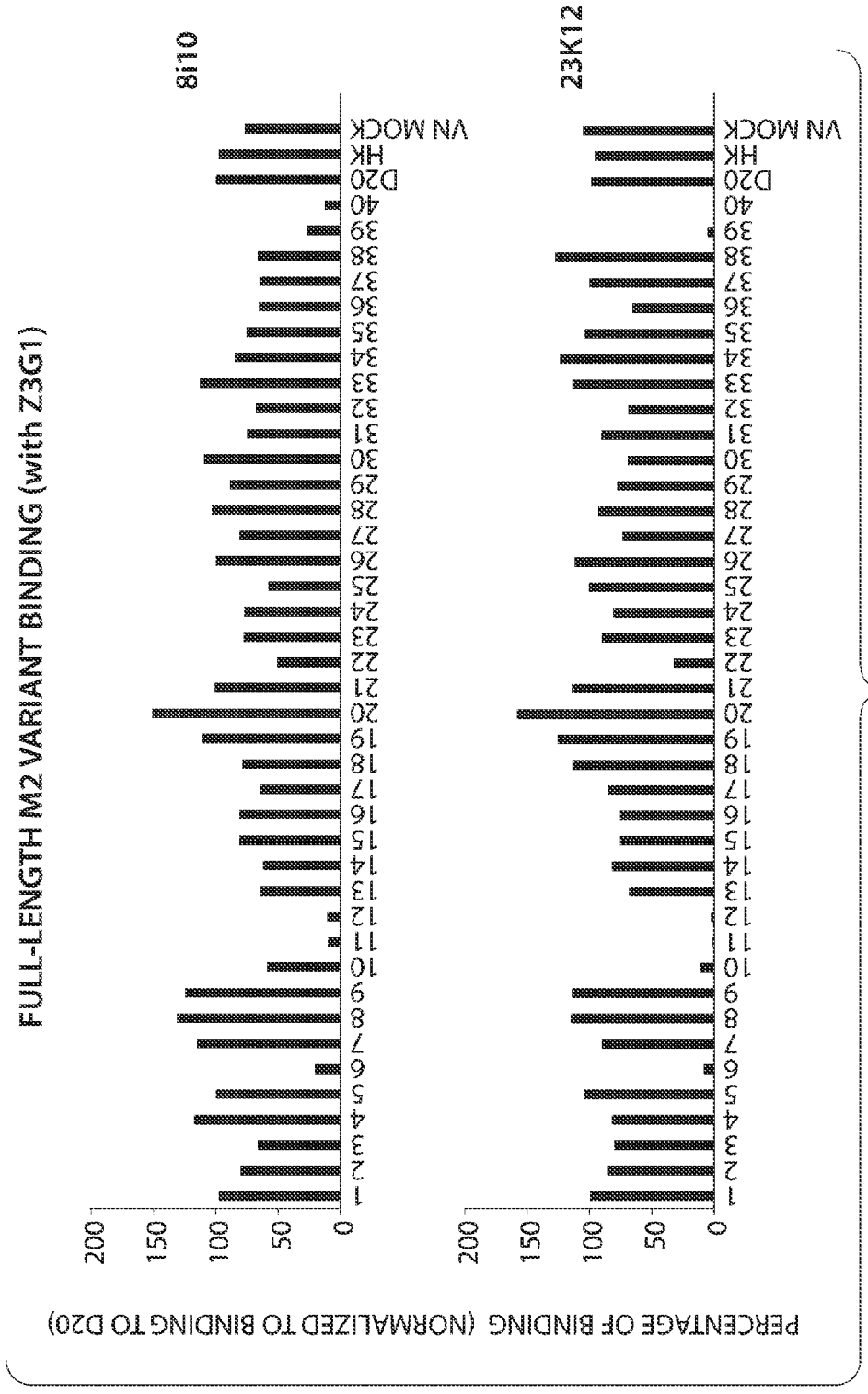

FULL-LENGTH M2 VARIANT BINDING (with Z3G1)
8i10
23K12
PERCENTAGE OF BINDING (NORMALIZED TO BINDING TO D20)
0
50
100
150
200
VN MOCK
HK
D20
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40

FIG. 3B-1

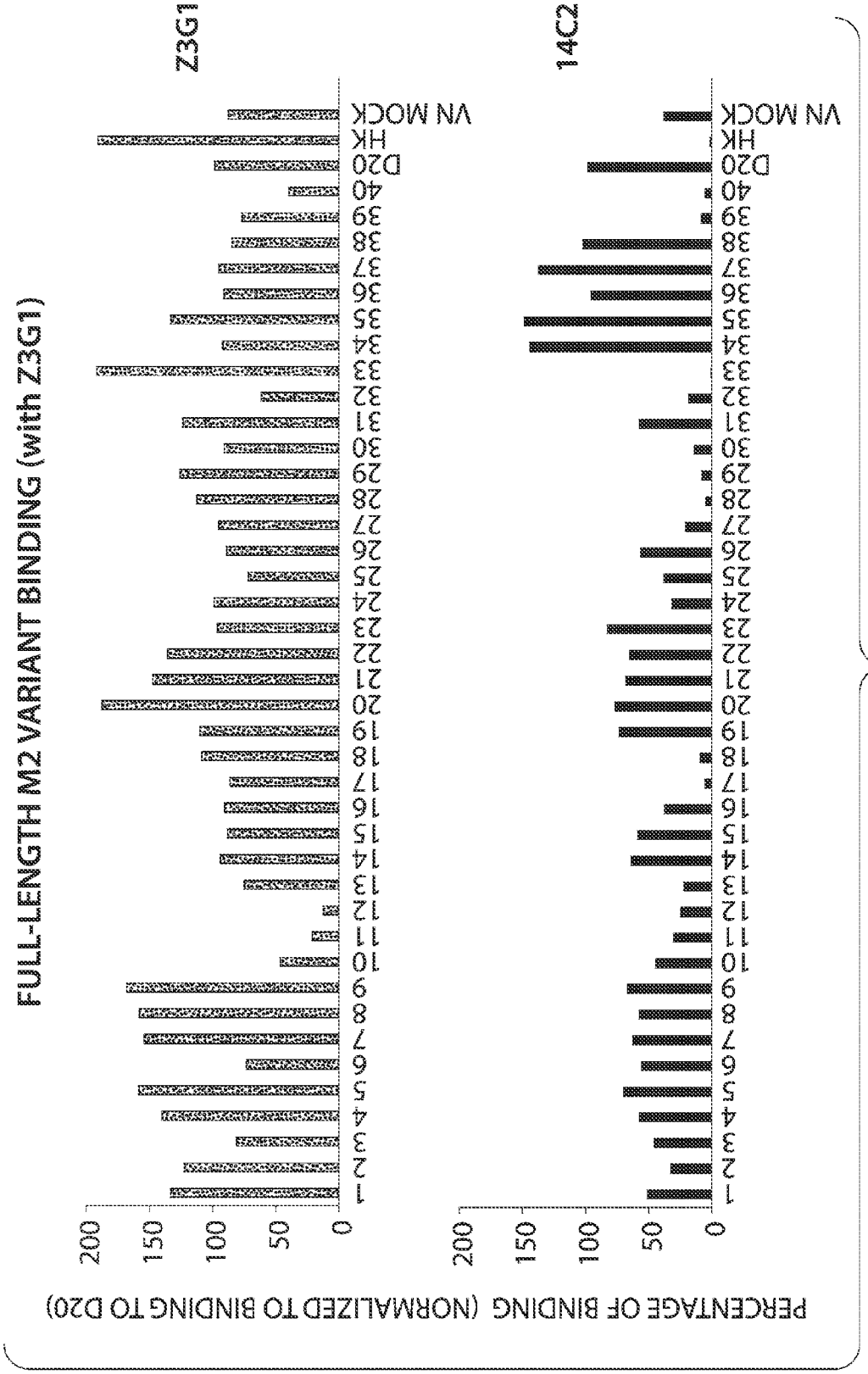

FULL-LENGTH M2 VARIANT BINDING (with Z3G1)
Z3G1
14C2
PERCENTAGE OF BINDING (NORMALIZED TO BINDING TO D20)
0
50
100
150
200
VN MOCK
HK
D20
40
39
38
37
36
35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1

FIG. 3B-2

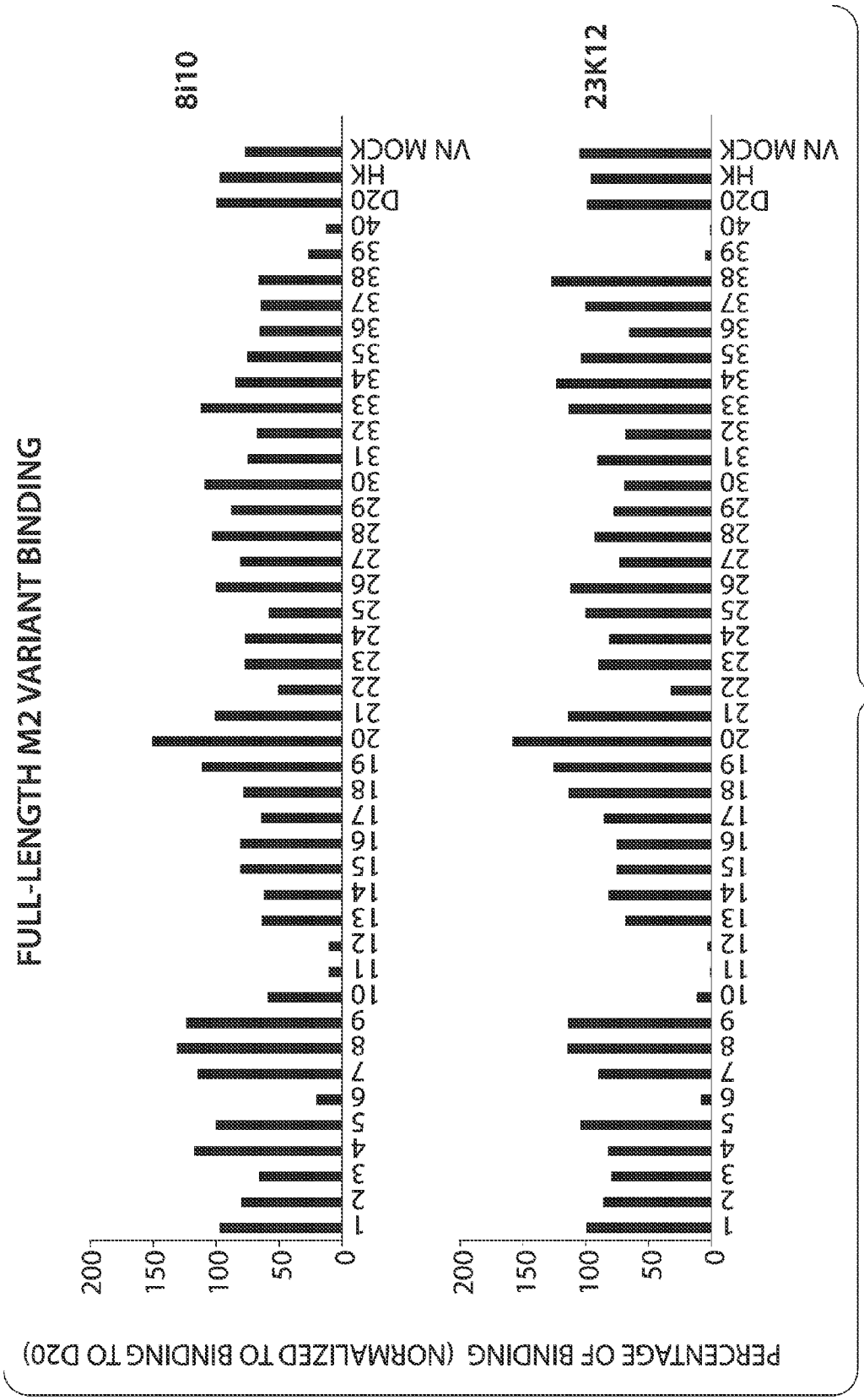

FULL-LENGTH M2 VARIANT BINDING
8i10
23K12
PERCENTAGE OF BINDING (NORMALIZED TO BINDING TO D20)
200
150
100
50
0
VN MOCK
HK
D20
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40

FIG. 3C-1

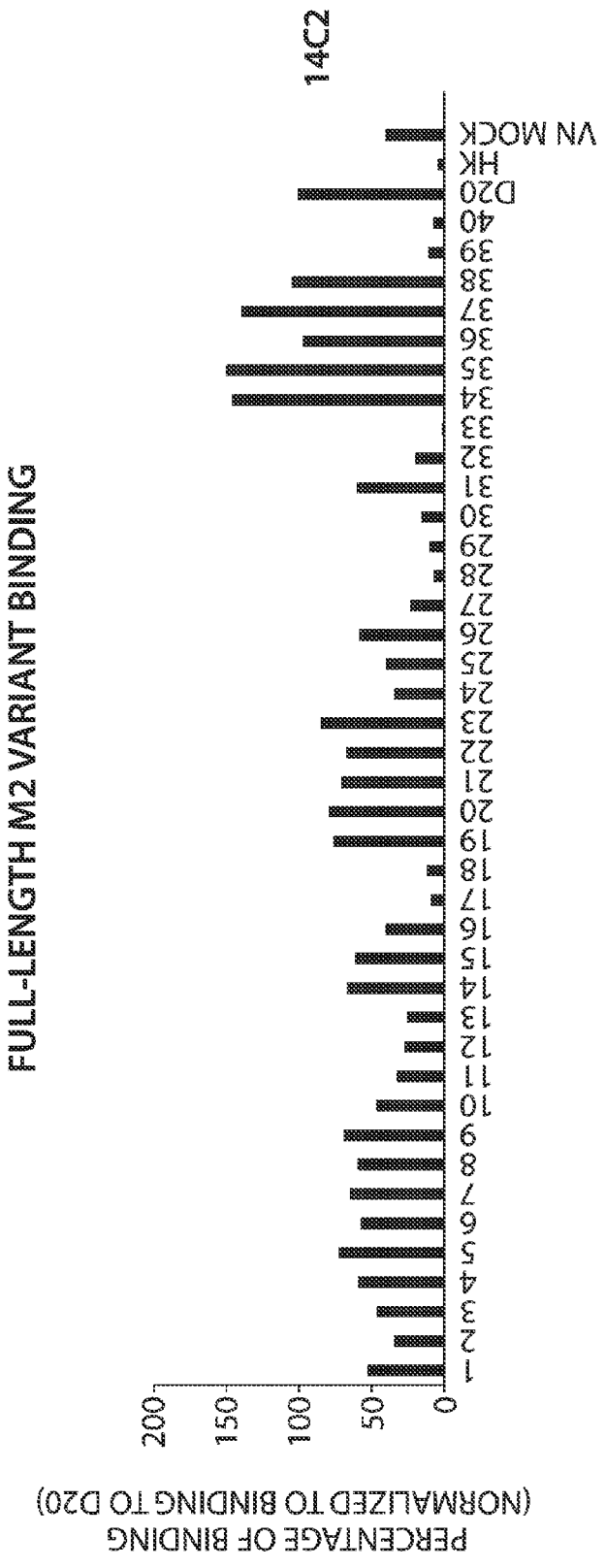

14C2
FULL-LENGTH M2 VARIANT BINDING
PERCENTAGE OF BINDING
(NORMALIZED TO BINDING TO D20)
200
150
100
50
0
VN MOCK
HK
D20
40
39
38
37
36
35
34
33
32
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1

FIG. 3C-2

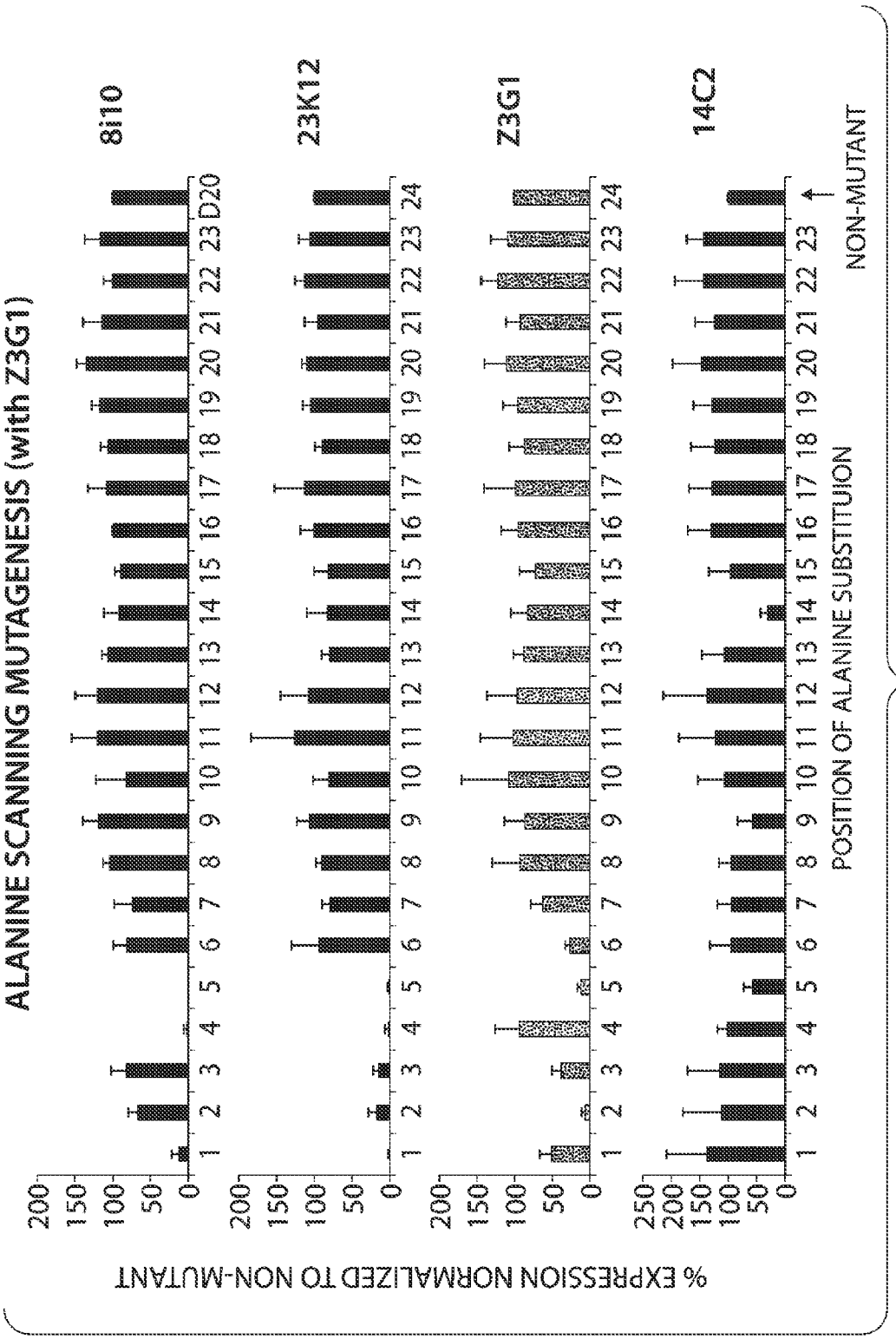

ALANINE SCANNING MUTAGENESIS (with Z3G1)
8i10
23K12
Z3G1
14C2
% EXPRESSION NORMALIZED TO NON-MUTANT
POSITION OF ALANINE SUBSTITUION
NON-MUTANT

FIG. 4A

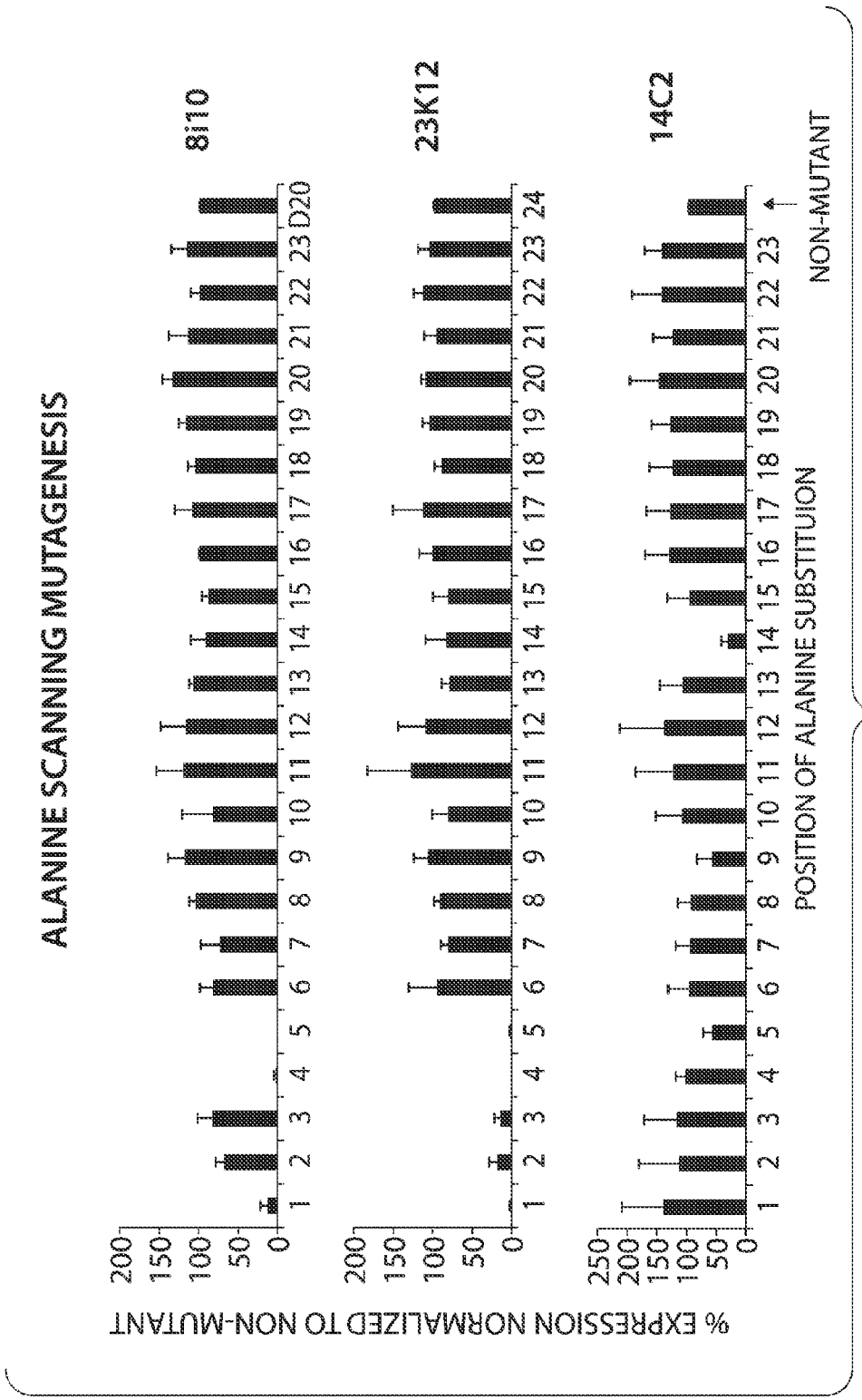

ALANINE SCANNING MUTAGENESIS
8i10
23K12
14C2
% EXPRESSION NORMALIZED TO NON-MUTANT
POSITION OF ALANINE SUBSTITUION
NON-MUTANT

FIG. 4B

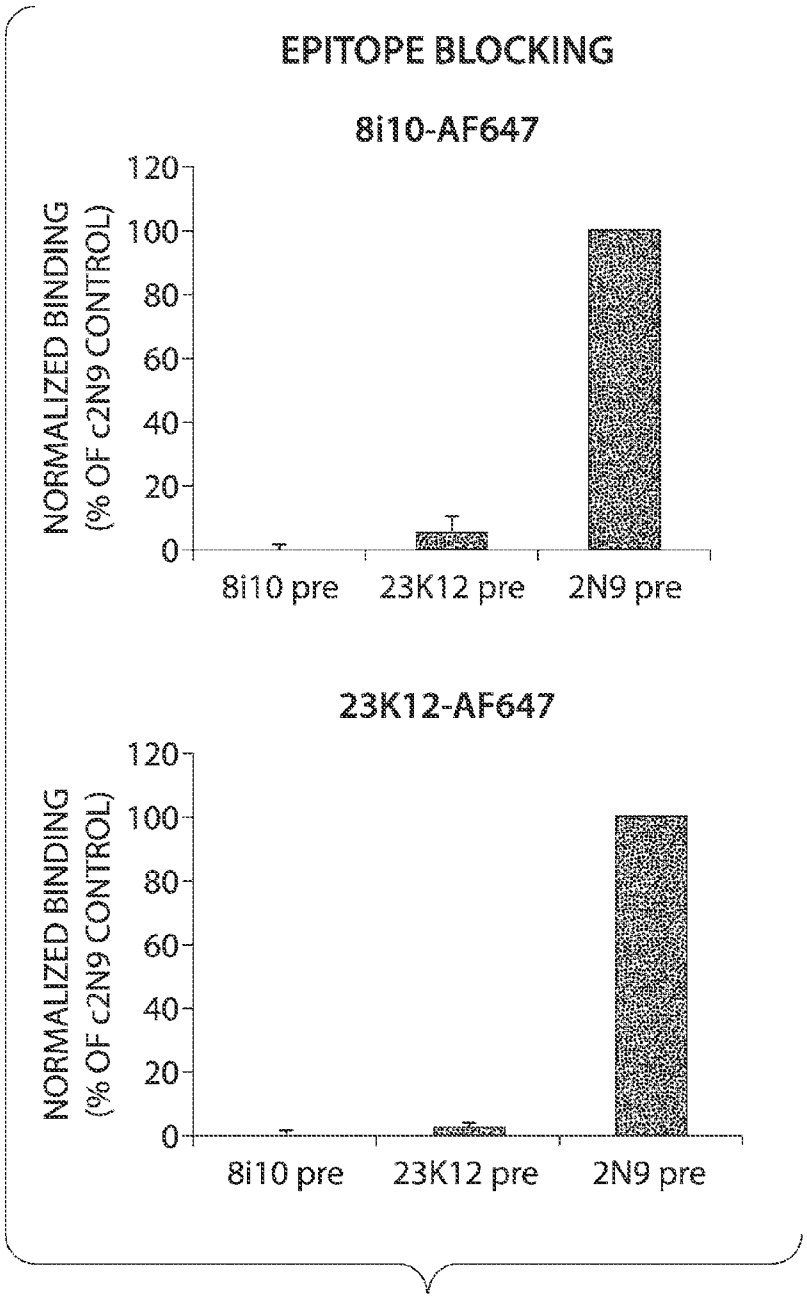

EPITOPE BLOCKING
8i10-AF647
NORMALIZED BINDING (% OF c2N9 CONTROL)
120
100
80
60
40
20
0
8i10 pre
23K12 pre
2N9 pre
23K12-AF647
NORMALIZED BINDING (% OF c2N9 CONTROL)
120
100
80
60
40
20
0
8i10 pre
23K12 pre
2N9 pre

FIG. 5

CROSS REACTIVITY BINDING OF ANTI-M2 ANTIBODIES TO VARIANT M2 PEPTIDES

				ELISA (OD 450)			
seqNo	Name	Size	Description	14C2	8i10	23K12	2N9
680	M2	23 aa	SLLTEVETPIRNEWGCRCNDSSD	+	-	-	-
681	M2SG	23 aa	SLLTEVETPIRSEWGCRCNDSGD	+	-	-	-
682	M2EG	23 aa	SLLTEVETPIRNEWECRCNGSSD	+	-	-	-
683	M2P	23 aa	SLPTEVETPIRNEWGCRCNDSSD	+	-	-	-
684	M2G	23 aa	SLLTEVETPIRNEWGCRCNGSSD	+	-	-	-
685	M2DLTGS	23 aa	SLLTEVDTLTRNGWGCRCSDSSD	-	-	+	-
686	M2KNS	23 aa	SLLTEVETPIRKEWGCNCSDSSD	+	-	-	-
687	M2LGS	23 aa	SLLTEVETLIRNGWGCRCSDSSD	-	-	-	-
688	M2LTKGS	23 aa	SLLTEVETLTKNGWGCRCSDSSD	-	-	-	-
689	M2SY	23 aa	SLLTEVETPIRSEWGCRYNDSSD	+	-	-	-
690	M2TGEKS	23 aa	SLLTEVETPTRNGWECKCSDSSD	+	-	-	-
691	M2HTGEKS	23 aa	SLLTEVETHTRNGWECKCSDSSD	-	-	-	-
692	M2KTGEKS	23 aa	SLLTEVKTPTRNGWECKCSDSSD	-	-	-	-
693	M2LTGS	23 aa	SLLTEVETLTRNGWGCRCSDSSD	-	-	+	-
694	M2TDGEKS	23 aa	SLLTEVETPTRDGWECKCSDSSD	+	-	-	-
695	M2TGS	23 aa	SLLTEVETPTRNGWGCRCSDSSD	+	-	W	-
696	M2TGEK	23 aa	SLLTEVETPTRNGWECKCNDSSD	+	-	-	-
697	M2LTGEKS	23 aa	SLLTEVETLTRNGWECKCSDSSD	-	-	W	-
698	M2K	23 aa	SLLTEVETPIRNEWGCKCNDSSD	+	W	+	-
699	M2FG	23 aa	SFLTEVETPIRNEWGCRCNGSSD	+	W	-	-
700	M2TGE	23 aa	SLLTEVETPTRNGWECRCNDSSD	+	-	-	-
701	M2KGENS	23 aa	SLLTEVETPIRKGWECNCSDSSD	+	-	-	-
702	M2TES	23 aa	SLLTEVETPTRNEWECRCSDSSD	+	-	-	-
703	M2GHTGKS	23 aa	SLLTGVETHTRNGWGCKCSDSSD	-	-	-	-
704	M2PHTGS	23 aa	SLLPEVETHTRNGWGCRCSDSSD	-	-	-	-

PERCENTAGE COMPARED RELATIVE TO BINDING TO WILD-TYPE PEPTIDE (Seq 1) NOTE: mAbs WERE TESTED AT 5 µg/mL

>25 %	-	NO BINDING
25 - 40 %	W	WEAK BINDING
> 40 %	+	POSITIVE BINDING

FIG. 6A

BINDING ACTIVITY OF M2 ANTIBODIES TO TRUNCATED M2 PEPTIDES

seqNo	Name	Size	Description	14C2	8i10	23K12	2N9
680	M2	23 aa	SLLTEVETPIRNEWGCRCNDSSD	3.85	0.11	0.22	0.06
705	M16	16 aa	LLTEVETPIRNEWGCR	3.94	0.09	0.21	0.09
706	M15	15 aa	LTEVETPIRNEWGCR	3.95	0.09	0.21	0.09
707	M12	12 aa	VETPIRNEWGCR	0.15	0.09	0.20	0.09
708	CM17	17 aa	ETPIRNEWGCRCNDSSD	0.19	0.11	0.34	0.11
709	CM16	16 aa	TPIRNEWGCRCNDSSD	0.23	0.13	0.35	0.12
710	CM15	15 aa	PIRNEWGCRCNDSSD	0.19	0.12	0.34	0.11
711	CM14	14 aa	IRNEWGCRCNDSSD	0.23	0.14	0.36	0.13
712	CM13	13 aa	RNEWGCRCNDSSD	0.22	0.14	0.34	0.13
713	CM12	12 aa	NEWGCRCNDSSD	0.27	0.14	0.39	0.14
714	NM17	17 aa	SLLTEVETPIRNEWGCR	3.99	0.26	0.58	0.10
715	NM16	16 aa	SLLTEVETPIRNEWGC	3.90	0.29	0.62	0.09
716	NM15	15 aa	SLLTEVETPIRNEWG	3.97	0.12	0.30	0.11
717	NM14	14 aa	SLLTEVETPIRNEW	3.97	0.11	0.24	0.09
718	NM13	13 aa	SLLTEVETPIRNE	0.18	0.11	0.25	0.10
719	NM12	12 aa	SLLTEVETPIRN	0.20	0.10	0.24	0.09
720	NM11	11 aa	SLLTEVETPIR	0.21	0.13	0.30	0.12
721	NM10	10 aa	SLLTEVETPI	0.17	0.10	0.24	0.10
722	NM8	8 aa	SLLTEVET	0.15	0.10	0.20	0.09
723	NM7	7 aa	SLLTEVE	0.14	0.10	0.20	0.08
724	NM9	9 aa	SLLTEVETP	0.21	0.12	0.30	0.19
19	M2e	24 aa	MSLLTEVETPIRNEWGCRCNDSSD	3.98	0.13	0.43	0.10
CMV	HVIR1			0.16	0.11	0.21	3.99

NOTE: mAbs WERE TESTED AT 5 µg/mL

FIG. 6B

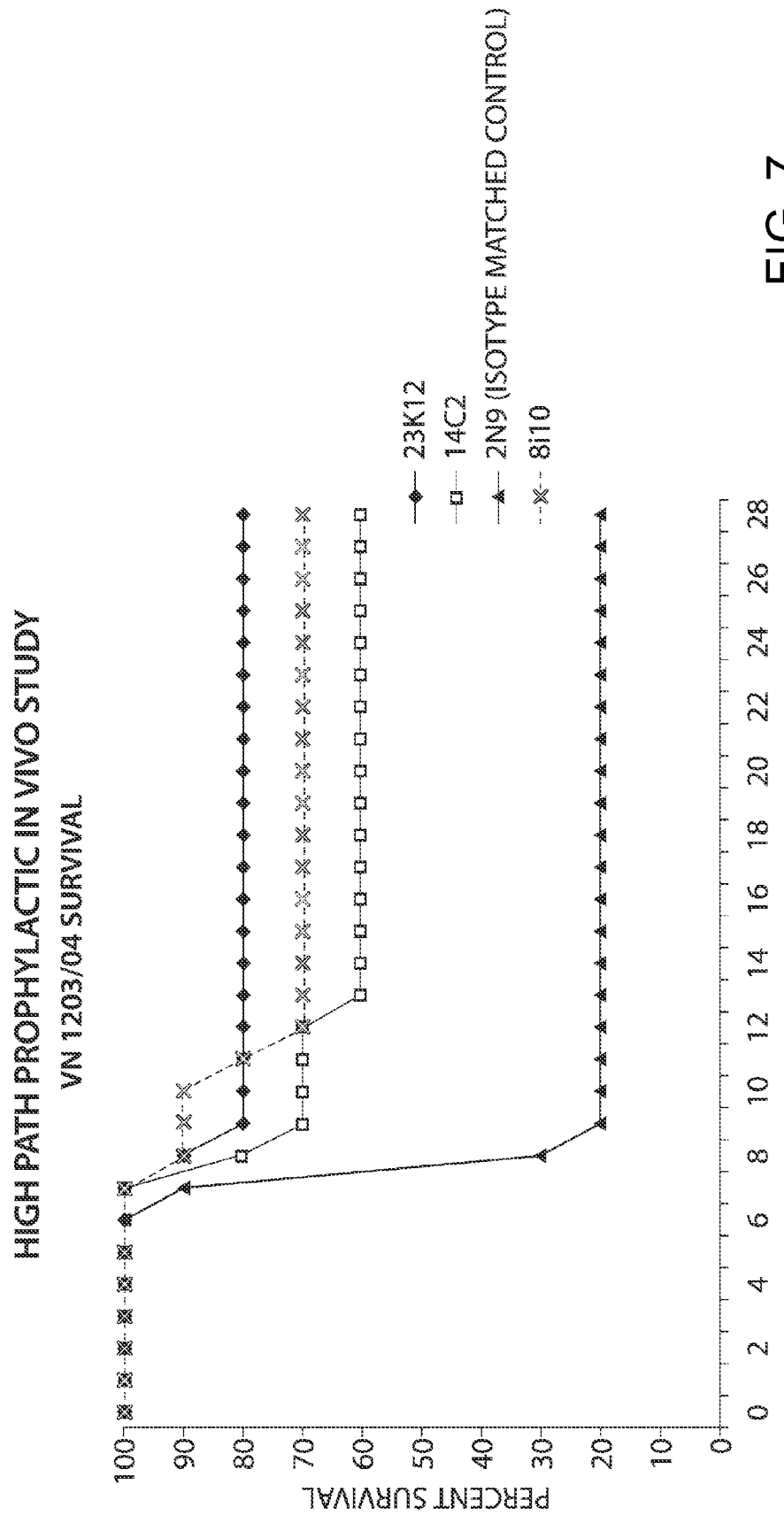

HIGH PATH PROPHYLACTIC IN VIVO STUDY
VN 1203/04 SURVIVAL
PERCENT SURVIVAL
100
90
80
70
60
50
40
30
20
10
0
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28
DAYS POST INFECTION
23K12
14C2
2N9 (ISOTYPE MATCHED CONTROL)
8i10

FIG. 7

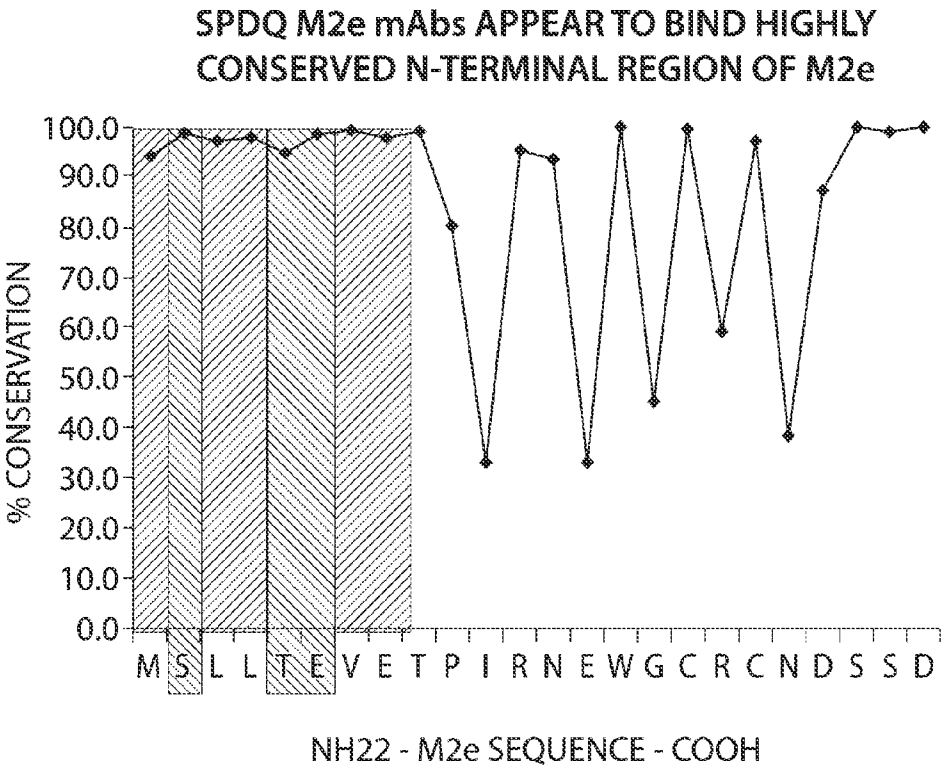

SPDQ M2e mAbs APPEAR TO BIND HIGHLY CONSERVED N-TERMINAL REGION OF M2e
% CONSERVATION
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
M S L L T E V E T P I R N E W G C R C N D S S D
NH22 - M2e SEQUENCE - COOH

FIG. 8

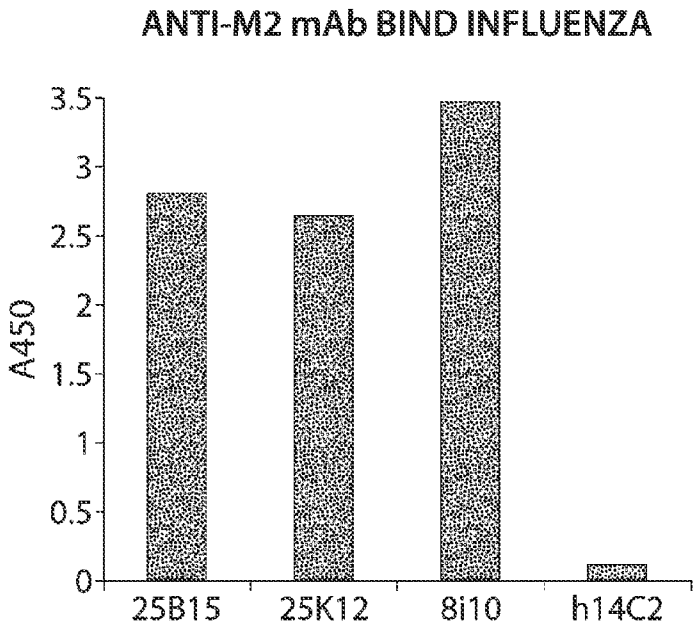

ANTI-M2 mAb BIND INFLUENZA
A450
3.5
3
2.5
2
1.5
1
0.5
0
25B15
25K12
8i10
h14C2

FIG. 9

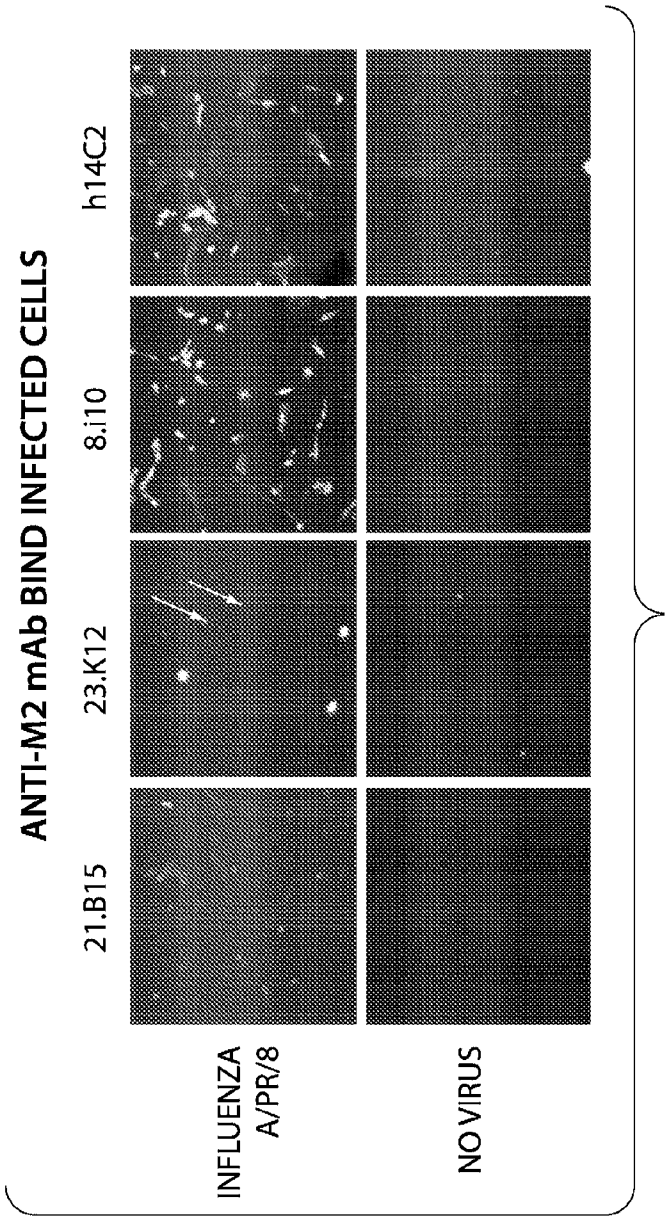

ANTI-M2 mAb BIND INFECTED CELLS
21.B15
23.K12
8.i10
h14C2
INFLUENZA A/PR/8
NO VIRUS

FIG. 10

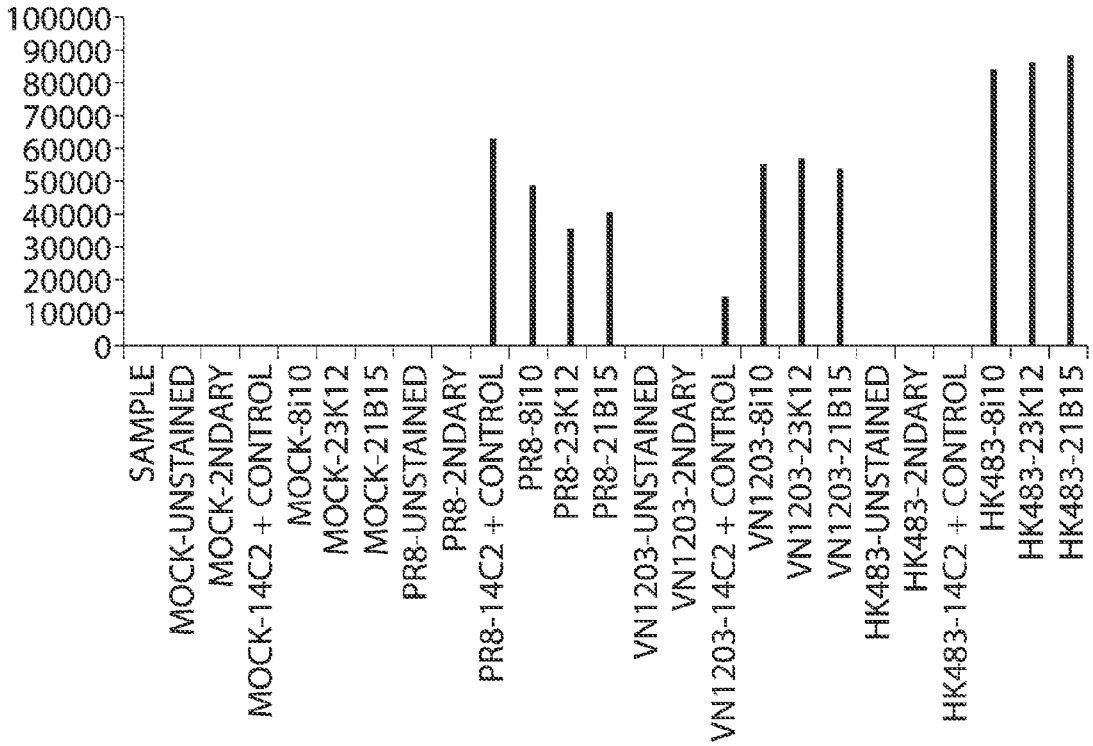

100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
SAMPLE
MOCK-UNSTAINED
MOCK-2NDARY
MOCK-14C2 + CONTROL
MOCK-8i10
MOCK-23K12
MOCK-21B15
PR8-UNSTAINED
PR8-2NDARY
PR8-14C2 + CONTROL
PR8-8i10
PR8-23K12
PR8-21B15
VN1203-UNSTAINED
VN1203-2NDARY
VN1203-14C2 + CONTROL
VN1203-8i10
VN1203-23K12
VN1203-21B15
HK483-UNSTAINED
HK483-2NDARY
HK483-14C2 + CONTROL
HK483-8i10
HK483-23K12
HK483-21B15

FIG. 11

FIG. 12A

Heavy Chain

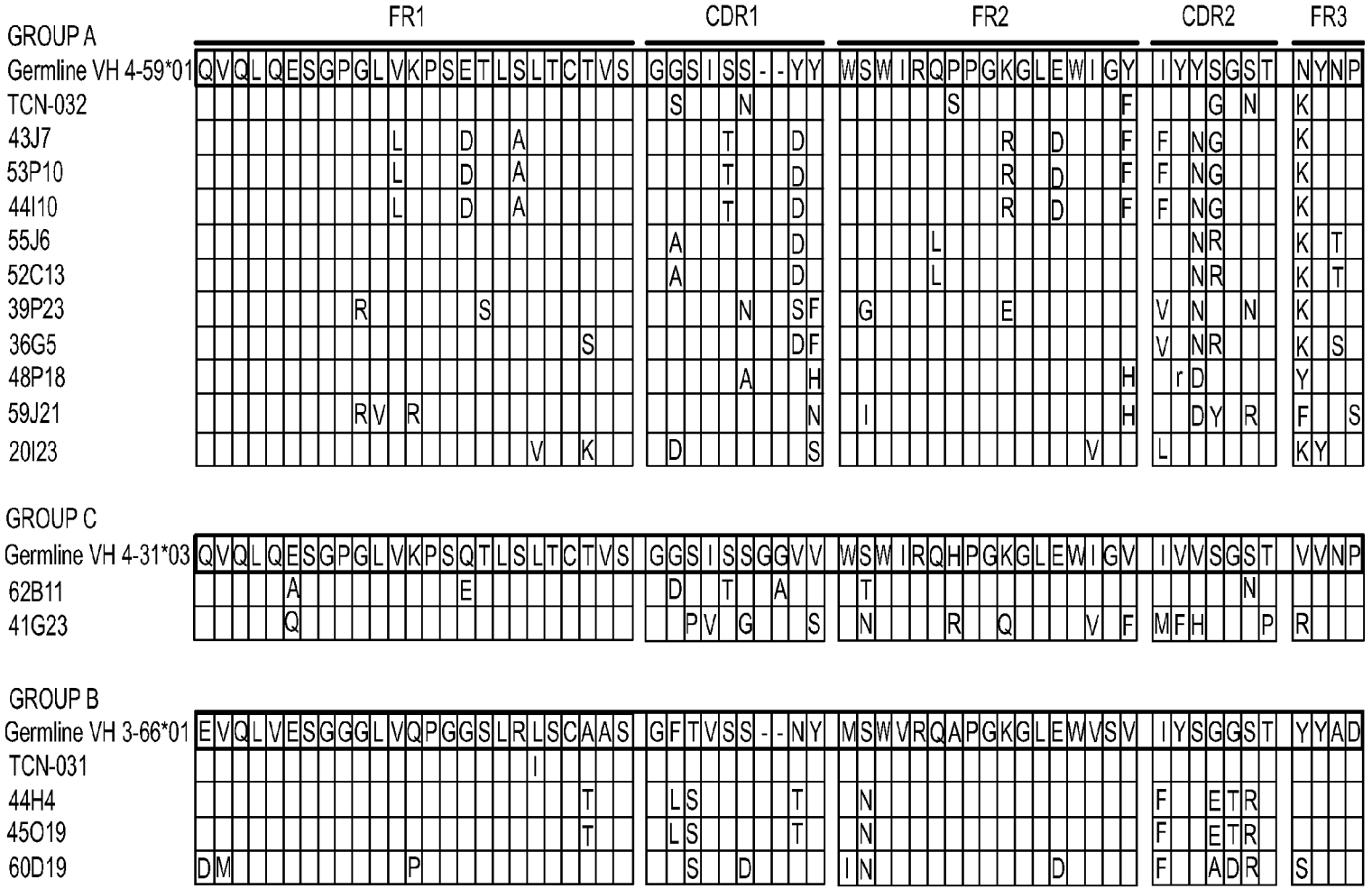


FIG. 12A (continued)

Heavy Chain

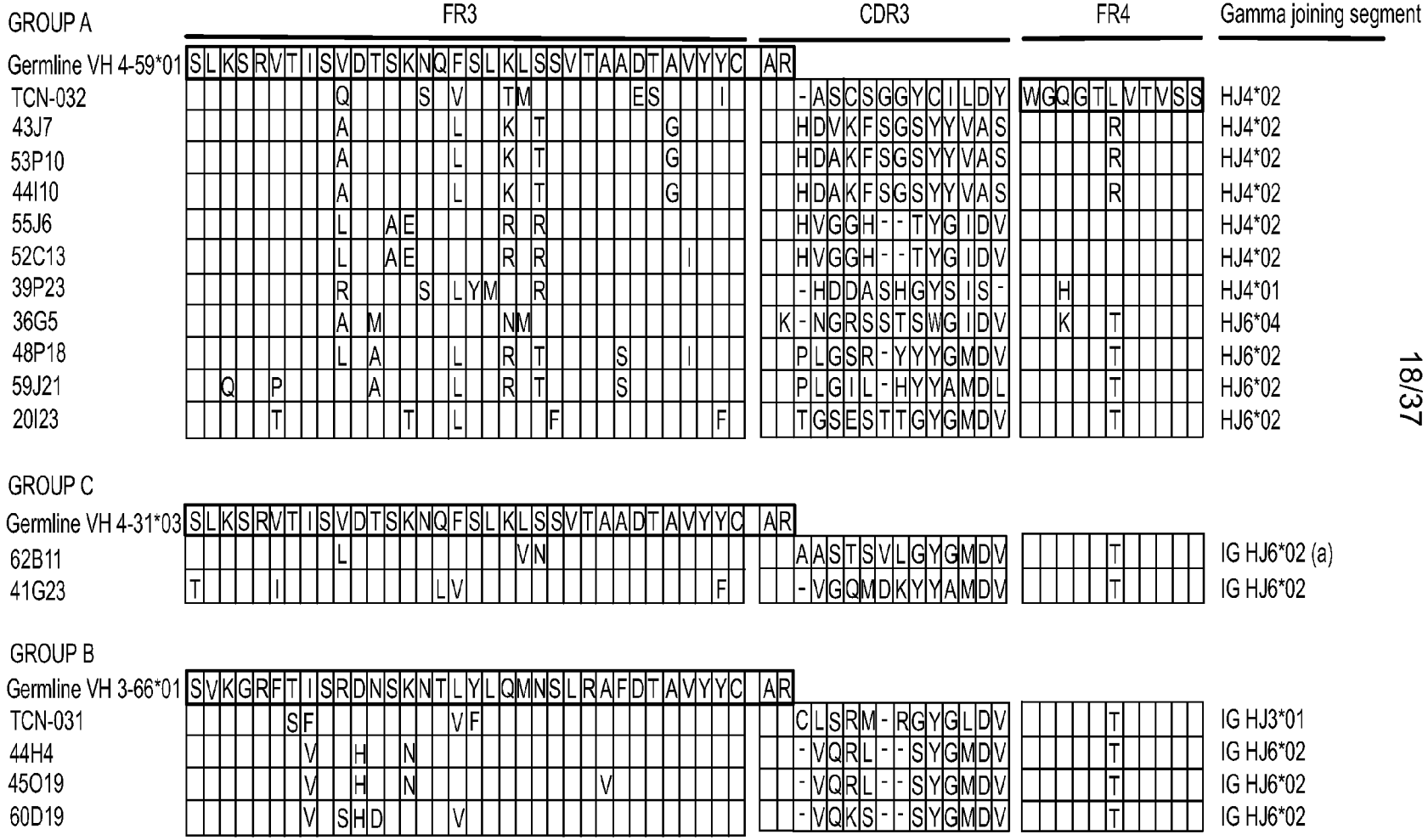


FIG. 12B

Kappa Chain

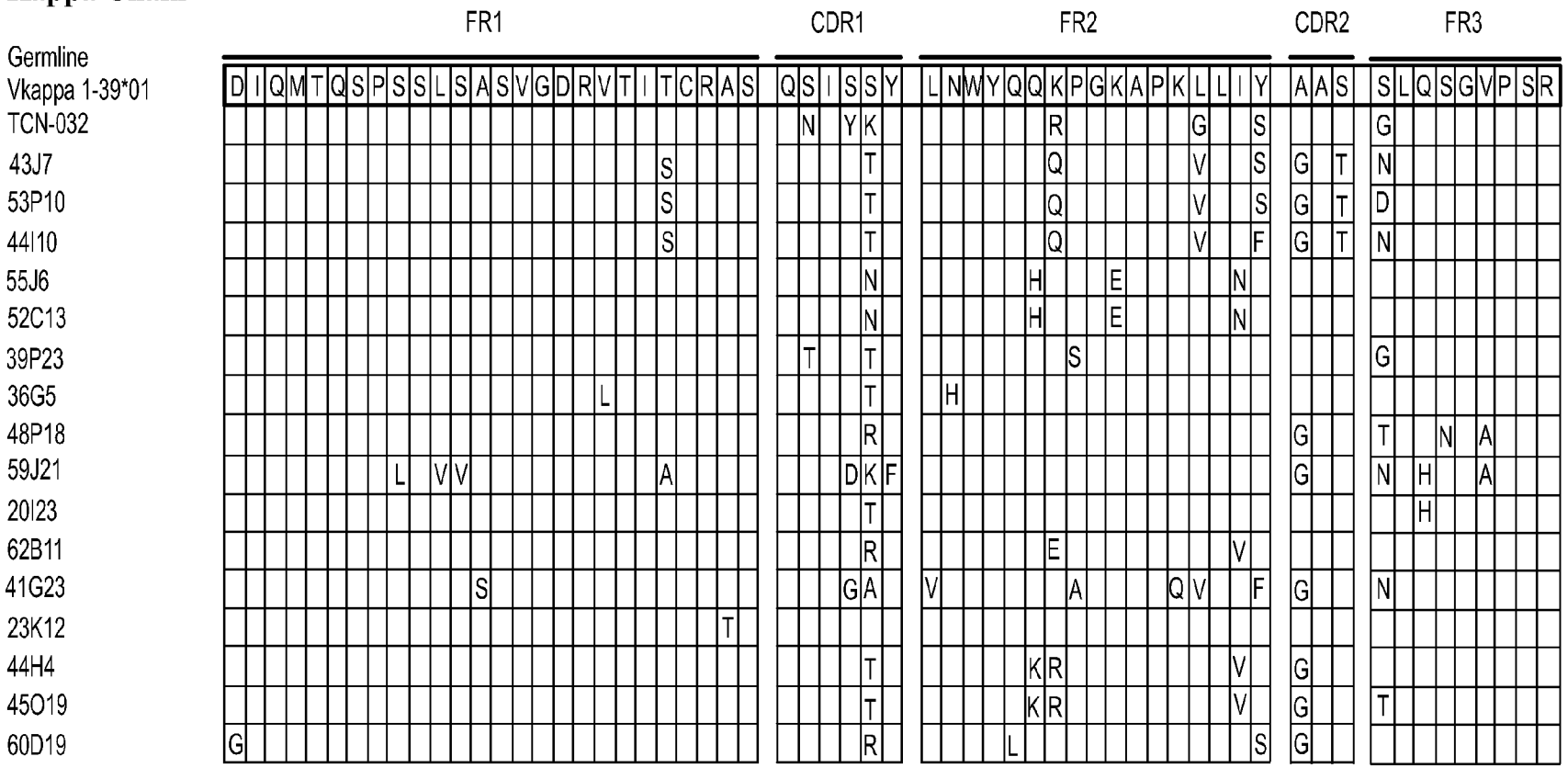
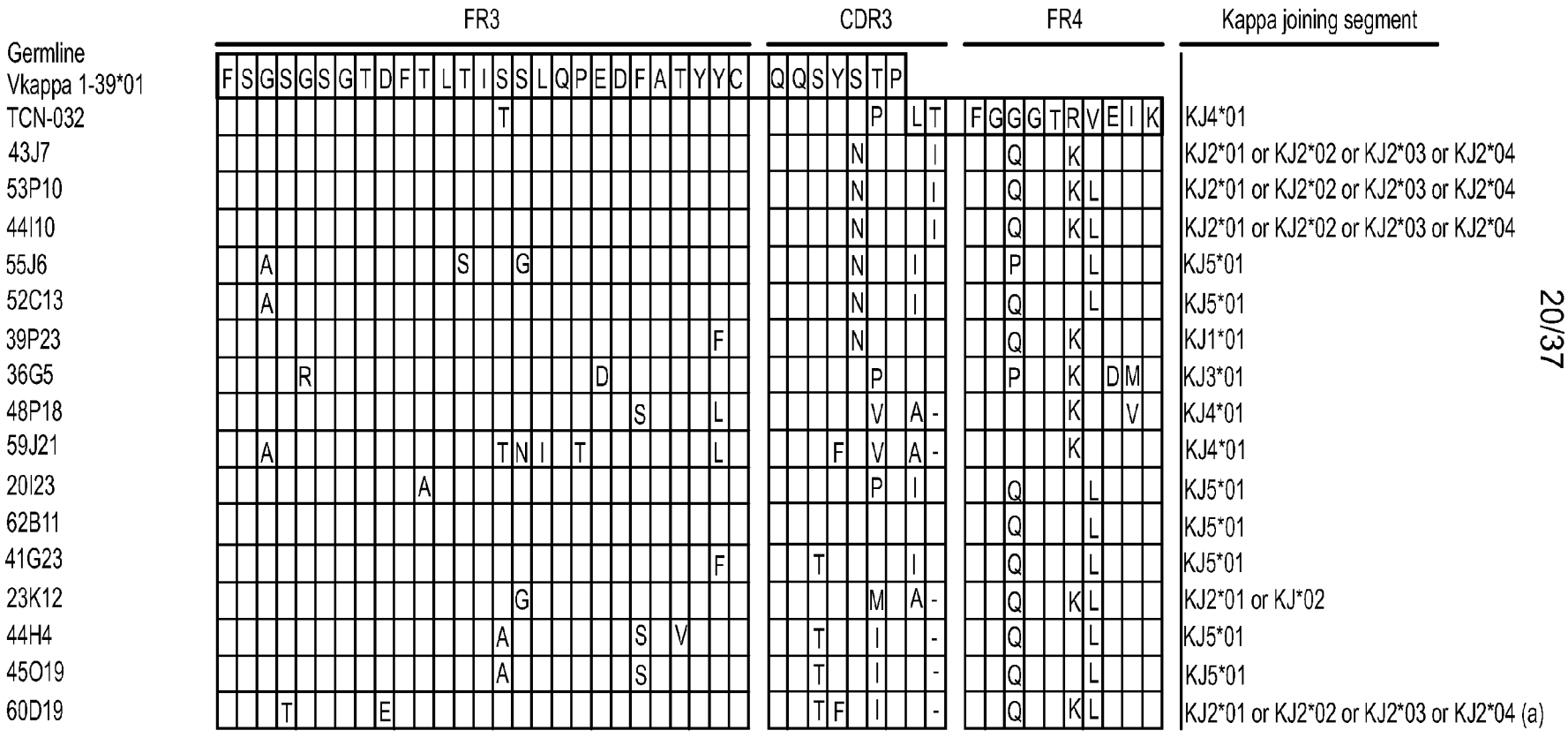


FIG. 12B (continued)



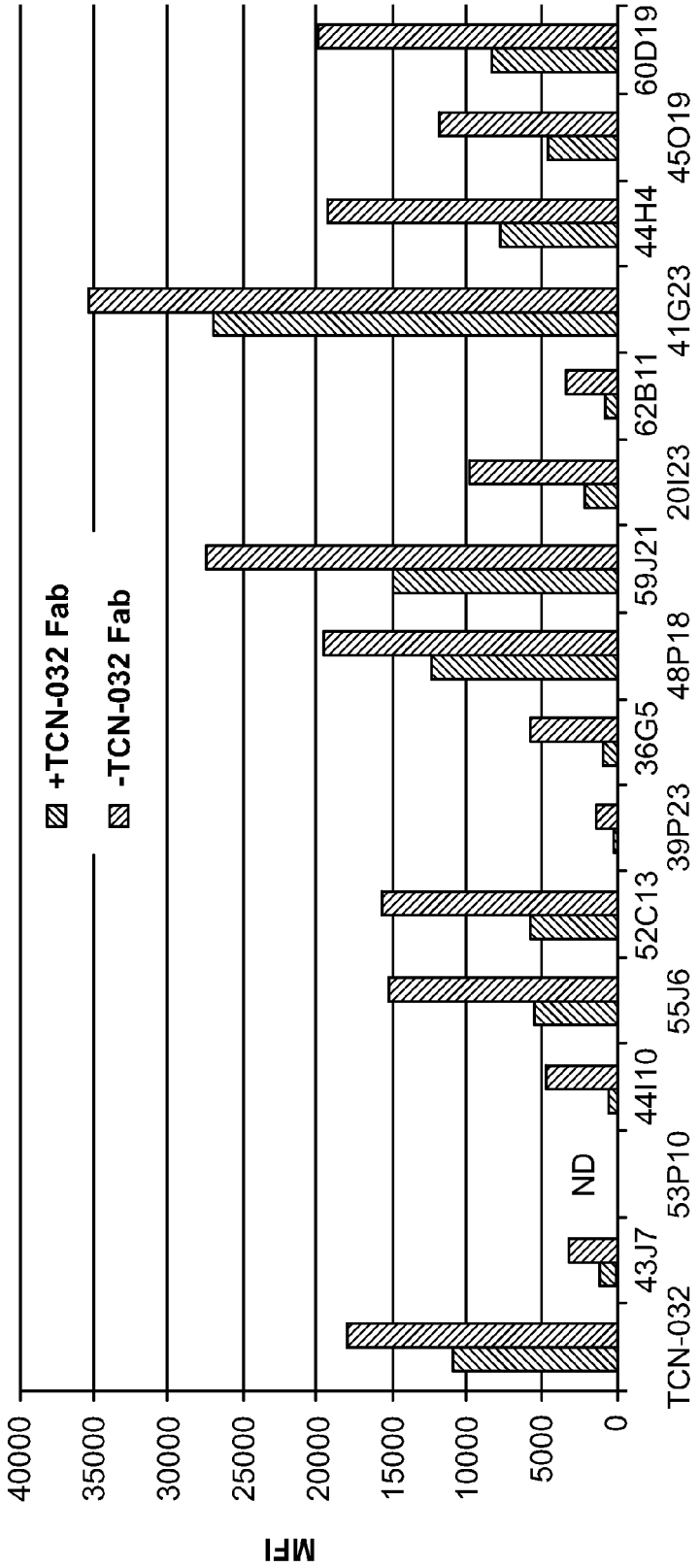

+TCN-032 Fab
-TCN-032 Fab
MFI
40000
35000
30000
25000
20000
15000
10000
5000
0
mAb
TCN-032
43J7
53P10
ND
44I10
55J6
52C13
39P23
36G5
48P18
59J21
20I23
62B11
41G23
44H4
45O19
60D19

FIG. 13

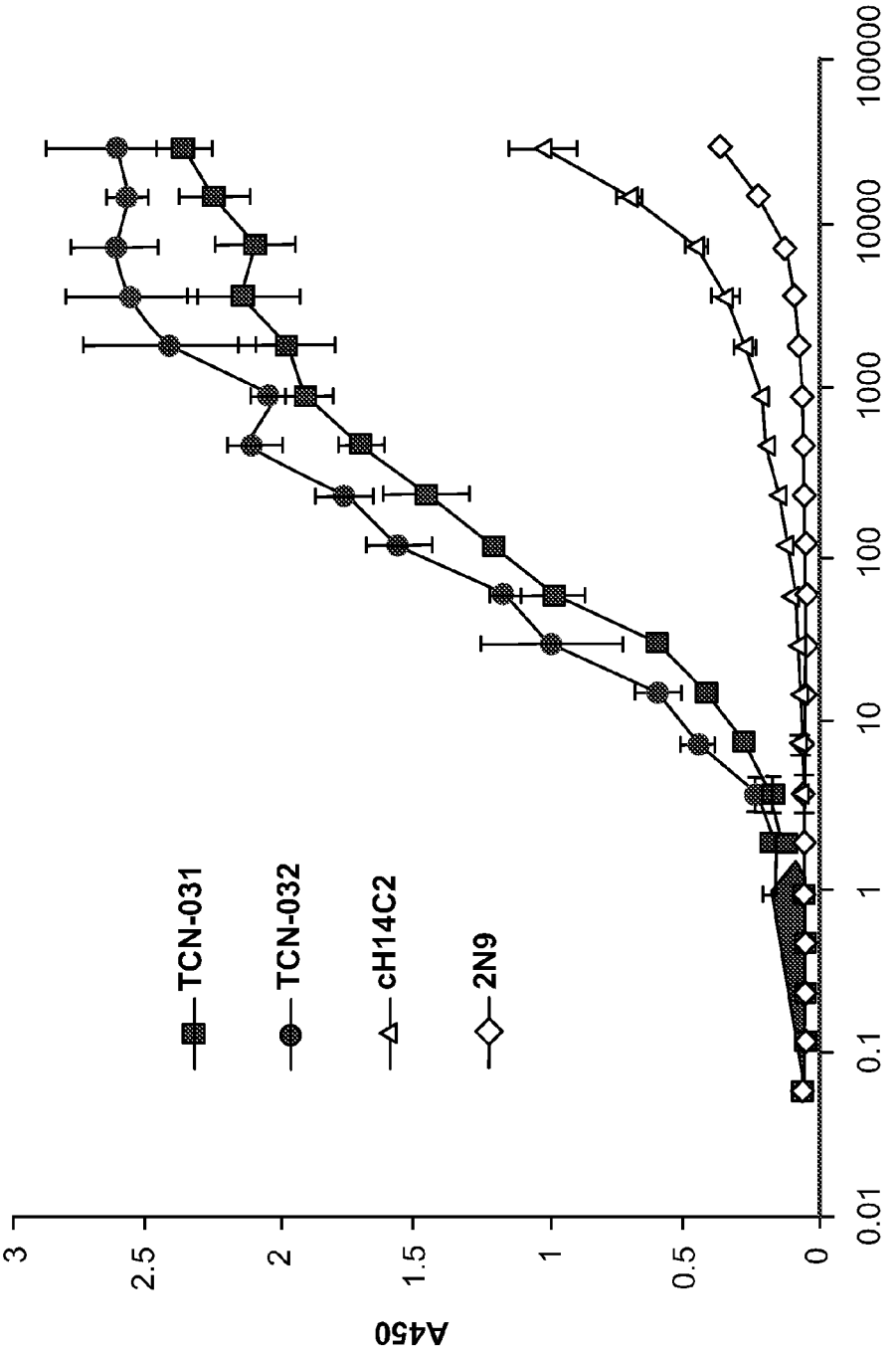

A450
3
2.5
2
1.5
1
0.5
0
0.01
0.1
1
10
100
1000
10000
100000
mAb(ng/ml)
TCN-031
TCN-032
cH14C2
2N9

FIG. 14A

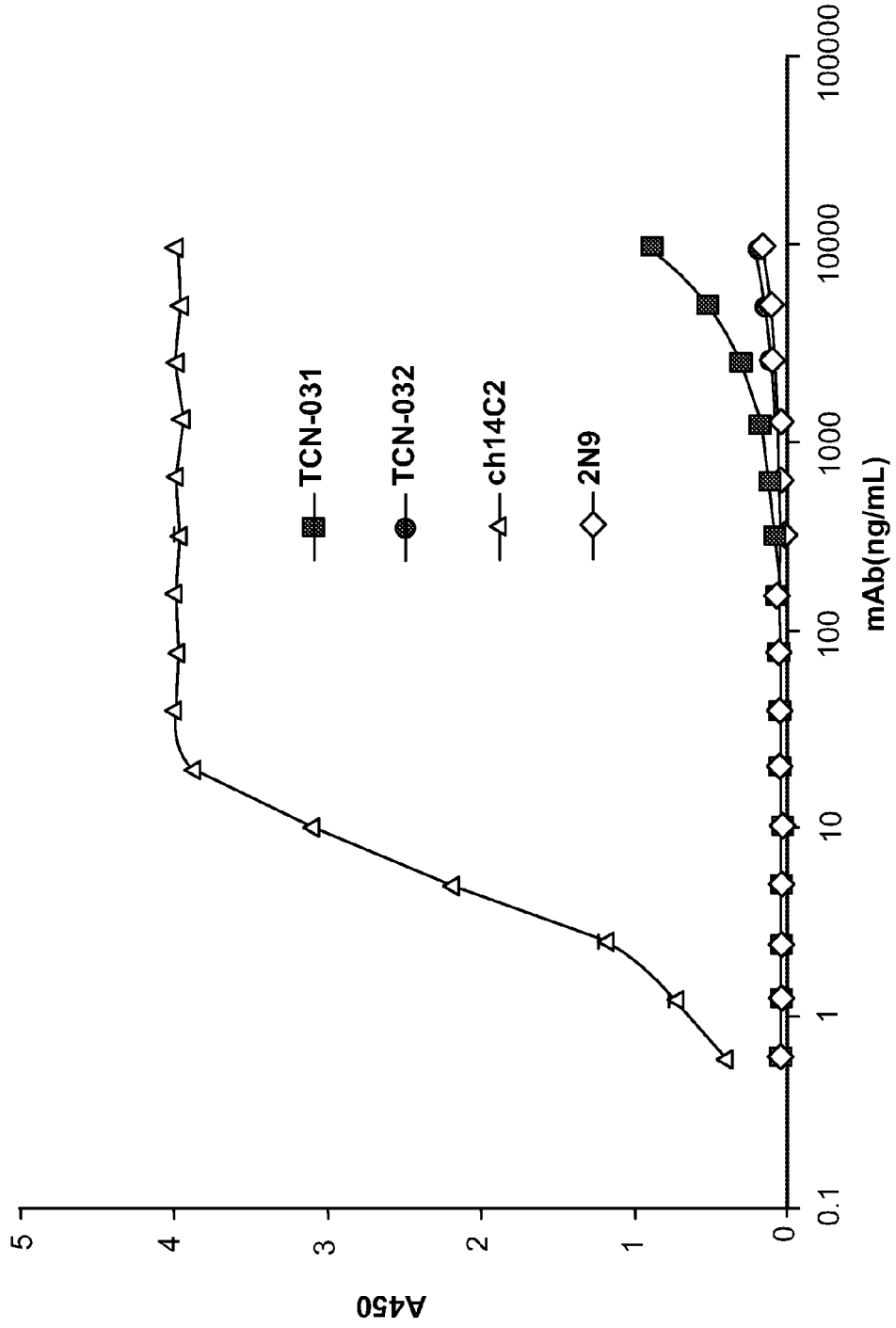

A450
0
1
2
3
4
5
0.1
1
10
100
1000
10000
100000
mAb(ng/mL)
TCN-031
TCN-032
ch14C2
2N9

FIG. 14B

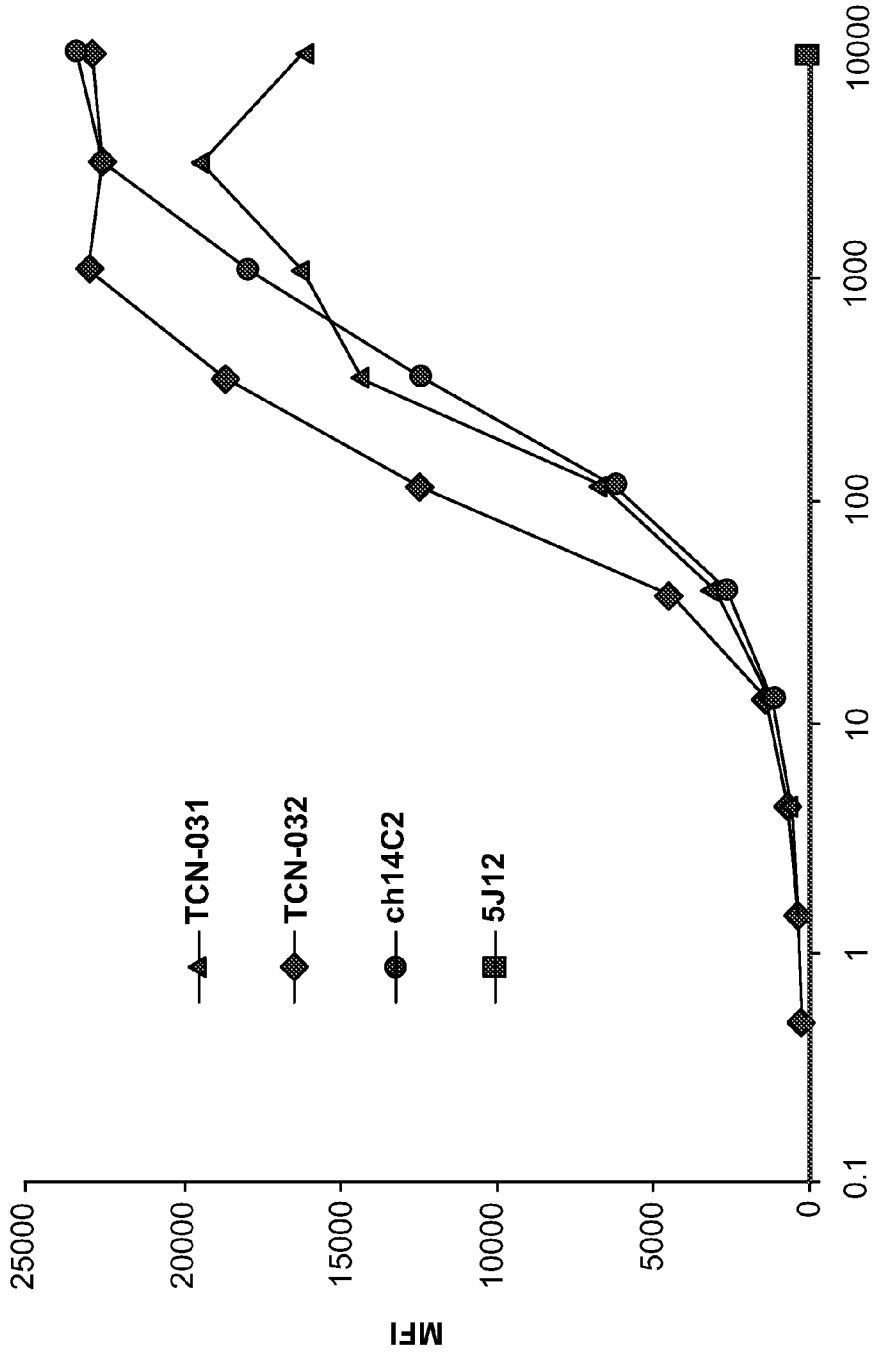

MFI
25000
20000
15000
10000
5000
0
0.1
1
10
100
1000
10000
mAb (ng/ml)
TCN-031
TCN-032
ch14C2
5J12

FIG. 14C

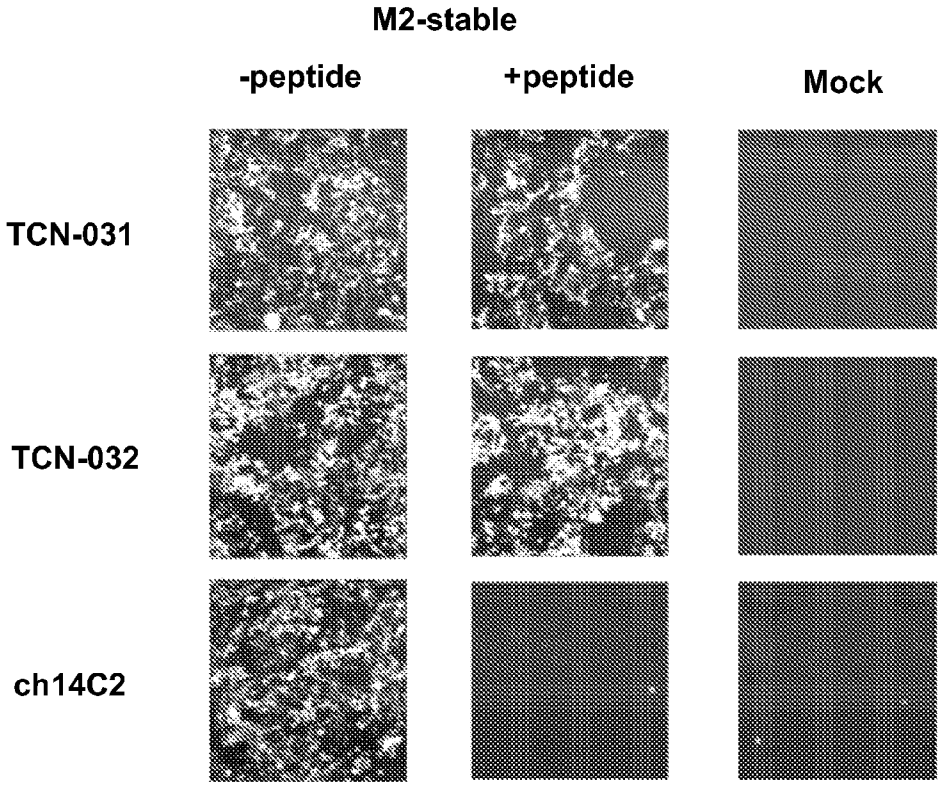


FIG. 14D

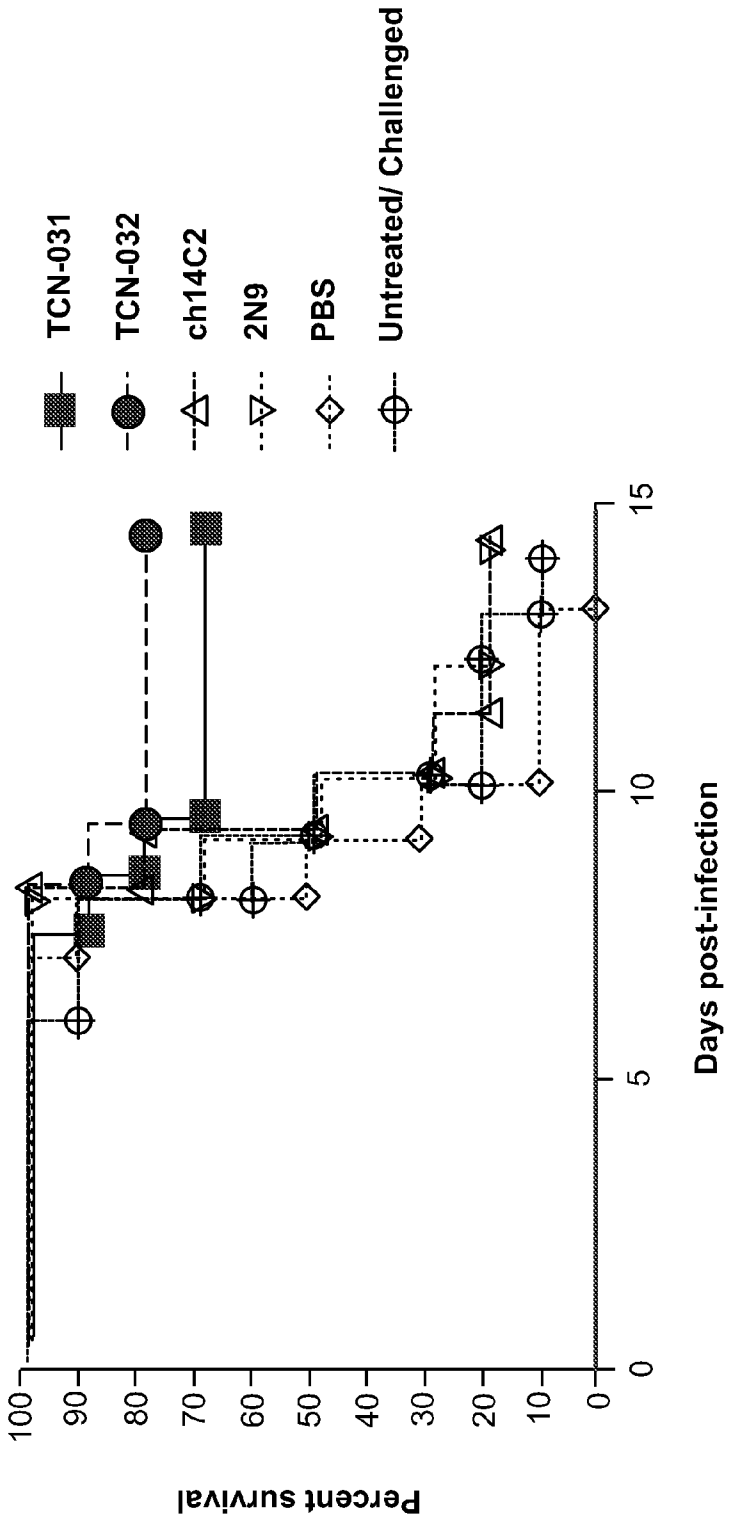

TCN-031
TCN-032
ch14C2
2N9
PBS
Untreated/ Challenged
Percent survival
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
Days post-infection

FIG. 15A

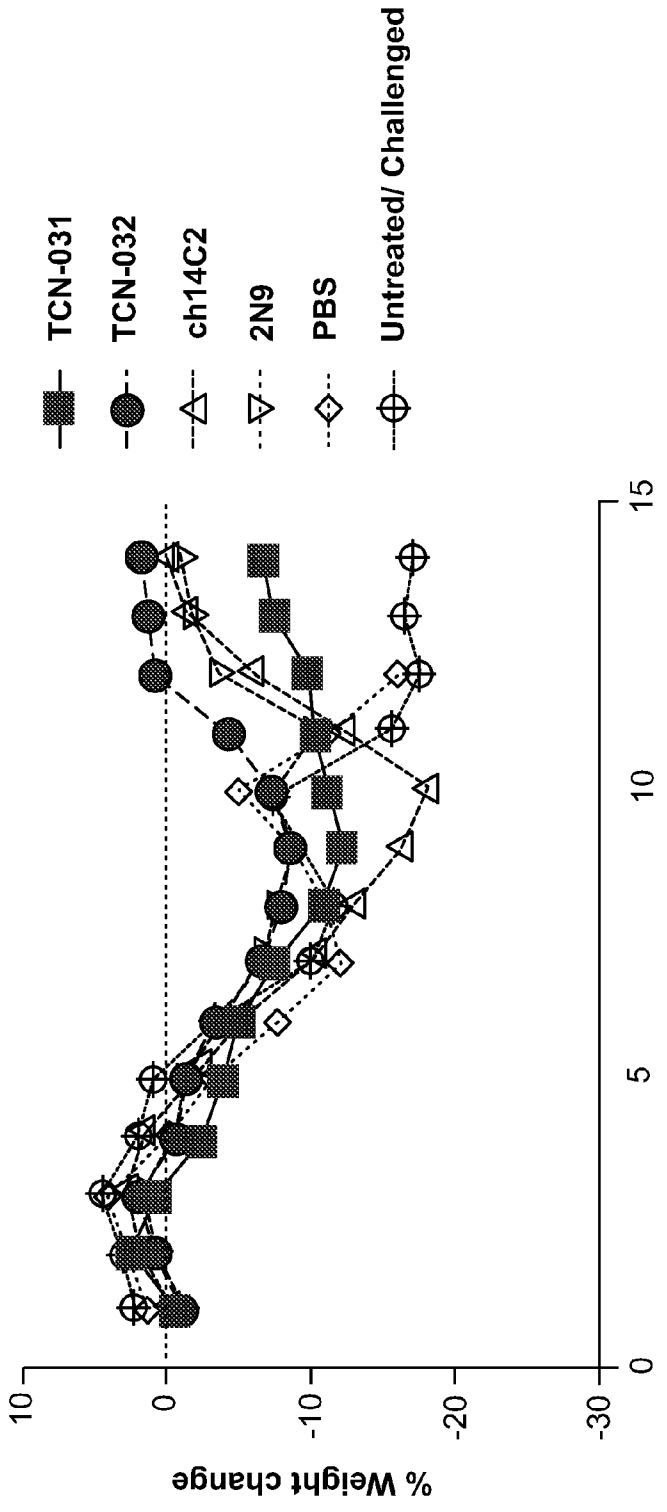

TCN-031
TCN-032
ch14C2
2N9
PBS
Untreated/ Challenged
% Weight change
10
0
-10
-20
-30
0
5
10
15
Days post-infection

FIG. 15B

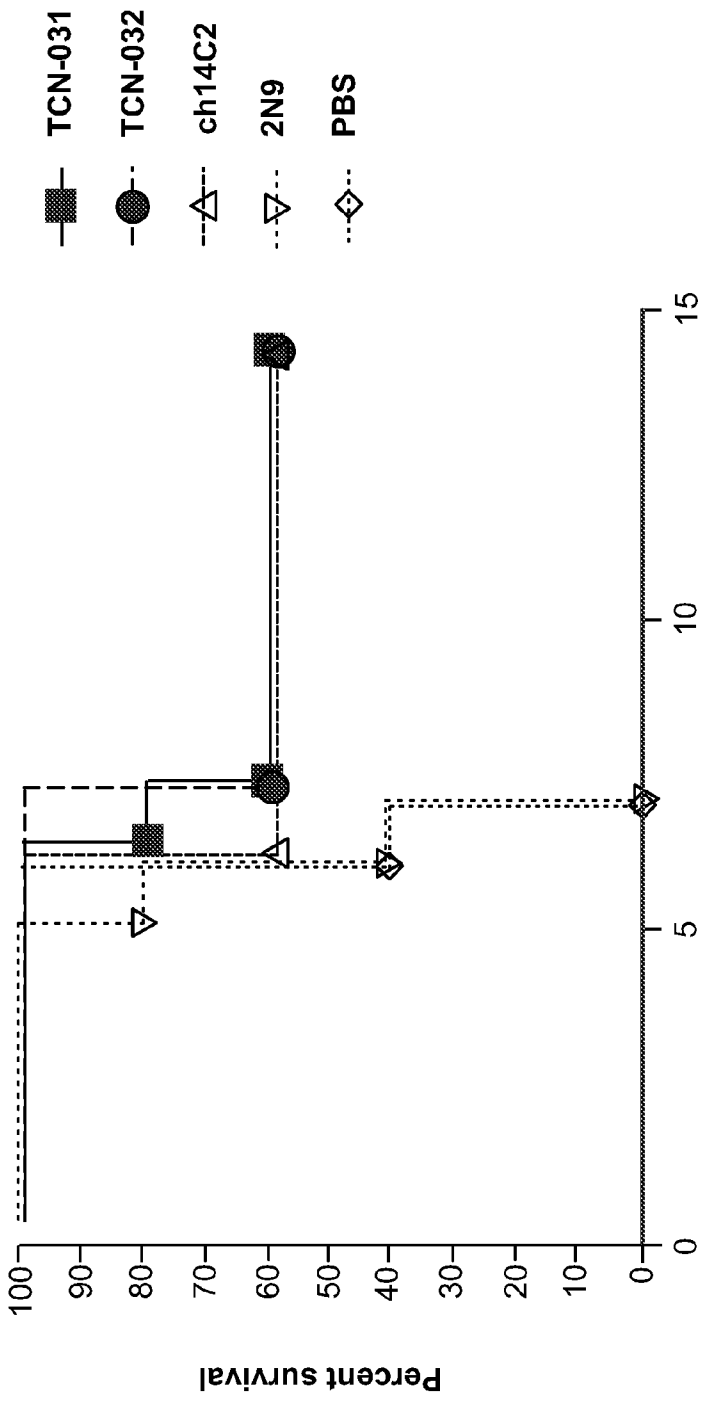

TCN-031
TCN-032
ch14C2
2N9
PBS
Percent survival
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
Days post-infection

FIG. 15C

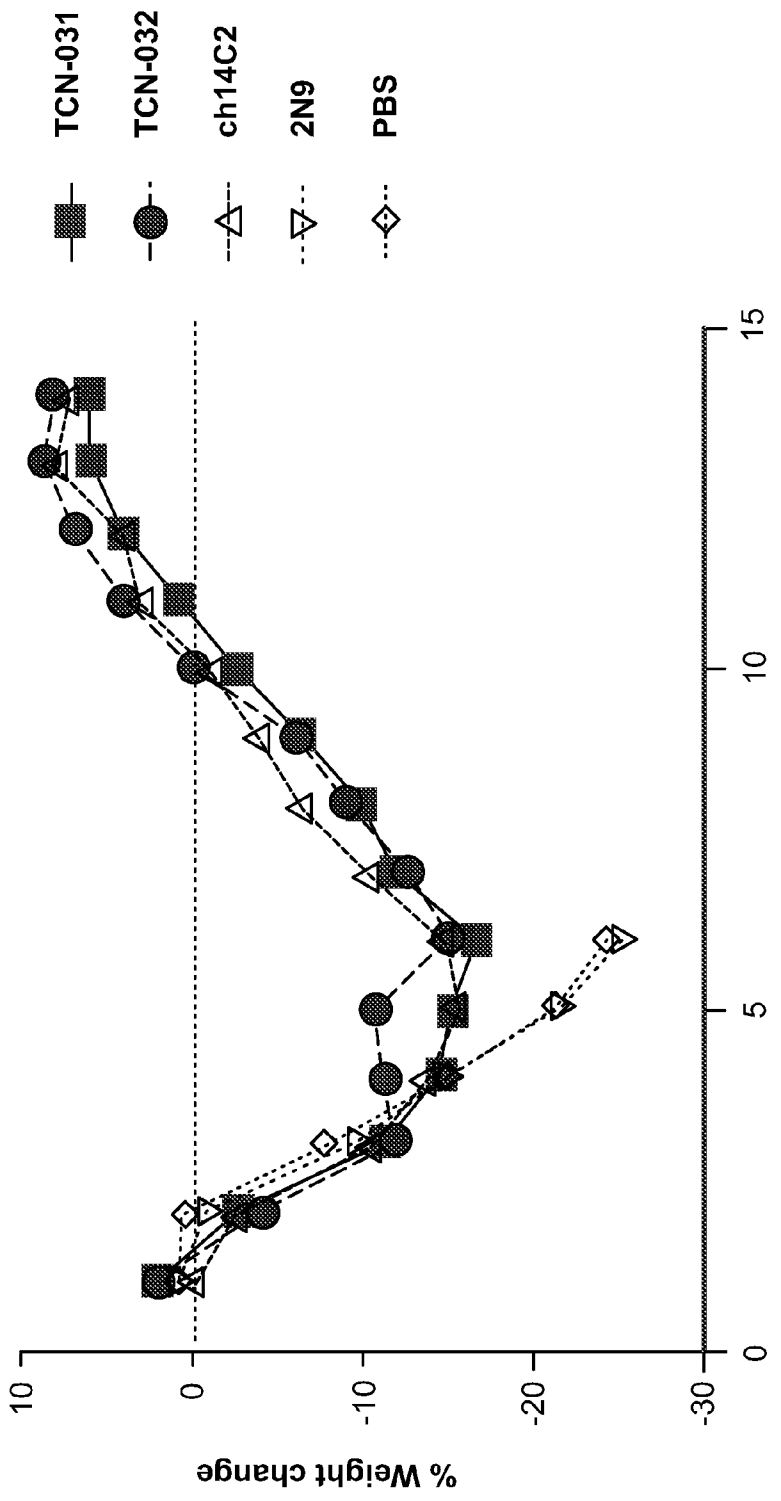

TCN-031
TCN-032
ch14C2
2N9
PBS
% Weight change
10
0
-10
-20
-30
0
5
10
15
Days post-infection

FIG. 15D

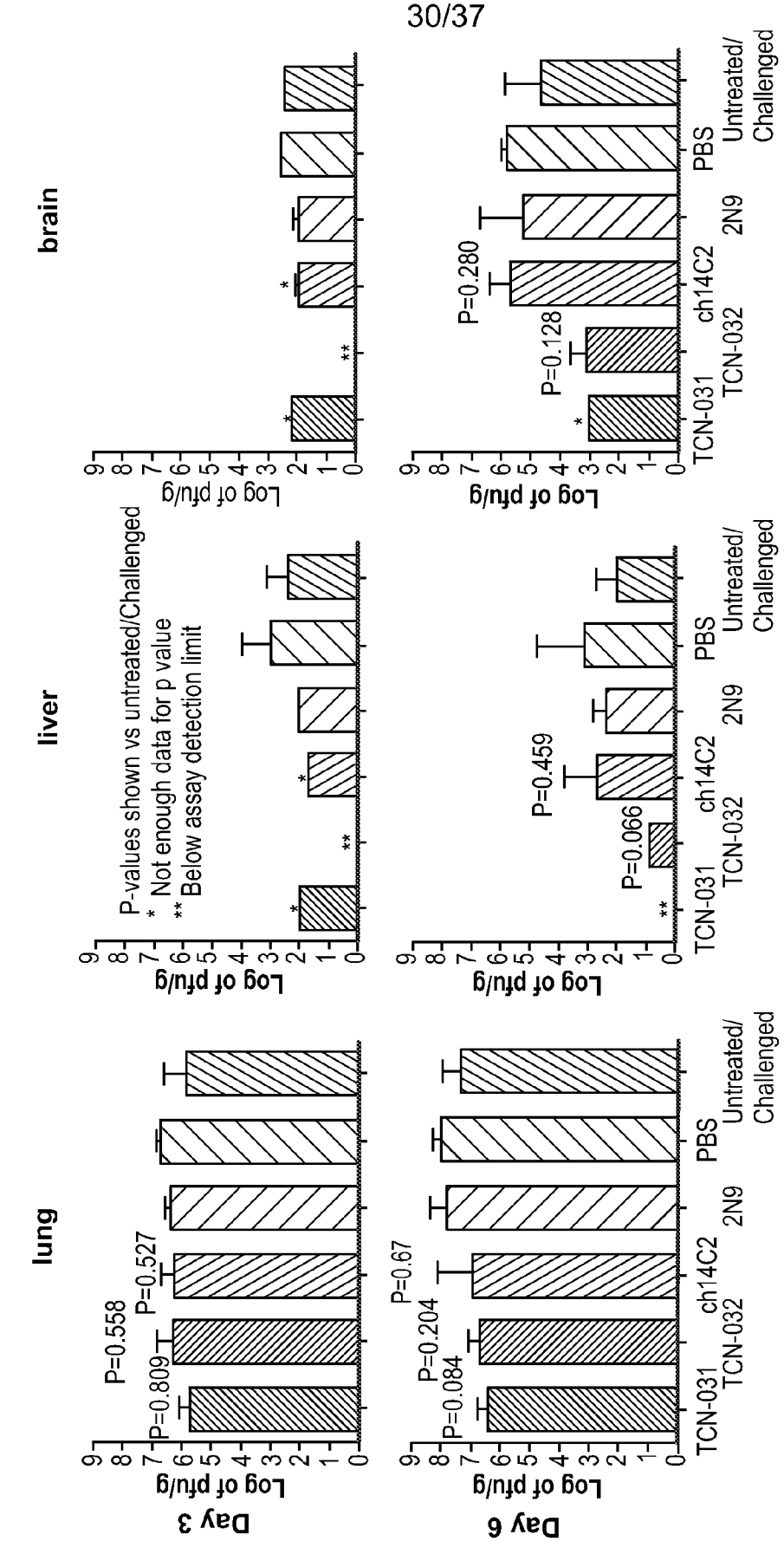

lung
liver
brain
Day 3
Day 6
Log of pfu/g
P=0.558
P=0.809
P=0.527
P=0.084
P=0.204
P=0.67
P=0.066
P=0.459
P=0.128
P=0.280
P-values shown vs untreated/Challenged
* Not enough data for p value
** Below assay detection limit
TCN-031
TCN-032
ch14C2
2N9
PBS
Untreated/
Challenged

FIG. 16

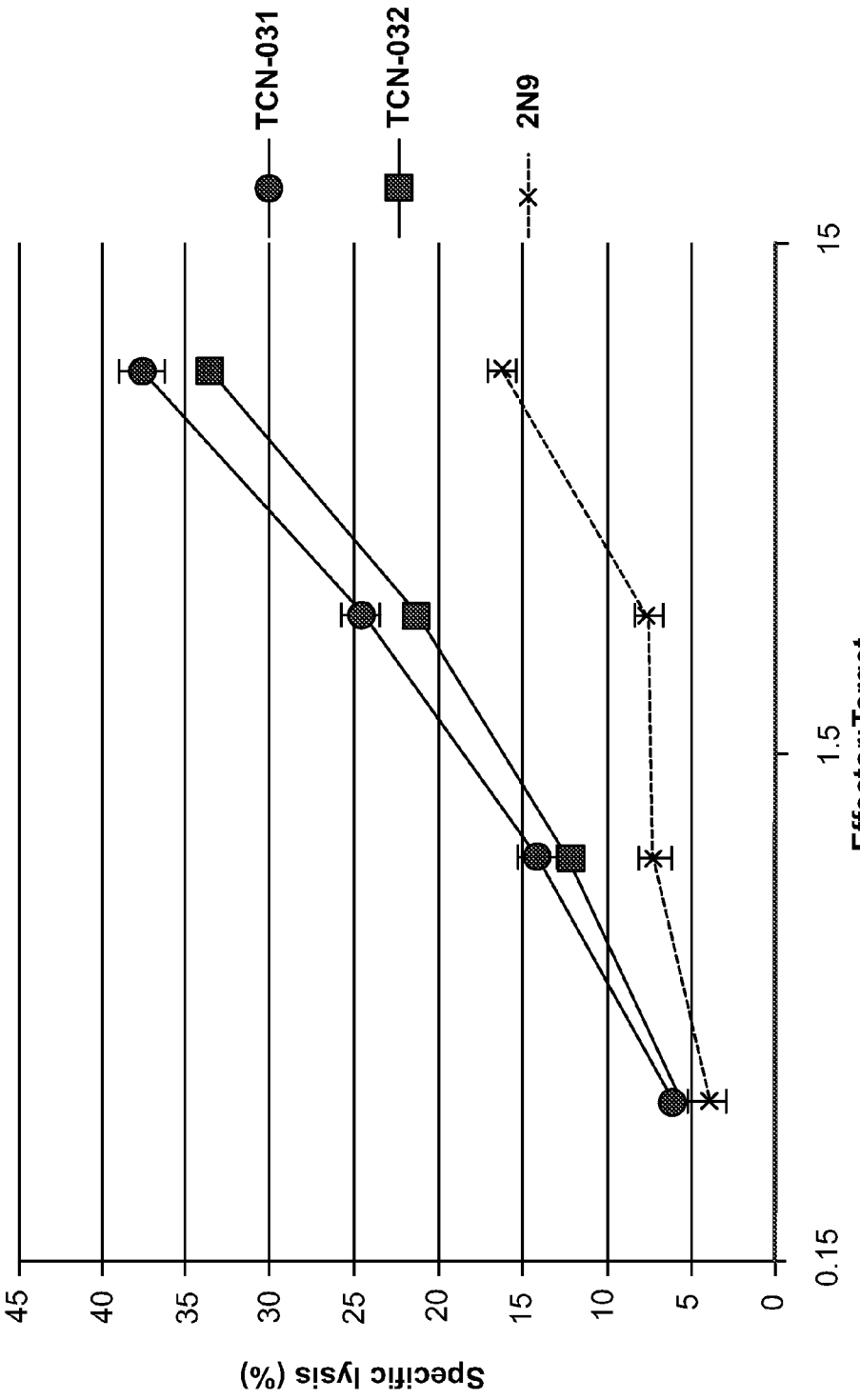

TCN-031
TCN-032
2N9
Specific lysis (%)
45
40
35
30
25
20
15
10
5
0
0.15
1.5
15
Effector:Target

FIG. 17

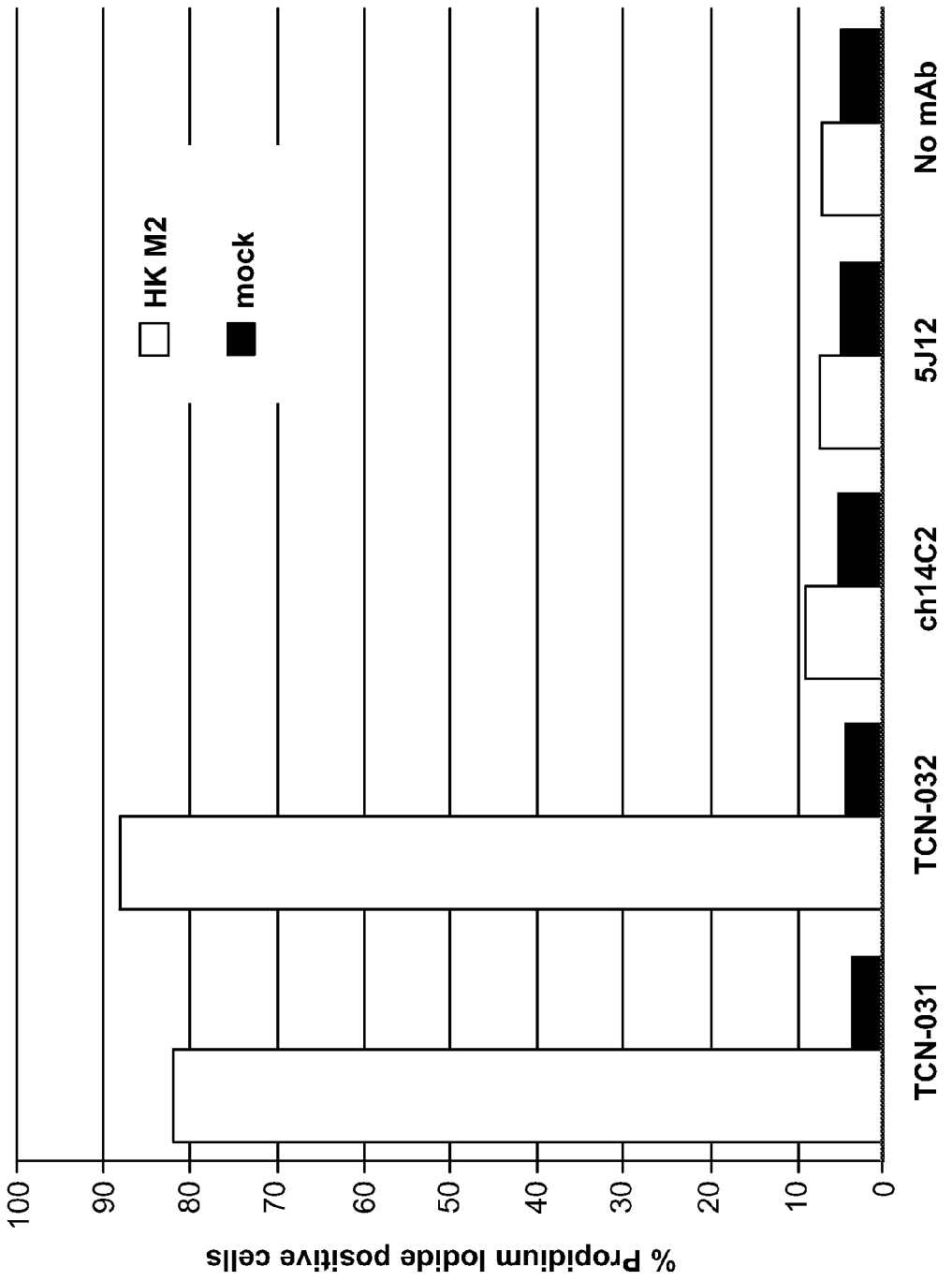

% Propidium Iodide positive cells
0
10
20
30
40
50
60
70
80
90
100
HK M2
mock
TCN-031
TCN-032
ch14C2
5J12
No mAb

FIG. 18

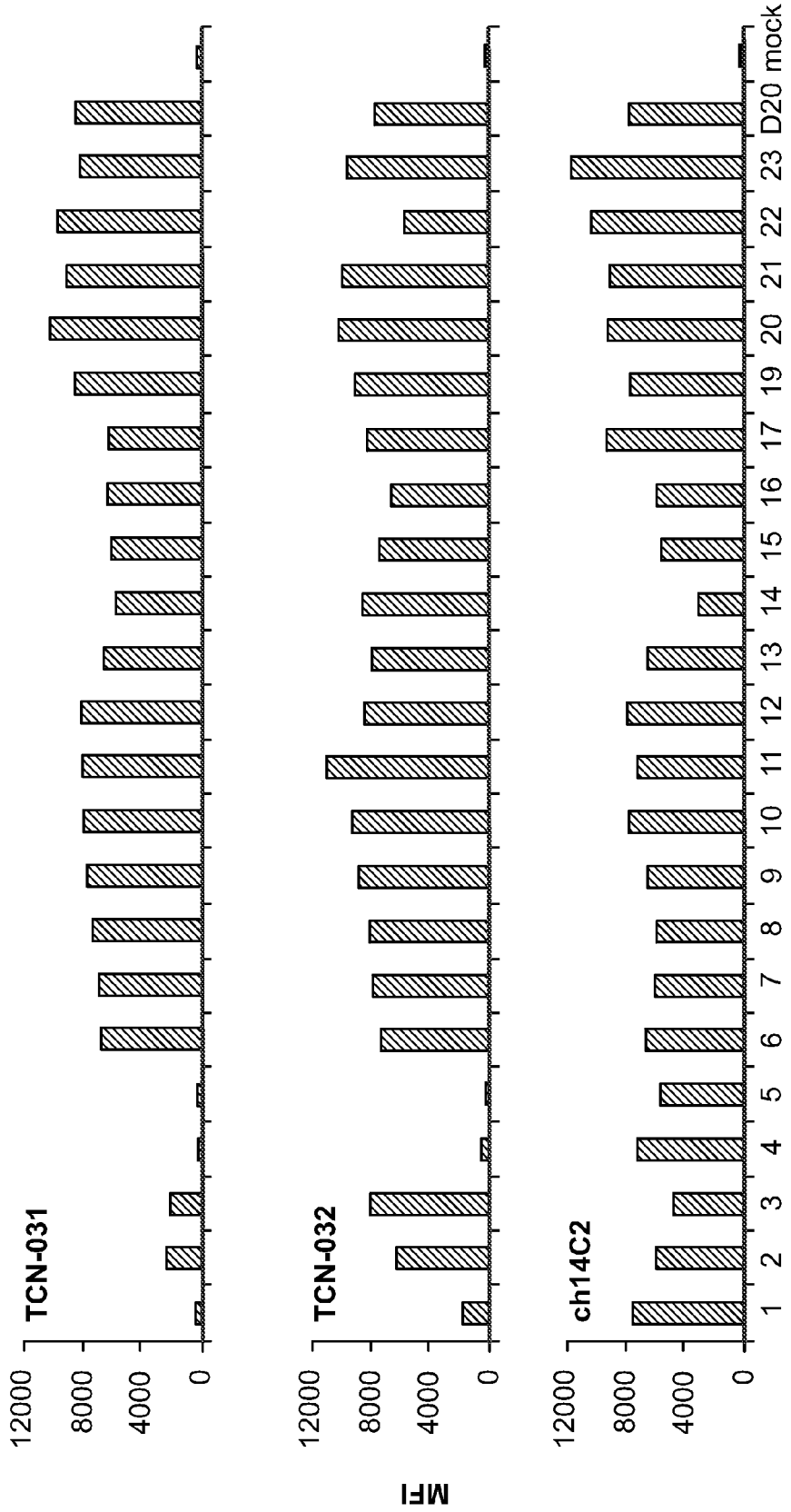

TCN-031
TCN-032
ch14C2
MFI
12000
8000
4000
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 19 20 21 22 23 D20 mock
Position of Alanine substitution in M2e

FIG. 19A

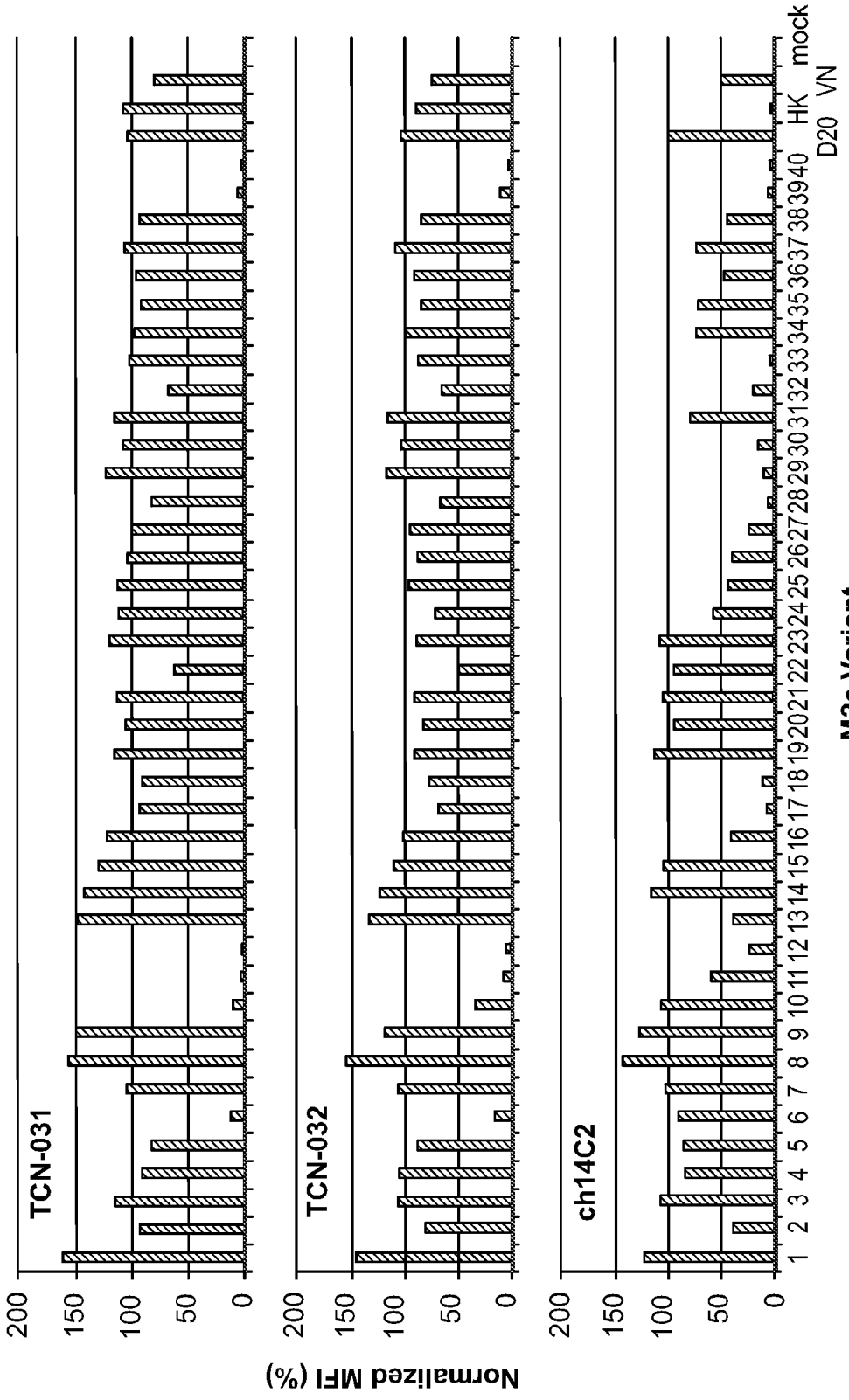

TCN-031
TCN-032
ch14C2
Normalized MFI (%)
200
150
100
50
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 HK mock
D20 VN
M2e Variant

FIG. 19B

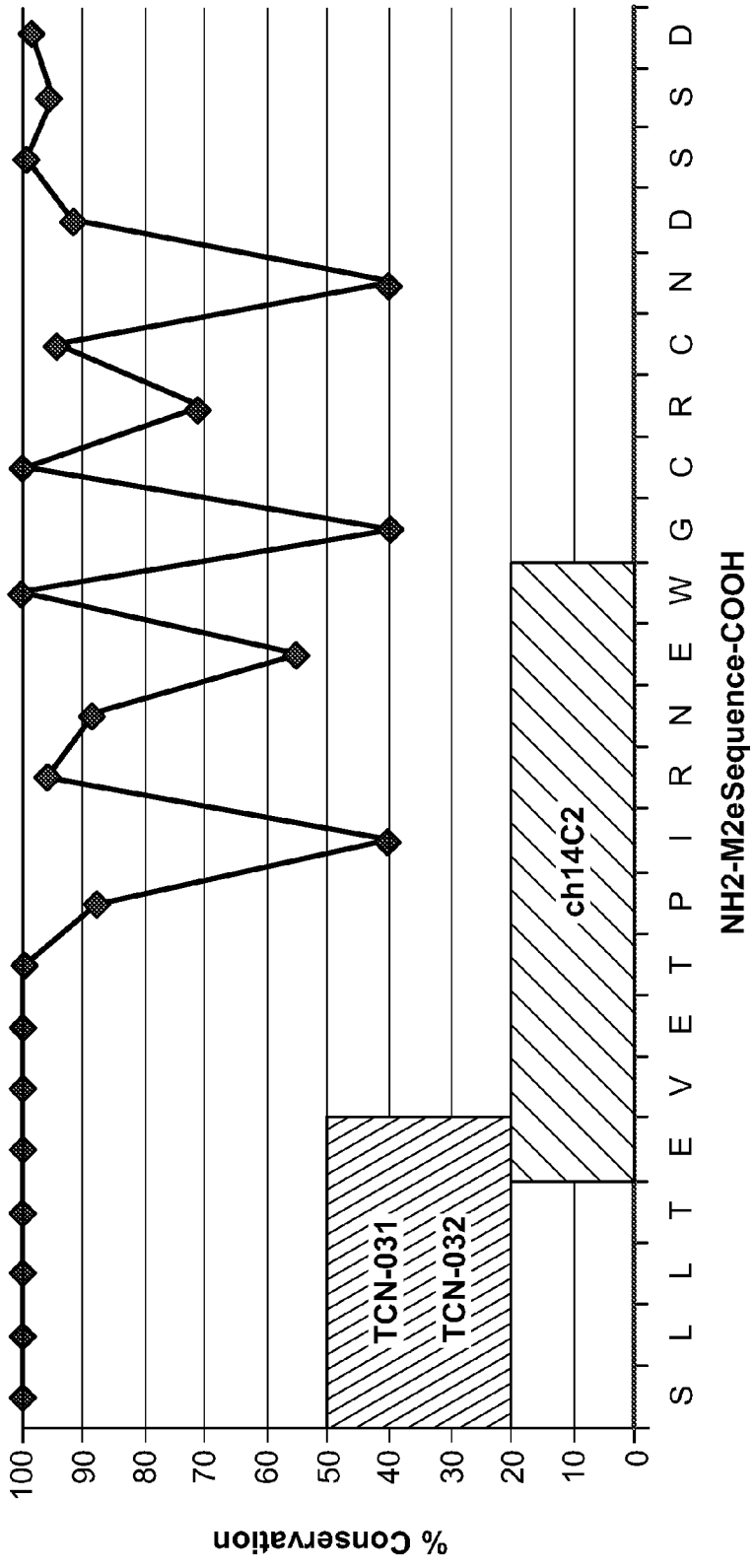

% Conservation
100
90
80
70
60
50
40
30
20
10
0
TCN-031
TCN-032
ch14C2
S L L T E V E T P I R N E W G C R C N D S S D
NH2-M2eSequence-COOH

FIG. 19C

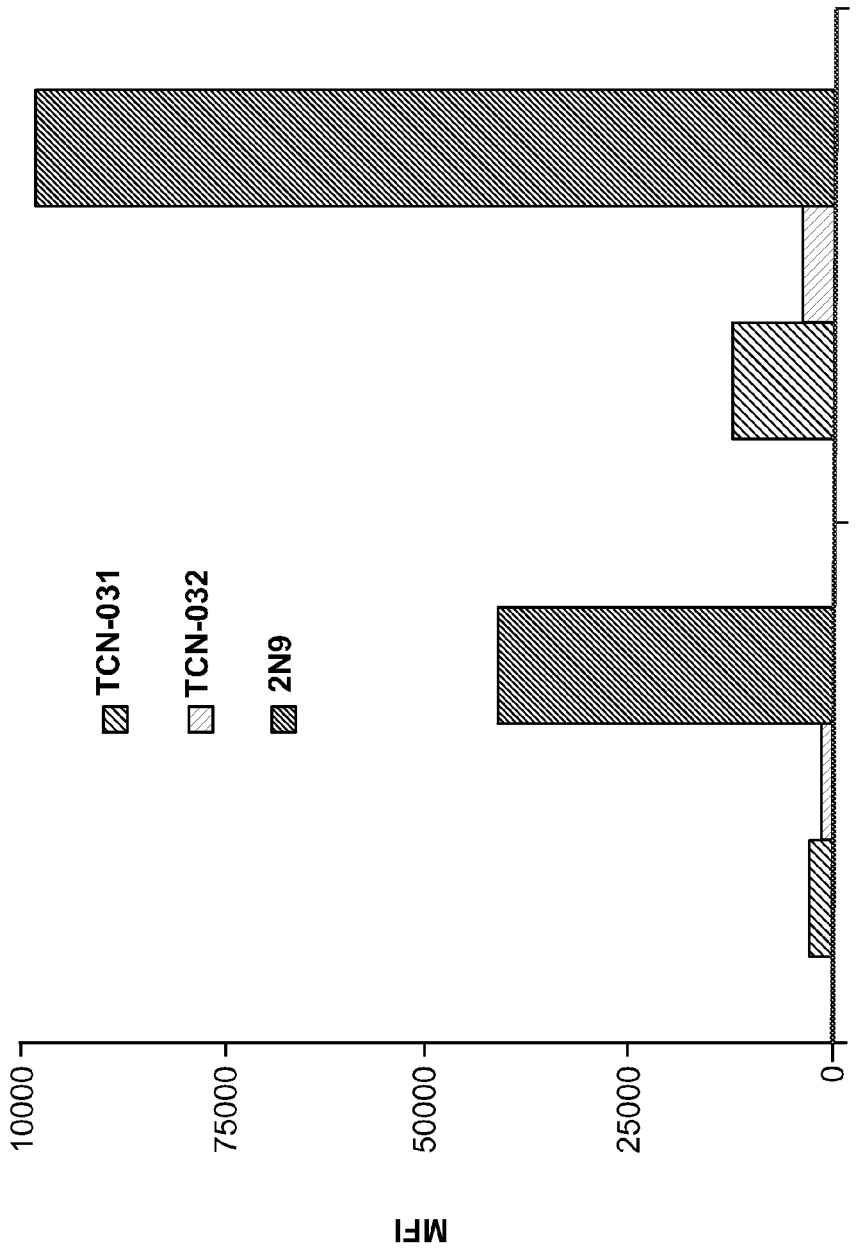
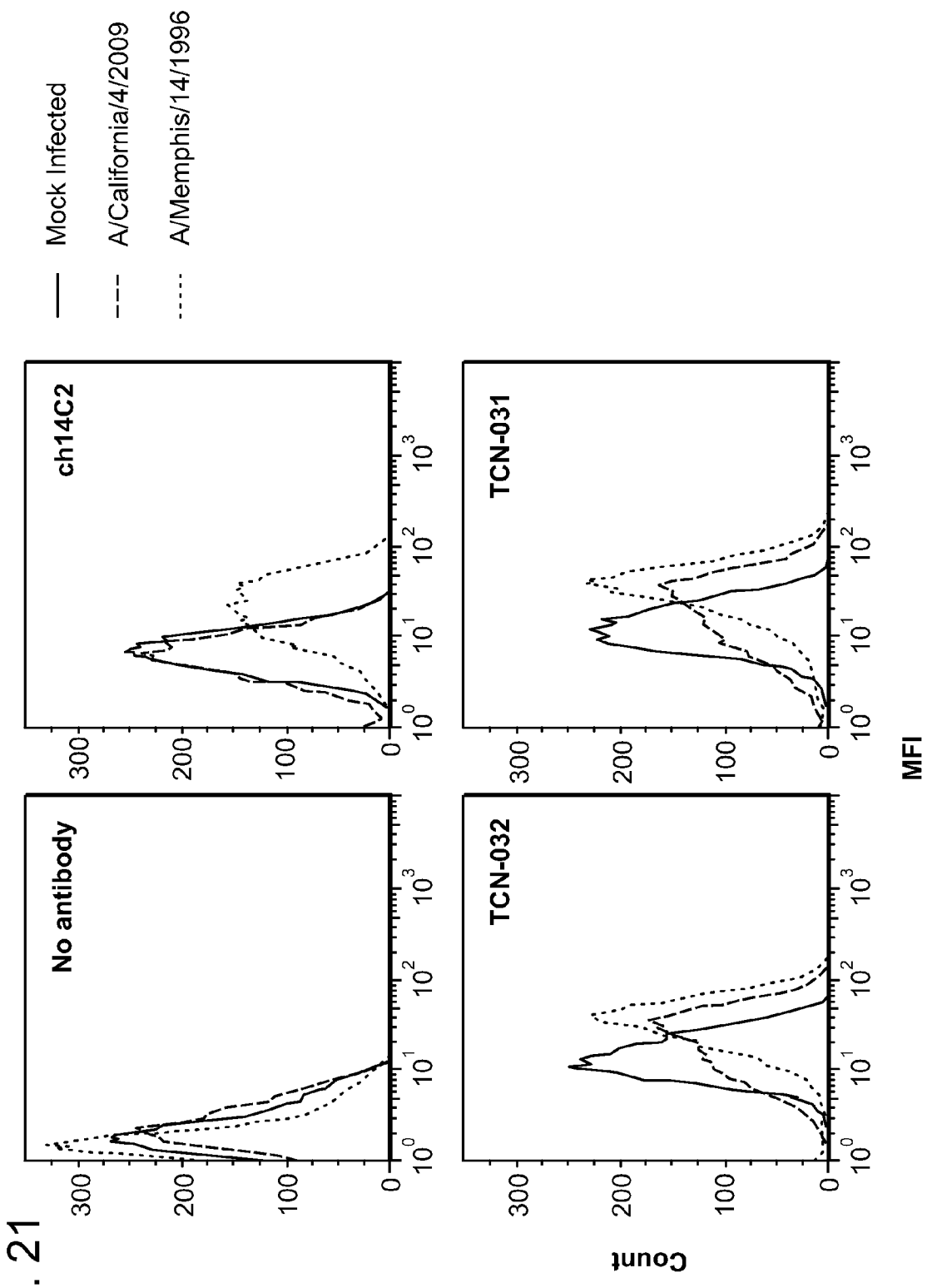

TCN-031
TCN-032
2N9
MFI
10000
75000
50000
25000
0
TCN-031 AF647
TCN-032 AF647

FIG. 20

FIG. 21


Mock Infected
A/California/4/2009
A/Memphis/14/1996
No antibody
ch14C2
TCN-032
TCN-031
Count
MFI

SEQUENCE LISTING

<110> THERACLONE SCIENCES, INC.
Grandea, Andres G. III
King, Gordon
Cox, Thomas C.
Olsen, Cle
Mitcham, Jennifer
Moyle, Matthew
Hammond, Phillip

<120> COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF INFLUENZA

<130> 37418-518001WO

<150> 61/442733
<151> 2011-02-14

<160> 1345

<170> PatentIn version 3.5

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<212> PRT
<213> Influenza A virus

<400> 1

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 2
<211> 24
<212> PRT
<213> Influenza A virus

<400> 2

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Lys Asn Glu Trp Glu
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 3
<211> 24
<212> PRT
<213> Influenza A virus

<400> 3

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Glu
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 4
<211> 24
<212> PRT
<213> Influenza A virus

<400> 4

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Gly Trp Glu
1 5 10 15

Cys Lys Cys Asn Asp Ser Ser Asp
20

<210> 5
<211> 24
<212> PRT
<213> Influenza A virus

<400> 5

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Ser Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 6
<211> 24
<212> PRT
<213> Influenza A virus

<400> 6

Met Ser Phe Leu Pro Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 7
<211> 24
<212> PRT
<213> Influenza A virus

<400> 7

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asn
20

<210> 8
<211> 24
<212> PRT
<213> Influenza A virus

<400> 8

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Lys Glu Trp Gly

1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 9
<211> 24
<212> PRT
<213> Influenza A virus

<400> 9

Met Ser Phe Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 10
<211> 24
<212> PRT
<213> Influenza A virus

<400> 10

Met Ser Leu Pro Thr Glu Val Glu Thr Pro Ile Arg Ser Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 11
<211> 24
<212> PRT
<213> Influenza A virus

<400> 11

Met Ser Leu Leu Pro Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 12
<211> 24
<212> PRT
<213> Influenza A virus

<400> 12

Met Ser Leu Leu Pro Glu Val Glu Thr Pro Ile Arg Asn Gly Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 13

<211> 24
<212> PRT
<213> Influenza A virus

<400> 13

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Glu
1 5 10 15

Cys Arg Cys Ser Gly Ser Ser Asp
20

<210> 14
<211> 24
<212> PRT
<213> Influenza A virus

<400> 14

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Glu
1 5 10 15

Tyr Arg Cys Asn Asp Ser Ser Asp
20

<210> 15
<211> 24
<212> PRT
<213> Influenza A virus

<400> 15

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Glu
1 5 10 15

Tyr Arg Cys Ser Asp Ser Ser Asp
20

<210> 16
<211> 24
<212> PRT
<213> Influenza A virus

<400> 16

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Glu
1 5 10 15

Cys Arg Tyr Ser Asp Ser Ser Asp
20

<210> 17
<211> 24
<212> PRT
<213> Influenza A virus

<400> 17

Met Ser Phe Leu Thr Glu Val Glu Thr Leu Thr Arg Asn Gly Trp Glu
1 5 10 15

Cys Arg Cys Ser Asp Ser Ser Asp
20

<210> 18
<211> 24
<212> PRT
<213> Influenza A virus

<400> 18

Met Ser Leu Leu Thr Glu Val Glu Thr Leu Thr Arg Asn Gly Trp Glu
1 5 10 15

Cys Lys Cys Arg Asp Ser Ser Asp
20

<210> 19
<211> 24
<212> PRT
<213> Influenza A virus

<400> 19

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 20
<211> 24
<212> PRT
<213> Influenza A virus

<400> 20

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Ser Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Gly Asp
20

<210> 21
<211> 24
<212> PRT
<213> Influenza A virus

<400> 21

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Glu
1 5 10 15

Cys Arg Cys Asn Gly Ser Ser Asp
20

<210> 22
<211> 24

<212> PRT
<213> Influenza A virus

<400> 22

Met Ser Leu Pro Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 23
<211> 24
<212> PRT
<213> Influenza A virus

<400> 23

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Gly Ser Ser Asp
20

<210> 24
<211> 24
<212> PRT
<213> Influenza A virus

<400> 24

Met Ser Leu Leu Thr Glu Val Asp Thr Leu Thr Arg Asn Gly Trp Gly
1 5 10 15

Cys Arg Cys Ser Asp Ser Ser Asp
20

<210> 25
<211> 24
<212> PRT
<213> Influenza A virus

<400> 25

Met Ser Leu Leu Thr Glu Val Glu Thr Leu Thr Lys Asn Gly Trp Gly
1 5 10 15

Cys Arg Cys Ser Asp Ser Ser Asp
20

<210> 26
<211> 24
<212> PRT
<213> Influenza A virus

<400> 26

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Glu
1 5 10 15

```
Cys Lys Cys Ser Asp Ser Ser Asp
            20


<210>  27
<211>  24
<212>  PRT
<213>  Influenza A virus

<400>  27

Met Ser Leu Leu Thr Glu Val Glu Thr His Thr Arg Asn Gly Trp Glu
1               5                   10                  15


Cys Lys Cys Ser Asp Ser Ser Asp
            20


<210>  28
<211>  24
<212>  PRT
<213>  Influenza A virus

<400>  28

Met Ser Leu Leu Thr Glu Val Lys Thr Pro Thr Arg Asn Gly Trp Glu
1               5                   10                  15


Cys Lys Cys Ser Asp Ser Ser Asp
            20


<210>  29
<211>  24
<212>  PRT
<213>  Influenza A virus

<400>  29

Met Ser Leu Leu Thr Glu Val Glu Thr Leu Thr Arg Asn Gly Trp Gly
1               5                   10                  15


Cys Arg Cys Ser Asp Ser Ser Asp
            20


<210>  30
<211>  24
<212>  PRT
<213>  Influenza A virus

<400>  30

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asp Gly Trp Glu
1               5                   10                  15


Cys Lys Cys Ser Asp Ser Ser Asp
            20


<210>  31
<211>  24
<212>  PRT
```

<213> Influenza A virus

<400> 31

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Gly
1 5 10 15

Cys Arg Cys Ser Asp Ser Ser Asp
20

<210> 32
<211> 24
<212> PRT
<213> Influenza A virus

<400> 32

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Glu
1 5 10 15

Cys Lys Cys Asn Asp Ser Ser Asp
20

<210> 33
<211> 24
<212> PRT
<213> Influenza A virus

<400> 33

Met Ser Leu Leu Thr Glu Val Glu Thr Leu Thr Arg Asn Gly Trp Glu
1 5 10 15

Cys Lys Cys Ser Asp Ser Ser Asp
20

<210> 34
<211> 24
<212> PRT
<213> Influenza A virus

<400> 34

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

Cys Lys Cys Asn Asp Ser Ser Asp
20

<210> 35
<211> 24
<212> PRT
<213> Influenza A virus

<400> 35

Met Ser Phe Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

Cys Arg Cys Asn Gly Ser Ser Asp
20

<210> 36
<211> 24
<212> PRT
<213> Influenza A virus

<400> 36

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Glu
1 5 10 15

Cys Arg Cys Asn Asp Ser Ser Asp
20

<210> 37
<211> 24
<212> PRT
<213> Influenza A virus

<400> 37

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Lys Gly Trp Glu
1 5 10 15

Cys Asn Cys Ser Asp Ser Ser Asp
20

<210> 38
<211> 24
<212> PRT
<213> Influenza A virus

<400> 38

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Glu Trp Glu
1 5 10 15

Cys Arg Cys Ser Asp Ser Ser Asp
20

<210> 39
<211> 24
<212> PRT
<213> Influenza A virus

<400> 39

Met Ser Leu Leu Thr Gly Val Glu Thr His Thr Arg Asn Gly Trp Gly
1 5 10 15

Cys Lys Cys Ser Asp Ser Ser Asp
20

<210> 40
<211> 24
<212> PRT
<213> Influenza A virus

<400> 40

Met Ser Leu Leu Pro Glu Val Glu Thr His Thr Arg Asn Gly Trp Gly
1 5 10 15

Cys Arg Cys Ser Asp Ser Ser Asp
20

<210> 41
<211> 8
<212> PRT
<213> Influenza A virus

<400> 41

Ser Leu Leu Thr Glu Val Glu Thr
1 5

<210> 42
<211> 6
<212> PRT
<213> Influenza A virus

<400> 42

Ser Leu Leu Thr Glu Val
1 5

<210> 43
<211> 357
<212> DNA
<213> Homo sapiens

<400> 43
caggtgcaat tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggttc gtccatcagt aattactact ggagctggat ccggcagtcc 120

ccagggaagg gactggagtg gattgggtat atctattacg gtggaaacac caagtacaat 180

ccctccctca agagccgcgt caccatatca caagacactt ccaagagtca ggtctccctg 240

acgatgagct ctgtgaccgc tgcggaatcg gccgtctatt tctgtgcgag agcgtcttgt 300

agtggtggtt actgtatcct tgactactgg ggccagggaa ccctggtcac cgtctcg 357

<210> 44
<211> 119
<212> PRT
<213> Homo sapiens

<400> 44

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

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

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

35 40 45

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

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

Thr Met Ser Ser Val Thr Ala Ala Glu Ser Ala Val Tyr Phe Cys Ala
85 90 95

Arg Ala Ser Cys Ser Gly Gly Tyr Cys Ile Leu Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser
115

<210> 45
<211> 322
<212> DNA
<213> Homo sapiens

<400> 45
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcgagtca gaacatttac aagtatttaa attggtatca gcagagacca 120

gggaaagccc ctaagggcct gatctctgct gcatccgggt tgcaaagtgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcaccag tctgcaacct 240

gaagattttg caacttacta ctgtcaacag agttacagtc cccctctcac tttcggcgga 300

gggaccaggg tggagatcaa ac 322

<210> 46
<211> 107
<212> PRT
<213> Homo sapiens

<400> 46

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 Asn Ile Tyr Lys Tyr
20 25 30

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

Ser Ala Ala Ser Gly 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 Thr Ser Leu Gln Pro
65 70 75 80

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

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

<210> 47
<211> 357
<212> DNA
<213> Homo sapiens

<400> 47
caggtgcaat tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggttc gtccatcagt aattactact ggagctggat ccggcagtcc 120

ccagggaagg gactggagtg gattgggtat atctattacg gtggaaacac caagtacaat 180

ccctccctca agagccgcgt caccatatca caagacactt ccaagagtca ggtctccctg 240

acgatgagct ctgtgaccgc tgcggaatcg gccgtctatt tctgtgcgag agcgtcttgt 300

agtggtggtt actgtatcct tgactactgg ggccagggaa ccctggtcac cgtctcg 357

<210> 48
<211> 322
<212> DNA
<213> Homo sapiens

<400> 48
gacatccagg tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gcgcgagtca gaacatttac aagtatttaa attggtatca gcagagacca 120

gggaaagccc ctaagggcct gatctctgct gcatccgggt tgcaaagtgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcaccag tctgcaacct 240

gaagattttg caacttacta ctgtcaacag agttacagtc ccccttcac tttcggcgga 300

gggaccaggg tggatatcaa ac 322

<210> 49
<211> 357
<212> DNA
<213> Homo sapiens

<400> 49
gaggtgcagc tggtggagtc tgggggaggc ttggtccagc ctgggggtc cctgagaatc 60

tcctgtgcag cctctggatt caccgtcagt agcaactaca tgagttgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagtt attttatagt gtggtagcac atactacgca 180

gactccgtga agggcagatt ctcctctcc agagacaact ccaagaacac agtgtttctt 240

caaatgaaca gcctgagagc cgaggacacg gctgtgtatt actgtgcgag atgtctgagc 300

aggatgcggg gttacggttt agacgtctgg ggccaaggga ccacggtcac cgtctcg 357

<210> 50
<211> 119

<212> PRT
<213> Homo sapiens

<400> 50

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

Ser Leu Arg Ile Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
20 25 30

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

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

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

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

Arg Cys Leu Ser Arg Met Arg Gly Tyr Gly Leu Asp Val Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser
115

<210> 51
<211> 318
<212> DNA
<213> Homo sapiens

<400> 51
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc ggacaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120

gggaaagccc ctaaactcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcgg tctgcaacct 240

gaagattttg caacctacta ctgtcaacag agttacagta tgcctgcctt tggccagggg 300

accaagctgg agatcaaa 318

<210> 52
<211> 106
<212> PRT
<213> Homo sapiens

<400> 52

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 Thr Ser Gln Ser Ile Ser Ser Tyr

20 25 30

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

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

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

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

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

<210> 53
<211> 291
<212> DNA
<213> Influenza A virus

<400> 53
atgagtcttc taaccgaggt cgaaacgcct atcagaaacg aatgggggtg cagatgcaac 60

gattcaagtg atcctcttgt tgttgccgca agtatcattg ggatcctgca cttgatattg 120

tggattcttg atcgtctttt tttcaaatgc attttatcgt tctttaaaca cggtctgaaa 180

agagggcctt ctacggaagg agtaccagag tctatgaggg aagaatatcg aaaggaacag 240

cagagtgctg tggatgctga cgatagtcat tttgtcaaca tagagctgga g 291

<210> 54
<211> 404
<212> DNA
<213> Homo sapiens

<400> 54
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tccgaggtgc cagatgtgac atccagatga cccagtctcc atcctccctg tctgcatctg 120

taggagacag agtcaccatc acttgccggg cgagtcagaa catttacaag tatttaaatt 180

ggtatcagca gagaccaggg aaagccccta agggcctgat ctctgctgca tccgggttgc 240

aaagtggggt cccatcaagg ttcagtggca gtggatctgg gacagatttc actctcacca 300

tcaccagtct gcaacctgaa gattttgcaa cttactactg tcaacagagt tacagtcccc 360

ctctcacttt cggcggaggg accagggtgg agatcaaacg tacg 404

<210> 55
<211> 404
<212> DNA
<213> Homo sapiens

<400> 55
cgtacgtttg atctccaccc tggtccctcc gccgaaagtg agagggggac tgtaactctg 60

ttgacagtag taagttgcaa aatcttcagg ttgcagactg gtgatggtga gagtgaaatc 120

tgtcccagat ccactgccac tgaaccttga tgggacccca ctttgcaacc cggatgcagc 180

agagatcagg ccctt agggg ctttccctgg tctctgctga taccaatt ta aatacttgta 240

aatgttctga ctcgcccggc aagtgatggt gactctgtct cctacagatg cagacaggga 300

ggatggagac tgggtcatct ggatgtcaca tctggcacct cggagccaga gtagcaggag 360

ccccaggagc tgagcgagga ccctcatgtc catggtggaa gctt 404

<210> 56
<211> 236
<212> PRT
<213> Homo sapiens

<400> 56

Met Asp Met Arg Val Leu Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15

Leu Arg Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
35 40 45

Gln Asn Ile Tyr Lys Tyr Leu Asn Trp Tyr Gln Gln Arg Pro Gly Lys
50 55 60

Ala Pro Lys Gly Leu Ile Ser Ala Ala Ser Gly Leu Gln Ser Gly Val
65 70 75 80

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
85 90 95

Ile Thr Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
100 105 110

Ser Tyr Ser Pro Pro Leu Thr Phe Gly Gly Gly Thr Arg Val Glu Ile
115 120 125

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
130 135 140

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
145 150 155 160

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
165 170 175

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
180 185 190

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Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
        195                 200                 205

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
    210                 215                 220

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225                 230                 235


<210>  57
<211>  22
<212>  PRT
<213>  Homo sapiens

<400>  57

Met Asp Met Arg Val Leu Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1               5                   10                  15

Leu Arg Gly Ala Arg Cys
            20


<210>  58
<211>  23
<212>  PRT
<213>  Homo sapiens

<400>  58

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
            20


<210>  59
<211>  11
<212>  PRT
<213>  Homo sapiens

<400>  59

Arg Ala Ser Gln Asn Ile Tyr Lys Tyr Leu Asn
1               5                   10


<210>  60
<211>  15
<212>  PRT
<213>  Homo sapiens

<400>  60

Trp Tyr Gln Gln Arg Pro Gly Lys Ala Pro Lys Gly Leu Ile Ser
1               5                   10                  15


<210>  61
<211>  7
<212>  PRT
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<213> Homo sapiens

<400> 61

Ala Ala Ser Gly Leu Gln Ser
1 5

<210> 62
<211> 32
<212> PRT
<213> Homo sapiens

<400> 62

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Thr Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
20 25 30

<210> 63
<211> 9
<212> PRT
<213> Homo sapiens

<400> 63

Gln Gln Ser Tyr Ser Pro Pro Leu Thr
1 5

<210> 64
<211> 10
<212> PRT
<213> Homo sapiens

<400> 64

Phe Gly Gly Gly Thr Arg Val Glu Ile Lys
1 5 10

<210> 65
<211> 800
<212> DNA
<213> Artificial Sequence

<220>
<223> Recombinant human sequence

<400> 65
tcgaaattaa tacgactcac tatagggaga cccaagctgg ctagcgttta aacttaagct 60

tccaccatgg acatgagggt cctcgctcag ctcctggggc tcctgctact ctggctccga 120

ggtgccagat gtgacatcca gatgacccag tctccatcct ccctgtctgc atctgtagga 180

gacagagtca ccatcacttg ccgggcgagt cagaacattt acaagtattt aaattggtat 240

cagcagagac cagggaaagc ccctaagggc ctgatctctg ctgcatccgg gttgcaaagt 300

ggggtcccat caaggttcag tggcagtgga tctgggacag atttcactct caccatcacc 360

agtctgcaac ctgaagattt tgcaacttac tactgtcaac agagttacag tccccctctc 420

actttcggcg gagggaccag ggtggagatc aaacgtacgg tggctgcacc atctgtcttc 480

atcttcccgc catctgatga gcagttgaaa tctggaactg cctctgttgt gtgcctgctg 540

aataacttct atcccagaga ggccaaagta cagtggaagg tggataacgc cctccaatcg 600

ggtaactccc aggagagtgt cacagagcag gacagcaagg acagcaccta cagcctcagc 660

agcaccctga cgctgagcaa agcagactac gagaaacaca aagtctacgc ctgcgaagtc 720

acccatcagg gcctgagctc gcccgtcaca aagagcttca acaggggaga gtgttagagg 780

gtctagaggg cccgtttaaa 800

<210> 66
<211> 800
<212> DNA
<213> Artificial Sequence

<220>
<223> Recombinant Human sequence

<400> 66
tttaaacggg ccctctagac cctctaacac tctcccctgt tgaagctctt tgtgacgggc 60

gagctcaggc cctgatgggt gacttcgcag gcgtagactt tgtgtttctc gtagtctgct 120

ttgctcagcg tcagggtgct gctgaggctg taggtgctgt ccttgctgtc ctgctctgtg 180

acactctcct gggagttacc cgattggagg gcgttatcca ccttccactg tacttttggcc 240

tctctgggat agaagttatt cagcaggcac acaacagagg cagttccaga tttcaactgc 300

tcatcagatg gcgggaagat gaagacagat ggtgcagcca ccgtacgttt gatctccacc 360

ctggtccctc cgccgaaagt gagaggggga ctgtaactct gttgacagta gtaagttgca 420

aaatcttcag gttgcagact ggtgatggtg agagtgaaat ctgtcccaga tccactgcca 480

ctgaaccttg atgggacccc actttgcaac ccggatgcag cagagatcag gcccttaggg 540

gctttccctg gtctctgctg ataccaattt aaatacttgt aaatgttctg actcgcccgg 600

caagtgatgg tgactctgtc tcctacagat gcagacaggg aggatggaga ctgggtcatc 660

tggatgtcac atctggcacc tcggagccag agtagcagga gccccaggag ctgagcgagg 720

accctcatgt ccatggtgga agcttaagtt taaacgctag ccagcttggg tctccctata 780

gtgagtcgta ttaatttcga 800

<210> 67
<211> 427
<212> DNA
<213> Homo sapiens

<400> 67
aagcttccac catgaaacac ctgtggttct tccttctcct ggtggcagct cccagctggg 60

tcctgtccca ggtgcaattg caggagtcgg gcccaggact ggtgaagcct tcggagaccc 120

tgtccctcac ctgcactgtc tctggttcgt ccatcagtaa ttactactgg agctggatcc 180

ggcagtcccc agggaaggga ctggagtgga ttgggtttat ctattacggt ggaaacacca 240

agtacaatcc ctccctcaag agccgcgtca ccatatcaca agacacttcc aagagtcagg 300

tctccctgac gatgagctct gtgaccgctg cggaatcggc cgtctatttc tgtgcgagag 360

cgtcttgtag tggtggttac tgtatccttg actactgggg ccagggaacc ctggtcaccg 420

tctcgag 427

<210> 68
<211> 427
<212> DNA
<213> Homo sapiens

<400> 68
ctcgagacgg tgaccagggt tccctggccc cagtagtcaa ggatacagta accaccacta 60

caagacgctc tcgcacagaa atagacggcc gattccgcag cggtcacaga gctcatcgtc 120

agggagacct gactcttgga agtgtcttgt gatatggtga cgcggctctt gagggaggga 180

ttgtacttgg tgttttccacc gtaatagata aacccaatcc actccagtcc ctttccctggg 240

gactgccgga tccagctcca gtagtaatta ctgatggacg aaccagagac agtgcaggtg 300

agggacaggg tctccgaagg ctttcaccagt cctgggcccg actcctgcaa ttgcacctgg 360

gacaggaccc agctgggagc tgccaccagg agaaggaaga accacaggtg tttcatggtg 420

gaagctt 427

<210> 69
<211> 469
<212> PRT
<213> Homo sapiens

<400> 69

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Ser Trp
1 5 10 15

Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys
20 25 30

Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ser Ser Ile
35 40 45

Ser Asn Tyr Tyr Trp Ser Trp Ile Arg Gln Ser Pro Gly Lys Gly Leu
50 55 60

Glu Trp Ile Gly Phe Ile Tyr Tyr Gly Gly Asn Thr Lys Tyr Asn Pro
65 70 75 80

Ser Leu Lys Ser Arg Val Thr Ile Ser Gln Asp Thr Ser Lys Ser Gln
85 90 95

Val Ser Leu Thr Met Ser Ser Val Thr Ala Ala Glu Ser Ala Val Tyr
100 105 110

Phe Cys Ala Arg Ala Ser Cys Ser Gly Gly Tyr Cys Ile Leu Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg Ala Ser Thr Lys Gly
130 135 140

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
145 150 155 160

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
165 170 175

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
180 185 190

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
195 200 205

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
210 215 220

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
225 230 235 240

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
245 250 255

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
260 265 270

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
275 280 285

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
290 295 300

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
305 310 315 320

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
325 330 335

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
340 345 350

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
355 360 365

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
370 375 380

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
385 390 395 400

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
405 410 415

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
420 425 430

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
435 440 445

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
450 455 460

Leu Ser Pro Gly Lys
465

<210> 70
<211> 19
<212> PRT
<213> Homo sapiens

<400> 70

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Ser Trp
1 5 10 15

Val Leu Ser

<210> 71
<211> 30
<212> PRT
<213> Homo sapiens

<400> 71

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

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

<210> 72
<211> 5
<212> PRT
<213> Homo sapiens

<400> 72

Asn Tyr Tyr Trp Ser
1 5

<210> 73
<211> 14
<212> PRT
<213> Homo sapiens

<400> 73

Trp Ile Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Ile Gly
1 5 10

<210> 74
<211> 16
<212> PRT
<213> Homo sapiens

<400> 74

Phe Ile Tyr Tyr Gly Gly Asn Thr Lys Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 75
<211> 32
<212> PRT
<213> Homo sapiens

<400> 75

Arg Val Thr Ile Ser Gln Asp Thr Ser Lys Ser Gln Val Ser Leu Thr
1 5 10 15

Met Ser Ser Val Thr Ala Ala Glu Ser Ala Val Tyr Phe Cys Ala Arg
20 25 30

<210> 76
<211> 11
<212> PRT
<213> Homo sapiens

<400> 76

Ala Ser Cys Ser Gly Gly Tyr Cys Ile Leu Asp
1 5 10

<210> 77
<211> 11
<212> PRT
<213> Homo sapiens

<400> 77

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

<210> 78
<211> 1557
<212> DNA
<213> Artificial Sequence

<220>
<223> Recombinant Human Sequence

<400> 78
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ttaagcttcc accatgaaac acctgtggtt cttccttctc ctggtggcag ctcccagctg 120

ggtcctgtcc caggtgcaat tgcaggagtc gggcccagga ctggtgaagc cttcggagac 180

cctgtccctc acctgcactg tctctggttc gtccatcagt aattactact ggagctggat 240

ccggcagtcc ccagggaagg gactggagtg gattgggttt atctattacg gtggaaacac 300

caagtacaat ccctccctca agagccgcgt caccatatca caagacactt ccaagagtca 360

ggtctccctg acgatgagct ctgtgaccgc tgcggaatcg gccgtctatt tctgtgcgag 420

agcgtcttgt agtggtggtt actgtatcct tgactactgg ggccagggaa ccctggtcac 480

cgtctcgaga gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag 540

cacctctggg ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt 600

gacggtgtcg tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct 660

acagtcctca ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg 720

cacccagacc tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagag 780

agttgagccc aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact 840

cctgggggga ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc 900

ccggacccct gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa 960

gttcaactgg tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga 1020

gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct 1080

gaatggcaag gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa 1140

aaccatctcc aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc 1200

ccgggaggag atgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc 1260

cagcgacatc gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac 1320

gcctcccgtg ctggactccg acggctcctt ctttcctcta tagcaagctca ccgtggacaa 1380

gagcaggtgg cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa 1440

ccactacacg cagaagagcc tctccctgtc tccgggtaaa tgagttctag agggcccgtt 1500

taaacccgct gatcagcctc gactgtgcct tctagttgcc agccatctgt tgtttgc 1557

<210> 79
<211> 1557
<212> DNA
<213> Artificial Sequence

<220>
<223> Recombinant Human Sequence

<400> 79
gcaaacaaca gatggctggc aactagaagg cacagtcgag gctgatcagc gggtttaaac 60

gggccctcta gaactcattt acccggagac agggagaggc tcttctgcgt gtagtggttg 120

tgcagagcct catgcatcac ggagcatgag aagacgttcc cctgctgcca cctgctcttg 180

tccacggtga gcttgctata gaggaagaag gagccgtcgg agtccagcac gggaggcgtg 240

gtcttgtagt tgttctccgg ctgcccattg ctctcccact ccacggcgat gtcgctggga 300

tagaagcctt tgaccaggca ggtcaggctg acctggttct tggtcatctc ctcccgggat 360

ggggggcaggg tgtacacctg tggttctcgg ggctgccctt tggctttgga gatggttttc 420

tcgatggggg ctgggagggc tttgttggag accttgcact tgtacttctt gccattcagc 480

cagtcctggt gcaggacggt gaggacgctg accacacggt acgtgctgtt gtactgctcc 540

tcccgcggct ttgtcttggc attatgcacc tccacgccgt ccacgtacca gttgaacttg 600

acctcagggt cttcgtggct cacgtccacc accacgcatg tgacctcagg ggtccgggag 660

atcatgaggg tgtccttggg ttttgggggg aagaggaaga ctgacggtcc ccccaggagt 720

tcaggtgctg ggcacggtgg gcatgtgtga gttttgtcac aagatttggg ctcaactctc 780

ttgtccacct tggtgttgct gggcttgtga ttcacgttgc agatgtaggt ctgggtgccc 840

aagctgctgg agggcacggt caccacgctg ctgagggagt agagtcctga ggactgtagg 900

acagccggga aggtgtgcac gccgctggtc agggcgcctg agttccacga caccgtcacc 960

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accagggttc cctggcccca gtagtcaagg atacagtaac caccactaca agacgctctc 1140

gcacagaaat agacggccga ttccgcagcg gtcacagagc tcatcgtcag ggagacctga 1200

ctcttggaag tgtcttgtga tatggtgacg cggctcttga gggagggatt gtacttggtg 1260

tttccaccgt aatagataaa cccaatccac tccagtccct tccctgggga ctgccggatc 1320

cagctccagt agtaattact gatggacgaa ccagagacag tgcaggtgag ggacagggtc 1380

tccgaaggct tcaccagtcc tgggcccgac tcctgcaatt gcacctggga caggacccag 1440

ctgggagctg ccaccaggag aaggaagaac cacaggtgtt tcatggtgga agcttaagtt 1500

taaacgctag ccagcttggg tctccctata gtgagtcgta ttaatttcga taagcca 1557

<210> 80
<211> 11
<212> PRT
<213> Homo sapiens

<400> 80

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> 81
<211> 6
<212> DNA
<213> Artificial Sequence

<220>
<223> Restriction site

<400> 81
ctcgag 6

<210> 82
<211> 11
<212> PRT

<213> Homo sapiens

<400> 82

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Arg
1 5 10

<210> 83
<211> 404
<212> DNA
<213> Homo sapiens

<400> 83
aagcttccac catggacatg agggtcctcg ctcagctcct ggggctcctg ctactctggc 60

tccgaggtgc cagatgtgac atccaggtga cccagtctcc atcctccctg tctgcatctg 120

taggagacag agtcaccatc acttgccgcg cgagtcagaa catttacaag tatttaaatt 180

ggtatcagca gagaccaggg aaagccccta agggcctgat ctctgctgca tccgggttgc 240

aaagtggggt cccatcaagg ttcagtggca gtggatctgg gacagatttc actctcacca 300

tcaccagtct gcaacctgaa gattttgcaa cttactactg tcaacagagt tacagtcccc 360

ctctcacttt cggcggaggg accagggtgg atatcaaacg tacg 404

<210> 84
<211> 404
<212> DNA
<213> Homo sapiens

<400> 84
cgtacgtttg atatccaccc tggtccctcc gccgaaagtg agagggggac tgtaactctg 60

ttgacagtag taagttgcaa aatcttcagg ttgcagactg gtgatggtga gagtgaaatc 120

tgtcccagat ccactgccac tgaacctgga tgggacccca ctttgcaacc cggatgcagc 180

agagatcagg ccctt agggg ctttccctgg tctctgctga taccaatttа aatacttgta 240

aatgttctga ctcgcgcggc aagtgatggt gactctgtct cctacagatg cagacaggga 300

ggatggagac tgggtcacct ggatgtcaca tctggcacct cggagccaga gtagcaggag 360

ccccaggagc tgagcgagga ccctcatgtc catggtggaa gctt 404

<210> 85
<211> 427
<212> DNA
<213> Homo sapiens

<400> 85
aagcttccac catgaaacac ctgtggttct tccttctcct ggtggcagct cccagctggg 60

tcctgtccca ggtgcaattg caggagtcgg gcccaggact ggtgaagcct tcggagaccc 120

tgtccctcac ctgcactgtc tctggttcgt ccatcagtaa ttactactgg agctggatcc 180

ggcagtcccc agggaaggga ctggagtgga ttgggtttat ctattacggt ggaaacacca 240

agtacaatcc ctccctcaag agccgcgtca ccatatcaca agacacttcc aagagtcagg 300

tctccctgac gatgagcttc gtgaccgctg cggaatcggc cgtctatttc tgtgcgagag 360

cgtcttgtag tggtggttac tgtatccttg actactgggg ccagggaacc ctggtcaccg 420

tctcgag 427

<210> 86
<211> 427
<212> DNA
<213> Homo sapiens

<400> 86
ctcgagacgg tgaccagggt tccctggccc cagtagtcaa ggatacagta accaccacta 60

caagacgctc tcgcacagaa atagacggcc gattccgcag cggtcacaga gctcatcgtc 120

agggagacct gactcttgga agtgtcttgt gatatggtga cgcggcttt gagggaggga 180

ttgtacttgg tgttttccacc gtaatagata aacccaatcc actccagtcc cttccctggg 240

gactgccgga tccagctcca gtagtaatta ctgatggacg aaccagagac agtgcaggtg 300

agggacaggg tctccgaagg ctttaccagt cctgggcccg actcctgcaa ttgcacctgg 360

gacaggaccc agctgggagc tgccaccagg agaaggaaga accacaggtg tttcatggtg 420

gaagctt 427

<210> 87
<211> 427
<212> DNA
<213> Homo sapiens

<400> 87
aagcttccac catgaaacac ctgtggttct tccttctcct ggtggcagct cccagctggg 60

tcctgtccca ggtgcaattg caggagtcgg gcccaggact ggtgaagcct tcggagaccc 120

tgtccctcac ctgcactgtc tctggttcgt ccatcagtaa ttactactgg agctggatcc 180

ggcagtcccc agggaaggga ctggagtgga ttgggtttat ctattacggt ggaaacacca 240

agtacaatcc ctccctcaag agccgcgtca ccatatcaca agacacttcc aagagtcagg 300

tctccctgac gatgagctct gtgaccgctg cggaatcggc cgtctatttc tgtgcgagag 360

cgtcttgtag tggtggttac tgtatccttg actactgggg ccagggaacc ctggtcaccg 420

tctcgag 427

<210> 88
<211> 401
<212> DNA
<213> Homo sapiens

<400> 88
aagcttccac catggacatg agggtcctcg ctcagctcct ggggctcctg ctactctggc 60

tccgaggtgc cagatgtgac atccagatga cccagtctcc atcctccctg tctgcatctg 120

taggagacag agtcaccatc acttgccgga caagtcagag cattagcagc tatttaaatt 180

ggtatcagca gaaaccaggg aaagcccctaa aactcctgat ctatgctgca tccagtttgc 240

aaagtggggt cccatcaagg ttcagtggca gtggatctgg gacagatttc actctcacca 300

tcagcggtct gcaacctgaa gatttttgcaa cctactactg tcaacagagt tacagtatgc 360

ctgcctttgg ccaggggacc aagctggaga tcaaacgtac g 401

<210> 89
<211> 401
<212> DNA
<213> Homo sapiens

<400> 89
cgtacgtttg atctccagct tggtcccctg gccaaaggca ggcatactgt aactctgttg 60

acagtagtag gtttgcaaaat ctttcaggtt g cagaccgctg atggtgagag tgaaatctgt 120

cccagatcca ctgccactga acctttgatgg gaccccactt tgcaaactgg atgcagcata 180

gatcaggagt ttaggggctt tccctggttt ctgctgatac caatttaaat agctgctaat 240

gctctgactt gtccggcaag tgatggtgac tctgtctcct acagatgcag acagggagga 300

tggagactgg gtcatctgga tgtcacatct ggcacctcgg agccagagta gcaggagccc 360

caggagctga gcgaggaccc tcatgtccat ggtggaagct t 401

<210> 90
<211> 401
<212> DNA
<213> Homo sapiens

<400> 90
aagcttccac catggacatg agggtcctcg ctcagctcct ggggctcctg ctactctggc 60

tccgaggtgc cagatgtgac atccagatga cccagtctcc atcctccctg tctgcatctg 120

taggagacag agtcaccatc acttgccgga caagtcagag cattagcagc tatttaaatt 180

ggtatcagca gaaaccaggg aaagccccta aactcctgat ctatgctgca tccagtttgc 240

aaagtggggt cccatcaagg ttcagtggca gtggatctgg gacagatttc actctcacca 300

tcagcggtct gcaacctgaa gatttttgcaa cctactactg tcaacagagt tacagtatgc 360

ctgcctttgg ccaggggacc aagctggaga tcaaacgtac g 401

<210> 91
<211> 130
<212> PRT
<213> Homo sapiens

<400> 91

Met Asp Met Arg Val Leu Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15

Leu Arg Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Thr Ser
35 40 45

Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
50 55 60

```
Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val
65                  70                  75                  80

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
                85                  90                  95

Ile Ser Gly Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
            100                 105                 110

Ser Tyr Ser Met Pro Ala Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Arg Thr
    130
```

<210> 92
<211> 11
<212> PRT
<213> Homo sapiens

<400> 92

```
Arg Thr Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1               5                   10
```

<210> 93
<211> 15
<212> PRT
<213> Homo sapiens

<400> 93

```
Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
1               5                   10                  15
```

<210> 94
<211> 13
<212> PRT
<213> Homo sapiens

<400> 94

```
Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe
1               5                   10
```

<210> 95
<211> 26
<212> PRT
<213> Homo sapiens

<400> 95

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Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Gly Leu
1               5                   10                  15

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
            20                  25
```

<210> 96
<211> 8
<212> PRT
<213> Homo sapiens

<400> 96

Gln Gln Ser Tyr Ser Met Pro Ala
1 5

<210> 97
<211> 427
<212> DNA
<213> Homo sapiens

<400> 97
aagcttccac catggagttg gggctgtgct gggttttcct tgttgctatt ttaaaaggtg 60

tccagtgtga ggtgcagctg gtggagtctg gggaggcttt ggtccagcct gggggtccc 120

tgagaatctc ctgtgcagcc tctggattca ccgtcagtag caactacatg agttgggtcc 180

gccaggctcc agggaagggg ctggagtggg tctcagttat ttatagtggt ggtagcacat 240

actacgcaga ctccgtgaag ggcagattct cctttctccag agacaactcc aagaacacag 300

tgttcttca aatgaacagc ctgagagccg aggacacggc tgtgtattac tgtgcgagat 360

gtctgagcag gatgcggggt tacggttag acgtctgggg ccaagggacc acggtcaccg 420

tctcgag 427

<210> 98
<211> 427
<212> DNA
<213> Homo sapiens

<400> 98
ctcgagacgg tgaccgtggt cccttggccc cagacgtcta aaccgtaacc ccgcatcctg 60

ctcagacatc tcgcacagta atacacagcc gtgtcctcgg ctctcaggct gttcatttga 120

agaaacactg tgttcttgga gttgtctctg gagaaggaga atctgcccct cacggagtct 180

gcgtagtatg tgctaccacc actataaata actgagaccc actccagccc cttccctgga 240

gcctggcgga cccaactcat gtagttgcta ctgacggtga atccagaggc tgcacaggag 300

attctcaggg acccccccagg ctggaccaag cctcccccag actccaccag ctgcacctca 360

cactggacac cttttaaaat agcaacaagg aaaacccagc acagccccaa ctccatggtg 420

gaagctt 427

<210> 99
<211> 427
<212> DNA
<213> Homo sapiens

<400> 99
aagcttccac catggagttg gggctgtgct gggttttcct tgttgctatt ttaaaaggtg 60

tccagtgtga ggtgcagctg gtggagtctg gggaggcttt ggtccagcct gggggtccc 120

tgagaatctc ctgtgcagcc tctggattca ccgtcagtag caactacatg agttgggtcc 180

gccaggctcc agggaagggg ctggagtggg tctcagttat ttatagtggt ggtagcacat 240

actacgcaga ctccgtgaag ggcagattct cctttctccag agacaactcc aagaacacag 300

tgttttcttca aatgaacagc ctgagagccg aggacacggc tgtgtattac tgtgcgagat 360

gtctgagcag gatgcggggt tacggttttag acgtctgggg ccaagggacc acggtcaccg 420

tctcgag 427

<210> 100
<211> 138
<212> PRT
<213> Homo sapiens

<400> 100

Met Glu Leu Gly Leu Cys Trp Val Phe Leu Val Ala Ile Leu Lys Gly
1 5 10 15

Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Ile Ser Cys Ala Ala Ser Gly Phe Thr Val
35 40 45

Ser Ser Asn Tyr Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp
65 70 75 80

Ser Val Lys Gly Arg Phe Ser Phe Ser Arg Asp Asn Ser Lys Asn Thr
85 90 95

Val Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
100 105 110

Tyr Cys Ala Arg Cys Leu Ser Arg Met Arg Gly Tyr Gly Leu Asp Val
115 120 125

Trp Gly Gln Gly Thr Thr Val Thr Val Ser
130 135

<210> 101
<211> 19
<212> PRT
<213> Homo sapiens

<400> 101

Met Glu Leu Gly Leu Cys Trp Val Phe Leu Val Ala Ile Leu Lys Gly
1 5 10 15

Val Gln Cys

<210> 102
<211> 30
<212> PRT
<213> Homo sapiens

<400> 102

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

Ser Leu Arg Ile Ser Cys Ala Ala Ser Gly Phe Thr Val Ser
20 25 30

<210> 103
<211> 5
<212> PRT
<213> Homo sapiens

<400> 103

Ser Asn Tyr Met Ser
1 5

<210> 104
<211> 14
<212> PRT
<213> Homo sapiens

<400> 104

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser
1 5 10

<210> 105
<211> 15
<212> PRT
<213> Homo sapiens

<400> 105

Val Ile Tyr Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

<210> 106
<211> 33
<212> PRT
<213> Homo sapiens

<400> 106

Gly Arg Phe Ser Phe Ser Arg Asp Asn Ser Lys Asn Thr Val Phe Leu
1 5 10 15

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
20 25 30

Arg

<210> 107
<211> 12
<212> PRT
<213> Homo sapiens

<400> 107

Cys Leu Ser Arg Met Arg Gly Tyr Gly Leu Asp Val
1 5 10

<210> 108
<211> 10
<212> PRT
<213> Homo sapiens

<400> 108

Trp Gly Gln Gly Thr Thr Val Thr Val Ser
1 5 10

<210> 109
<211> 6
<212> PRT
<213> Homo sapiens

<400> 109

Gly Ser Ser Ile Ser Asn
1 5

<210> 110
<211> 9
<212> PRT
<213> Homo sapiens

<400> 110

Phe Ile Tyr Tyr Gly Gly Asn Thr Lys
1 5

<210> 111
<211> 11
<212> PRT
<213> Homo sapiens

<400> 111

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
1 5 10

<210> 112
<211> 7
<212> PRT
<213> Homo sapiens

<400> 112

Gly Phe Thr Val Ser Ser Asn
1 5

<210> 113
<211> 9
<212> PRT
<213> Homo sapiens

<400> 113

Val Ile Tyr Ser Gly Gly Ser Thr Tyr
1 5

<210> 114
<211> 10
<212> PRT
<213> Homo sapiens

<400> 114

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
1 5 10

<210> 115
<211> 366
<212> DNA
<213> Homo sapiens

<400> 115
caggtgcagc tgcagcagtc gggcccagga ctggtgaagc cttcacagac cctgtccctc 60

acttgcactg tctctggtgg ccccgtcagc ggtggtggtt actcctggaa ctggatccgc 120

caacgcccag gacagggcct ggagtgggtt gggttcatgt ttcacagtgg gagtccccgc 180

tacaatccga ccctcaagag tcgaattacc atctcagtcg acacgtctaa gaacctggtc 240

tccctgaagc tgagctctgt gacggccgcg gacacggccg tgtatttttg tgcgcgagtg 300

gggcagatgg acaagtacta tgccatggac gtctggggcc aagggaccac ggtcaccgtc 360

tcgagc 366

<210> 116
<211> 122
<212> PRT
<213> Homo sapiens

<400> 116

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 Thr Val Ser Gly Gly Pro Val Ser Gly Gly
20 25 30

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

Trp Val Gly Phe Met Phe His Ser Gly Ser Pro Arg Tyr Asn Pro Thr
50 55 60

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

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

Cys Ala Arg Val Gly Gln Met Asp Lys Tyr Tyr Ala Met Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 117
<211> 323
<212> DNA
<213> Homo sapiens

<400> 117
gacatccaga tgacccagtc tccatcctcc ctgtcttcct ctgtcggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattggc gcctatgtaa attggtatca acagaaagca 120

gggaaagccc cccaggtcct gatctttggt gcttccaatt tacaaagcgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaagactttg caacttactt ctgtcaacag acttacagta ccccgatcac cttcggccaa 300

gggacacgac tggagattaa acg 323

<210> 118
<211> 107
<212> PRT
<213> Homo sapiens

<400> 118

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

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

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

Phe Gly Ala Ser Asn 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 Phe Cys Gln Gln Thr Tyr Ser Thr Pro Ile
85 90 95

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

<210> 119
<211> 363
<212> DNA
<213> Homo sapiens

<400> 119
caggtccagc tgcaggagtc gggcccagga ctgctgaagc cttcggacac cctggccctc 60

acttgcactg tctctggtgg ctccatcacc agtgactact ggagctggat ccggcaaccc 120

ccagggaggg gactggactg gatcggattc ttctataacg gcggaagcac caagtacaat 180

ccctccctca agagtcgagt caccatttca gcggacacgt ccaagaacca gttgtccctg 240

aaattgacct ctgtgaccgc cgcagacacg ggcgtgtatt attgtgcgag acatgatgcc 300

aaatttagtg ggagctacta cgttgcctcc tggggccagg gaacccgagt caccgtctcg 360

agc 363

<210> 120
<211> 121
<212> PRT
<213> Homo sapiens

<400> 120

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

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

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

Gly Phe Phe Tyr Asn Gly Gly Ser Thr Lys Tyr Asn Pro Ser Leu Lys
50 55 60

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

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

Arg His Asp Ala Lys Phe Ser Gly Ser Tyr Tyr Val Ala Ser Trp Gly
100 105 110

Gln Gly Thr Arg Val Thr Val Ser Ser
115 120

<210> 121
<211> 323
<212> DNA
<213> Homo sapiens

<400> 121
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atctcttgcc gggcaagtca gagcattagc acctatttaa attggtatca gcagcaacct 120

gggaaagccc ctaaggtcct cattttggt gcaaccaact tgcaaagtgg ggtcccatct 180

cgcttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg caacttacta ctgtcaacag agttacaata ccccctcat ttttggccag 300

gggaccaagc tggagatcaa acg 323

<210> 122
<211> 107
<212> PRT
<213> Homo sapiens

<400> 122

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 Ser Cys Arg Ala Ser Gln Ser Ile Ser Thr Tyr
20 25 30

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

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

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

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

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

<210> 123
<211> 363
<212> DNA
<213> Homo sapiens

<400> 123
caggtccagc tgcaggagtc gggcccagga ctgctgaagc cttcggacac cctggccctc 60

acttgcactg tctctggtgg ctccatcacc agtgactact ggagctggat ccggcaaccc 120

ccagggaggg gactggactg gatcggattc ttctataacg gcgggagcac caagtacaat 180

ccctccctca agagtcgagt caccatatca gcggacacgt ccaagaacca gttgtccctg 240

aaattgacct ctgtgaccgc cgcagacacg ggcgtgtatt attgtgcgag acatgatgtc 300

aaatttagtg ggagctacta cgttgcctcc tggggccagg gaacccgagt caccgtctcg 360

agc 363

<210> 124

<211> 121
<212> PRT
<213> Homo sapiens

<400> 124

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

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

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

Gly Phe Phe Tyr Asn Gly Gly Ser Thr Lys Tyr Asn Pro Ser Leu Lys
50 55 60

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

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

Arg His Asp Val Lys Phe Ser Gly Ser Tyr Tyr Val Ala Ser Trp Gly
100 105 110

Gln Gly Thr Arg Val Thr Val Ser Ser
115 120

<210> 125
<211> 323
<212> DNA
<213> Homo sapiens

<400> 125
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcttgcc gggcaagtca gagcattagc acctatttaa attggtatca gcagcaacct 120

gggaaagccc ctaaggtcct gatctctggt gcaaccaact tgcaaagtgg ggtcccatct 180

cgcttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg caacttacta ctgtcaacag agttacaata ccccctcat ttttggccag 300

gggaccaagc tggagatcaa acg 323

<210> 126
<211> 107
<212> PRT
<213> Homo sapiens

<400> 126

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 Ser Cys Arg Ala Ser Gln Ser Ile Ser Thr Tyr
20 25 30

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

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

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

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

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

<210> 127
<211> 360
<212> DNA
<213> Homo sapiens

<400> 127
caggtgcagc tgcaggagtc gggcccacga gtggtgaggc cttcggagac cctgtccctc 60

acctgcactg tctcgggggg ctccatcagt tcttacaact ggattttgat ccggcagccc 120

cctgggaagg gactggagtg gattgggcac atatatgact atgggaggac ctttctacaac 180

tcctccctcc agagtcgacc taccatatct gtagacgcgt ccaagaatca gctctccctg 240

cgattgacct ctgtgaccgc tcagacacg gccgtctatt actgtgcgag acctctcggt 300

atactccact actacgcgat ggacctctgg ggccaaggga ccacggtcac cgtctcgagc 360

<210> 128
<211> 120
<212> PRT
<213> Homo sapiens

<400> 128

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

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

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

Gly His Ile Tyr Asp Tyr Gly Arg Thr Phe Tyr Asn Ser Ser Leu Gln
50 55 60

Ser Arg Pro Thr Ile Ser Val Asp Ala Ser Lys Asn Gln Leu Ser Leu
65 70 75 80

```
Arg Leu Thr Ser Val Thr Ala Ser Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Pro Leu Gly Ile Leu His Tyr Tyr Ala Met Asp Leu Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210>  129
<211>  320
<212>  DNA
<213>  Homo sapiens

<400>  129
gacatccaga tgacccagtc tccattatcc gtgtctgtat ctgtcgggga cagggtcacc        60

atcgcttgcc gggcaagtca gagtattgac aagttttaa attggtatca gcagaaacca        120

gggaaagccc ctaaactcct gatctatggt gcctccaatt tgcacagtgg ggccccatca        180

aggttcagtg ccagtgggtc tgggacagac ttcactctaa caatcaccaa tatacagact        240

gaagatttcg caacttacct ctgtcaacag agttttcagtg tccccgcttt cggcggaggg       300

accaaggttg agatcaaacg                                                   320


<210>  130
<211>  106
<212>  PRT
<213>  Homo sapiens

<400>  130

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

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

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

Tyr Gly Ala Ser Asn Leu His Ser Gly Ala Pro Ser Arg Phe Ser Ala
    50                  55                  60

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

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

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

<210> 131
<211> 354
<212> DNA
<213> Homo sapiens

<400> 131
gaggtgcaac tggtggagtc tggaggggc ttggtccagc ctgggggtc cctgagactc 60

tcctgtacgg cctctgggtt aagtgtcagt tccacctaca tgaactgggt ccgccaggct 120

ccagggaagg ggctggaatg ggtctcagtt ttttatagtg agaccaggac gtactacgca 180

gactccgtga agggccgatt caccgtctcc agacacaatt ccaacaacac gctctatctt 240

cagatgaaca gcctgagagt tgaagacacg gccgtgtatt attgtgcgag agtccagaga 300

ttgtcgtacg gtatggacgt ctggggccaa gggaccacgg tcaccgtctc gagc 354

<210> 132
<211> 118
<212> PRT
<213> Homo sapiens

<400> 132

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 Thr Ala Ser Gly Leu Ser Val Ser Ser Thr
20 25 30

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

Ser Val Phe Tyr Ser Glu Thr Arg Thr Tyr Tyr Ala Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Val Ser Arg His Asn Ser Asn Asn Thr Leu Tyr Leu
65 70 75 80

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

Arg Val Gln Arg Leu Ser Tyr Gly Met Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> 133
<211> 320
<212> DNA
<213> Homo sapiens

<400> 133
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgttggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagc acctatttaa attggtatca gaagagacca 120

gggaaagccc ctaaactcct ggtctatggt gcatccactt tgcagagtgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcgccag tctgcaacct 240

gaagattctg caacttacta ctgtcaacag acttacagta tccccctctt cggccagggg 300

acacggctgg agattaaacg 320

<210> 134
<211> 106
<212> PRT
<213> Homo sapiens

<400> 134

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

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

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

Tyr Gly Ala Ser Thr 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 Ala Ser Leu Gln Pro
65 70 75 80

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

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

<210> 135
<211> 354
<212> DNA
<213> Homo sapiens

<400> 135
gaggtgcagc tggtggaatc tggagggggc ttggtccagc ctgggggtc cctgagactc 60

tcctgtacag cctctgggtt aagcgtcagt tccacctaca tgaactgggt ccgccaggct 120

ccagggaagg ggctggaatg ggtctcagtt tttatagtg aaaccaggac gtattacgca 180

gactccgtga agggccgatt caccgtctcc agacacaatt ccaacaacac gctgtatctt 240

caaatgaaca gcctgagagc tgaagacacg gccgtgtatt attgtgcgag agtccagaga 300

ctgtcatacg gtatggacgt ctggggccaa gggaccacgg tcaccgtctc gagc 354

<210> 136
<211> 118
<212> PRT
<213> Homo sapiens

<400> 136

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 Thr Ala Ser Gly Leu Ser Val Ser Ser Thr
20 25 30

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

Ser Val Phe Tyr Ser Glu Thr Arg Thr Tyr Tyr Ala Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Val Ser Arg His Asn Ser Asn Asn Thr Leu Tyr Leu
65 70 75 80

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

Arg Val Gln Arg Leu Ser Tyr Gly Met Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> 137
<211> 320
<212> DNA
<213> Homo sapiens

<400> 137
gacatccaga tgacccagtc tccatcgtcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagc acctatttaa attggtatca gaagagacca 120

gggaaagccc ctaaactcct ggtctatggt gcatccagtt tgcagagtgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcgccag tctgcaacct 240

gaagattctg cagtttatta ctgtcaacag acttacagta tccccctctt cggccagggg 300

acacgactgg agattaaacg 320

<210> 138
<211> 106
<212> PRT
<213> Homo sapiens

<400> 138

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

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

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

Tyr Gly 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 Ala Ser Leu Gln Pro
65 70 75 80

Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Thr Tyr Ser Ile Pro Leu
85 90 95

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

<210> 139
<211> 360
<212> DNA
<213> Homo sapiens

<400> 139
caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cctcggagac cctgtccctc 60

acctgcagtg tctctggtgg ctccattagt agtgatttct ggagttggat ccgacagccc 120

ccagggaagg gactggagtg gattgggtat gtctataaca gagggagcac taagtacagt 180

ccctccctca agagtcgagt caccatatca gcagacatgt ccaagaacca gttttccctg 240

aatatgagtt ctgtgaccgc tgcggacacg gccgtgtatt actgtgcgaa aaatggtcga 300

agtagcacca gttggggcat cgacgtctgg ggcaaaggga ccacggtcac cgtctcgagc 360

<210> 140
<211> 120
<212> PRT
<213> Homo sapiens

<400> 140

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

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

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

Gly Tyr Val Tyr Asn Arg Gly Ser Thr Lys Tyr Ser Pro Ser Leu Lys
50 55 60

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

Asn Met Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Lys Asn Gly Arg Ser Ser Thr Ser Trp Gly Ile Asp Val Trp Gly Lys
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 141
<211> 323
<212> DNA
<213> Homo sapiens

<400> 141
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtgggaga cagactcacc 60

atcacttgcc gggcaagtca gagcattagc acctatttac attggtatca gcagaaacca 120

gggaaagccc ctaaactcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180

aggttcagtg gcagtagatc aggaacagat ttcactctca ccatcagcag tctgcaacct 240

gatgatttg caacttacta ctgtcaacag agttacagtc ccccctcac tttcggccct 300

gggaccaaag tggatatgaa acg 323

<210> 142
<211> 107
<212> PRT
<213> Homo sapiens

<400> 142

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

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

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

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

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

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

Thr Phe Gly Pro Gly Thr Lys Val Asp Met Lys
100 105

<210> 143
<211> 357
<212> DNA
<213> Homo sapiens

<400> 143
caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggtgc ctccatcagt agtgactact ggagctggat ccggctgccc 120

ccagggaagg gactggagtg gattgggtat atctataata gagggagtac caagtacacc 180

ccctccctga agagtcgagt caccatatca ctagacacgg ccgagaacca gttctccctg 240

aggctgaggt cggtgaccgc cgcagacacg gccatctatt actgtgcgag acatgtaggt 300

ggccacacct atggaattga ttactggggc cagggaaccc tggtcaccgt ctcgagc 357

<210> 144
<211> 119
<212> PRT
<213> Homo sapiens

<400> 144

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

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

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

Gly Tyr Ile Tyr Asn Arg Gly Ser Thr Lys Tyr Thr Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Leu Asp Thr Ala Glu Asn Gln Phe Ser Leu
65 70 75 80

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

Arg His Val Gly Gly His Thr Tyr Gly Ile Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 145
<211> 323
<212> DNA
<213> Homo sapiens

<400> 145
gacatccaga tgacccagtc tccatcgtcc ctgtctgcct ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagc aactatttaa attggtatca acacaaacct 120

ggggaagccc ccaagctcct gaactatgct gcgtccagtt tgcaaagtgg ggtcccatca 180

aggttcagtg ccagtggatc tgggacagat ttcactctca ccatcagcag tcttcaacct 240

gaagattttg ccacttacta ctgtcaacag agttacaata ctccgatcac cttcggccaa 300

gggacacgac tggaaattaa acg 323

<210> 146
<211> 107
<212> PRT
<213> Homo sapiens

<400> 146

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

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

Leu Asn Trp Tyr Gln His Lys Pro Gly Glu Ala Pro Lys Leu Leu Asn
35 40 45

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

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

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

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

<210> 147
<211> 357
<212> DNA
<213> Homo sapiens

<400> 147
caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggtgc ctccatcagt agtgactact ggagctggat ccggctgccc 120

ccagggaagg gactggagtg gattgggtat atctataata gagggagtac caagtacacc 180

ccctccctga agagtcgagt caccatatca ctagacacgg ccgagaacca gttctccctg 240

aggctgaggt cggtgaccgc cgcagacacg gccgtctatt actgtgcgag acatgtgggt 300

ggccacacct atggaattga ttactggggc cagggaaccc tggtcaccgt ctcgagc 357

<210> 148
<211> 119
<212> PRT
<213> Homo sapiens

<400> 148

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

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

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

Gly Tyr Ile Tyr Asn Arg Gly Ser Thr Lys Tyr Thr Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Leu Asp Thr Ala Glu Asn Gln Phe Ser Leu
65 70 75 80

Arg Leu Arg Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Val Gly Gly His Thr Tyr Gly Ile Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 149
<211> 323
<212> DNA
<213> Homo sapiens

<400> 149
gacatccaga tgacccagtc tccatcgtcc ctgtctgcct ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagc aactatttaa attggtatca acacaaacct 120

ggggaagccc ccaagctcct gaactatgct gcgtccagtt tgcaaagtgg ggtcccatca 180

aggttcagtg ccagtggatc tgggacagat ttcactctca gcatcagcgg tcttcaacct 240

gaagattttg ccacttacta ctgtcaacag agctacaata ctccgatcac cttcggccca 300

gggacacgac tggaaattaa acg 323

<210> 150
<211> 107
<212> PRT
<213> Homo sapiens

<400> 150

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

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

Leu Asn Trp Tyr Gln His Lys Pro Gly Glu Ala Pro Lys Leu Leu Asn
35 40 45

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

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

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

Thr Phe Gly Pro Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 151
<211> 363
<212> DNA
<213> Homo sapiens

<400> 151
caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccgtc 60

acctgcaaag tctctggtga ctccatcagt agttattcct ggagctggat ccggcagccc 120

ccagggaagg gactggagtg ggttggctat ttgtattata gtgggagcac caagtacaac 180

ccctccctca agagtcgaac caccatatca gtagacacgt ccacgaacca gttgtccctg 240

aagttgagtt ttgtgaccgc cgcggacacg gccgtgtatt tctgtgcgag aaccggctcg 300

gaatctacta ccggctacgg tatggacgtc tggggccaag ggaccacggt caccgtctcg 360

agc 363

<210> 152
<211> 121
<212> PRT
<213> Homo sapiens

<400> 152

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

Thr Leu Ser Val Thr Cys Lys Val Ser Gly Asp Ser Ile Ser Ser Tyr
20 25 30

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

Gly Tyr Leu Tyr Tyr Ser Gly Ser Thr Lys Tyr Asn Pro Ser Leu Lys
50 55 60

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

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

Arg Thr Gly Ser Glu Ser Thr Thr Gly Tyr Gly Met Asp Val Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 153
<211> 323
<212> DNA
<213> Homo sapiens

<400> 153
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagc acctatttaa attggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcacagtgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcgctctca ccatcagcag tctgcaacct 240

gaagattttg caacttacta ctgtcaacag agttacagtc ccccgatcac cttcggccaa 300

gggacacgac tggagattaa acg 323

<210> 154
<211> 107
<212> PRT
<213> Homo sapiens

<400> 154

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

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

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

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

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

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

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

<210> 155
<211> 357
<212> DNA
<213> Homo sapiens

<400> 155

caggtgcagc tgcaggagtc gggcccaaga ctggtgaagc cttcggagag cctgtccctc 60

acctgcactg tctctggtgg ctccattagt aattccttct ggggctggat ccggcagccc 120

ccaggggagg gactggagtg gattggttat gtctataaca gtggcaacac caagtacaat 180

ccctccctca agagtcgagt caccatttcg cgcgacacgt ccaagagtca actctacatg 240

aagctgaggt ctgtgaccgc cgctgacacg gccgtgtact actgtgcgag gcatgacgac 300

gcaagtcatg gctacagcat ctcctggggc cacggaaccc tggtcaccgt ctcgagc 357

<210> 156
<211> 119
<212> PRT
<213> Homo sapiens

<400> 156

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

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

Phe Trp Gly Trp Ile Arg Gln Pro Pro Gly Glu Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Val Tyr Asn Ser Gly Asn Thr Lys Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Arg Asp Thr Ser Lys Ser Gln Leu Tyr Met
65 70 75 80

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

Arg His Asp Asp Ala Ser His Gly Tyr Ser Ile Ser Trp Gly His Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 157
<211> 321
<212> DNA
<213> Homo sapiens

<400> 157
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtagggga cagagtcacc 60

atcacttgcc gggcaagtca gaccattagt acttatttaa attggtatca acagaaatca 120

gggaaagccc ctaagcctcct gatctatgct gcatccggtt tgcaaagtgg agtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tcttcaacct 240

gaagattttg caacttactt ctgtcaacag agttacaata ctcccctgac gttcggccaa 300

gggaccaagg tggaaatcaa a 321

<210> 158
<211> 107
<212> PRT
<213> Homo sapiens

<400> 158

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 Thr Ile Ser Thr Tyr
20 25 30

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

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

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

<210> 159
<211> 360
<212> DNA
<213> Homo sapiens

<400> 159
caggtgcaac tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctcgggtgg ctccatcagt gcttaccact ggagctggat ccgccagccc 120

ccagggaagg gactggagtg gattgggcac atctttgaca gtgggagcac ttactacaac 180

ccctccctta agagtcgagt caccatatca ctagacgcgt ccaagaacca gctctccctg 240

agattgacct ctgtgaccgc ctcagacacg gccatattat actgtgcgag acctctcggg 300

agtcggtact attacggaat ggacgtctgg ggccaaggga ccacggtcac cgtctcgagc 360

<210> 160
<211> 120
<212> PRT
<213> Homo sapiens

<400> 160

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

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

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

Gly His Ile Phe Asp Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys
50 55 60

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

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

Arg Pro Leu Gly Ser Arg Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 161
<211> 318
<212> DNA
<213> Homo sapiens

<400> 161
gacatccaga tgacccagtc tccgtcctcc ctgtctgcat ctgtcggaga cagagtcacc 60

atcacttgcc gggcaagtca gagtattagc aggtatttaa attggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctatggt gcctccactt tgcaaaatgg ggccccatca 180

aggttcagcg gcagtggatc tgggacagat ttcactctca ccatcagcag tctacaacct 240

gaagattccg caacttacct ctgtcaacag agttacagtg tccctgcttt cggcggagga 300

accaaggtgg aggtcaaa 318

<210> 162
<211> 106
<212> PRT
<213> Homo sapiens

<400> 162

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

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

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

Tyr Gly Ala Ser Thr Leu Gln Asn Gly Ala 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 Ser Ala Thr Tyr Leu Cys Gln Gln Ser Tyr Ser Val Pro Ala
85 90 95

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

<210> 163
<211> 363
<212> DNA
<213> Homo sapiens

<400> 163
caggtccagc tgcaggagtc gggcccagga ctgctgaagc cttcggacac cctggccctc 60

acttgcactg tctctggtgg ctccatcacc agtgactact ggagctggat ccggcaaccc 120

ccagggaggg gactggactg gatcggattc ttctataacg gcgggagcac caagtacaat 180

ccctccctca agagtcgagt caccatatca gcggacacgt ccaagaacca gttgtccctg 240

aaattgacct ctgtgaccgc cgcagacacg ggcgtgtatt attgtgcgag acatgatgcc 300

aaatttagtg ggagctacta cgttgcctcc tggggccagg gaacccgagt caccgtctcg 360

agc 363

<210> 164
<211> 121
<212> PRT
<213> Homo sapiens

<400> 164

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

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

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

Gly Phe Phe Tyr Asn Gly Gly Ser Thr Lys Tyr Asn Pro Ser Leu Lys
50 55 60

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

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

Arg His Asp Ala Lys Phe Ser Gly Ser Tyr Tyr Val Ala Ser Trp Gly
100 105 110

Gln Gly Thr Arg Val Thr Val Ser Ser
115 120

<210> 165
<211> 321
<212> DNA
<213> Homo sapiens

<400> 165
gacatccaga tgacccagtc tccctcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atctcttgcc gggcaagtca gagcattagc acctatttaa attggtatca gcagcaacct 120

gggaaagccc ctaaggtcct gatctctggt gcaaccgact tgcaaagtgg ggtcccatct 180

cgcttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg caacttacta ctgtcaacag agttacaata ccccctcat ttttggccag 300

gggaccaagc tggagatcaa a 321

<210> 166
<211> 107
<212> PRT
<213> Homo sapiens

<400> 166

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 Ser Cys Arg Ala Ser Gln Ser Ile Ser Thr Tyr
20 25 30

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

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

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

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

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

<210> 167
<211> 354
<212> DNA
<213> Homo sapiens

<400> 167
gacatgcagc tggtggagtc tggaggaggc ttggtcccgc cgggggggtc cctgagactc 60

tcctgcgcag cctctgggtt ttccgtcagt gacaactaca taaactgggt ccgccaggct 120

ccagggaagg ggctggactg ggtctcagtc ttttatagtg ctgatagaac atcctacgca 180

gactccgtga agggccgatt caccgtctcc agccacgatt ccaagaacac agtgtacctt 240

caaatgaaca gtctgagagc tgaggacacg gccgttttat actgtgcgag agttcagaag 300

tcctattacg gtatggacgt ctggggccaa gggaccacgg tcaccgtctc gagc 354

<210> 168
<211> 118
<212> PRT
<213> Homo sapiens

<400> 168

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Val Ser Asp Asn
20 25 30

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

Ser Val Phe Tyr Ser Ala Asp Arg Thr Ser Tyr Ala Asp Ser Val Lys
50 55 60

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

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

Arg Val Gln Lys Ser Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> 169
<211> 318
<212> DNA
<213> Homo sapiens

<400> 169
ggcatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagc agatatttaa attggtatct gcagaaacca 120

gggaaagccc ctaagctcct gatctctggt gcatccagtt tgcaaagtgg ggtcccatca 180

aggttcagtg gcactgggtc tgggacagaa ttcactctca ccatcagcag tttgcaacct 240

gaagattttg caacttacta ctgtcaacag actttcagta tccctctttt tggccagggg 300

accaaggtgg agatcaaa 318

<210> 170
<211> 106
<212> PRT
<213> Homo sapiens

<400> 170

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

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

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

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

Thr 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 Thr Phe Ser Ile Pro Leu
85 90 95

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

<210> 171
<211> 369
<212> DNA
<213> Homo sapiens

<400> 171
caggtgcagc tgcaggcgtc gggcccagga ctggtgaagc cttcagagac cctgtccctc 60

acctgcactg tctctggtga ctccatcacc agtggtgctt actactggac ctggatccgc 120

cagcacccag ggaagggcct ggagtggatt gggtacatct attacagtgg gaacacctac 180

tacaacccgt ccctcaagag tcgagttacc atatcactag acacgtctaa gaaccagttc 240

tccctgaagg tgaactctgt gactgccgcg gacacggccg tatattactg tgcgcgagct 300

gcttcgactt cagtgctagg atacggtatg gacgtctggg gccaagggac cacggtcacc 360

gtctcgagc 369

<210> 172
<211> 123
<212> PRT
<213> Homo sapiens

<400> 172

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

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

Ala 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 Asn Thr Tyr Tyr Asn Pro Ser
50 55 60

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

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

Cys Ala Arg Ala Ala Ser Thr Ser Val Leu Gly Tyr Gly Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 173
<211> 321
<212> DNA
<213> Homo sapiens

<400> 173
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atcacttgcc gggcaagtca gagcattagc agatatttaa attggtatca gcaggaacca 120

gggaaggccc ctaagctcct ggtctatgct gcatccagtt tgcaaagtgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccataagcag tcttcaacct 240

gaagattttg caacttacta ctgtcaacag agttatagta ccccctcac cttcggccaa 300

gggacacgac tggagattaa a 321

<210> 174
<211> 107
<212> PRT
<213> Homo sapiens

<400> 174

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

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

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

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

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

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

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

<210> 175
<211> 354
<212> DNA
<213> Homo sapiens

<400> 175
gacatgcagc tggtggagtc tggaggaggc ttggtcccgc cgggggggtc cctgagactc 60

tcctgcgcag cctctgggtt ttccgtcagt gacaactaca taaactgggt ccgccaggct 120

ccagggaagg ggctggactg ggtctcagtc ttttatagtg ctgatagaac atcctacgca 180

gactccgtga agggccgatt caccgtctcc agccacgatt ccaagaacac agtgtacctt 240

caaatgaaca gtctgagagc tgaggacacg gccgttttat tactgtgcgag agttcagaag 300

tcctattacg gtatggacgt ctggggccaa gggaccacgg tcaccgtctc gagc 354

<210> 176
<211> 118
<212> PRT
<213> Homo sapiens

<400> 176

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Val Ser Asp Asn
20 25 30

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

Ser Val Phe Tyr Ser Ala Asp Arg Thr Ser Tyr Ala Asp Ser Val Lys
50 55 60

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

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

Arg Val Gln Lys Ser Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> 177
<211> 318
<212> DNA
<213> Homo sapiens

<400> 177
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atcacttgcc gggcaagtca gagcattagc agatatttaa attggtatct gcagaaacca 120

gggaaagccc ctaagctcct gatctctggt gcatccagtt tgcaaagtgg ggtcccatca 180

aggttcagtg gcactgggtc tgggacagaa ttcactctca ccatcagcag tttgcaacct 240

gaagattttg caacttacta ctgtcaacag actttcagta tccctctttt tggccagggg 300

accaaggtgg agatcaaa 318

<210> 178
<211> 106
<212> PRT
<213> Homo sapiens

<400> 178

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

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

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

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

Thr 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 Thr Phe Ser Ile Pro Leu
85 90 95

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

<210> 179
<211> 7
<212> PRT
<213> Homo sapiens

<400> 179

Gly Gly Gly Tyr Ser Trp Asn
1 5

<210> 180
<211> 16
<212> PRT
<213> Homo sapiens

<400> 180

Phe Met Phe His Ser Gly Ser Pro Arg Tyr Asn Pro Thr Leu Lys Ser
1 5 10 15

<210> 181
<211> 12
<212> PRT
<213> Homo sapiens

<400> 181

Val Gly Gln Met Asp Lys Tyr Tyr Ala Met Asp Val
1 5 10

<210> 182
<211> 8
<212> PRT
<213> Homo sapiens

<400> 182

Gly Gly Pro Val Ser Gly Gly Gly
1 5

<210> 183
<211> 9
<212> PRT
<213> Homo sapiens

<400> 183

Phe Met Phe His Ser Gly Ser Pro Arg
1 5

<210> 184
<211> 11
<212> PRT
<213> Homo sapiens

<400> 184

Arg Ala Ser Gln Ser Ile Gly Ala Tyr Val Asn
1 5 10

<210> 185
<211> 7
<212> PRT
<213> Homo sapiens

<400> 185

Gly Ala Ser Asn Leu Gln Ser
1 5

<210> 186

<211> 9
<212> PRT
<213> Homo sapiens

<400> 186

Gln Gln Thr Tyr Ser Thr Pro Ile Thr
1 5

<210> 187
<211> 5
<212> PRT
<213> Homo sapiens

<400> 187

Ser Asp Tyr Trp Ser
1 5

<210> 188
<211> 16
<212> PRT
<213> Homo sapiens

<400> 188

Phe Phe Tyr Asn Gly Gly Ser Thr Lys Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 189
<211> 13
<212> PRT
<213> Homo sapiens

<400> 189

His Asp Ala Lys Phe Ser Gly Ser Tyr Tyr Val Ala Ser
1 5 10

<210> 190
<211> 6
<212> PRT
<213> Homo sapiens

<400> 190

Gly Gly Ser Ile Thr Ser
1 5

<210> 191
<211> 9
<212> PRT
<213> Homo sapiens

<400> 191

Phe Phe Tyr Asn Gly Gly Ser Thr Lys
1 5

<210> 192
<211> 11
<212> PRT

<213> Homo sapiens

<400> 192

Arg Ala Ser Gln Ser Ile Ser Thr Tyr Leu Asn
1 5 10

<210> 193
<211> 7
<212> PRT
<213> Homo sapiens

<400> 193

Gly Ala Thr Asn Leu Gln Ser
1 5

<210> 194
<211> 9
<212> PRT
<213> Homo sapiens

<400> 194

Gln Gln Ser Tyr Asn Thr Pro Leu Ile
1 5

<210> 195
<211> 360
<212> DNA
<213> Homo sapiens

<400> 195
gaggtgcagc tggtggagtc tgggggaggc ttggtccagc ctgggggtc cctgagaatc 60

tcctgtgcag cctctggatt caccgtcagt agcaactaca tgagttgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagtt attttatagt gtggtagcac atactacgca 180

gactccgtga agggcagatt ctcctttctcc agagacaact ccaagaacac agtgttttctt 240

caaatgaaca gcctgagagc cgaggacacg gctgtgtatt actgtgcgag atgtctgagc 300

aggatgcggg gttacggttt agacgtctgg ggccaaggga ccacggtcac cgtctcgagc 360

<210> 196
<211> 360
<212> DNA
<213> Homo sapiens

<400> 196
caggtgcaat tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggttc gtccatcagt aattactact ggagctggat ccggcagtcc 120

ccagggaagg gactggagtg gattgggttt atctattacg gtggaaacac caagtacaat 180

ccctccctca agagccgcgt caccatatca caagacactt ccaagagtca ggtctccctg 240

acgatgagct ctgtgaccgc tgcggaatcg gccgtctatt tctgtgcgag agcgtcttgt 300

agtggtggtt actgtatcct tgactactgg ggccagggaa ccctggtcac cgtctcgagc 360

<210> 197
<211> 13
<212> PRT
<213> Homo sapiens

<400> 197

His Asp Val Lys Phe Ser Gly Ser Tyr Tyr Val Ala Ser
1 5 10

<210> 198
<211> 12
<212> PRT
<213> Influenza A virus

<400> 198

Gly Val Thr Asn Lys Val Asn Ser Ile Ile Asp Lys
1 5 10

<210> 199
<211> 115
<212> PRT
<213> Homo sapiens

<400> 199

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 Thr Gly Tyr
20 25 30

Tyr Val Tyr 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 Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr 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 Ser Arg Ser Leu Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 200
<211> 5
<212> PRT
<213> Influenza A virus

<400> 200

Thr Gly Leu Arg Asn
1 5

<210> 201
<211> 12
<212> PRT
<213> Influenza A virus

<400> 201

Gly Val Thr Asn Lys Val Asn Arg Ile Ile Asp Lys
1 5 10

<210> 202
<211> 12
<212> PRT
<213> Influenza A virus

<400> 202

Gly Val Thr Asn Lys Glu Asn Ser Ile Ile Asp Lys
1 5 10

<210> 203
<211> 5
<212> PRT
<213> Homo sapiens

<400> 203

Ser Tyr Asn Trp Ile
1 5

<210> 204
<211> 16
<212> PRT
<213> Homo sapiens

<400> 204

His Ile Tyr Asp Tyr Gly Arg Thr Phe Tyr Asn Ser Ser Leu Gln Ser
1 5 10 15

<210> 205
<211> 12
<212> PRT
<213> Homo sapiens

<400> 205

Pro Leu Gly Ile Leu His Tyr Tyr Ala Met Asp Leu
1 5 10

<210> 206
<211> 6
<212> PRT
<213> Homo sapiens

<400> 206

Gly Gly Ser Ile Ser Ser
1 5

<210> 207
<211> 9
<212> PRT
<213> Homo sapiens

<400> 207

His Ile Tyr Asp Tyr Gly Arg Thr Phe
1 5

<210> 208
<211> 11
<212> PRT
<213> Homo sapiens

<400> 208

Arg Ala Ser Gln Ser Ile Asp Lys Phe Leu Asn
1 5 10

<210> 209
<211> 7
<212> PRT
<213> Homo sapiens

<400> 209

Gly Ala Ser Asn Leu His Ser
1 5

<210> 210
<211> 8
<212> PRT
<213> Homo sapiens

<400> 210

Gln Gln Ser Phe Ser Val Pro Ala
1 5

<210> 211
<211> 5
<212> PRT
<213> Homo sapiens

<400> 211

Ser Thr Tyr Met Asn
1 5

<210> 212
<211> 16
<212> PRT
<213> Homo sapiens

<400> 212

Val Phe Tyr Ser Glu Thr Arg Thr Tyr Tyr Ala Asp Ser Val Lys Gly
1 5 10 15

<210> 213
<211> 10
<212> PRT
<213> Homo sapiens

<400> 213

Val Gln Arg Leu Ser Tyr Gly Met Asp Val
1 5 10

<210> 214
<211> 6
<212> PRT
<213> Homo sapiens

<400> 214

Gly Leu Ser Val Ser Ser
1 5

<210> 215
<211> 9
<212> PRT
<213> Homo sapiens

<400> 215

Val Phe Tyr Ser Glu Thr Arg Thr Tyr
1 5

<210> 216
<211> 12
<212> PRT
<213> Influenza A virus

<400> 216

Lys Ile Thr Ser Lys Val Asn Asn Ile Val Asp Lys
1 5 10

<210> 217
<211> 7
<212> PRT
<213> Homo sapiens

<400> 217

Gly Ala Ser Thr Leu Gln Ser
1 5

<210> 218
<211> 8
<212> PRT
<213> Homo sapiens

<400> 218

Gln Gln Thr Tyr Ser Ile Pro Leu
1 5

<210> 219
<211> 14

<212> PRT
<213> Homo sapiens

<400> 219

Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His
1 5 10

<210> 220
<211> 14
<212> PRT
<213> Homo sapiens

<400> 220

Ile Pro His Tyr Asn Phe Gly Ser Gly Ser Tyr Phe Asp Tyr
1 5 10

<210> 221
<211> 17
<212> PRT
<213> Homo sapiens

<400> 221

Gly Ile Ile Ala Ile Phe Gly Thr Pro Lys Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 222
<211> 5
<212> PRT
<213> Homo sapiens

<400> 222

Asn Tyr Ala Met Ser
1 5

<210> 223
<211> 7
<212> PRT
<213> Homo sapiens

<400> 223

Asp Asn Ser Asp Arg Pro Ser
1 5

<210> 224
<211> 11
<212> PRT
<213> Homo sapiens

<400> 224

Gly Gly His Asn Ile Gly Ser Asn Ser Val His
1 5 10

<210> 225
<211> 12
<212> PRT
<213> Influenza A virus

<400> 225

Gly Ile Thr Asn Lys Val Asn Ser Ile Ile Asp Lys
1 5 10

<210> 226
<211> 7
<212> PRT
<213> Homo sapiens

<400> 226

Gly Ala Ser Ser Leu Gln Ser
1 5

<210> 227
<211> 9
<212> PRT
<213> Homo sapiens

<400> 227

Gln Val Trp Gly Ser Ser Ser Asp His
1 5

<210> 228
<211> 5
<212> PRT
<213> Homo sapiens

<400> 228

Ser Asp Phe Trp Ser
1 5

<210> 229
<211> 16
<212> PRT
<213> Homo sapiens

<400> 229

Tyr Val Tyr Asn Arg Gly Ser Thr Lys Tyr Ser Pro Ser Leu Lys Ser
1 5 10 15

<210> 230
<211> 12
<212> PRT
<213> Homo sapiens

<400> 230

Asn Gly Arg Ser Ser Thr Ser Trp Gly Ile Asp Val
1 5 10

<210> 231
<211> 7

<212> PRT
<213> Homo sapiens

<400> 231

Gly Asn Ser Asn Arg Pro Ser
1 5

<210> 232
<211> 9
<212> PRT
<213> Homo sapiens

<400> 232

Tyr Val Tyr Asn Arg Gly Ser Thr Lys
1 5

<210> 233
<211> 11
<212> PRT
<213> Homo sapiens

<400> 233

Arg Ala Ser Gln Ser Ile Ser Thr Tyr Leu His
1 5 10

<210> 234
<211> 7
<212> PRT
<213> Homo sapiens

<400> 234

Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 235
<211> 120
<212> PRT
<213> Homo sapiens

<400> 235

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

Ser Leu Arg Ile Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
20 25 30

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

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

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

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

Arg Cys Leu Ser Arg Met Arg Gly Tyr Gly Leu Asp Val Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210>  236
<211>  119
<212>  PRT
<213>  Homo sapiens

<400>  236

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

Ser Leu Arg Ile Ser Cys Ala Ala Ser Gly Phe Thr Val Ser Ser Asn
            20                  25                  30

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

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

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

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

Arg Cys Leu Ser Arg Met Arg Gly Tyr Gly Leu Asp Val Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser
        115


<210>  237
<211>  16
<212>  PRT
<213>  Homo sapiens

<400>  237

Tyr Ile Tyr Asn Arg Gly Ser Thr Lys Tyr Thr Pro Ser Leu Lys Ser
1               5                   10                  15


<210>  238
<211>  11
<212>  PRT
<213>  Homo sapiens
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<400> 238

His Val Gly Gly His Thr Tyr Gly Ile Asp Tyr
1 5 10

<210> 239
<211> 6
<212> PRT
<213> Homo sapiens

<400> 239

Gly Ala Ser Ile Ser Ser
1 5

<210> 240
<211> 9
<212> PRT
<213> Homo sapiens

<400> 240

Tyr Ile Tyr Asn Arg Gly Ser Thr Lys
1 5

<210> 241
<211> 11
<212> PRT
<213> Homo sapiens

<400> 241

Arg Ala Ser Gln Ser Ile Ser Asn Tyr Leu Asn
1 5 10

<210> 242
<211> 5
<212> PRT
<213> Homo sapiens

<400> 242

Tyr Tyr Ala Met Ser
1 5

<210> 243
<211> 9
<212> PRT
<213> Homo sapiens

<400> 243

Gln Gln Ser Tyr Asn Thr Pro Ile Thr
1 5

<210> 244
<211> 353
<212> DNA
<213> Homo sapiens

<400> 244
gaggtgcagc tggtggagtc tgggggaggc ttggtccagc ctgggggtc cctgagaatc 60

tcctgtgcag cctctggatt caccgtcagt agcaactaca tgagttgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagtt attttatagt ggtggtagcac atactacgca 180

gactccgtga agggcagatt ctcctttctcc agagacaact ccaagaacac agtgttttctt 240

caaatgaaca gcctgagagc cgaggacacg gctgtgtatt actgtgcgag atgtctgagc 300

aggatgcggg gttacggttt agacgtctgg ggccaaggga ccacggtcac cgt 353

<210> 245
<211> 17
<212> PRT
<213> Homo sapiens

<400> 245

Lys Ser Ser Gln Ser Ile Leu Asn Ser Ser Asn Asn Lys Asn Tyr Leu
1 5 10 15

Ala

<210> 246
<211> 19
<212> PRT
<213> Homo sapiens

<400> 246

Leu Asn Tyr His Asp Ser Gly Thr Tyr Tyr Asn Ala Pro Arg Gly Trp
1 5 10 15

Phe Asp Pro

<210> 247
<211> 5
<212> PRT
<213> Homo sapiens

<400> 247

Gly Tyr Tyr Val Tyr
1 5

<210> 248
<211> 17
<212> PRT
<213> Homo sapiens

<400> 248

Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 249
<211> 17
<212> PRT
<213> Homo sapiens

<400> 249

Gly Val Ile Pro Ile Phe Arg Thr Ala Asn Tyr Ala Gln Asn Phe Gln
1 5 10 15

Gly

<210> 250
<211> 9
<212> PRT
<213> Homo sapiens

<400> 250

Gln Gln Tyr Tyr Ser Ser Pro Pro Thr
1 5

<210> 251
<211> 5
<212> PRT
<213> Homo sapiens

<400> 251

Ser Tyr Ala Ile Ser
1 5

<210> 252
<211> 5
<212> PRT
<213> Homo sapiens

<400> 252

Ser Tyr Ser Trp Ser
1 5

<210> 253
<211> 16
<212> PRT
<213> Homo sapiens

<400> 253

Tyr Leu Tyr Tyr Ser Gly Ser Thr Lys Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 254
<211> 13
<212> PRT
<213> Homo sapiens

<400> 254

Thr Gly Ser Glu Ser Thr Thr Gly Tyr Gly Met Asp Val
1 5 10

<210> 255
<211> 6
<212> PRT
<213> Homo sapiens

<400> 255

Gly Asp Ser Ile Ser Ser
1 5

<210> 256
<211> 9
<212> PRT
<213> Homo sapiens

<400> 256

Tyr Leu Tyr Tyr Ser Gly Ser Thr Lys
1 5

<210> 257
<211> 12
<212> PRT
<213> Influenza A virus

<400> 257

Gly Ile Thr Asn Lys Glu Asn Ser Val Ile Glu Lys
1 5 10

<210> 258
<211> 7
<212> PRT
<213> Homo sapiens

<400> 258

Ala Ala Ser Ser Leu His Ser
1 5

<210> 259
<211> 9
<212> PRT
<213> Homo sapiens

<400> 259

Gln Gln Ser Tyr Ser Pro Pro Ile Thr
1 5

<210> 260
<211> 5
<212> PRT
<213> Homo sapiens

<400> 260

Asn Ser Phe Trp Gly
1 5

<210> 261
<211> 16
<212> PRT
<213> Homo sapiens

<400> 261

Tyr Val Tyr Asn Ser Gly Asn Thr Lys Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 262
<211> 11
<212> PRT
<213> Homo sapiens

<400> 262

His Asp Asp Ala Ser His Gly Tyr Ser Ile Ser
1 5 10

<210> 263
<211> 6
<212> PRT
<213> Homo sapiens

<400> 263

Gly Gly Ser Ile Ser Asn
1 5

<210> 264
<211> 9
<212> PRT
<213> Homo sapiens

<400> 264

Tyr Val Tyr Asn Ser Gly Asn Thr Lys
1 5

<210> 265
<211> 11
<212> PRT
<213> Homo sapiens

<400> 265

Arg Ala Ser Gln Thr Ile Ser Thr Tyr Leu Asn
1 5 10

<210> 266
<211> 12
<212> PRT
<213> Homo sapiens

<400> 266

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

<210> 267
<211> 9

<212> PRT
<213> Homo sapiens

<400> 267

Gln Gln Ser Tyr Asn Thr Pro Leu Thr
1 5

<210> 268
<211> 5
<212> PRT
<213> Homo sapiens

<400> 268

Ala Tyr His Trp Ser
1 5

<210> 269
<211> 16
<212> PRT
<213> Homo sapiens

<400> 269

His Ile Phe Asp Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 270
<211> 12
<212> PRT
<213> Homo sapiens

<400> 270

Pro Leu Gly Ser Arg Tyr Tyr Tyr Gly Met Asp Val
1 5 10

<210> 271
<211> 6
<212> PRT
<213> Homo sapiens

<400> 271

Gly Gly Ser Ile Ser Ala
1 5

<210> 272
<211> 9
<212> PRT
<213> Homo sapiens

<400> 272

His Ile Phe Asp Ser Gly Ser Thr Tyr
1 5

<210> 273
<211> 11
<212> PRT
<213> Homo sapiens

<400> 273

Arg Ala Ser Gln Ser Ile Ser Arg Tyr Leu Asn
1 5 10

<210> 274
<211> 7
<212> PRT
<213> Homo sapiens

<400> 274

Gly Ala Ser Thr Leu Gln Asn
1 5

<210> 275
<211> 8
<212> PRT
<213> Homo sapiens

<400> 275

Gln Gln Ser Tyr Ser Val Pro Ala
1 5

<210> 276
<211> 120
<212> PRT
<213> Homo sapiens

<400> 276

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

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

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

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

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

Thr Met Ser Ser Val Thr Ala Ala Glu Ser Ala Val Tyr Phe Cys Ala
85 90 95

Arg Ala Ser Cys Ser Gly Gly Tyr Cys Ile Leu Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 277
<211> 117
<212> PRT
<213> Homo sapiens

<400> 277

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

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

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

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

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

Thr Met Ser Ser Val Thr Ala Ala Glu Ser Ala Val Tyr Phe Cys Ala
85 90 95

Arg Ala Ser Cys Ser Gly Gly Tyr Cys Ile Leu Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr
115

<210> 278
<211> 353
<212> DNA
<213> Homo sapiens

<400> 278
caggtgcaat tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc 60

acctgcactg tctctggttc gtccatcagt aattactact ggagctggat ccggcagtcc 120

ccagggaagg gactggagtg gattgggtat atctattacg gtggaaacac caagtacaat 180

ccctccctca agagccgcgt caccatatca caagacactt ccaagagtca ggtctccctg 240

acgatgagct ctgtgaccgc tgcggaatcg gccgtctatt tctgtgcgag agcgtcttgt 300

agtggtggtt actgtatcct tgactactgg ggccagggaa ccctggtcac cgt 353

<210> 279
<211> 1335
<212> DNA
<213> Homo sapiens

<400> 279
gaggtccagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctgggta caccttcacc ggctactatg tgtactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagt tccagggcag agtcacgatt accgcggaca aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaagac acggctgtgt attactgtgc gagaagtaga 300

tccctggacg tctggggcca agggaccacg gtcaccgtct cgagtgctag caccaagggc 360

cccagcgtgt tccccctggc ccccagcagc aagagcacca gcggcggcac agccgccctg 420

ggctgcctgg tgaaggacta cttccccgag cccgtgaccg tgagctggaa cagcggcgcc 480

ttgaccagcg gcgtgcacac cttccccgcc gtgctgcaga gcagcggcct gtacagcctg 540

agcagcgtgg tgaccgtgcc cagcagcagc ctgggcaccc agacctacat ctgcaacgtg 600

aaccacaagc ccagcaacac caaggtggac aaacgcgtgg agcccaagag ctgcgacaag 660

acccacacct gcccccctg ccctgccccc gagctgctgg gcggaccctc cgtgttcctg 720

ttccccccca agcccaagga caccctcatg atcagccgga ccccgaggt gacctgcgtg 780

gtggtggacg tgagccacga ggaccccgag gtgaagttca actggtacgt ggacggcgtg 840

gaggtgcaca acgccaagac caagccccgg gaggagcagt acaacagcac ctaccgggtg 900

gtgagcgtgc tcaccgtgct gcaccaggac tggctgaacg gcaaggagta caagtgcaag 960

gtgagcaaca aggccctgcc tgcccccatc gagaagacca tcagcaaggc caagggccag 1020

ccccgggagc cccaggtgta caccctgccc cccagccggg aggagatgac caagaaccag 1080

gtgtccctca cctgtctggt gaagggcttc tatccccagcg acatcgccgt ggagtgggag 1140

agcaacggcc agcccgagaa caactacaag accacccccc ctgtgctgga cagcgacggc 1200

agcttcttcc tgtacagcaa gctcaccgtg gacaagagcc ggtggcagca gggcaacgtg 1260

ttcagctgca gcgtgatgca cgaggccctg cacaaccact acacccagaa gagcctgagc 1320

ctgagccccg gcaag 1335

<210> 280
<211> 11
<212> PRT
<213> Homo sapiens

<400> 280

Gly Thr Trp Asp Ser Ser Leu Ser Ala Tyr Val
1 5 10

<210> 281
<211> 12
<212> PRT
<213> Influenza A virus

<400> 281

Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu Lys
1 5 10

<210> 282
<211> 7
<212> PRT

<213> Homo sapiens

<400> 282

Gly Ala Thr Asp Leu Gln Ser
1 5

<210> 283
<211> 12
<212> PRT
<213> Influenza A virus

<400> 283

Gly Val Thr Asn Lys Val Asn Ser Ile Ile Asn Lys
1 5 10

<210> 284
<211> 5
<212> PRT
<213> Influenza A virus

<400> 284

Asp Asn Tyr Ile Asn
1 5

<210> 285
<211> 16
<212> PRT
<213> Homo sapiens

<400> 285

Val Phe Tyr Ser Ala Asp Arg Thr Ser Tyr Ala Asp Ser Val Lys Gly
1 5 10 15

<210> 286
<211> 10
<212> PRT
<213> Homo sapiens

<400> 286

Val Gln Lys Ser Tyr Tyr Gly Met Asp Val
1 5 10

<210> 287
<211> 6
<212> PRT
<213> Homo sapiens

<400> 287

Gly Phe Ser Val Ser Asp
1 5

<210> 288
<211> 9
<212> PRT
<213> Homo sapiens

<400> 288

Val Phe Tyr Ser Ala Asp Arg Thr Ser
1 5

<210> 289
<211> 9
<212> PRT
<213> Homo sapiens

<400> 289

Gln Gln Tyr Tyr Ser Thr Pro Leu Thr
1 5

<210> 290
<211> 11
<212> PRT
<213> Homo sapiens

<400> 290

Ser Ser Asn Tyr Tyr Asp Ser Val Tyr Asp Tyr
1 5 10

<210> 291
<211> 8
<212> PRT
<213> Homo sapiens

<400> 291

Gln Gln Thr Phe Ser Ile Pro Leu
1 5

<210> 292
<211> 107
<212> PRT
<213> Homo sapiens

<400> 292

Asp Ile Gln Val 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 Asn Ile Tyr Lys Tyr
20 25 30

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

Ser Ala Ala Ser Gly 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 Thr Ser Leu Gln Pro
65 70 75 80

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

Thr Phe Gly Gly Gly Thr Arg Val Asp Ile Lys
100 105

<210> 293
<211> 7
<212> PRT
<213> Homo sapiens

<400> 293

Ser Gly Ala Tyr Tyr Trp Thr
1 5

<210> 294
<211> 16
<212> PRT
<213> Homo sapiens

<400> 294

Tyr Ile Tyr Tyr Ser Gly Asn Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 295
<211> 13
<212> PRT
<213> Homo sapiens

<400> 295

Ala Ala Ser Thr Ser Val Leu Gly Tyr Gly Met Asp Val
1 5 10

<210> 296
<211> 8
<212> PRT
<213> Homo sapiens

<400> 296

Gly Asp Ser Ile Thr Ser Gly Ala
1 5

<210> 297
<211> 9
<212> PRT
<213> Homo sapiens

<400> 297

Tyr Ile Tyr Tyr Ser Gly Asn Thr Tyr
1 5

<210> 298

<400> 298
000

<210> 299
<211> 5

<212> PRT
<213> Homo sapiens

<400> 299

Ser Tyr Ala Phe Ser
1 5

<210> 300
<211> 9
<212> PRT
<213> Homo sapiens

<400> 300

Gln Gln Ser Tyr Ser Thr Pro Leu Thr
1 5

<210> 301
<211> 7
<212> PRT
<213> Homo sapiens

<400> 301

Val Ser Asp Asn Tyr Ile Asn
1 5

<210> 302
<211> 5
<212> PRT
<213> Homo sapiens

<400> 302

Thr Asn Ala Phe Ser
1 5

<210> 303

<400> 303
000

<210> 304
<211> 5
<212> PRT
<213> Homo sapiens

<400> 304

Ser Gly Phe Ser Val
1 5

<210> 305
<211> 5
<212> PRT
<213> Homo sapiens

<400> 305

Ala Tyr Ala Phe Thr
1 5

<210> 306
<211> 17
<212> PRT
<213> Homo sapiens

<400> 306

Gly Ile Ile Ala Ile Phe His Thr Pro Lys Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 307
<211> 17
<212> PRT
<213> Homo sapiens

<400> 307

Gly Ile Ser Pro Met Phe Gly Thr Thr Thr Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 308
<211> 9
<212> PRT
<213> Homo sapiens

<400> 308

Gln Gln Tyr Gly Ser Ser Ser Leu Thr
1 5

<210> 309
<211> 115
<212> PRT
<213> Homo sapiens

<400> 309

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 Thr Gly Tyr
20 25 30

Tyr Val Tyr 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 Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr 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 Ser Arg Ser Leu Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 310
<211> 114
<212> PRT
<213> Homo sapiens

<400> 310

Asp Val 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 Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile
100 105 110

Lys Arg

<210> 311
<211> 735
<212> DNA
<213> Homo sapiens

<400> 311
gaggtccagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctgggta cacctcacc ggctactatg tgtactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagt tccagggcag agtcacgatt accgcggaca aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaagac acggctgtgt attactgtgc gagaagtaga 300

tccctggacg tctggggcca agggaccacg gtcaccgtct cgagcggtac gggcggttca 360

ggcggaaccg gcagcggcac tggcgggtcg acggatgttg tgatgactca gtctccagac 420

tccctggctg tgtctctggg cgagagggcc accatcaact gcaagtccag ccagagtgtt 480

ttatacagct ccaacaataa gaacttactta gcttggtacc agcagaaacc aggacagcct 540

cctaagctgc tcatttactg ggcatctacc cgggaatccg gggtccctga ccgattcagt 600

ggcagcgggt ctgggacaga tttcactctc accatcagca gcctgcaggc tgaagatgtg 660

gcagttatt actgtcagca atattatagt actcctctca ctttcggcgg agggaccaaa 720

gtggatatca aacgt 735

<210> 312
<211> 245
<212> PRT
<213> Homo sapiens

<400> 312

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 Thr Gly Tyr
20 25 30

Tyr Val Tyr 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 Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr 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 Ser Arg Ser Leu Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Gly Thr Gly Gly Ser Gly Gly Thr Gly Ser Gly Thr Gly
115 120 125

Gly Ser Thr Asp Val Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val
130 135 140

Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val
145 150 155 160

Leu Tyr Ser Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys
165 170 175

Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu
180 185 190

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr
210 215 220

Cys Gln Gln Tyr Tyr Ser Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Val Asp Ile Lys Arg
245

<210> 313
<211> 121
<212> PRT
<213> Homo sapiens

<400> 313

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 314
<211> 111
<212> PRT
<213> Homo sapiens

<400> 314

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

Arg Val Thr Ile Ser Cys Ser Gly Ser Thr Phe Asn Ile Gly Ser Asn
20 25 30

Ala Val Asp Trp Tyr Arg Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Arg Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ile Leu
85 90 95

Asn Val Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> 315
<211> 744
<212> DNA
<213> Homo sapiens

<400> 315
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggtac aacaaaatac 180

gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt attactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gtcctatgtg 420

ctgactcagc caccctcagc gtctgggacc cccgggcaga gggtcaccat ctcttgttct 480

ggaagcacgt tcaacatcgg aagtaatgct gtagactggt accggcagct cccaggaacg 540

gcccccaaac tcctcatcta tagtaataat cagcggccct caggggtccc tgaccgattc 600

tctggctcca ggtctggcac tcagcctcc ctggccatca gtgggctcca gtctgaggat 660

gaggctgatt attactgtgc agcatgggat gacatcctga atgttccggt attcggcgga 720

gggaccaagc tgaccgtcct aggt 744

<210> 316
<211> 248
<212> PRT
<213> Homo sapiens

<400> 316

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Gly Ser Thr Ser Tyr Val Leu Thr Gln Pro
130 135 140

Pro Ser Ala Ser Gly Thr Pro Gly Gln Arg Val Thr Ile Ser Cys Ser
145 150 155 160

Gly Ser Thr Phe Asn Ile Gly Ser Asn Ala Val Asp Trp Tyr Arg Gln
165 170 175

Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Ser Asn Asn Gln Arg
180 185 190

Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Arg Ser Gly Thr Ser
195 200 205

Ala Ser Leu Ala Ile Ser Gly Leu Gln Ser Glu Asp Glu Ala Asp Tyr
210 215 220

Tyr Cys Ala Ala Trp Asp Asp Ile Leu Asn Val Pro Val Phe Gly Gly
225 230 235 240

Gly Thr Lys Leu Thr Val Leu Gly
245

<210> 317
<211> 121
<212> PRT
<213> Homo sapiens

<400> 317

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 318
<211> 111
<212> PRT
<213> Homo sapiens

<400> 318

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

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

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

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> 319
<211> 744
<212> DNA
<213> Homo sapiens

<400> 319
caggtccagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggtac aacaaaatac 180

gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gcagtctgcc 420

ctgactcagc ctgccgccgt gtctgggtct cctggacagt cgatcaccat ctcctgcact 480

ggaaccagca gtgacgttgg tggttataac tatgtctcct ggtaccaaca gcacccaggc 540

aaagccccca aactcatgat ttatgaggtc agtaatcggc cctcaggggt ttctaatcgc 600

ttctctggct ccaagtctgg caacacggcc tccctgacca tctctgggct ccaggctgag 660

gacgaggctg attattactg cagctcatat acaagcagca gcacttatgt cttcggaact 720

gggaccaagg tcaccgtcct aggt 744

<210> 320
<211> 248
<212> PRT
<213> Homo sapiens

<400> 320

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Gly Ser Thr Gln Ser Ala Leu Thr Gln Pro
130 135 140

Ala Ala Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser Cys Thr
145 150 155 160

Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln
165 170 175

Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Glu Val Ser Asn
180 185 190

Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn
195 200 205

Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp
210 215 220

Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr Tyr Val Phe Gly Thr
225 230 235 240

Gly Thr Lys Val Thr Val Leu Gly
245

<210> 321
<211> 121
<212> PRT
<213> Homo sapiens

<400> 321

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly

100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 322
<211> 111
<212> PRT
<213> Homo sapiens

<400> 322

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Arg Ser Asn Val Gly Asp Asn
20 25 30

Ser Val Tyr Trp Tyr Gln His Val Pro Glu Met Ala Pro Lys Leu Leu
35 40 45

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

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ile Gly Leu Gln
65 70 75 80

Ser Gly Asp Glu Ala Asp Tyr Tyr Cys Val Ala Trp Asp Asp Ser Val
85 90 95

Asp Gly Tyr Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> 323
<211> 744
<212> DNA
<213> Homo sapiens

<400> 323
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggtac aacaaaatac 180

gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agcggtacgg gcggttcagg cggaaccggc agcgacactg gcgggtcgac gtcctatgtg 420

ctgactcagc caccctcagt ctctgggacc cccgggcaga gggtcaccat ctcttgctct 480

ggaagccgct ccaacgtcgg agataattct gtatattggt atcaacacgt cccagaaatg 540

gcccccaaac tcctcgtcta taagaatact caacggccct caggagtccc tgcccggttt 600

tccggctcca agtctggcac ttcagcctcc ctggccatca ttggcctcca gtccggcgat 660

gaggctgatt attattgtgt ggcatgggat gacagcgtag atggctatgt cttcggatct 720

gggaccaagg tcaccgtcct aggt 744

<210> 324
<211> 248
<212> PRT
<213> Homo sapiens

<400> 324

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Gly Ser Thr Ser Tyr Val Leu Thr Gln Pro
130 135 140

Pro Ser Val Ser Gly Thr Pro Gly Gln Arg Val Thr Ile Ser Cys Ser
145 150 155 160

Gly Ser Arg Ser Asn Val Gly Asp Asn Ser Val Tyr Trp Tyr Gln His
165 170 175

Val Pro Glu Met Ala Pro Lys Leu Leu Val Tyr Lys Asn Thr Gln Arg
180 185 190

Pro Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser
195 200 205

Ala Ser Leu Ala Ile Ile Gly Leu Gln Ser Gly Asp Glu Ala Asp Tyr
210 215 220

Tyr Cys Val Ala Trp Asp Asp Ser Val Asp Gly Tyr Val Phe Gly Ser
225 230 235 240

Gly Thr Lys Val Thr Val Leu Gly
245

<210> 325
<211> 121
<212> PRT
<213> Homo sapiens

<400> 325

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 326
<211> 111
<212> PRT
<213> Homo sapiens

<400> 326

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

Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Asn Asp Tyr
20 25 30

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

Tyr Asp Asn Asn Lys Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly
50 55 60

Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln Thr
65 70 75 80

Gly Asp Glu Ala Asn Tyr Tyr Cys Ala Thr Trp Asp Arg Arg Pro Thr
85 90 95

Ala Tyr Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> 327
<211> 747
<212> DNA
<213> Homo sapiens

<400> 327
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggtac aacaaaatac 180

gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gcagtctgtg 420

ttgacgcagc cgccctcagt gtctgcggcc ccaggacaga aggtcaccat ctcctgctct 480

ggaagcagct ccaacattgg gaatgattat gtatcctggt accagcagct cccaggaaca 540

gcccccaaac tcctcatta tgacaataat aagcgaccct cagggattcc tgaccgattc 600

tctggctcca agtctggcac gtcagccacc ctgggcatca ccggactcca gactggggac 660

gaggccaact attactgcgc aacatgggat cgccgcccga ctgcttatgt tgtcttcggc 720

ggagggacca agctgaccgt cctaggt 747

<210> 328
<211> 249
<212> PRT
<213> Homo sapiens

<400> 328

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Gly Ser Thr Gln Ser Val Leu Thr Gln Pro
130 135 140

Pro Ser Val Ser Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys Ser
145 150 155 160

Gly Ser Ser Ser Asn Ile Gly Asn Asp Tyr Val Ser Trp Tyr Gln Gln
165 170 175

Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Asp Asn Asn Lys Arg
180 185 190

Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser
195 200 205

Ala Thr Leu Gly Ile Thr Gly Leu Gln Thr Gly Asp Glu Ala Asn Tyr
210 215 220

Tyr Cys Ala Thr Trp Asp Arg Arg Pro Thr Ala Tyr Val Val Phe Gly
225 230 235 240

Gly Gly Thr Lys Leu Thr Val Leu Gly
245

<210> 329
<211> 120
<212> PRT
<213> Homo sapiens

<400> 329

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

Ser Val Lys Val Ser Cys Lys Val Ser Gly Val Ile Phe Ser Gly Ser
20 25 30

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

35 40 45

Gly Gly Ile Ser Pro Leu Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Gln Ser Thr Asn Thr Thr Tyr
65 70 75 80

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

Ala Arg Gly Pro Lys Tyr Tyr Ser Glu Tyr Met Asp Val Trp Gly Lys
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 330
<211> 109
<212> PRT
<213> Homo sapiens

<400> 330

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

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

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

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

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

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

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

<210> 331
<211> 735
<212> DNA
<213> Homo sapiens

<400> 331
caggtacagc tgcagcagtc aggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg tttccggagt cattttcagc ggcagtgcga tcagctgggt gcgacaggcc 120

cctggacaag gccttgagtg gatgggaggg atcagccctc tctttggcac aacaaattac 180

gcacaaaagt tccagggcag agtcacgatt accgcggacc aatccacgaa cacaacctac 240

atggaggtga acagcctgag atatgaggac acggccgtgt attctgtgc gcgaggtcca 300

aaatattaca gtgagtacat ggacgtctgg ggcaaaggga ccacggtcac cgtctcgagc 360

ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgga catccagatg 420

acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg 480

gcgagtcagg gcattagcag ttatttagcc tggtatcagc agaagccagg gaaagttcct 540

acactcctga tctatgatgc atccactttg cgatcagggg tcccatctcg cttcagtggc 600

agtggatctg cgacagattt cactctcacc atcagcagcc tgcagcctga agatgttgca 660

acttattact gtcaaaggta taacagtgcc cccccgatca ccttcggcca agggacacga 720

ctggagatta aacgt 735

<210> 332
<211> 245
<212> PRT
<213> Homo sapiens

<400> 332

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

Ser Val Lys Val Ser Cys Lys Val Ser Gly Val Ile Phe Ser Gly Ser
20 25 30

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

Gly Gly Ile Ser Pro Leu Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Gln Ser Thr Asn Thr Thr Tyr
65 70 75 80

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

Ala Arg Gly Pro Lys Tyr Tyr Ser Glu Tyr Met Asp Val Trp Gly Lys
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly Thr
115 120 125

Gly Ser Gly Thr Gly Gly Ser Thr Asp Ile Gln Met Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

Ala Ser Gln Gly Ile Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Val Pro Thr Leu Leu Ile Tyr Asp Ala Ser Thr Leu Arg Ser
180 185 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Ala Thr Asp Phe Thr
195 200 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Val Ala Thr Tyr Tyr Cys
210 215 220

Gln Arg Tyr Asn Ser Ala Pro Pro Ile Thr Phe Gly Gln Gly Thr Arg
225 230 235 240

Leu Glu Ile Lys Arg
245

<210> 333
<211> 120
<212> PRT
<213> Homo sapiens

<400> 333

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

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

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

Gly Gly Ile Met Gly Met Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Ala Ala Tyr
65 70 75 80

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

Ala Arg Ser Ser Gly Tyr Tyr Pro Glu Tyr Phe Gln Asp Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 334
<211> 107
<212> PRT

<213> Homo sapiens

<400> 334

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

Thr Ala Ser Val Thr Cys Ser Gly His Lys Leu Gly Asp Lys Tyr Val
20 25 30

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

Gln Asp Asn Arg Arg Pro Ser Gly Ile Pro Glu Arg Phe Ile Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Leu
65 70 75 80

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

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

<210> 335
<211> 729
<212> DNA
<213> Homo sapiens

<400> 335
caggtccagc tggtacagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccttcagt agttatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggagga atcatgggta tgttggcac aactaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aattcacgag cgcagcctac 240

atggagctga ggagcctgag atctgaggac acggccgtct actactgtgc gaggtctagt 300

ggttattacc ccgaatactt ccaggactgg ggccagggca ccctggtcac cgtctcgagc 360

ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgca gtctgtgctg 420

actcagccac cctcagagtc cgtgtcccca ggacagacag ccagcgtcac ctgctctgga 480

cataaattgg gggataaata tgtttcgtgg tatcagcaga agccaggcca gtccctgta 540

ttactcatct atcaagataa caggcggccc tcagggatcc ctgagcgatt catggctcc 600

aactctggga acacagccac tctgaccatc agcgggaccc aggctctgga tgaggctgac 660

tattactgtc aggcgtggga cagcagcact gcggttttcg gcggagggac caagctgacc 720

gtcctaggt 729

<210> 336
<211> 243
<212> PRT

<213> Homo sapiens

<400> 336

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

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

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

Gly Gly Ile Met Gly Met Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Ala Ala Tyr
65 70 75 80

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

Ala Arg Ser Ser Gly Tyr Tyr Pro Glu Tyr Phe Gln Asp Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly Thr
115 120 125

Gly Ser Gly Thr Gly Gly Ser Thr Gln Ser Val Leu Thr Gln Pro Pro
130 135 140

Ser Glu Ser Val Ser Pro Gly Gln Thr Ala Ser Val Thr Cys Ser Gly
145 150 155 160

His Lys Leu Gly Asp Lys Tyr Val Ser Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Ser Pro Val Leu Leu Ile Tyr Gln Asp Asn Arg Arg Pro Ser Gly
180 185 190

Ile Pro Glu Arg Phe Ile Gly Ser Asn Ser Gly Asn Thr Ala Thr Leu
195 200 205

Thr Ile Ser Gly Thr Gln Ala Leu Asp Glu Ala Asp Tyr Tyr Cys Gln
210 215 220

Ala Trp Asp Ser Ser Thr Ala Val Phe Gly Gly Gly Thr Lys Leu Thr
225 230 235 240

Val Leu Gly

<210> 337
<211> 120
<212> PRT
<213> Homo sapiens

<400> 337

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

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

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

Gly Gly Ile Ile Gly Met Phe Gly Ser Thr Asn Tyr Ala Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr 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 Ser Thr Gly Tyr Tyr Pro Ala Tyr Leu His His Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 338
<211> 111
<212> PRT
<213> Homo sapiens

<400> 338

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

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

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

Met Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr His Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> 339
<211> 741
<212> DNA
<213> Homo sapiens

<400> 339
cagatgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccttctcc agttatgcta tcacctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcggta tgtttggttc aacaaactac 180

gcacagaact tccagggcag agtcacgatt accgcggacg aatccacgag cacagcctac 240

atggagctga gcagcctcag atctgaggac acggccgtgt attactgtgc gagaagtact 300

ggttattacc ctgcatacct ccaccactgg ggccagggca ccctggtcac cgtctcgagc 360

ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgca gtctgccctg 420

actcagcctc gctcagtgtc cgggtctcct ggacagtcag tcaccatctc ctgcactgga 480

accagcagtg atgttggtgg ttatAactat gtctcctggt accaacagca cccaggcaaa 540

gcccccaaac tcatgattta tgatgtcagt aagcggccct caggggtccc tgatcgcttc 600

tctggctcca agtctggcaa cacggcctcc ctgaccatct ctgggctcca ggctgaggat 660

gaggctgatt attactgcag ctcatatACa agcagcagca ctcatgtctt cggaactggg 720

accaaggtca ccgtcctagg t 741

<210> 340
<211> 246
<212> PRT
<213> Homo sapiens

<400> 340

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

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

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

Gly Gly Ile Ile Gly Met Phe Gly Ser Thr Tyr Ala Gln Asn Phe Gln
50 55 60

Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr Met
65 70 75 80

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

Arg Ser Thr Gly Tyr Tyr Pro Ala Tyr Leu His His Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly Thr Gly
115 120 125

Ser Gly Thr Gly Gly Ser Thr Gln Ser Ala Leu Thr Gln Pro Arg Ser
130 135 140

Val Ser Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr
145 150 155 160

Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His
165 170 175

Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Lys Arg Pro
180 185 190

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala
195 200 205

Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr
210 215 220

Cys Ser Ser Tyr Thr Ser Ser Ser Thr His Val Phe Gly Thr Gly Thr
225 230 235 240

Lys Val Thr Val Leu Gly
245

<210> 341
<211> 121
<212> PRT
<213> Homo sapiens

<400> 341

Glu Val Gln Leu Val Glu Thr 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 Ser Tyr
20 25 30

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

Gly Trp Ile Asn Pro 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 Glu Gly Lys Trp Gly Pro Gln Ala Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 342
<211> 109
<212> PRT
<213> Homo sapiens

<400> 342

Glu 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 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 Asp Ala Ser Ser Arg Ala Thr Asp 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 Leu
85 90 95

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

<210> 343
<211> 738
<212> DNA
<213> Homo sapiens

<400> 343
gaggtgcagc tggtggagac cggggctgag gtgaagaagc ctggggcctc agtgaaggtt 60

tcctgcaagg catctggata cacctcacc agctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaaccct acagtggtgg cacaaactat 180

gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcag cacagcctac 240

atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gagagagggg 300

aaatggggac ctcaagcggc ttttgatatc tggggccaag ggacaatggt caccgtctcg 360

agcggtacgg gcggttcagg cggaaccggc agtggcagtg gcgggtcgac ggaaattgtg 420

atgacgcagt ctccaggcac cctgtctttg tctccagggg aaagagccac cctctcctgc 480

agggccagtc agagtgttag cagcagctac ttagcctggt accagcagaa acctggccag 540

gctcccaggc tcctcatcta tgatgcatcc agcagggcca ctgacatccc agacaggttc 600

agtggcagtg ggtctgggac agacttcact ctcaccatca gcagactgga gcctgaagat 660

tttgcagtgt attactgtca gcagtatggt agctcacttt ggacgttcgg ccaagggacc 720

aaggtggaga tcaaacgt 738

<210> 344
<211> 246
<212> PRT
<213> Homo sapiens

<400> 344

Glu Val Gln Leu Val Glu Thr 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 Ser Tyr
20 25 30

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

Gly Trp Ile Asn Pro 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 Glu Gly Lys Trp Gly Pro Gln Ala Ala Phe Asp Ile Trp Gly
100 105 110

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

Thr Gly Ser Gly Thr Gly Gly Ser Thr Glu Ile Val Met Thr Gln Ser
130 135 140

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln
165 170 175

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Ser Arg
180 185 190

Ala Thr Asp Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
210 215 220

Tyr Cys Gln Gln Tyr Gly Ser Ser Leu Trp Thr Phe Gly Gln Gly Thr
225 230 235 240

Lys Val Glu Ile Lys Arg
245

<210> 345
<211> 117
<212> PRT
<213> Homo sapiens

<400> 345

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

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

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

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

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg 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 Ala Tyr Gly Tyr Thr Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 346
<211> 113
<212> PRT
<213> Homo sapiens

<400> 346

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

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

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

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

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

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

Arg

<210> 347
<211> 738
<212> DNA
<213> Homo sapiens

<400> 347
gaggtgcagc tggtagagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt caccttt agc atctatgcca tgagctgggt ccgccaggca 120

ccagggaagg ggctggagtg ggtctcagct attagtagta gtggtgatag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca acgccaggaa cacgctgtat 240

ctgcaaatga acagtctgag agccgaggac acggctgtgt attactgtgc gagagcgtat 300

ggctacacgt tcgacccctg gggccaggga accctggtca ccgtctcgag cggtacgggc 360

ggttcaggcg gaaccggcag cggcactggc gggtcgacgg aaattgtgct gactcagtct 420

ccactctccc tgcccgtcac ccctggagag ccggcctcca tctcctgcag gtctagtcag 480

agcctcctgc atagtaatgg atacaactat ttggattggt acctgcagaa gccagggcag 540

tctccacagc tcctgatcta tttgggttct aatcgggcct ccggggtccc tgacaggttc 600

agtggcagtg gatcaggcac agattttaca ctgaaaatca gcagagtgga ggctgaggat 660

gttggggttt attactgcat gcaagctcta caaactcccc tcactttcgg cggagggacc 720

aaggtggaga tcaaacgt 738

<210> 348
<211> 246
<212> PRT
<213> Homo sapiens

<400> 348

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

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

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

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

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg 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 Ala Tyr Gly Tyr Thr Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly Thr Gly Ser Gly
115 120 125

Thr Gly Gly Ser Thr Glu Ile Val Leu Thr Gln Ser Pro Leu Ser Leu
130 135 140

Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln
145 150 155 160

Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln
165 170 175

Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg
180 185 190

Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr
210 215 220

Tyr Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr
225 230 235 240

Lys Val Glu Ile Lys Arg
245

<210> 349
<211> 122
<212> PRT
<213> Homo sapiens

<400> 349

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

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

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

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Gly Gly Gly Ser Tyr Gly Ala Tyr Glu Gly Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 350
<211> 108
<212> PRT
<213> Homo sapiens

<400> 350

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

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

Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Arg Thr Pro Leu
85 90 95

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

<210> 351
<211> 738
<212> DNA
<213> Homo sapiens

<400> 351
caggtccagc tggtgcagtc tgggggaggc ctggtcaagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt caccttcagt agctatagca tgaactgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcatcc attagtagta gtagttacat acactactac 180

gtagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat 240

ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagaggtggt 300

gggagctacg gggcctacga aggcttttgac tactggggcc agggcaccct ggtcaccgtc 360

tcgagcggta cgggcggttc aggcggaacc ggcagcggca ctggcgggtc gacggaaatt 420

gtgctgactc agtctccagg caccctgtct ttgtctccag gggaaagagc caccctctcc 480

tgcagggcca gtcagcgtgt tagcagctac ttagcctggt accaacagaa acctggccag 540

gctcccaggc tcctcatcta tggtgcatcc accagggccg ctggcatccc agacaggttc 600

agtggcagtg ggtctgggac agacttcact ctcaccatca gcagactgga gcctgaagat 660

tctgcagtgt attactgtca gcagtatggt aggacaccgc tcacttttcgg cggagggacc 720

aaggtggaga tcaaacgt 738

<210> 352
<211> 246
<212> PRT
<213> Homo sapiens

<400> 352

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

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

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

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Gly Gly Gly Ser Tyr Gly Ala Tyr Glu Gly Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly
115 120 125

Gly Thr Gly Ser Gly Thr Gly Gly Ser Thr Glu Ile Val Leu Thr Gln
130 135 140

Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser
145 150 155 160

Cys Arg Ala Ser Gln Arg Val Ser Ser Tyr Leu Ala Trp Tyr Gln Gln
165 170 175

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg
180 185 190

Ala Ala Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Ser Ala Val Tyr
210 215 220

Tyr Cys Gln Gln Tyr Gly Arg Thr Pro Leu Thr Phe Gly Gly Gly Thr
225 230 235 240

Lys Val Glu Ile Lys Arg
245

<210> 353
<211> 121
<212> PRT
<213> Homo sapiens

<400> 353

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly

100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 354
<211> 109
<212> PRT
<213> Homo sapiens

<400> 354

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

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Ala Val Phe Gly Gly Gly Thr Gln Leu Thr Val Leu Gly
100 105

<210> 355
<211> 738
<212> DNA
<213> Homo sapiens

<400> 355
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggtac aacaaaatac 180

gcaccgaagt tccagagcag agtcacgatt accacggacg atttcgcggg cacagttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gtcctatgtg 420

ctgactcagc caccctcggt gtcagtggcc ccaggacaga cggccaggat tacctgtggg 480

ggaaacaaca ttggaagtaa aagtgtgcac tggtaccagc agaagccagg ccaggccct 540

gtgctggtcg tctatgatga tagcgaccgg ccctcaggga tccctgagcg attctctggc 600

tccaactctg ggaacacggc cacccctgacc atcagcaggg tcgaagccgg ggatgaggcc 660

gactattact gtcaggtgtg ggatagtagt agtgatcatg ctgtgttcgg aggaggcacc 720

cagctgaccg tcctcggt 738

<210> 356
<211> 246
<212> PRT
<213> Homo sapiens

<400> 356

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Gly Ser Thr Ser Tyr Val Leu Thr Gln Pro
130 135 140

Pro Ser Val Ser Val Ala Pro Gly Gln Thr Ala Arg Ile Thr Cys Gly
145 150 155 160

Gly Asn Asn Ile Gly Ser Lys Ser Val His Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Gln Ala Pro Val Leu Val Val Tyr Asp Asp Ser Asp Arg Pro Ser
180 185 190

Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr
195 200 205

Leu Thr Ile Ser Arg Val Glu Ala Gly Asp Glu Ala Asp Tyr Tyr Cys
210 215 220

Gln Val Trp Asp Ser Ser Ser Asp His Ala Val Phe Gly Gly Gly Thr
225 230 235 240

Gln Leu Thr Val Leu Gly
245

<210> 357
<211> 121
<212> PRT
<213> Homo sapiens

<400> 357

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 358
<211> 111
<212> PRT
<213> Homo sapiens

<400> 358

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

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

Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Arg Asp Gly Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65 70 75 80

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

Ser Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> 359
<211> 744
<212> DNA
<213> Homo sapiens

<400> 359
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggtac aacaaaatac 180

gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagtttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gtcctatgtg 420

ctgactcagc caccctcagc gtctgggacc cccgggcaga gggtcaccat ctcttgttct 480

ggaagcagct ccaacatcgg aagtaattat gtatactggt accagcagct cccaggcacg 540

gcccccaaac tcctcatcta tagggatggt cagcggccct caggggtccc tgaccgattc 600

tctggctcca agtctggcac ctcagcctcc ctggccatca gtggactccg gtccgatgat 660

gaggctgatt attactgtgc aacatgggat gacaacctga gtggtccagt attcggcgga 720

gggaccaagc tgaccgtcct aggt 744

<210> 360
<211> 248
<212> PRT
<213> Homo sapiens

<400> 360

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Gly Ser Thr Ser Tyr Val Leu Thr Gln Pro
130 135 140

Pro Ser Ala Ser Gly Thr Pro Gly Gln Arg Val Thr Ile Ser Cys Ser
145 150 155 160

Gly Ser Ser Ser Asn Ile Gly Ser Asn Tyr Val Tyr Trp Tyr Gln Gln
165 170 175

Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Arg Asp Gly Gln Arg
180 185 190

Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser
195 200 205

Ala Ser Leu Ala Ile Ser Gly Leu Arg Ser Asp Asp Glu Ala Asp Tyr
210 215 220

Tyr Cys Ala Thr Trp Asp Asp Asn Leu Ser Gly Pro Val Phe Gly Gly
225 230 235 240

Gly Thr Lys Leu Thr Val Leu Gly
245

<210> 361
<211> 120
<212> PRT
<213> Homo sapiens

<400> 361

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

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

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

35 40 45

Gly Asp Ile Ile Gly Met Phe Gly Ser Thr Asn Tyr Ala Gln Asn Phe
50 55 60

Gln Gly Arg Leu Thr Ile Thr Ala Asp Glu Ser Thr 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 Ser Ser Gly Tyr Tyr Pro Ala Tyr Leu Pro His Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 362
<211> 109
<212> PRT
<213> Homo sapiens

<400> 362

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

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

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

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

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

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

<210> 363
<211> 735
<212> DNA
<213> Homo sapiens

<400> 363
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc cagggtcctc ggtgaaggtc 60

tcctgtaagg cctctggagg caccttctcc agctatggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggagac atcatcggta tgttttggtt caacaaactac 180

gcacagaact tccagggcag actcacgatt accgcggacg aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagaagtagt 300

ggttattacc ctgcatacct ccccactgg ggccagggca ccttggtcac cgtctcgagc 360

ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgga aattgtgttg 420

acccagtctc caggcaccct gtctttgtct ccaggggaaa gagccaccct ctcctgcagg 480

gccagtcaga gtgttagcag cagctacttа gcctggtacc agcagaaacc tggccaggct 540

cccaggctcc tcatctatgg tgcatccagc agggccactg gcatcccaga caggttcagt 600

ggcagtgggt ctgggacaga cttcactctc accatcagca gactggagcc tgaagatttt 660

gcagtgtatt actgtcagca gtatggtagc tcacccagaa ctttcggcgg agggaccaag 720

gtggagatca aacgt 735

<210> 364
<211> 245
<212> PRT
<213> Homo sapiens

<400> 364

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

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

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

Gly Asp Ile Ile Gly Met Phe Gly Ser Thr Asn Tyr Ala Gln Asn Phe
50 55 60

Gln Gly Arg Leu Thr Ile Thr Ala Asp Glu Ser Thr 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 Ser Ser Gly Tyr Tyr Pro Ala Tyr Leu Pro His Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly Thr
115 120 125

Gly Ser Gly Thr Gly Gly Ser Thr Glu Ile Val Leu Thr Gln Ser Pro
130 135 140

Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg
145 150 155 160

Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys
165 170 175

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala
180 185 190

Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr
210 215 220

Cys Gln Gln Tyr Gly Ser Ser Pro Arg Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Val Glu Ile Lys Arg
245

<210> 365
<211> 121
<212> PRT
<213> Homo sapiens

<400> 365

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

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

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

Gly Gly Ile Ile Pro Met Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Val Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Gly Asp Lys Gly Ile Tyr Tyr Tyr Tyr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 366
<211> 111
<212> PRT

<213> Homo sapiens

<400> 366

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

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

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

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> 367
<211> 744
<212> DNA
<213> Homo sapiens

<400> 367
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc cggggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccttcagc ttctattcta tgagctgggt gcgacaggcc 120

cctggacaag gacttgagtg gatgggaggg atcatcccta tgtttggtac aacaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggtcg aatccacgag cacagcctac 240

atggaggtga gcagcctgag atctgaggac acggccgttt attactgtgc gagaggtgat 300

aagggtatct actactacta catggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gcagtctgcc 420

ctgactcagc ctgcctccgt gtctgggtct cctggacagt cgatcaccat ctcctgcact 480

ggaaccagca gtgacgttgg tggttataac tatgtctcct ggtaccaaca gcacccaggc 540

aaagccccca aactcatgat ttatgaggtc agtaatcggc ctcaggggtt tctctaatcgc 600

ttctctggct ccaagtctgg caacacggcc tccctgacca tctctgggct ccaggctgag 660

gacgaggctg attattactg cagctcatat acaagcagca gcactcttgt ctttcggaact 720

gggaccaagg tcaccgtcct aggt 744

<210> 368
<211> 248
<212> PRT

<213> Homo sapiens

<400> 368

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

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

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

Gly Gly Ile Ile Pro Met Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Val Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Gly Asp Lys Gly Ile Tyr Tyr Tyr Tyr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Gly Ser Thr Gln Ser Ala Leu Thr Gln Pro
130 135 140

Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser Cys Thr
145 150 155 160

Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln
165 170 175

Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Glu Val Ser Asn
180 185 190

Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn
195 200 205

Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp
210 215 220

Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr Leu Val Phe Gly Thr
225 230 235 240

Gly Thr Lys Val Thr Val Leu Gly
245

<210> 369
<211> 121
<212> PRT
<213> Homo sapiens

<400> 369

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Arg Thr His
20 25 30

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

Gly Gly Ile Ile Ala Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Ile Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Gly Ser Gly Tyr His Ile Ser Thr Pro Phe Asp Asn Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 370
<211> 109
<212> PRT
<213> Homo sapiens

<400> 370

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

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Gly Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

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

<210> 371
<211> 738
<212> DNA
<213> Homo sapiens

<400> 371
gaggtgcagc tggtggagac cggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cctctggagg caccttcagg acccatgcta tcagttgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcgcta tcttcggaac agcaaactac 180

gcacagaagt tccagggcag aatcacgatt accgcggacg aatccacgag tacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attttctgtg cgagaggcagt 300

ggttatcata tatcgacacc ctttgacaac tggggccagg gaaccctggt caccgtctcg 360

agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gtcctatgtg 420

ctgactcagc caccctcggt gtcagtggcc ccaggacaga cggccaggat tacctgtggg 480

ggaaacaaca ttggaagtaa aggtgtgcac tggtaccagc agaagcctgg ccaggccct 540

gtgctggtcg tctatgatga tagcgaccgg ccctcaggga tccctgagcg attctctggc 600

tccaactctg ggaacacggc caccctgacc atcagcaggg tcgaagccgg ggatgaggcc 660

gactattact gtcaggtgtg ggatagtagt agtgatcatg tggtattcgg cggagggacc 720

aagctgaccg tcctaggt 738

<210> 372
<211> 246
<212> PRT
<213> Homo sapiens

<400> 372

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Arg Thr His
20 25 30

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

Gly Gly Ile Ile Ala Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Ile Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Gly Ser Gly Tyr His Ile Ser Thr Pro Phe Asp Asn Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Gly Ser Thr Ser Tyr Val Leu Thr Gln Pro
130 135 140

Pro Ser Val Ser Val Ala Pro Gly Gln Thr Ala Arg Ile Thr Cys Gly
145 150 155 160

Gly Asn Asn Ile Gly Ser Lys Gly Val His Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Gln Ala Pro Val Leu Val Val Tyr Asp Asp Ser Asp Arg Pro Ser
180 185 190

Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr
195 200 205

Leu Thr Ile Ser Arg Val Glu Ala Gly Asp Glu Ala Asp Tyr Tyr Cys
210 215 220

Gln Val Trp Asp Ser Ser Ser Asp His Val Val Phe Gly Gly Gly Thr
225 230 235 240

Lys Leu Thr Val Leu Gly
245

<210> 373
<211> 128
<212> PRT
<213> Homo sapiens

<400> 373

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly His Ile Phe Ser Gly Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Gln Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Val Lys Asp Gly Tyr Cys Thr Leu Thr Ser Cys Pro Val Gly
100 105 110

Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 374
<211> 108
<212> PRT
<213> Homo sapiens

<400> 374

Glu 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 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 Leu
85 90 95

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

<210> 375
<211> 756
<212> DNA
<213> Homo sapiens

<400> 375
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggaca catcttcagc ggctatgcaa tcagttgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttggtac aacaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggacc aatccacgag cacagcctac 240

atggacctga gcaacttgag atctgaggac acggccgtct attactgtgc gagagtgaaa 300

gatggatatt gtactcttac cagcggcact gtcggctggt acttcgatct ctggggccgt 360

ggcaccctgg tcactgtctc gagcggtacg ggcggttcag gcggaaccgg cagcggcact 420

ggcgggtcga cggaaattgt gatgacgcag tctccaggca ccctgtcttt gtctccaggg 480

gaaagagcca ccctctcgtg cagggccagt cagagtgtta gcagcagcta cttagcctgg 540

taccagcaga aacctggcca ggctcccagg ctcctcatct ttggtgcctc cagcagggcc 600

actggcatcc cagacaggtt cagtggcagt gggtctggga cagacttcac tctcaccatc 660

agcagactgg agcctgaaga ttttgcagtg tattactgtc agcagtatgg tagctcactc 720

actttcggcg gagggaccaa gctggagatc aaacgt 756

<210> 376
<211> 252
<212> PRT
<213> Homo sapiens

<400> 376

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly His Ile Phe Ser Gly Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Gln Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Val Lys Asp Gly Tyr Cys Thr Leu Thr Ser Cys Pro Val Gly
100 105 110

Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120 125

Gly Thr Gly Gly Ser Gly Gly Thr Gly Ser Gly Thr Gly Gly Ser Thr
130 135 140

Glu Ile Val Met Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
145 150 155 160

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
165 170 175

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
180 185 190

Ile Phe Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
195 200 205

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
210 215 220

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Leu
225 230 235 240

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
245 250

<210> 377
<211> 121
<212> PRT
<213> Homo sapiens

<400> 377

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Ile Phe Arg Ser Asn
20 25 30

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

Gly Gly Ile Phe Ala Leu Phe Gly Thr Thr Asp Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Ser Thr Thr Val Tyr
65 70 75 80

Leu Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 378
<211> 109
<212> PRT
<213> Homo sapiens

<400> 378

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 Asn
20 25 30

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

Ile Tyr Gly Ala Ser Ser Arg Ala Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Gly 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 Arg
100 105

<210> 379
<211> 738
<212> DNA
<213> Homo sapiens

<400> 379
gaggtccagc tggtacagtc tggggctgag gttaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg catcttcaga agcaattcta tcagttgggt gcgacaggcc 120

cctgggcaag ggcttgagtg gatgggaggg atcttcgctc ttttcggaac aacagactac 180

gcgcagaagt tccagggcag agtcacgatt accgcggacg aatcttcgac cacagtctac 240

ctggagcttga gtagcctgac atctgaggac acggccgttt attactgtgc gagaggcagt 300

ggctacacca cacgcaacta ctttgactac tggggccagg gcaccctggt caccgtctcg 360

agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac ggaaattgtg 420

ctgactcagt ctccaggcac cctgtctttg tctccagggg aaagagccac actctcctgc 480

agggccagtc agagtgttag cagcaactac ttaggctggt accagcagaa acctggccag 540

gctcccaggc tcctgatcta tggtgcatcc agcagggcca gtggcatccc agacaggttc 600

agtggcggtg ggtctgggac agacttcact ctcaccatca gcagactgga gcctgaagat 660

tttgcagtgt attactgtca gcagtatggt agctcacccc tcactttcgg cggagggacc 720

aaggtggaga tcaaacgt 738

<210> 380
<211> 246
<212> PRT
<213> Homo sapiens

<400> 380

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Ile Phe Arg Ser Asn
20 25 30

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

Gly Gly Ile Phe Ala Leu Phe Gly Thr Thr Asp Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Ser Thr Thr Val Tyr
65 70 75 80

Leu Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Gly Ser Thr Glu Ile Val Leu Thr Gln Ser
130 135 140

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ser Ser Asn Tyr Leu Gly Trp Thr Gln Gln
165 170 175

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg
180 185 190

Ala Ser Gly Ile Pro Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
210 215 220

Tyr Cys Gln Gln Tyr Gly Ser Ser Pro Leu Thr Phe Gly Gly Gly Thr
225 230 235 240

Lys Val Glu Ile Lys Arg
245

<210> 381
<211> 120
<212> PRT
<213> Homo sapiens

<400> 381

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

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

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

Gly Gly Ile Ile Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr 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 Gly Asn Tyr Tyr Tyr Glu Ser Ser Leu Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 382
<211> 109
<212> PRT
<213> Homo sapiens

<400> 382

Gln Ser Val Val Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105

<210> 383
<211> 735
<212> DNA
<213> Homo sapiens

<400> 383
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcggta tgttcggtac agcaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatttacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagaggaaat 300

tatttactat g agagtagtct cgactactgg ggccagggaa ccctggtcac cgtctcgagc 360

ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgca gtctgtcgtg 420

acgcagccgc cctcggtgtc agtggcccca ggacagacgg ccaggattac ctgtggggga 480

aacaacatt g gaagtaaaag tgtgcactgg taccagcaga agccaggcca ggccccgtg g 540

ctggtcgtct atgatgatag cgaccggccc tcagggatcc ctgagcgatt ctctggctcc 600

aactctggga acacggccac cctgaccatc agcagggtcg aagccgggga tgaggccgac 660

tattactgtc aggtgtggga tagtagtagt gatcattatg tcttcggaac tgggaccaag 720

gtcaccgtcc taggt 735

<210> 384
<211> 245
<212> PRT
<213> Homo sapiens

<400> 384

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

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

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

Gly Gly Ile Ile Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr 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 Gly Asn Tyr Tyr Tyr Glu Ser Ser Leu Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly Thr
115 120 125

Gly Ser Gly Thr Gly Gly Ser Thr Gln Ser Val Val Thr Gln Pro Pro
130 135 140

Ser Val Ser Val Ala Pro Gly Gln Thr Ala Arg Ile Thr Cys Gly Gly
145 150 155 160

Asn Asn Ile Gly Ser Lys Ser Val His Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Ala Pro Val Leu Val Val Tyr Asp Asp Ser Asp Arg Pro Ser Gly
180 185 190

Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr Leu
195 200 205

Thr Ile Ser Arg Val Glu Ala Gly Asp Glu Ala Asp Tyr Tyr Cys Gln
210 215 220

Val Trp Asp Ser Ser Ser Asp His Tyr Val Phe Gly Thr Gly Thr Lys
225 230 235 240

Val Thr Val Leu Gly
245

<210> 385
<211> 120
<212> PRT
<213> Homo sapiens

<400> 385

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Asn Phe
20 25 30

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

Gly Gly Ile Ile Ala Val Phe Gly Thr Thr Lys Tyr Ala His Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Gly Ser Leu Lys Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Pro His Tyr Tyr Ser Ser Tyr Met Asp Val Trp Gly Glu
100 105 110

Gly Thr Thr Val Thr Val Ser Ser

115 120

<210> 386
<211> 107
<212> PRT
<213> Homo sapiens

<400> 386

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

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

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

Tyr Ala Ala Ser Thr 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 Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Ser
85 90 95

Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg
100 105

<210> 387
<211> 729
<212> DNA
<213> Homo sapiens

<400> 387
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtaaaggtc 60

tcctgcaagg cttctggagg ccccttccgc aatttgctat caactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcgctg tctttgggac gacaaagtac 180

gcacataagt tccagggcag agtcaccatc accgcggacg actccacaaa tacagcttac 240

atggagctgg gcagcctgaa atctgaggac acggccgtgt attactgtgc gagaggtccc 300

cactactact cctcctacat ggacgtctgg ggcgaaggga ccacggtcac cgtctcgagc 360

ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgga tccagttg 420

acccagtctc catcctccct gtctgcatct gtaggagaca gagtcaccat cacttgccgg 480

gcgagtcagg gcattagcac ttatttagcc tggtatcagc agaaacccgg gaaagttcct 540

aaactcctga tctatgctgc atccactttg caatcagggg tcccatctcg gttcagtggc 600

agtggatctg ggacagattt cactctcacc atcagcagcc tgcagcctga agatgttgca 660

acttattact gtcaaaagta taacagtgcc ccttctttcg gccctgggac caaagtggat 720

atcaaacgt 729

<210> 388
<211> 243
<212> PRT
<213> Homo sapiens

<400> 388

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Asn Phe
20 25 30

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

Gly Gly Ile Ile Ala Val Phe Gly Thr Thr Lys Tyr Ala His Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Gly Ser Leu Lys Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Pro His Tyr Tyr Ser Ser Tyr Met Asp Val Trp Gly Glu
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Thr Gly Gly Asp Gly Gly Thr
115 120 125

Gly Ser Gly Thr Gly Gly Ser Thr Asp Ile Gln Leu Thr Gln Ser Pro
130 135 140

Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg
145 150 155 160

Ala Ser Gln Gly Ile Ser Thr Tyr Leu Ala Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Lys Val Pro Lys Leu Leu Ile Tyr Ala Ala Ser Thr Leu Gln Ser
180 185 190

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
195 200 205

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Val Ala Thr Tyr Tyr Cys
210 215 220

Gln Lys Tyr Asn Ser Ala Pro Ser Phe Gly Pro Gly Thr Lys Val Asp
225 230 235 240

Ile Lys Arg

<210> 389
<211> 120
<212> PRT
<213> Homo sapiens

<400> 389

Glu Val Ala Leu Val Glu Thr Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Pro Cys Lys Ser Ser Gly Ser Pro Phe Arg Ser Asn
20 25 30

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

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

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Val His
65 70 75 80

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

Ala Arg Gly Pro Thr Tyr Tyr Tyr Ser Tyr Met Asp Val Trp Gly Lys
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 390
<211> 109
<212> PRT
<213> Homo sapiens

<400> 390

Ser Tyr Val Leu Thr Gln Pro Pro Ser Glu Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Arg Asn Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp His Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105

<210> 391
<211> 735
<212> DNA
<213> Homo sapiens

<400> 391
gaggtgcagc tggtggagac tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

ccctgcaaat cttctggaag ccccttcagg agtaatgctg tcagctgggt gcgacaggcc 120

cccggacaag ggcttgagtg ggtgggagga atcctcggtg tctttggttc accaagctac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatccaccaa cacagtccac 240

atggagctga gaggtttgag atctgaggac acggccgtgt attattgtgc gagaggtcct 300

acctactact actcctacat ggacgtctgg ggcaaaggga ccacggtcac cgtctcgagc 360

ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgtc ctatgtgctg 420

actcagccac cctcggagtc agtggcccca ggacagacgg ccaggattac ctgtgggggа 480

aataacattg gaagaaatag tgtgcactgg tatcagcaga agccaggcca ggccctgtg 540

ctggtcgtgt atgatgatag cgaccggccc tcagggatcc ctgagcgatt ttctggctcc 600

aagtctggga acacggccac cctgattatc agcagggtcg aagtcgggga tgaggccgac 660

tactactgtc aggtgtggca tagtagtagt gatcattatg tcttcggaac tgggaccaag 720

gtcaccgtcc taggt 735

<210> 392
<211> 245
<212> PRT
<213> Homo sapiens

<400> 392

Glu Val Ala Leu Val Glu Thr Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Pro Cys Lys Ser Ser Gly Ser Pro Phe Arg Ser Asn
20 25 30

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

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

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Val His
65 70 75 80

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

Ala Arg Gly Pro Thr Tyr Tyr Tyr Ser Tyr Met Asp Val Trp Gly Lys
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly Thr
115 120 125

Gly Ser Gly Thr Gly Gly Ser Thr Ser Tyr Val Leu Thr Gln Pro Pro
130 135 140

Ser Glu Ser Val Ala Pro Gly Gln Thr Ala Arg Ile Thr Cys Gly Gly
145 150 155 160

Asn Asn Ile Gly Arg Asn Ser Val His Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Ala Pro Val Leu Val Val Tyr Asp Asp Ser Asp Arg Pro Ser Gly
180 185 190

Ile Pro Glu Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Thr Leu
195 200 205

Ile Ile Ser Arg Val Glu Val Gly Asp Glu Ala Asp Tyr Tyr Cys Gln
210 215 220

Val Trp His Ser Ser Ser Asp His Tyr Val Phe Gly Thr Gly Thr Lys
225 230 235 240

Val Thr Val Leu Gly
245

<210> 393
<211> 120
<212> PRT
<213> Homo sapiens

<400> 393

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

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

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

Gly Gly Ile Phe Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe

50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Ala Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Gly Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

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

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 394
<211> 109
<212> PRT
<213> Homo sapiens

<400> 394

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

Gln 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

Met 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 Ser
85 90 95

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

<210> 395
<211> 735
<212> DNA
<213> Homo sapiens

<400> 395
cagatgcagc tggtacaatc tggagctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcttcggta tgttgggac agcaaactac 180

gcgcagaagt tccagggcag agtcacgatt accgcggacg aattcacgag cgcggcctac 240

atggagctga gcagcctggg atctgaggac acggccatgt attactgtgc gaggtctagt 300

ggttattacc cccaatactt ccaggactgg ggccagggca ccctggtcac cgtctcgagc 360

ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgga attgtgatg 420

acacagtctc caggcaccct gtctttgtct ccagggcaaa gagccaccct ctcctgcagg 480

gccagtcaga gtgttagcag cagctactta gcctggtacc agcagaaacc tggccaggct 540

cccagactcc tcatgtatgg tgcatccagc agggccactg gcatcccaga caggttcagt 600

ggcagtgggt ctgggacaga cttcactctc accatcagca gactggagcc tgaagatttt 660

gcagtgtatt actgtcagca gtatggtagc tcatcgctca ctttcggcgg agggaccaag 720

ctggagatca aacgt 735

<210> 396
<211> 245
<212> PRT
<213> Homo sapiens

<400> 396

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

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

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

Gly Gly Ile Phe Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Ala Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Gly Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

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

Gly Thr Leu Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly Thr
115 120 125

Gly Ser Gly Thr Gly Gly Ser Thr Glu Ile Val Met Thr Gln Ser Pro
130 135 140

Gly Thr Leu Ser Leu Ser Pro Gly Gln Arg Ala Thr Leu Ser Cys Arg
145 150 155 160

Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys
165 170 175

```
Pro Gly Gln Ala Pro Arg Leu Leu Met Tyr Gly Ala Ser Ser Arg Ala
            180                 185                 190

Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
        195                 200                 205

Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr
    210                 215                 220

Cys Gln Gln Tyr Gly Ser Ser Ser Leu Thr Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Leu Glu Ile Lys Arg
                245
```

<210> 397
<211> 121
<212> PRT
<213> Homo sapiens

<400> 397

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Ile Phe Asn Ser Tyr
            20                  25                  30

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

Gly Gly Ile Ile Ala Ile Phe His Thr Pro Lys Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Arg Ser Leu Lys Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
                85                  90                  95

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

Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120
```

<210> 398
<211> 109
<212> PRT
<213> Homo sapiens

<400> 398

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

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

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

<210> 399
<211> 738
<212> DNA
<213> Homo sapiens

<400> 399
gaggtgcagc tggtggagtc cggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg catcttcaac agttatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggc atcatcgcta tctttcatac accaaagtac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatccacgaa cacagcctac 240

atggaactga gaagcctgaa atctgaggac acggccctgt attactgtgc gagagggtcc 300

acttacgatt tttcgagtgg ccttgactac tggggccagg gaaccctggt caccgtctcg 360

agcggtacgg gcggttcagg cggaaccggc agcggcactg gcgggtcgac gcaggcaggg 420

ctgactcagc caccctcggt gtcagtggcc ccaggacaga cggccaggat tacctgtggg 480

ggaaacaaca ttggaagtaa aagtgtgcac tggtaccagc agaagccagg ccaggccct 540

gtcctagtcg tctatgatga tagcgaccgg ccctcaggga tccctgagcg attctctggc 600

tccaactctg ggaacacggc caccctgacc atcagcaggg tcgaagccgg ggatgaggcc 660

gactattact gtcaggtgtg ggatagtagt agtgatcatg tggtattcgg cggagggacc 720

aagctgaccg tcctaggt 738

<210> 400
<211> 246
<212> PRT
<213> Homo sapiens

<400> 400

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Ile Phe Asn Ser Tyr
20 25 30

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

Gly Gly Ile Ile Ala Ile Phe His Thr Pro Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Lys Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

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

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Gly Ser Thr Gln Ala Gly Leu Thr Gln Pro
130 135 140

Pro Ser Val Ser Val Ala Pro Gly Gln Thr Ala Arg Ile Thr Cys Gly
145 150 155 160

Gly Asn Asn Ile Gly Ser Lys Ser Val His Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Gln Ala Pro Val Leu Val Val Tyr Asp Asp Ser Asp Arg Pro Ser
180 185 190

Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr
195 200 205

Leu Thr Ile Ser Arg Val Glu Ala Gly Asp Glu Ala Asp Tyr Tyr Cys
210 215 220

Gln Val Trp Asp Ser Ser Ser Asp His Val Val Phe Gly Gly Gly Thr
225 230 235 240

Lys Leu Thr Val Leu Gly
245

<210> 401
<211> 126
<212> PRT
<213> Homo sapiens

<400> 401

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

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

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

Gly Gly Val Ile Pro Ile Phe Arg Thr Ala Asn Tyr Ala Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Tyr Met Glu
65 70 75 80

Leu Ser Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg
85 90 95

Leu Asn Tyr His Asp Ser Gly Thr Tyr Tyr Asn Ala Pro Arg Gly Trp
100 105 110

Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 402
<211> 114
<212> PRT
<213> Homo sapiens

<400> 402

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

Glu Lys Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Ile Leu Asn 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 Ser Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys Arg

<210> 403
<211> 768
<212> DNA
<213> Homo sapiens

<400> 403
caggtccagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg cttcttcagc agctatgcta tcagctgggt gcgccaggcc 120

cctggacaag gacttgagtg gatgggggggg gtcatcccta tctttcgtac agcaaactac 180

gcacagaact tccagggcag agtcaccatt accgcggacg aattcacatc gtatatggag 240

ctgagcagcc tgagatctga cgacacggcc gtgtattact gtgcgaggtt gaattaccat 300

gattcgggga cttattataa cgccccccgg ggctggttcg acccctgggg ccagggaacc 360

ctggtcaccg tctcgagcgg tacgggcggt tcaggcggaa ccggcagcgg cactggcggg 420

tcgacggaca tccagatgac ccagtctcca gactccctgg ctgtgtctct gggcgagaag 480

gccaccatca actgcaagtc cagccagagt attttaaaca gctccaacaa taagaactac 540

ttagcttggt accagcagaa accaggacag cctcctaagc tgctcattta ctgggcatct 600

acccgggaat ccggggtccc tgaccgattc agtggcagcg ggtctgggac agatttcact 660

ctcaccatca gcagcctgca ggctgaagat gtggcagttt attactgtca gcaatattat 720

agtagtccgc cgacgttcgg ccaagggacc aaggtggaaa tcaaacgt 768

<210> 404
<211> 256
<212> PRT
<213> Homo sapiens

<400> 404

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

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

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

Gly Gly Val Ile Pro Ile Phe Arg Thr Ala Asn Tyr Ala Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Tyr Met Glu
65 70 75 80

Leu Ser Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg
85 90 95

Leu Asn Tyr His Asp Ser Gly Thr Tyr Tyr Asn Ala Pro Arg Gly Trp
100 105 110

Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Thr
115 120 125

Gly Gly Ser Gly Gly Thr Gly Ser Gly Thr Gly Gly Ser Thr Asp Ile
130 135 140

Gln Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu Lys
145 150 155 160

Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Ile Leu Asn Ser Ser Asn
165 170 175

Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
180 185 190

Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp
195 200 205

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
210 215 220

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr
225 230 235 240

Ser Ser Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
245 250 255

<210> 405
<211> 120
<212> PRT
<213> Homo sapiens

<400> 405

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

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

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

Gly Gly Ile Ser Pro Met Phe Gly Thr Thr Thr Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

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

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 406
<211> 109
<212> PRT
<213> Homo sapiens

<400> 406

Gln Ser Val Val Thr Gln Pro Pro Ser Glu Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly His Asn Ile Gly Ser Asn Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asn Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Gly Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105

<210> 407
<211> 735
<212> DNA
<213> Homo sapiens

<400> 407
caggtccagc tggtgcagtc tggagctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagt cacctttagt tactatgcta tgagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggagga atcagcccta tgtttgggac aacaacctac 180

gcacagaagt tccagggcag agtcacgatt actgcggacg actccacgag tacagcctac 240

atggaggtga ggagcctgag atctgaggac acggccgtgt attactgtgc gagatcttcg 300

aatttactat gatagtgtat atgactactg gggccagggaa ccctggtcac cgtctcgagc 360

ggtacgggcg gttcaggcgg aaccggcagc ggcactggcg ggtcgacgca gtctgtcgtg 420

acgcagccgc cctcggagtc agtggcccca ggacagacgg ccaggattac ctgtggggga 480

cataacattg gaagtaatag tgtgcactgg taccagcaga agccaggcca ggccctgtg 540

ctggtcgtgt atgataatag cgaccggccc tcagggatcc ctgagcgatt ctctggctcc 600

aactctggga acacggccac cctgaccatc agcagggtcg aagccyyyga tgaggccgac 660

tattactgtc aggtgtgggg tagtagtagt gaccattatg tcttcggaac tgggaccaag 720

gtcaccgtcc taggt 735

<210> 408
<211> 245
<212> PRT
<213> Homo sapiens

<400> 408

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

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

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

Gly Gly Ile Ser Pro Met Phe Gly Thr Thr Thr Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

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

Gly Thr Leu Val Thr Val Ser Ser Gly Thr Gly Gly Ser Gly Gly Thr
115 120 125

Gly Ser Gly Thr Gly Gly Ser Thr Gln Ser Val Val Thr Gln Pro Pro
130 135 140

Ser Glu Ser Val Ala Pro Gly Gln Thr Ala Arg Ile Thr Cys Gly Gly
145 150 155 160

His Asn Ile Gly Ser Asn Ser Val His Trp Tyr Gln Gln Lys Pro Gly
165 170 175

Gln Ala Pro Val Leu Val Val Tyr Asp Asn Ser Asp Arg Pro Ser Gly
180 185 190

Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr Leu
195 200 205

Thr Ile Ser Arg Val Glu Ala Gly Asp Glu Ala Asp Tyr Tyr Cys Gln
210 215 220

Val Trp Gly Ser Ser Ser Asp His Tyr Val Phe Gly Thr Gly Thr Lys
225 230 235 240

Val Thr Val Leu Gly
245

<210> 409
<211> 123
<212> PRT
<213> Homo sapiens

<400> 409

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

Ser Val Arg Val Ser Cys Lys Ala Ser Gly Ser Ile Phe Arg Asn Tyr
20 25 30

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

Gly Gly Ile Ile Ala Ile Phe Gly Thr Pro Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Gly Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ile Pro His Tyr Asn Phe Gly Ser Gly Ser Tyr Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 410
<211> 111
<212> PRT
<213> Homo sapiens

<400> 410

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

Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr
20 25 30

Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Gly Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
65 70 75 80

Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Gly Thr Trp Asp Ser Ser Leu
85 90 95

Ser Ala Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> 411
<211> 750
<212> DNA
<213> Homo sapiens

<400> 411
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgagagtc 60

tcctgcaagg cttctggaag catcttcaga aactatgcta tgagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcgcta ttttt gggac accaaagtac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatcgacgag cactgtctac 240

atggaactga gcggactgag atctgaggac acggccatgt attactgtgc gaggattccc 300

cactataatt ttggttcggg gagttatttc gactactggg gccagggaac cctggtcacc 360

gtctcgagcg gtacgggcgg ttcaggcgga accggcagcg gcactggcgg gtcgacgact 420

gtgttgacac agccgccctc agtgtctggg gccccagggc agagggtcac catctcctgc 480

actgggagca gctccaacat cggggcaggt tatgatgtac actggtacca gcagcttcca 540

ggaacagccc ccaaactcct catctatggt aacagcaatc ggccctcagg ggtccctgac 600

cgattctctg gctccaagtc tggcacgtca gccaccctgg gcatcaccgg actccagact 660

ggggacgagg ccgattatta ctgcggaaca tgggatagca gcctgagtgc ttatgtcttc 720

ggaactggga ccaaggtcac cgtcctaggt 750

<210> 412
<211> 250
<212> PRT
<213> Homo sapiens

<400> 412

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

Ser Val Arg Val Ser Cys Lys Ala Ser Gly Ser Ile Phe Arg Asn Tyr
20 25 30

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

Gly Gly Ile Ile Ala Ile Phe Gly Thr Pro Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Gly Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ile Pro His Tyr Asn Phe Gly Ser Gly Ser Tyr Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Thr Gly Gly Ser
115 120 125

Gly Gly Thr Gly Ser Gly Thr Gly Gly Ser Thr Thr Val Leu Thr Gln
130 135 140

Pro Pro Ser Val Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys
145 150 155 160

Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His Trp Tyr
165 170 175

Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Gly Asn Ser
180 185 190

Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly
195 200 205

Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln Thr Gly Asp Glu Ala
210 215 220

Asp Tyr Tyr Cys Gly Thr Trp Asp Ser Ser Leu Ser Ala Tyr Val Phe
225 230 235 240

Gly Thr Gly Thr Lys Val Thr Val Leu Gly
245 250

<210> 413
<211> 445
<212> PRT
<213> Homo sapiens

<400> 413

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 Thr Gly Tyr
20 25 30

Tyr Val Tyr 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 Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr 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 Ser Arg Ser Leu Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
115 120 125

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
130 135 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145 150 155 160

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
165 170 175

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
180 185 190

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
195 200 205

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
210 215 220

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

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Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
    290                 295                 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305                 310                 315                 320

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
                325                 330                 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
            340                 345                 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
        355                 360                 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
    370                 375                 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385                 390                 395                 400

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
                405                 410                 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
            420                 425                 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        435                 440                 445
```

<210> 414
<211> 114
<212> PRT
<213> Homo sapiens

<400> 414

```
Asp Val 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 Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile
100 105 110

Lys Arg

<210> 415
<211> 657
<212> DNA
<213> Homo sapiens

<400> 415
gatgttgtga tgactcagtc tccagactcc ctggctgtgt ctctgggcga gagggccacc 60

atcaactgca agtccagcca gagtgttta tacagctcca acaataagaa ctacttagct 120

tggtaccagc agaaaccagg acagcctcct aagctgctca tttactgggc atctacccgg 180

gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240

atcagcagcc tgcaggctga agatgtggca gtttattact gtcagcaata tttatagtact 300

cctctcactt tcggcggagg gaccaaagtg gatatcaaac gtgcggccgc acccagcgtg 360

ttcatcttcc ccccctccga cgagcagctg aagagcggca ccgccagcgt ggtgtgcctg 420

ctgaacaact tctaccccg ggaggccaag gtgcagtgga aggtggacaa cgccctgcag 480

agcggcaaca gccaggagag cgtgaccgag caggacagca aggactccac ctacagcctg 540

agcagcaccc tcaccctgag caaggccgac tacgagaagc acaaggtgta cgcctgcgag 600

gtgacccacc agggcctgag cagccccgtg accaagagct tcaaccgggg cgagtgt 657

<210> 416
<211> 219
<212> PRT
<213> Homo sapiens

<400> 416

Asp Val 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 Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile
100 105 110

Lys Arg Ala Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 417
<211> 121
<212> PRT
<213> Homo sapiens

<400> 417

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly

100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 418
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 418
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggtac aacaaaatac 180

gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agtgctagca ccaagggccc cagcgtgttc ccccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg 480

agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag 660

cccaagagct gcgacaagac ccacacctgc ccccccctgcc ctgccccga gctgctgggc 720

ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc 780

cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac 900

aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc 960

aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc 1020

agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag 1080

gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac 1140

atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaaga gcctgagcct gagccccggc aag 1353

<210> 419
<211> 451
<212> PRT
<213> Homo sapiens

<400> 419

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

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val

275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 420
<211> 111
<212> PRT
<213> Homo sapiens

<400> 420

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

Arg Val Thr Ile Ser Cys Ser Gly Ser Thr Phe Asn Ile Gly Ser Asn
20 25 30

Ala Val Asp Trp Tyr Arg Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Arg Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ile Leu
85 90 95

Asn Val Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> 421
<211> 660
<212> DNA
<213> Homo sapiens

<400> 421
tcctatgtgc tgactcagcc accctcagcg tctgggaccc ccgggcagag ggtcaccatc 60

tcttgttctg gaagcacgtt caacatcgga agtaatgctg tagactggta ccggcagctc 120

ccaggaacgg cccccaaact cctcatctat agtaataatc agcggccctc aggggtccct 180

gaccgattct ctggctccag gtctggcacc tcagcctccc tggccatcag tgggctccag 240

tctgaggatg aggctgatta ttactgtgca gcatgggatg acatcctgaa tgttccggta 300

ttcggcggag ggaccaagct gaccgtccta ggtgcggccg caggccagcc caaggccgct 360

cccagcgtga ccctgttccc ccctcctcc gaggagctgc aggccaacaa ggccaccctg 420

gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc 480

agccccgtga aggccggcgt ggagaccacc acccccagca agcagagcaa caacaagtac 540

gccgccagca gctacctgag cctcaccccc gagcagtgga agagccaccg gagctacagc 600

tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggcccccac cgagtgcagc 660

<210> 422
<211> 220
<212> PRT
<213> Homo sapiens

<400> 422

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

Arg Val Thr Ile Ser Cys Ser Gly Ser Thr Phe Asn Ile Gly Ser Asn
20 25 30

Ala Val Asp Trp Tyr Arg Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Arg Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ile Leu
85 90 95

Asn Val Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
115 120 125

Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130 135 140

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145 150 155 160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
165 170 175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180 185 190

Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195 200 205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215 220

<210> 423
<211> 121
<212> PRT
<213> Homo sapiens

<400> 423

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 424
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 424
caggtccagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggtac aacaaaatac 180

gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agtgctagca ccaagggccc cagcgtgttc ccccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg 480

agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag 660

cccaagagct gcgacaagac ccacacctgc cccccctgcc ctgccccga gctgctgggc 720

ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc 780

cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac 900

aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc 960

aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc 1020

agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag 1080

gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac 1140

atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaaga gcctgagcct gagccccggc aag 1353

<210> 425
<211> 451
<212> PRT
<213> Homo sapiens

<400> 425

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

```
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys
    450


<210>  426
<211>  111
<212>  PRT
<213>  Homo sapiens

<400>  426

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

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
            20                  25                  30

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

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> 427
<211> 660
<212> DNA
<213> Homo sapiens

<400> 427
cagtctgccc tgactcagcc tgccgccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtaccaacag 120

cacccaggca aagcccccaa actcatgatt tatgaggtca gtaatcggcc ctcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

caggctgagg acgaggctga ttattactgc agctcatata caagcagcag cacttatgtc 300

ttcggaactg ggaccaaggt caccgtccta ggtgcggccg caggccagcc caaggccgct 360

cccagcgtga ccctgttccc ccctcctcc gaggagctgc aggccaacaa ggccaccctg 420

gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc 480

agccccgtga aggccggcgt ggagaccacc acccccagca agcagagcaa caacaagtac 540

gccgccagca gctacctgag cctcaccccc gagcagtgga agagccaccg gagctacagc 600

tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggcccccac cgagtgcagc 660

<210> 428
<211> 220
<212> PRT
<213> Homo sapiens

<400> 428

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

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

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

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
115 120 125

Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130 135 140

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145 150 155 160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
165 170 175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180 185 190

Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195 200 205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215 220

<210> 429
<211> 121
<212> PRT
<213> Homo sapiens

<400> 429

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

85 90 95

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 430
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 430
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggtac aacaaaatac 180

gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agtgctagca ccaagggccc cagcgtgttc ccctggcccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg 480

agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag 660

cccaagagct gcgacaagac ccacacctgc cccccctgcc ctgccccga gctgctgggc 720

ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc 780

cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac 900

aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc 960

aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc 1020

agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag 1080

gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac 1140

atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaaga gcctgagcct gagccccggc aag 1353

<210> 431
<211> 451
<212> PRT
<213> Homo sapiens

<400> 431

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His

260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 432
<211> 111
<212> PRT
<213> Homo sapiens

<400> 432

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Arg Ser Asn Val Gly Asp Asn
20 25 30

Ser Val Tyr Trp Tyr Gln His Val Pro Glu Met Ala Pro Lys Leu Leu
35 40 45

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

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ile Gly Leu Gln
65 70 75 80

Ser Gly Asp Glu Ala Asp Tyr Tyr Cys Val Ala Trp Asp Asp Ser Val
85 90 95

Asp Gly Tyr Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> 433
<211> 660
<212> DNA
<213> Homo sapiens

<400> 433
tcctatgtgc tgactcagcc accctcagtc tctgggaccc ccgggcagag ggtcaccatc 60

tcttgctctg gaagccgctc caacgtcgga gataattctg tatattggta tcaacacgtc 120

ccagaaatgg ccccccaaact cctcgtctat aagaatactc aacggccctc aggagtccct 180

gcccggtttt ccggctccaa gtctggcact tcagcctccc tggccatcat tggcctccag 240

tccggcgatg aggctgatta ttattgtgtg gcatgggatg acagcgtaga tggctatgtc 300

ttcggatctg ggaccaaggt caccgtccta ggtgcggccg caggccagcc caaggccgct 360

cccagcgtga ccctgttccc ccctcctccc gaggagctgc aggccaacaa ggccaccctg 420

gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc 480

agccccgtga aggccggcgt ggagaccacc acccccagca agcagagcaa caacaagtac 540

gccgccagca gctacctgag cctcaccccc gagcagtgga agagccaccg gagctacagc 600

tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggcccccac cgagtgcagc 660

<210> 434
<211> 220
<212> PRT
<213> Homo sapiens

<400> 434

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Arg Ser Asn Val Gly Asp Asn
20 25 30

Ser Val Tyr Trp Tyr Gln His Val Pro Glu Met Ala Pro Lys Leu Leu
35 40 45

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

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ile Gly Leu Gln
65 70 75 80

Ser Gly Asp Glu Ala Asp Tyr Tyr Cys Val Ala Trp Asp Asp Ser Val
85 90 95

Asp Gly Tyr Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
115 120 125

Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130 135 140

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145 150 155 160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
165 170 175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180 185 190

Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195 200 205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215 220

<210> 435
<211> 121
<212> PRT
<213> Homo sapiens

<400> 435

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 436
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 436
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggta caacaaaatac 180

gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agtgctagca ccaagggccc cagcgtgttc ccccctggcc ccagcagcaa gagcaccagc 420

ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg 480

agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag 660

cccaagagct gcgacaagac ccacacctgc ccccccctgc ctgccccga gctgctgggc 720

ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc 780

cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac 900

aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc 960

aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc 1020

agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag 1080

gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac 1140

atcgccgtgg agtgggagag caacggccag cccaaggaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaaga gcctgagcct gagccccggc aag 1353

<210> 437
<211> 451

<212> PRT
<213> Homo sapiens

<400> 437

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

```
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys
    450
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<210> 438
<211> 112
<212> PRT
<213> Homo sapiens

<400> 438

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

Lys Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Asn Asp
            20                  25                  30
```

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

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
65 70 75 80

Thr Gly Asp Glu Ala Asn Tyr Tyr Cys Ala Thr Trp Asp Arg Arg Pro
85 90 95

Thr Ala Tyr Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> 439
<211> 660
<212> DNA
<213> Homo sapiens

<400> 439
cagtctgtgt tgacgcagcc gccctcagtg tctgcggccc caggacagaa ggtcaccatc 60

tcctgctctg gaagcagctc caacattggg aatgattatg tatcctggta ccagcagctc 120

ccaggaacag cccccaaact cctcatttat gacaataata agcgaccctc agggattcct 180

gaccgattct ctggctccaa gtctggcacg tcagccaccc tgggcatcac cggactccag 240

actggggacg aggccaacta ttactgcgca acatgggatc gccgcccgac tgcttatgtt 300

gtcttcggcg gagggaccaa gctgaccgtc ctaggtgcgg ccgcaggcca gcccaaggcc 360

gctcccagcg tgaccctgtt ccccccctcc tccgaggagc tgcaggccaa caaggccacc 420

ctggtgtgcc tcatcagcga cttctaccct ggcgccgtga ccgtggcctg gaaggccgac 480

agcagccccg tgaaggccgg cgtggagacc accaccccca gcaagcagag caacaacaag 540

tacgccgcca gcagctacct gagcctcacc cccgagcagt ggaagagcca ccggagctac 600

agctgccagg tgacccacga gggcagcacc gtggagaaga ccgtggcccc caccgagtgc 660

<210> 440
<211> 221
<212> PRT
<213> Homo sapiens

<400> 440

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

Lys Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Asn Asp
20 25 30

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

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
65 70 75 80

Thr Gly Asp Glu Ala Asn Tyr Tyr Cys Ala Thr Trp Asp Arg Arg Pro
85 90 95

Thr Ala Tyr Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

Ala Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro
115 120 125

Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu
130 135 140

Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp
145 150 155 160

Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln
165 170 175

Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu
180 185 190

Gln Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly
195 200 205

Ser Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215 220

<210> 441
<211> 120
<212> PRT
<213> Homo sapiens

<400> 441

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

Ser Val Lys Val Ser Cys Lys Val Ser Gly Val Ile Phe Ser Gly Ser
20 25 30

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

Gly Gly Ile Ser Pro Leu Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Gln Ser Thr Asn Thr Thr Tyr

65 70 75 80

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

Ala Arg Gly Pro Lys Tyr Tyr Ser Glu Tyr Met Asp Val Trp Gly Lys
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 442
<211> 1350
<212> DNA
<213> Homo sapiens

<400> 442
caggtacagc tgcagcagtc aggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg tttccggagt catttcagc ggcagtgcga tcagctgggt gcgacaggcc 120

cctggacaag gcctgagtgg gatgggaggg atcagccctc tctttggcac aacaaatcac 180

gcacaaaagt tccagggcag agtcacgatt accgcggacc aatccacgaa cacaacctac 240

atggaggtga acagcctgag atatgaggac acggccgtgt atttctgtgc gcgaggtcca 300

aaatatcaca gtgagtacat ggacgtctgg ggcaaaggga ccacggtcac cgtctcgagt 360

gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc 420

ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc 480

tggaacagcg gcgcctgac cagcggcgtg cacacctcc ccgccgtgct gcagagcagc 540

ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc 600

tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc 660

aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga 720

ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccct 780

gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg 840

tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac 900

agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag 960

gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc 1020

aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag 1080

atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc 1140

gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccctgtg 1200

ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg 1260

cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc 1320

cagaagagcc tgagcctgag ccccggcaag 1350

<210> 443
<211> 450
<212> PRT
<213> Homo sapiens

<400> 443

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

Ser Val Lys Val Ser Cys Lys Val Ser Gly Val Ile Phe Ser Gly Ser
20 25 30

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

Gly Gly Ile Ser Pro Leu Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Gln Ser Thr Asn Thr Thr Tyr
65 70 75 80

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

Ala Arg Gly Pro Lys Tyr Tyr Ser Glu Tyr Met Asp Val Trp Gly Lys
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile

245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 444
<211> 109
<212> PRT
<213> Homo sapiens

<400> 444

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

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

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

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

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

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

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

<210> 445
<211> 642
<212> DNA
<213> Homo sapiens

<400> 445
gacatccaga tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcgagtca gggcattagc agttatttag cctggtatca gcagaagcca 120

gggaaagttc ctacactcct gatctatgat gcatccactt tgcgatcagg ggtcccatct 180

cgcttcagtg gcagtggatc tgcgacagat ttcactctca ccatcagcag cctgcagcct 240

gaagatgttg caacttatta ctgtcaaagg tataacagtg ccccccgat cacctt cggc 300

caagggacac gactggagat taaacgtgcg gccgcaccca gcgtgttcat cttccccccc 360

tccgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtga ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctcacc 540

ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgagcagcc ccgtgaccaa gagcttcaac cggggcgagt gt 642

<210> 446
<211> 214
<212> PRT
<213> Homo sapiens

<400> 446

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

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

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

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

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

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

Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Ala Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 447
<211> 120
<212> PRT
<213> Homo sapiens

<400> 447

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

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

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

Gly Gly Ile Met Gly Met Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Ala Ala Tyr
65 70 75 80

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

Ala Arg Ser Ser Gly Tyr Tyr Pro Glu Tyr Phe Gln Asp Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 448
<211> 1350
<212> DNA
<213> Homo sapiens

<400> 448
caggtccagc tggtacagtc ttggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccttcagt agttatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggagga atcatgggta tgttggcac aactaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aattcacgag cgcagcctac 240

atggagctga ggagcctgag atctgaggac acggccgtct actactgtgc gaggtctagt 300

ggttattacc ccgaatactt ccaggactgg ggccagggca ccctggtcac cgtctcgagt 360

gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc 420

ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc 480

tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc 540

ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc 600

tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc 660

aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga 720

ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccct 780

gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg 840

tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac 900

agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag 960

gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc 1020

aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag 1080

atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc 1140

gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccctgtg 1200

ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg 1260

cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc 1320

cagaagagcc tgagcctgag ccccggcaag 1350

<210> 449
<211> 450
<212> PRT
<213> Homo sapiens

<400> 449

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

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

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

Gly Gly Ile Met Gly Met Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Ala Ala Tyr
65 70 75 80

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

Ala Arg Ser Ser Gly Tyr Tyr Pro Glu Tyr Phe Gln Asp Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

```
Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Asp Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Lys
    450


<210>  450
<211>  107
<212>  PRT
<213>  Homo sapiens

<400>  450

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

Thr Ala Ser Val Thr Cys Ser Gly His Lys Leu Gly Asp Lys Tyr Val
20 25 30

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

Gln Asp Asn Arg Arg Pro Ser Gly Ile Pro Glu Arg Phe Ile Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Leu
65 70 75 80

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

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

<210> 451
<211> 648
<212> DNA
<213> Homo sapiens

<400> 451
cagtctgtgc tgactcagcc accctcagag tccgtgtccc caggacagac agccagcgtc 60

acctgctctg gacataaatt gggggataaa tatgtttcgt ggtatcagca gaagccaggc 120

cagtcccctg tattactcat ctatcaagat aacaggcggc cctcagggat ccctgagcga 180

ttcataggct ccaactctgg gaacacagcc actctgacca tcagcgggac ccaggctctg 240

gatgaggctg actattactg tcaggcgtgg gacagcagca ctgcggtttt cggcggaggg 300

accaagctga ccgtcctagg tgcggccgca ggccagccca aggccgctcc cagcgtgacc 360

ctgttccccc cctcctccga ggagctgcag gccaacaagg ccaccctggt gtgcctcatc 420

agcgacttct accctggcgc cgtgaccgtg gcctggaagg ccgacagcag ccccgtgaag 480

gccggcgtgg agaccaccac ccccagcaag cagagcaaca acaagtacgc cgccagcagc 540

tacctgagcc tcacccccga gcagtggaag agccaccgga gctacagctg ccaggtgacc 600

cacgagggca gcaccgtgga gaagaccgtg gcccccaccg agtgcagc 648

<210> 452
<211> 216
<212> PRT
<213> Homo sapiens

<400> 452

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

Thr Ala Ser Val Thr Cys Ser Gly His Lys Leu Gly Asp Lys Tyr Val
20 25 30

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

Gln Asp Asn Arg Arg Pro Ser Gly Ile Pro Glu Arg Phe Ile Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Leu
65 70 75 80

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

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala Ala Ala Gly Gln
100 105 110

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
115 120 125

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
130 135 140

Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
145 150 155 160

Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
165 170 175

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
180 185 190

Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
195 200 205

Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 453
<211> 120
<212> PRT
<213> Homo sapiens

<400> 453

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

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

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

Gly Gly Ile Ile Gly Met Phe Gly Ser Thr Asn Tyr Ala Gln Asn Phe

50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr 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 Ser Thr Gly Tyr Tyr Pro Ala Tyr Leu His His Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 454
<211> 1350
<212> DNA
<213> Homo sapiens

<400> 454
cagatgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccttctcc agttatgcta tcacctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcggta tgttggttc aacaaactac 180

gcacagaact tccagggcag agtcacgatt accgcggacg aatccacgag cacagcctac 240

atggagctga gcagcctcag atctgaggac acggccgtgt attactgtgc gagaagtact 300

ggttattacc ctgcatacct ccaccactgg ggccagggca ccctggtcac cgtctcgagt 360

gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc 420

ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc 480

tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc 540

ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc 600

tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc 660

aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga 720

ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccct 780

gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg 840

tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac 900

agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag 960

gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc 1020

aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag 1080

atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc 1140

gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccccctg 1200

ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg 1260

cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc 1320

cagaagagcc tgagcctgag ccccggcaag 1350

<210> 455
<211> 450
<212> PRT
<213> Homo sapiens

<400> 455

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

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

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

Gly Gly Ile Ile Gly Met Phe Gly Ser Thr Asn Tyr Ala Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr 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 Ser Thr Gly Tyr Tyr Pro Ala Tyr Leu His His Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly

225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 456
<211> 111
<212> PRT
<213> Homo sapiens

<400> 456

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

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

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

Met Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr His Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> 457
<211> 660
<212> DNA
<213> Homo sapiens

<400> 457
cagtctgccc tgactcagcc tcgctcagtg tccgggtctc ctggacagtc agtcaccatc 60

tcctgcactg gaaccagcag tgatgttggt ggttataact atgtctcctg gtaccaacag 120

cacccaggca aagcccccaa actcatgatt tatgatgtca gtaagcggcc tcaggggtc 180

cctgatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

caggctgagg atgaggctga ttattactgc agctcatata caagcagcag cactcatgtc 300

ttcggaactg ggaccaaggt caccgtccta ggtgcggccg caggccagcc caaggccgct 360

cccagcgtga ccctgttccc ccctcctcc gaggagctgc aggccaacaa ggccaccctg 420

gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc 480

agccccgtga aggccggcgt ggagaccacc acccccagca agcagagcaa caacaagtac 540

gccgccagca gctacctgag cctcaccccc gagcagtgga agagccaccg gagctacagc 600

tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggcccccac cgagtgcagc 660

<210> 458
<211> 220
<212> PRT
<213> Homo sapiens

<400> 458

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

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

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

Met Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
    50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
                85                  90                  95

Ser Thr His Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala
            100                 105                 110

Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
        115                 120                 125

Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
    130                 135                 140

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145                 150                 155                 160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
                165                 170                 175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
            180                 185                 190

Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
        195                 200                 205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
    210                 215                 220


<210>  459
<211>  121
<212>  PRT
<213>  Homo sapiens

<400>  459

Glu Val Gln Leu Val Glu Thr 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 Ser Tyr
            20                  25                  30

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

Gly Trp Ile Asn Pro 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 Glu Gly Lys Trp Gly Pro Gln Ala Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 460
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 460
gaggtgcagc tggtggagac cggggctgag gtgaagaagc ctggggcctc agtgaaggtt 60

tcctgcaagg catctggata cacctcacc agctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtggtgg cacaaactat 180

gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcag cacagcctac 240

atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gagagagggg 300

aaatggggac ctcaagcggc ttttgatatc tggggccaag ggacaatggt caccgtctcg 360

agtgctagca ccaagggccc cagcgtgttc ccctggcccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg 480

agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag 660

cccaagagct gcgacaagac ccacacctgc ccccctgcc ctgccccga gctgctgggc 720

ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc 780

cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac 900

aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc 960

aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc 1020

agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag 1080

gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac 1140

atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaaga gcctgagcct gagccccggc aag 1353

<210> 461
<211> 451
<212> PRT
<213> Homo sapiens

<400> 461

Glu Val Gln Leu Val Glu Thr 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 Ser Tyr
20 25 30

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

Gly Trp Ile Asn Pro 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 Glu Gly Lys Trp Gly Pro Gln Ala Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 462
<211> 109
<212> PRT
<213> Homo sapiens

<400> 462

Glu 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 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 Asp Ala Ser Ser Arg Ala Thr Asp 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 Leu
85 90 95

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

<210> 463
<211> 642
<212> DNA
<213> Homo sapiens

<400> 463
gaaattgtga tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa 120

cctggccagg ctcccaggct cctcatctat gatgcatcca gcagggccac tgacatccca 180

gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcactttg gacgttcggc 300

caagggacca aggtggagat caaacgtgcg gccgcaccca gcgtgttcat cttccccccc 360

tccgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtga ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctcacc 540

ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgagcagcc ccgtgaccaa gagcttcaac cggggcgagt gt 642

<210> 464
<211> 214
<212> PRT
<213> Homo sapiens

<400> 464

Glu 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 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 Asp Ala Ser Ser Arg Ala Thr Asp 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 Leu
85 90 95

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

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 465
<211> 117
<212> PRT
<213> Homo sapiens

<400> 465

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

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

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

35 40 45

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

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg 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 Ala Tyr Gly Tyr Thr Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 466
<211> 1341
<212> DNA
<213> Homo sapiens

<400> 466
gaggtgcagc tggtagagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc atctatgcca tgagctgggt ccgccaggca 120

ccagggaagg ggctggagtg ggtctcagct attagtagta gtggtgatag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca acgccaggaa cacgctgtat 240

ctgcaaatga acagtctgag agccgaggac acggctgtgt attactgtgc gagagcgtat 300

ggctacacgt tcgacccctg gggccaggga accctggtca ccgtctcgag tgctagcacc 360

aagggcccca gcgtgttccc cctggccccc agcagcaaga gcaccagcgg cggcacagcc 420

gccctgggct gcctggtgaa ggactacttc cccgagcccg tgaccgtgag ctggaacagc 480

ggcgccttga ccagcggcgt gcacaccttc cccgccgtgc tgcagagcag cggcctgtac 540

agcctgagca gcgtggtgac cgtgcccagc agcagcctgg gcacccagac ctacatctgc 600

aacgtgaacc acaagcccag caacaccaag gtggacaaac gcgtggagcc caagagctgc 660

gacaagaccc acacctgccc ccctgccct gcccccgagc tgctgggcgg accctccgtg 720

ttcctgttcc ccccaagcc caagaacacc ctcatgatca gccggacccc cgaggtgacc 780

tgcgtggtgg tggacgtgag ccacgaggac cccgaggtga agttcaactg gtacgtggac 840

ggcgtggagg tgcacaacgc caagaccaag ccccgggagg agcagtacaa cagcacctac 900

cgggtggtga gcgtgctcac cgtgctgcac caggactggc tgaacggcaa ggagtacaag 960

tgcaaggtga gcaacaaggc cctgcctgcc cccatcgaga agaccatcag caaggccaag 1020

ggccagcccc gggagcccca ggtgtacacc ctgccccca gccgggagga gatgaccaag 1080

aaccaggtgt ccctcacctg tctggtgaag ggcttctacc ccagcgacat cgccgtggag 1140

tgggagagca acggccagcc cgagaacaac tacaagacca ccccccct gt gctggacagc 1200

gacggcagct tcttcctgta cagcaagctc accgtggaca agagccggtg gcagcagggc 1260

aacgtgttca gctgcagcgt gatgcacgag gccctgcaca accactacac ccagaagagc 1320

ctgagcctga gccccggcaa g 1341

<210> 467
<211> 447
<212> PRT
<213> Homo sapiens

<400> 467

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

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

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

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

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg 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 Ala Tyr Gly Tyr Thr Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
115 120 125

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
130 135 140

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
145 150 155 160

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
165 170 175

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
180 185 190

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
195 200 205

Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His

210 215 220

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
225 230 235 240

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
245 250 255

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
260 265 270

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
275 280 285

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
290 295 300

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
305 310 315 320

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
325 330 335

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
340 345 350

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
355 360 365

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
370 375 380

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
385 390 395 400

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
405 410 415

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
420 425 430

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 468
<211> 113
<212> PRT
<213> Homo sapiens

<400> 468

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

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

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

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

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

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

Arg

<210> 469
<211> 654
<212> DNA
<213> Homo sapiens

<400> 469
gaaattgtgc tgactcagtc tccactctcc ctgcccgtca cccctggaga gccggcctcc 60

atctcctgca ggtctagtca gagcctcctg catagtaatg gatacaacta tttggattgg 120

tacctgcaga agccagggca gtctccacag ctcctgatct atttgggttc taatcgggcc 180

tccggggtcc ctgacaggtt cagtggcagt ggatcaggca cagattttac actgaaaatc 240

agcagagtgg aggctgagga tgttggggtt tattactgca tgcaagctct acaaactccc 300

ctcactttcg gcggagggac caaggtggag atcaaacgtg cggccgcacc agcgtgttc 360

atcttccccc cctccgacga gcagctgaag agcggcaccg ccagcgtggt gtgcctgctg 420

aacaacttct acccccggga ggccaaggtg cagtggaagg tggacaacgc cctgcagagc 480

ggcaacagcc aggagagcgt gaccgagcag gacagcaagg actccaccta cagcctgagc 540

agcaccctca ccctgagcaa ggccgactac gagaagcaca aggtgtacgc ctgcgaggtg 600

acccaccagg gcctgagcag ccccgtgacc aagagcttca accggggcga gtgt 654

<210> 470
<211> 218
<212> PRT
<213> Homo sapiens

<400> 470

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

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

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

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

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

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

Arg Ala Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 471
<211> 122
<212> PRT
<213> Homo sapiens

<400> 471

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

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

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

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Gly Gly Gly Ser Tyr Gly Ala Tyr Glu Gly Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 472
<211> 1356
<212> DNA
<213> Homo sapiens

<400> 472
caggtccagc tggtgcagtc tgggggaggc ctggtcaagc ctgggggtcc tgagactc 60

tcctgtgcag cctctggatt caccttcagt agctatagca tgaactgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcatcc attagtagta gtagttacat atactac 180

gtagactcag tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat 240

ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagaggtggt 300

gggagctacg gggcctacga aggcttttgac tactggggcc agggcaccct ggtcaccgtc 360

tcgagtgcta gcaccaaggg ccccagcgtg ttccccctgg ccccccagcag caagagcacc 420

agcggcggca cagccgccct gggctgcctg gtgaaggact acttccccga gcccgtgacc 480

gtgagctgga acagcggcgc cttgaccagc ggcgtgcaca ccttccccgc cgtgctgcag 540

agcagcggcc tgtacagcct gagcagcgtg gtgaccgtgc ccagcagcag cctgggcacc 600

cagacctaca tctgcaacgt gaaccacaag cccagcaaca ccaaggtgga caaacgcgtg 660

gagcccaaga gctgcgacaa gacccacacc tgccccccct gccctgcccc cgagctgctg 720

ggcggaccct ccgtgttcct gttccccccc aagcccaagg acaccctcat gatcagccgg 780

acccccgagg tgacctgcgt ggtggtggac gtgagccacg aggaccccga ggtgaagttc 840

aactggtacg tggacggcgt ggaggtgcac aacgccaaga ccaagccccg ggaggagcag 900

tacaacagca cctaccgggt ggtgagcgtg ctcaccgtgc tgcaccagga ctggctgaac 960

ggcaaggagt acaagtgcaa ggtgagcaac aaggccctgc ctgccccat cgagaagacc 1020

atcagcaagg ccaagggcca gccccgggag ccccaggtgt acaccctgcc ccccagccgg 1080

gaggagatga ccaagaacca ggtgtccctc acctgtctgg tgaagggctt ctaccccagc 1140

gacatcgccg tggagtggga gagcaacggc cagcccgaga acaactacaa gaccaccccc 1200

cctgtgctgg acagcgacgg cagcttcttc ctgtacagca agctcaccgt ggacaagagc 1260

cggtggcagc agggcaacgt gttcagctgc agcgtgatgc acgaggccct gcacaaccac 1320

tacacccaga agagcctgag cctgagcccc ggcaag 1356

<210> 473
<211> 452
<212> PRT
<213> Homo sapiens

<400> 473

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

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

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

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Val Asp Ser Val
50 55 60

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

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

Ala Arg Gly Gly Gly Ser Tyr Gly Ala Tyr Glu Gly Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
115 120 125

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
130 135 140

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145 150 155 160

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
165 170 175

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180 185 190

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
195 200 205

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His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser
    210                 215                 220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
225                 230                 235                 240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
    290                 295                 300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305                 310                 315                 320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
                325                 330                 335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350

Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445

Ser Pro Gly Lys
    450
```

<210> 474
<211> 108
<212> PRT

<213> Homo sapiens

<400> 474

Glu Ile Val Leu Tyr 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 Arg 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 Gly Ala Ser Thr Arg Ala Ala Gly Ile Pro Asp Arg Phe Ser Gly
50 55 60

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

Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Arg Thr Pro Leu
85 90 95

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

<210> 475
<211> 639
<212> DNA
<213> Homo sapiens

<400> 475
gaaattgtgc tgactcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gcgtgttagc agcttactag cctggtacca acagaaacct 120

ggccaggctc ccaggctcct catctatggt gcatccacca gggccgctgg catcccagac 180

aggttcagtg gcagtgggtc tgggacagac ttcactctca ccatcagcag actggagcct 240

gaagattctg cagtgtatta ctgtcagcag tatggtagga caccgctcac tttcggcgga 300

gggaccaagg tggagatcaa acgtgcggcc gcacccagcg tgttcatctt ccccccctcc 360

gacgagcagc tgaagagcgg caccgccagc gtggtgtgcc tgctgaacaa ctttctaccc 420

cgggaggcca aggtgcagtg gaaggtggac aacgccctgc agagcggcaa cagccaggag 480

agcgtgaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctcaccctg 540

agcaaggccg actacgagaa gcacaaggtg tacgcctgcg aggtgaccca ccagggcctg 600

agcagccccg tgaccaagag ctttcaaccgg ggcgagtgt 639

<210> 476
<211> 213
<212> PRT
<213> Homo sapiens

<400> 476

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

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

Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Arg Thr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Ala Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 477
<211> 121
<212> PRT
<213> Homo sapiens

<400> 477

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr

20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 478
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 478
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggtac aacaaaatac 180

gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agtgctagca ccaagggccc cagcgtgttc ccccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg 480

agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag 660

cccaagagct gcgacaagac ccacacctgc cccccctgcc ctgccccga gctgctgggc 720

ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc 780

cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac 900

aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc 960

aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc 1020

agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag 1080

gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac 1140

atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaaga gcctgagcct gagccccggc aag 1353

<210> 479
<211> 451
<212> PRT
<213> Homo sapiens

<400> 479

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His

195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 480

<211> 109
<212> PRT
<213> Homo sapiens

<400> 480

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

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Ala Val Phe Gly Gly Gly Thr Gln Leu Thr Val Leu Gly
100 105

<210> 481
<211> 654
<212> DNA
<213> Homo sapiens

<400> 481
tcctatgtgc tgactcagcc accctcggtg tcagtggccc caggacagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcgt ctatgatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgc tgtgttcgga 300

ggaggcaccc agctgaccgt cctcggtgcg gccgcaggcc agcccaaggc cgctcccagc 360

gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc 420

ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc 480

gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc 540

agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag 600

gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc 654

<210> 482
<211> 218
<212> PRT
<213> Homo sapiens

<400> 482

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

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Ala Val Phe Gly Gly Gly Thr Gln Leu Thr Val Leu Gly Ala Ala Ala
100 105 110

Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser
115 120 125

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
130 135 140

Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
145 150 155 160

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
165 170 175

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
180 185 190

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
195 200 205

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 483
<211> 121
<212> PRT
<213> Homo sapiens

<400> 483

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 484
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 484
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaagtc 60

tcttgcaagg cttctggagg ccccttccgc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcctgagtg gatgggaggg atcatcccta ttttttggtac aacaaaatac 180

gcaccgaagt tccagggcag agtcacgatt accgcggacg atttcgcggg cacagttac 240

atggagctga gcagcctgcg atctgaggac acggccatgt actactgtgc gaaacatatg 300

gggtaccagg tgcgcgaaac tatggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agtgctagca ccaagggccc cagcgtgttc ccctggcccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg 480

agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag 660

cccaagagct gcgacaagac ccacacctgc ccccctgcc ctgccccga gctgctgggc 720

ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc 780

cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac 900

aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc 960

aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc 1020

agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag 1080

gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac 1140

atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac caccccccct 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaaga gcctgagcct gagccccggc aag 1353

<210> 485
<211> 451
<212> PRT
<213> Homo sapiens

<400> 485

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Ser Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Phe Ala Gly Thr Val Tyr
65 70 75 80

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

Ala Lys His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 486
<211> 111
<212> PRT
<213> Homo sapiens

<400> 486

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

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

Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Arg Asp Gly Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65 70 75 80

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

Ser Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> 487
<211> 660
<212> DNA
<213> Homo sapiens

<400> 487
tcctatgtgc tgactcagcc accctcagcg tctgggaccc ccgggcagag ggtcaccatc 60

tcttgttctg gaagcagctc caacatcgga agtaattatg tatactggta ccagcagctc 120

ccaggcacgg cccccaaact cctcatctat agggatggtc agcggccctc aggggtccct 180

gaccgattct ctggctccaa gtctggcacc tcagcctccc tggccatcag tggactccgg 240

tccgatgatg aggctgatta ttactgtgca acatgggatg acaacctgag tggtccagta 300

ttcggcggag ggaccaagct gaccgtccta ggtgcggccg caggccagcc caaggccgct 360

cccagcgtga ccctgttccc ccctcctccc gaggagctgc aggccaacaa ggccaccctg 420

gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc 480

agccccgtga aggccggcgt ggagaccacc acccccagca agcagagcaa caacaagtac 540

gccgccagca gctacctgag cctcaccccc gagcagtgga agagccaccg gagctacagc 600

tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggcccccac cgagtgcagc 660

<210> 488
<211> 220
<212> PRT

<213> Homo sapiens

<400> 488

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

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

Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Arg Asp Gly Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65 70 75 80

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

Ser Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

Ala Ala Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser
115 120 125

Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser
130 135 140

Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser
145 150 155 160

Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn
165 170 175

Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Gly Gln Trp
180 185 190

Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr
195 200 205

Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser Gly
210 215 220

<210> 489
<211> 120
<212> PRT
<213> Homo sapiens

<400> 489

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

1 5 10 15

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

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

Gly Asp Ile Ile Gly Met Phe Gly Ser Thr Asn Tyr Ala Gln Asn Phe
50 55 60

Gln Gly Arg Leu Thr Ile Thr Ala Asp Glu Ser Thr 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 Ser Ser Gly Tyr Tyr Pro Ala Tyr Leu Pro His Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 490
<211> 1350
<212> DNA
<213> Homo sapiens

<400> 490
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc cagggtcctc ggtgaaggtc 60

tcctgtaagg cctctggagg cacctttctc cagctatggt atcagctggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggagac atcatcggta tgtttggttc aacaaactac 180

gcacagaact tccagggcag actcacgatt accgcggacg aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagaagtagt 300

ggttattacc ctgcatacct ccccccactgg ggccagggca ccttggtcac cgtctcgagt 360

gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc 420

ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt ggacgtgagc 480

tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc 540

ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc 600

tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc 660

aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga 720

ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccccc 780

gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg 840

tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac 900

agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag 960

gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc 1020

aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag 1080

atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc 1140

gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccccgtg 1200

ctggacagcg acggcagctt ctttcctgtac agcaagctca ccgtggacaa gagccggtgg 1260

cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc 1320

cagaagagcc tgagcctgag ccccggcaag 1350

<210> 491
<211> 450
<212> PRT
<213> Homo sapiens

<400> 491

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

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

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

Gly Asp Ile Ile Gly Met Phe Gly Ser Thr Asn Tyr Ala Gln Asn Phe
50 55 60

Gln Gly Arg Leu Thr Ile Thr Ala Asp Glu Ser Thr 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 Ser Ser Gly Tyr Tyr Pro Ala Tyr Leu Pro His Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro

180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys

450

<210> 492
<211> 109
<212> PRT
<213> Homo sapiens

<400> 492

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

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

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

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

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

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

<210> 493
<211> 642
<212> DNA
<213> Homo sapiens

<400> 493
gaaattgtgt tgacccagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa 120

cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180

gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcacccag aacttttcggc 300

ggagggacca aggtggagat caaacgtgcg gccgcaccca gcgtgttcat cttccccccc 360

tccgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtga ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctcacc 540

ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgagcagcc ccgtgaccaa gagcttcaac cggggcgagt gt 642

<210> 494

<211> 214
<212> PRT
<213> Homo sapiens

<400> 494

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

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

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

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

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

Arg Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Ala Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 495
<211> 121
<212> PRT
<213> Homo sapiens

<400> 495

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

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

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

Gly Gly Ile Ile Pro Met Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Val Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Gly Asp Lys Gly Ile Tyr Tyr Tyr Tyr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 496
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 496
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc cggggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccttcagc ttctattcta tgagctgggt gcgacaggcc 120

cctggacaag gacttgagtg gatgggaggg atcatcccta tgttggtac aacaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggtcg aatccacgag cacagcctac 240

atggaggtga gcagcctgag atctgaggac acggccgttt atttactgtgc gagaggtgat 300

aagggtatct actactacta catggacgtc tggggcaaag ggaccacggt caccgtctcg 360

agtgctagca ccaagggccc cagcgtgttc ccctggcccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg 480

agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag 660

cccaagagct gcgacaagac ccacacctgc ccccctgcc ctgccccga gctgctgggc 720

ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc 780

cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac 900

aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc 960

aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc 1020

agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag 1080

gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac 1140

atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaaga gcctgagcct gagccccggc aag 1353

<210> 497
<211> 451
<212> PRT
<213> Homo sapiens

<400> 497

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

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

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

Gly Gly Ile Ile Pro Met Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Val Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Gly Asp Lys Gly Ile Tyr Tyr Tyr Tyr Met Asp Val Trp Gly
100 105 110

Lys Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 498
<211> 111
<212> PRT
<213> Homo sapiens

<400> 498

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

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

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

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> 499
<211> 660
<212> DNA
<213> Homo sapiens

<400> 499
cagtctgccc tgactcagcc tgcctccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt ggttatAact atgtctcctg gtaccaacag 120

cacccaggca aagccccaa actcatgatt tatgaggtca gtaatcggcc tcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

caggctgagg acgaggctga ttattactgc agctcatata caagcagcag cacttctgtc 300

ttcggaactg ggaccaaggt caccgtccta ggtgcggccg caggccagcc caaggccgct 360

cccagcgtga ccctgttccc ccctcctcc gaggagctgc aggccaacaa ggccaccctg 420

gtgtgcctca tcagcgactt ctaccctggc gccgtgaccg tggcctggaa ggccgacagc 480

agccccgtga aggccggcgt ggagaccacc acccccagca agcagagcaa caacaagtac 540

gccgccagca gctacctgag cctcacccc gagcagtgga agagccaccg gagctacagc 600

tgccaggtga cccacgaggg cagcaccgtg gagaagaccg tggcccccac cgagtgcagc 660

<210> 500
<211> 220
<212> PRT
<213> Homo sapiens

<400> 500

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

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

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

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
115 120 125

Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130 135 140

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145 150 155 160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
165 170 175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180 185 190

Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
195 200 205

Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215 220

<210> 501
<211> 121
<212> PRT
<213> Homo sapiens

<400> 501

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Arg Thr His
20 25 30

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

Gly Gly Ile Ile Ala Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Ile Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Gly Ser Gly Tyr His Ile Ser Thr Pro Phe Asp Asn Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 502
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 502
gaggtgcagc tggtggagac cggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cctctggagg cacctt cagg acccatgcta tcagttgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcgcta tcttcggaac agcaaactac 180

gcacagaagt tccagggcag aatcacgatt accgcggacg aatccacgag tacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attt ctgtgc gagaggcagt 300

ggttatcata tatcgacacc ctttgacaac tggggccagg gaaccctggt caccgtctcg 360

agtgctagca ccaagggccc cagcgtgttc ccccctggccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg 480

agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag 660

cccaagagct gcgacaagac ccacacctgc ccccccctgcc ctgccccga gctgctgggc 720

ggaccctccg tgttcctgtt cccccccaag cccaaggaca ccctcatgat cagccggacc 780

cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac 900

aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc 960

aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc 1020

agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag 1080

gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac 1140

atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac caccccccct 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaaga gcctgagcct gagccccggc aag 1353

<210> 503
<211> 451
<212> PRT
<213> Homo sapiens

<400> 503

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Arg Thr His
20 25 30

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

Gly Gly Ile Ile Ala Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Ile Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Gly Ser Gly Tyr His Ile Ser Thr Pro Phe Asp Asn Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala

165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser

435 440 445

Pro Gly Lys
450

<210> 504
<211> 109
<212> PRT
<213> Homo sapiens

<400> 504

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

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Gly Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

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

<210> 505
<211> 654
<212> DNA
<213> Homo sapiens

<400> 505
tcctatgtgc tgactcagcc accctcggtg tcagtggccc caggacagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa ggtgtgcact ggtaccagca gaagcctggc 120

caggcccctg tgctggtcgt ctatgatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgt ggtattcggc 300

ggagggacca agctgaccgt cctaggtgcg gccgcaggcc agcccaaggc cgctcccagc 360

gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc 420

ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc 480

gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc 540

agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag 600

gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc 654

<210> 506
<211> 218
<212> PRT
<213> Homo sapiens

<400> 506

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

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Gly Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala Ala Ala
100 105 110

Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser
115 120 125

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
130 135 140

Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
145 150 155 160

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
165 170 175

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
180 185 190

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
195 200 205

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 507
<211> 128

<212> PRT
<213> Homo sapiens

<400> 507

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly His Ile Phe Ser Gly Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Gln Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Val Lys Asp Gly Tyr Cys Thr Leu Thr Ser Cys Pro Val Gly
100 105 110

Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 508
<211> 1374
<212> DNA
<213> Homo sapiens

<400> 508
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggaca catcttcagc ggctatgcaa tcagttgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttggtac aacaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggacc aatccacgag cacagcctac 240

atggacctga gcaacttgag atctgaggac acggccgtct attactgtgc gagagtgaaa 300

gatggatatt gtactcttac cagctgccct gtcggctggt acttcgatct ctggggccgt 360

ggcaccctgg tcactgtctc gagtgctagc accaagggcc ccagcgtgtt ccccctggcc 420

cccagcagca agagcaccag cggcggcaca gccgccctgg gctgcctggt gaaggactac 480

ttccccgagc ccgtgaccgt gagctggaac agcggcgcct tgaccagcgg cgtgcacacc 540

ttccccgccg tgctgcagag cagcggcctg tacagcctga gcagcgtggt gaccgtgccc 600

agcagcagcc tgggcaccca gacctacatc tgcaacgtga accacaagcc cagcaacacc 660

aaggtggaca aacgcgtgga gcccaagagc tgcgacaaga cccacacctg ccccccctgc 720

cctgccccg agctgctggg cggaccctcc gtgttcctgt tccccccaa gcccaaggac 780

accctcatga tcagccggac ccccgaggtg acctgcgtgg tggtggacgt gagccacgag 840

gaccccgagg tgaagttcaa ctggtacgtg gacggcgtgg aggtgcacaa cgccaagacc 900

aagccccggg aggagcagta caacagcacc taccgggtgg tgagcgtgct caccgtgctg 960

caccaggact ggctgaacgg caaggagtac aagtgcaagg tgagcaacaa ggccctgcct 1020

gcccccatcg agaagaccat cagcaaggcc aagggccagc cccgggagcc ccaggtgtac 1080

accctgcccc ccagccggga ggagatgacc aagaaccagg tgtccctcac ctgtctggtg 1140

aagggcttct accccagcga catcgccgtg gagtgggaga gcaacggcca gcccgagaac 1200

aactacaaga ccacccccct gtgctggac agcgacggca gcttcttcct gtacagcaag 1260

ctcaccgtgg acaagagccg gtggcagcag ggcaacgtgt tcagctgcag cgtgatgcac 1320

gaggccctgc acaaccacta cacccagaag agcctgagcc tgagccccgg caag 1374

<210> 509
<211> 458
<212> PRT
<213> Homo sapiens

<400> 509

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly His Ile Phe Ser Gly Tyr
20 25 30

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

Gly Gly Ile Ile Pro Ile Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Gln Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Val Lys Asp Gly Tyr Cys Thr Leu Thr Ser Cys Pro Val Gly
100 105 110

Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120 125

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
130 135 140

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
145 150 155 160

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
165 170 175

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
180 185 190

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
195 200 205

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
210 215 220

Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
225 230 235 240

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
245 250 255

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
260 265 270

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
275 280 285

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
290 295 300

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
305 310 315 320

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
325 330 335

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
340 345 350

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
355 360 365

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
370 375 380

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
385 390 395 400

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
405 410 415

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
420 425 430

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
435 440 445

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
450 455

<210> 510
<211> 108
<212> PRT
<213> Homo sapiens

<400> 510

Glu 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 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 Leu
85 90 95

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

<210> 511
<211> 639
<212> DNA
<213> Homo sapiens

<400> 511
gaaattgtga tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60

ctctcgtgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa 120

cctggccagg ctcccaggct cctcatcttt ggtgcctcca gcagggccac tggcatccca 180

gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcactcac tttcggcgga 300

gggaccaagc tggagatcaa acgtgcggcc gcacccagcg tgttcatctt ccccccctcc 360

gacgagcagc tgaagagcgg caccgccagc gtggtgtgcc tgctgaacaa ctttctaccc 420

cgggaggcca aggtgcagtg gaaggtggac aacgccctgc agagcggcaa cagccaggag 480

agcgtgaccg agcaggacag caaggactcc acctacagcc tgagcagcac cctcaccctg 540

agcaaggccg actacgagaa gcacaaggtg tacgcctgcg aggtgaccca ccagggcctg 600

agcagccccg tgaccaagag cttcaaccgg ggcgagtgt 639

<210> 512
<211> 213
<212> PRT
<213> Homo sapiens

<400> 512

Glu 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 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 Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Ala Ala Pro
100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 513
<211> 121
<212> PRT
<213> Homo sapiens

<400> 513

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Ile Phe Arg Ser Asn
20 25 30

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

Gly Gly Ile Phe Ala Leu Phe Gly Thr Thr Asp Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Ser Thr Thr Val Tyr
65 70 75 80

Leu Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 514
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 514
gaggtccagc tggtacagtc tggggctgag gttaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg catcttcaga agcaattcta tcagttgggt gcgacaggcc 120

cctgggcaag ggcttgagtg gatgggaggg atcttcgctc ttttcggaac aacagactac 180

gcgcagaagt tccagggcag agtcacgatt accgcggacg aatcttcgac cacagtctac 240

ctggagctga gtagcctgac atctgaggac acggccgttt attactgtgc gagaggcagt 300

ggctacacca cacgcaacta ctttgactac tggggccagg gcaccctggt caccgtctcg 360

agtgctagca ccaagggccc cagcgtgttc ccctggcccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg 480

agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag 660

cccaagagct gcgacaggcc ccacacctgc ccccctgcc ctgccccga gctgctgggc 720

ggaccctccg tgttcctgtt ccccccccaag cccaaggaca ccctcatgat cagccggacc 780

cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac 900

aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc 960

aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc 1020

agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagactggag 1080

gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac 1140

atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaaga gcctgagcct gagccccggc aag 1353

<210> 515
<211> 451
<212> PRT
<213> Homo sapiens

<400> 515

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Ile Phe Arg Ser Asn
20 25 30

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

Gly Gly Ile Phe Ala Leu Phe Gly Thr Thr Asp Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Ser Thr Thr Val Tyr
65 70 75 80

Leu Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

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

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val

145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met

420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 516
<211> 109
<212> PRT
<213> Homo sapiens

<400> 516

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 Asn
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 Ser Arg Ala Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Gly 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 Arg
100 105

<210> 517
<211> 654
<212> DNA
<213> Homo sapiens

<400> 517
gaaattgtgc tgactcagtc tccaggcacc ctgtctttgt ctccagggga aagagccaca 60

ctctcctgca gggccagtca gagtgttagc agcaactact taggctggta ccagcagaaa 120

cctggccagg ctcccaggct cctgatctat ggtgcatcca gcagggccag tggcatccca 180

gacaggttca gtggcggtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcaccctt cactttcggc 300

ggagggacca aggtggagat caaacgtgcg gccgcaggcc agcccaaggc cgctcccagc 360

gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc 420

ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga caccaccccc 480

gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc 540

agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag 600

gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc 654

<210> 518
<211> 218
<212> PRT
<213> Homo sapiens

<400> 518

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 Asn
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 Ser Arg Ala Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Gly 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 Arg Ala Ala Ala
100 105 110

Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser
115 120 125

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
130 135 140

Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
145 150 155 160

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
165 170 175

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
180 185 190

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
195 200 205

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 519
<211> 120
<212> PRT
<213> Homo sapiens

<400> 519

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

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

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

Gly Gly Ile Ile Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr 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 Gly Asn Tyr Tyr Tyr Glu Ser Ser Leu Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 520
<211> 1350
<212> DNA
<213> Homo sapiens

<400> 520
gaggtgcagc tggtggagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcggta tgttcggtac agcaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatttacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagaggaaat 300

tattactatg agagtagtct cgactactgg ggccagggaa ccctggtcac cgtctcgagt 360

gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc 420

ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc 480

tggaacagcg gcgccttgac cagcggcgtg cacacctttcc ccgccgtgct gcagagcagc 540

ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc 600

tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc 660

aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga 720

ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggaccccc 780

gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg 840

tacgtggacg gcgtggtggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac 900

agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag 960

gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc 1020

aaggccaagg gccagccccg ggagccccag gtgtacaccc tgcccccag ccgggaggag 1080

atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc 1140

gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccctgtg 1200

ctggacagcg acggcagctt ctttcctgtac agcaagctca ccgtggacaa gagccggtgg 1260

cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc 1320

cagaagagcc tgagcctgag ccccggcaag 1350

<210> 521
<211> 450
<212> PRT
<213> Homo sapiens

<400> 521

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

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

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

Gly Gly Ile Ile Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr 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 Gly Asn Tyr Tyr Tyr Glu Ser Ser Leu Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 522
<211> 109
<212> PRT
<213> Homo sapiens

<400> 522

Gln Ser Val Val Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105

<210> 523
<211> 654
<212> DNA
<213> Homo sapiens

<400> 523
cagtctgtcg tgacgcagcc gccctcggtg tcagtggccc caggacagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcgt ctatgatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatta tgtcttcgga 300

actgggacca aggtcaccgt cctaggtgcg gccgcaggcc agcccaaggc cgctcccagc 360

gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc 420

ctcatcagcg actt ctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc 480

gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc 540

agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag 600

gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc 654

<210> 524
<211> 218
<212> PRT
<213> Homo sapiens

<400> 524

Gln Ser Val Val Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala Ala Ala
100 105 110

Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser
115 120 125

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
130 135 140

Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
145 150 155 160

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
165 170 175

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
180 185 190

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
195 200 205

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 525
<211> 120
<212> PRT
<213> Homo sapiens

<400> 525

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Asn Phe
20 25 30

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

Gly Gly Ile Ile Ala Val Phe Gly Thr Thr Lys Tyr Ala His Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Gly Ser Leu Lys Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Pro His Tyr Tyr Ser Ser Tyr Met Asp Val Trp Gly Glu
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 526
<211> 1350
<212> DNA
<213> Homo sapiens

<400> 526
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtaaaggtc 60

tcctgcaagg cttctggagg ccccttccgc aattttgcta tcaactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcgctg tctttgggac gacaaagtac 180

gcacataagt tccagggcag agtcaccatc accgcggacg actccacaaa tacagcttac 240

atggagctgg gcagcctgaa atctgaggac acggccgtgt attactgtgc gagaggtccc 300

cactactact cctcctacat ggacgtctgg ggcgaaggga ccacggtcac cgtctcgagt 360

gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc 420

ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc 480

tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc 540

ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc 600

tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc 660

aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga 720

ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggaccccc 780

gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg 840

tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac 900

agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag 960

gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc 1020

aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag 1080

atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc 1140

gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccccgtg 1200

ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg 1260

cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc 1320

cagaagagcc tgagcctgag ccccggcaag 1350

<210> 527
<211> 450
<212> PRT
<213> Homo sapiens

<400> 527

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Arg Asn Phe
20 25 30

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

Gly Gly Ile Ile Ala Val Phe Gly Thr Thr Lys Tyr Ala His Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Gly Ser Leu Lys Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Pro His Tyr Tyr Ser Ser Tyr Met Asp Val Trp Gly Glu
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala

130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp

405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 528
<211> 107
<212> PRT
<213> Homo sapiens

<400> 528

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

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

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

Tyr Ala Ala Ser Thr 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 Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Ser
85 90 95

Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg
100 105

<210> 529
<211> 636
<212> DNA
<213> Homo sapiens

<400> 529
gacatccagt tgacccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcgagtca gggcattagc acttatttag cctggtatca gcagaaaccc 120

gggaaagttc ctaaactcct gatctatgct gcatccactt tgcaatcagg ggtcccatct 180

cggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct 240

gaagatgttg caacttatta ctgtcaaaag tataacagtg ccccttcttt cggccctggg 300

accaaagtgg atatcaaacg tgcggccgca cccagcgtgt tcatcttccc ccctccgac 360

gagcagctga agagcggcac cgccagcgtg gtgtgcctgc tgaacaactt ctaccccgg 420

gaggccaagg tgcagtggaa ggtggacaac gccctgcaga gcggcaacag ccaggagagc 480

gtgaccgagc aggacagcaa ggactccacc tacagcctga gcagcaccct caccctgagc 540

aaggccgact acgagaagca caaggtgtac gcctgcgagg tgacccacca gggcctgagc 600

agccccgtga ccaagagctt caaccggggc gagtgt 636

<210> 530
<211> 212
<212> PRT
<213> Homo sapiens

<400> 530

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

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

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

Tyr Ala Ala Ser Thr 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 Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Ser
85 90 95

Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg Ala Ala Ala Pro Ser
100 105 110

Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala
115 120 125

Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
130 135 140

Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser
145 150 155 160

Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr
165 170 175

Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys
180 185 190

Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn
195 200 205

Arg Gly Glu Cys
210

<210> 531
<211> 120
<212> PRT
<213> Homo sapiens

<400> 531

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

Ser Val Lys Val Pro Cys Lys Ser Ser Gly Ser Pro Phe Arg Ser Asn
20 25 30

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

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

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Val His
65 70 75 80

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

Ala Arg Gly Pro Thr Tyr Tyr Tyr Ser Tyr Met Asp Val Trp Gly Lys
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 532
<211> 1350
<212> DNA
<213> Homo sapiens

<400> 532
gaggtgcagc tggtggagac tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

ccctgcaaat cttctggaag ccccttcagg agtaatgctg tcagctgggt gcgacaggcc 120

cccggacaag ggcttgagtg ggtgggagga atcctcggtg tctttggttc accaagctac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatccaccaa cacagtccac 240

atggagctga gaggttttgag atctgaggac acggccgtgt attattgtgc gagaggtcct 300

acctactact actcctacat ggacgtctgg ggcaaaggga ccacggtcac cgtctcgagt 360

gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc 420

ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc 480

tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc 540

ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc 600

tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggtgacc 660

aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga 720

ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccct 780

gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg 840

tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac 900

agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag 960

gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc 1020

aaggccaagg gccagccccg ggagccccag gtgtacaccc tgcccccag ccgggaggag 1080

atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc 1140

gccgtggaat gagagagcaa cggccagccc gagaacaact acaagaccac ccccctgtg 1200

ctggacagcg acggcagctt ctttcctgtac agcaagctca ccgtggacaa gagccggtgg 1260

cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc 1320

cagaagagcc tgagcctgag ccccggcaag 1350

<210> 533
<211> 450
<212> PRT
<213> Homo sapiens

<400> 533

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

Ser Val Lys Val Pro Cys Lys Ser Ser Gly Ser Pro Phe Arg Ser Asn
20 25 30

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

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

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Val His
65 70 75 80

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

Ala Arg Gly Pro Thr Tyr Tyr Tyr Ser Tyr Met Asp Val Trp Gly Lys
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

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Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400
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Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 534
<211> 109
<212> PRT
<213> Homo sapiens

<400> 534

Ser Tyr Val Leu Thr Gln Pro Pro Ser Glu Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Arg Asn Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp His Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105

<210> 535
<211> 654
<212> DNA
<213> Homo sapiens

<400> 535
tcctatgtgc tgactcagcc accctcggag tcagtggccc caggacagac ggccaggatt 60

acctgtgggg gaaataacat tggaagaaat agtgtgcact ggtatcagca gaagccaggc 120

caggcccctg tgctggtcgt gtatgatgat agcgaccggc cctcagggat ccctgagcga 180

ttttctggct ccaagtctgg gaacacggcc accctgatta tcagcagggt cgaagtcggg 240

gatgaggccg actactactg tcaggtgtgg catagtagta gtgatcatta tgtcttcgga 300

actgggacca aggtcaccgt cctaggtgcg gccgcaggcc agcccaaggc cgctcccagc 360

gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc 420

ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc 480

gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc 540

agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag 600

gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc 654

<210> 536
<211> 218
<212> PRT
<213> Homo sapiens

<400> 536

Ser Tyr Val Leu Thr Gln Pro Pro Ser Glu Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Arg Asn Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp His Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala Ala Ala
100 105 110

Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser
115 120 125

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
130 135 140

Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
145 150 155 160

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
165 170 175

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
180 185 190

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
195 200 205

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 537
<211> 120
<212> PRT
<213> Homo sapiens

<400> 537

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

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

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

Gly Gly Ile Phe Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Ala Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Gly Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

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

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 538
<211> 1350
<212> DNA
<213> Homo sapiens

<400> 538
cagatgcagc tggtacaatc tggagctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcttcggta tgttgggac agcaaactac 180

gcgcagaagt tccagggcag agtcacgatt accgcggacg aattcacgag cgcggcctac 240

atggagctga gcagcctggg atctgaggac acggccatgt attactgtgc gaggtctagt 300

ggttattacc cccaatactt ccaggactgg ggccagggca ccctggtcac cgtctcgagt 360

gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc 420

ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc 480

tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc 540

ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc 600

tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc 660

aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga 720

ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccct 780

gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg 840

tacgtggacg gcgtggaggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac 900

agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag 960

gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc 1020

aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag 1080

atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc 1140

gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccctgtg 1200

ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg 1260

cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc 1320

cagaagagcc tgagcctgag ccccggcaag 1350

<210> 539
<211> 450
<212> PRT
<213> Homo sapiens

<400> 539

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

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

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

Gly Gly Ile Phe Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Ala Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Gly Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

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

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val

115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val

385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 540
<211> 109
<212> PRT
<213> Homo sapiens

<400> 540

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

Gln 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

Met 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 Ser
85 90 95

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

<210> 541
<211> 642
<212> DNA
<213> Homo sapiens

<400> 541
gaaattgtga tgacacagtc tccaggcacc ctgtctttgt ctccagggca aagagccacc 60

ctctcctgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa 120

cctggccagg ctcccagact cctcatgtat ggtgcatcca gcagggccac tggcatccca 180

gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcatcgct cacttttcggc 300

ggagggacca agctggagat caaacgtgcg gccgcaccca gcgtgttcat cttccccccc 360

tccgacgagc agctgaagag cggcaccgcc agcgtggtgt gcctgctgaa caacttctac 420

ccccgggagg ccaaggtgca gtggaaggtg gacaacgccc tgcagagcgg caacagccag 480

gagagcgtga ccgagcagga cagcaaggac tccacctaca gcctgagcag caccctcacc 540

ctgagcaagg ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 600

ctgagcagcc ccgtgaccaa gagcttcaac cggggcgagt gt 642

<210> 542
<211> 214
<212> PRT
<213> Homo sapiens

<400> 542

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

Gln 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

Met 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 Ser
85 90 95

Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 543
<211> 121
<212> PRT
<213> Homo sapiens

<400> 543

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Ile Phe Asn Ser Tyr
20 25 30

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

Gly Gly Ile Ile Ala Ile Phe His Thr Pro Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Lys Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

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

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 544
<211> 5
<212> PRT
<213> Homo sapiens

<400> 544

Asp Ile Lys Arg Thr
1 5

<210> 545
<211> 1353
<212> DNA
<213> Homo sapiens

<400> 545
gaggtgcagc tggtggagtc cggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg catcttcaac agttatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggc atcatcgcta tctttcatac accaaagtac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatccacgaa cacagcctac 240

atggaactga gaagcctgaa atctgaggac acggccctgt attactgtgc gagagggtcc 300

acttacgatt tttcgagtgg ccttgactac tggggccagg gaaccctggt caccgtctcg 360

agtgctagca ccaagggccc cagcgtgttc ccctggcccc ccagcagcaa gagcaccagc 420

ggcggcacag ccgccctggg ctgcctggtg aaggactact tccccgagcc cgtgaccgtg 480

agctggaaca gcggcgcctt gaccagcggc gtgcacacct tccccgccgt gctgcagagc 540

agcggcctgt acagcctgag cagcgtggtg accgtgccca gcagcagcct gggcacccag 600

acctacatct gcaacgtgaa ccacaagccc agcaacacca aggtggacaa acgcgtggag 660

cccaagagct gcgacaagac ccacacctgc ccccctgcc ctgccccga gctgctgggc 720

ggaccctccg tgttcctgtt ccccccaag cccaaggaca ccctcatgat cagccggacc 780

cccgaggtga cctgcgtggt ggtggacgtg agccacgagg accccgaggt gaagttcaac 840

tggtacgtgg acggcgtgga ggtgcacaac gccaagacca agccccggga ggagcagtac 900

aacagcacct accgggtggt gagcgtgctc accgtgctgc accaggactg gctgaacggc 960

aaggagtaca agtgcaaggt gagcaacaag gccctgcctg ccccatcga gaagaccatc 1020

agcaaggcca agggccagcc ccgggagccc caggtgtaca ccctgccccc cagccgggag 1080

gagatgacca agaaccaggt gtccctcacc tgtctggtga agggcttcta ccccagcgac 1140

atcgccgtgg agtgggagag caacggccag cccgagaaca actacaagac cacccccct 1200

gtgctggaca gcgacggcag cttcttcctg tacagcaagc tcaccgtgga caagagccgg 1260

tggcagcagg gcaacgtgtt cagctgcagc gtgatgcacg aggccctgca caaccactac 1320

acccagaaga gcctgagcct gagccccggc aag 1353

<210> 546
<211> 451
<212> PRT
<213> Homo sapiens

<400> 546

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Ile Phe Asn Ser Tyr
20 25 30

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

Gly Gly Ile Ile Ala Ile Phe His Thr Pro Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Lys Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

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

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
210 215 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Pro Gly Lys
450

<210> 547
<211> 109
<212> PRT
<213> Homo sapiens

<400> 547

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

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

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

<210> 548

<211> 654
<212> DNA
<213> Homo sapiens

<400> 548
caggcagggc tgactcagcc accctcggtg tcagtggccc caggacagac ggccaggatt 60

acctgtgggg gaaacaacat tggaagtaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tcctagtcgt ctatgatgat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gatagtagta gtgatcatgt ggtattcggc 300

ggagggacca agctgaccgt cctaggtgcg gccgcaggcc agcccaaggc cgctcccagc 360

gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc 420

ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc 480

gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc 540

agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag 600

gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc 654

<210> 549
<211> 218
<212> PRT
<213> Homo sapiens

<400> 549

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

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala Ala Ala
100 105 110

Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser
115 120 125

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp

130 135 140

Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
145 150 155 160

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
165 170 175

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
180 185 190

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
195 200 205

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 550
<211> 126
<212> PRT
<213> Homo sapiens

<400> 550

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

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

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

Gly Gly Val Ile Pro Ile Phe Arg Thr Ala Asn Tyr Ala Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Tyr Met Glu
65 70 75 80

Leu Ser Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg
85 90 95

Leu Asn Tyr His Asp Ser Gly Thr Tyr Tyr Asn Ala Pro Arg Gly Trp
100 105 110

Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 551
<211> 1368
<212> DNA
<213> Homo sapiens

<400> 551

caggtccagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg cttcttcagc agctatgcta tcagctgggt gcgccaggcc 120

cctggacaag gacttgagtg gatgggggg gtcatcccta tctttcgtac agcaaactac 180

gcacagaact tccagggcag agtcaccatt accgcggacg aattcacatc gtatatggag 240

ctgagcagcc tgagatctga cgacacggcc gtgtattact gtgcgaggtt gaattaccat 300

gattcgggga cttattataa cgccccccgg ggctggttcg acccctgggg ccagggaacc 360

ctggtcaccg tctcgagtgc tagcaccaag ggccccagcg tgttcccct ggccccagc 420

agcaagagca ccagcggcgg cacagccgcc ctgggctgcc tggtgaagga ctacttcccc 480

gagcccgtga ccgtgagctg gaacagcggc gccttgacca gcggcgtgca cacctttccc 540

gccgtgctgc agagcagcgg cctgtacagc ctgagcagcg tggtgaccgt gcccagcagc 600

agcctgggca cccagacctacatctgcaac gtgaaccaca agcccagcaa caccaaggtg 660

gacaaacgcg tggagcccaa gagctgcgac aagacccaca cctgccccc ctgccctgcc 720

cccgagctgc tgggcggacc ctccgtgttc ctgttccccc ccaagcccaa ggacaccctc 780

atgatcagcc ggacccccga ggtgacctgc gtggtggtgg acgtgagcca cgaggacccc 840

gaggtgaagt tcaactggta cgtggacggc gtggaggtgc acaacgccaa gaccaagccc 900

cgggaggagc agtacaacag cacctaccgg gtggtgagcg tgctcaccgt gctgcaccag 960

gactggctga acggcaagga gtacaagtgc aaggtgagca acaaggccct gcctgccccc 1020

atcgagaaga ccatcagcaa ggccaagggc cagccccggg agccccaggt gtacaccctg 1080

cccccagcc gggaggagat gaccaagaac caggtgtccc tcacctgtct ggtgaagggc 1140

ttctacccca gcgacatcgc cgtggagtgg gagagcaacg gccagcccga gaacaactac 1200

aagaccaccc ccccgtgct ggacagcgac ggcagcttct tcctgtacag caagctcacc 1260

gtggacaaga gccggtggca gcagggcaac gtgttcagct gcagcgtgat gcacgaggcc 1320

ctgcacaacc actacaccca gaagagcctg agcctgagcc ccggcaag 1368

<210> 552
<211> 456
<212> PRT
<213> Homo sapiens

<400> 552

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

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

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

Gly Gly Val Ile Pro Ile Phe Arg Thr Ala Asn Tyr Ala Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Phe Thr Ser Tyr Met Glu
65 70 75 80

Leu Ser Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg
85 90 95

Leu Asn Tyr His Asp Ser Gly Thr Tyr Tyr Asn Ala Pro Arg Gly Trp
100 105 110

Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
115 120 125

Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr
130 135 140

Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145 150 155 160

Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
165 170 175

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
180 185 190

Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile
195 200 205

Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val
210 215 220

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
225 230 235 240

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
245 250 255

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
260 265 270

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
275 280 285

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
290 295 300

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
305 310 315 320

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
325 330 335

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
340 345 350

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
355 360 365

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
370 375 380

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
385 390 395 400

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
405 410 415

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
420 425 430

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
435 440 445

Ser Leu Ser Leu Ser Pro Gly Lys
450 455

<210> 553
<211> 114
<212> PRT
<213> Homo sapiens

<400> 553

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

Glu Lys Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Ile Leu Asn 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 Ser Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys Arg

<210> 554
<211> 657
<212> DNA
<213> Homo sapiens

<400> 554
gacatccaga tgacccagtc tccagactcc ctggctgtgt ctctgggcga gaaggccacc 60

atcaactgca agtccagcca gagtattta aacagctcca acaataagaa ctacttagct 120

tggtaccagc agaaaccagg acagcctcct aagctgctca tttactgggc atctacccgg 180

gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240

atcagcagcc tgcaggctga agatgtggca gtttattact gtcagcaata ttatagtagt 300

ccgccgacgt tcggccaagg gaccaaggtg gaaatcaaac gtgcggccgc acccagcgtg 360

ttcatcttcc ccccctccga cgagcagctg aagagcggca ccgccagcgt ggtgtgcctg 420

ctgaacaact tctaccccg ggaggccaag gtgcagtgga aggtggacaa cgccctgcag 480

agcggcaaca gccaggagag cgtgaccgag caggacagca aggactccac ctacagcctg 540

agcagcaccc tcaccctgag caaggccgac tacgagaagc acaaggtgta cgcctgcgag 600

gtgacccacc agggcctgag cagccccgtg accaagagct tcaaccgggg cgagtgt 657

<210> 555
<211> 219
<212> PRT
<213> Homo sapiens

<400> 555

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

Glu Lys Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Ile Leu Asn 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 Ser Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys Arg Ala Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 556
<211> 120
<212> PRT
<213> Homo sapiens

<400> 556

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

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

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

Gly Gly Ile Ser Pro Met Phe Gly Thr Thr Thr Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

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

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 557
<211> 1350
<212> DNA
<213> Homo sapiens

<400> 557
caggtccagc tggtgcagtc tggagctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagt cacctttagt tactatgcta tgagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggagga atcagccctt tgtttgggac aacaacctac 180

gcacagaagt tccagggcag agtcacgatt actgcggacg actccacgag tacagcctac 240

atggaggtga ggagcctgag atctgaggac acggccgtgt attactgtgc gagatcttcg 300

aatttactat gatagtgtta tttgactact ggggccaggg accctggtca ccgtctcgag t 360

gctagcacca agggccccag cgtgttcccc ctggccccca gcagcaagag caccagcggc 420

ggcacagccg ccctgggctg cctggtgaag gactacttcc ccgagcccgt gaccgtgagc 480

tggaacagcg gcgccttgac cagcggcgtg cacaccttcc ccgccgtgct gcagagcagc 540

ggcctgtaca gcctgagcag cgtggtgacc gtgcccagca gcagcctggg cacccagacc 600

tacatctgca acgtgaacca caagcccagc aacaccaagg tggacaaacg cgtggagccc 660

aagagctgcg acaagaccca cacctgcccc ccctgccctg cccccgagct gctgggcgga 720

ccctccgtgt tcctgttccc ccccaagccc aaggacaccc tcatgatcag ccggacccct 780

gaggtgacct gcgtggtggt ggacgtgagc cacgaggacc ccgaggtgaa gttcaactgg 840

tacgtggacg gcgtggtggt gcacaacgcc aagaccaagc cccgggagga gcagtacaac 900

agcacctacc gggtggtgag cgtgctcacc gtgctgcacc aggactggct gaacggcaag 960

gagtacaagt gcaaggtgag caacaaggcc ctgcctgccc ccatcgagaa gaccatcagc 1020

aaggccaagg gccagccccg ggagccccag gtgtacaccc tgccccccag ccgggaggag 1080

atgaccaaga accaggtgtc cctcacctgt ctggtgaagg gcttctaccc cagcgacatc 1140

gccgtggagt gggagagcaa cggccagccc gagaacaact acaagaccac ccccccgtg 1200

ctggacagcg acggcagctt cttcctgtac agcaagctca ccgtggacaa gagccggtgg 1260

cagcagggca acgtgttcag ctgcagcgtg atgcacgagg ccctgcacaa ccactacacc 1320

cagaagagcc tgagcctgag ccccggcaag 1350

<210> 558
<211> 450
<212> PRT
<213> Homo sapiens

<400> 558

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

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

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

Gly Gly Ile Ser Pro Met Phe Gly Thr Thr Thr Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Asp Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

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

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 559
<211> 109
<212> PRT
<213> Homo sapiens

<400> 559

Gln Ser Val Val Thr Gln Pro Pro Ser Glu Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly His Asn Ile Gly Ser Asn Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asn Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Gly Ser Ser Ser Asp His

85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105

<210> 560
<211> 654
<212> DNA
<213> Homo sapiens

<400> 560
cagtctgtcg tgacgcagcc gccctcggag tcagtggccc caggacagac ggccaggatt 60

acctgtgggg gacataacat tggaagtaat agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcgt gtatgataat agcgaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg ggtagtagta gtgaccatta tgtcttcgga 300

actgggacca aggtcaccgt cctaggtgcg gccgcaggcc agcccaaggc cgctcccagc 360

gtgaccctgt tccccccctc ctccgaggag ctgcaggcca acaaggccac cctggtgtgc 420

ctcatcagcg acttctaccc tggcgccgtg accgtggcct ggaaggccga cagcagcccc 480

gtgaaggccg gcgtggagac caccaccccc agcaagcaga gcaacaacaa gtacgccgcc 540

agcagctacc tgagcctcac ccccgagcag tggaagagcc accggagcta cagctgccag 600

gtgacccacg agggcagcac cgtggagaag accgtggccc ccaccgagtg cagc 654

<210> 561
<211> 218
<212> PRT
<213> Homo sapiens

<400> 561

Gln Ser Val Val Thr Gln Pro Pro Ser Glu Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly His Asn Ile Gly Ser Asn Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asn Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

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

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Gly Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala Ala Ala

100 105 110

Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser
115 120 125

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
130 135 140

Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
145 150 155 160

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
165 170 175

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
180 185 190

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
195 200 205

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 562
<211> 123
<212> PRT
<213> Homo sapiens

<400> 562

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

Ser Val Arg Val Ser Cys Lys Ala Ser Gly Ser Ile Phe Arg Asn Tyr
20 25 30

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

Gly Gly Ile Ile Ala Ile Phe Gly Thr Pro Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Gly Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ile Pro His Tyr Asn Phe Gly Ser Gly Ser Tyr Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 563
<211> 1359
<212> DNA
<213> Homo sapiens

<400> 563
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgagagtc 60

tcctgcaagg cttctggaag catcttcaga aactatgcta tgagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcgcta ttttgggac accaaagtac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatcgacgag cactgtctac 240

atggaactga gcggactgag atctgaggac acggccatgt attactgtgc gaggattccc 300

cactataatt ttggttcggg gagttatttc gactactggg gccagggaac cctggtcacc 360

ggcttgagtg ctagcaccaa gggccccagc gtgttccccc tggccccag cagcaagagc 420

accagcggcg gcacagccgc cctgggctgc ctggtgaagg actacttccc cgagcccgtg 480

accgtgagct ggaacagcgg cgccttgacc agcggcgtgc acaccttccc cgccgtgctg 540

cagagcagcg gcctgtacag cctgagcagc gtggtgaccg tgcccagcag cagcctgggc 600

acccagacct acatctgcaa cgtgaaccac aagcccagca acaccaaggt ggacaaacgc 660

gtggagccca agagctgcga caagacccac acctgccccc cctgccctgc ccccgagctg 720

ctgggcggac cctccgtgtt cctgttcccc cccaagccca aggacaccct catgatcagc 780

cggacccccg aggtgacctg cgtggtggtg gacgtgagcc acgaggaccc cgaggtgaag 840

ttcaactggt acgtggacgg cgtggaggtg cacaacgcca agaccaagcc ccgggaggag 900

cagtacaaca gcacctaccg ggtggtgagc gtgctcaccg tgctgcacca ggactggctg 960

aacggcaagg agtacaagtg caaggtgagc aacaaggccc tgcctgcccc catcgagaag 1020

accatcagca aggccaaggg ccagccccgg gagccccagg tgtacaccct gccccccagc 1080

cgggaggaga tgaccaagaa ccaggtgtcc ctcacctgtc tggtgaaggg cttctcccc 1140

agcgacatcg ccgtggagtg ggagagcaac ggccagcccg agaacaacta caagaccacc 1200

cccctgtgc tggacagcga cggcagcttc ttcctgtaca gcaagctcac cgtggacaag 1260

agccggtggc agcagggcaa cgtgttcagc tgcagcgtga tgcacgaggc cctgcacaac 1320

cactacaccc agaagagcct gagcctgagc cccggcaag 1359

<210> 564
<211> 453
<212> PRT
<213> Homo sapiens

<400> 564

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

Ser Val Arg Val Ser Cys Lys Ala Ser Gly Ser Ile Phe Arg Asn Tyr
20 25 30

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

Gly Gly Ile Ile Ala Ile Phe Gly Thr Pro Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Gly Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ile Pro His Tyr Asn Phe Gly Ser Gly Ser Tyr Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

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Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305                 310                 315                 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
                325                 330                 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
            340                 345                 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
        355                 360                 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
    370                 375                 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385                 390                 395                 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
                405                 410                 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
            420                 425                 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
        435                 440                 445

Leu Ser Pro Gly Lys
    450
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<210> 565
<211> 111
<212> PRT
<213> Homo sapiens

<400> 565

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

Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr
            20                  25                  30

Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
        35                  40                  45

Ile Tyr Gly Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
65                  70                  75                  80
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Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Gly Thr Trp Asp Ser Ser Leu
85 90 95

Ser Ala Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly
100 105 110

<210> 566
<211> 660
<212> PRT
<213> Homo sapiens

<400> 566

Ala Cys Thr Gly Thr Gly Thr Thr Gly Ala Cys Ala Cys Ala Gly Cys
1 5 10 15

Cys Gly Cys Cys Cys Thr Cys Ala Gly Thr Gly Thr Cys Thr Gly Gly
20 25 30

Gly Gly Cys Cys Cys Cys Ala Gly Gly Gly Cys Ala Gly Ala Gly Gly
35 40 45

Gly Thr Cys Ala Cys Cys Ala Thr Cys Thr Cys Cys Thr Gly Cys Ala
50 55 60

Cys Thr Gly Gly Gly Ala Gly Cys Ala Gly Cys Thr Cys Cys Ala Ala
65 70 75 80

Cys Ala Thr Cys Gly Gly Gly Gly Cys Ala Gly Gly Thr Thr Ala Thr
85 90 95

Gly Ala Thr Gly Thr Ala Cys Ala Cys Thr Gly Gly Thr Ala Cys Cys
100 105 110

Ala Gly Cys Ala Gly Cys Thr Thr Cys Cys Ala Gly Gly Ala Ala Cys
115 120 125

Ala Gly Cys Cys Cys Cys Cys Ala Ala Ala Cys Thr Cys Cys Thr Cys
130 135 140

Ala Thr Cys Thr Ala Thr Gly Gly Thr Ala Ala Cys Ala Gly Cys Ala
145 150 155 160

Ala Thr Cys Gly Gly Cys Cys Cys Thr Cys Ala Gly Gly Gly Gly Thr
165 170 175

Cys Cys Cys Thr Gly Ala Cys Cys Gly Ala Thr Thr Cys Thr Cys Thr
180 185 190

Gly Gly Cys Thr Cys Cys Ala Ala Gly Thr Cys Thr Gly Gly Cys Ala
195 200 205

Cys Gly Thr Cys Ala Gly Cys Cys Ala Cys Cys Cys Thr Gly Gly Gly
210 215 220

Cys Ala Thr Cys Ala Cys Cys Gly Gly Ala Cys Thr Cys Cys Ala Gly
225 230 235 240

Ala Cys Thr Gly Gly Gly Gly Ala Cys Gly Ala Gly Gly Cys Cys Gly
245 250 255

Ala Thr Thr Ala Thr Thr Ala Cys Thr Gly Cys Gly Gly Ala Ala Cys
260 265 270

Ala Thr Gly Gly Gly Ala Thr Ala Gly Cys Ala Gly Cys Cys Thr Gly
275 280 285

Ala Gly Thr Gly Cys Thr Thr Ala Thr Gly Thr Cys Thr Thr Cys Gly
290 295 300

Gly Ala Ala Cys Thr Gly Gly Gly Ala Cys Cys Ala Ala Gly Gly Thr
305 310 315 320

Cys Ala Cys Cys Gly Thr Cys Cys Thr Ala Gly Gly Thr Gly Cys Gly
325 330 335

Gly Cys Cys Gly Cys Ala Gly Gly Cys Cys Ala Gly Cys Cys Cys Ala
340 345 350

Ala Gly Gly Cys Cys Gly Cys Thr Cys Cys Cys Ala Gly Cys Gly Thr
355 360 365

Gly Ala Cys Cys Cys Thr Gly Thr Thr Cys Cys Cys Cys Cys Cys Cys
370 375 380

Thr Cys Cys Thr Cys Cys Gly Ala Gly Gly Ala Gly Cys Thr Gly Cys
385 390 395 400

Ala Gly Gly Cys Cys Ala Ala Cys Ala Ala Gly Gly Cys Cys Ala Cys
405 410 415

Cys Cys Thr Gly Gly Thr Gly Thr Gly Cys Cys Thr Cys Ala Thr Cys
420 425 430

Ala Gly Cys Gly Ala Cys Thr Thr Cys Thr Ala Cys Cys Cys Thr Gly
435 440 445

Gly Cys Gly Cys Cys Gly Thr Gly Ala Cys Cys Gly Thr Gly Gly Cys
450 455 460

Cys Thr Gly Gly Ala Ala Gly Gly Cys Cys Gly Ala Cys Ala Gly Cys
465 470 475 480

Ala Gly Cys Cys Cys Cys Gly Thr Gly Ala Ala Gly Gly Cys Cys Gly
485 490 495

Gly Cys Gly Thr Gly Gly Ala Gly Ala Cys Cys Ala Cys Cys Ala Cys
500 505 510

Cys Cys Cys Cys Ala Gly Cys Ala Ala Gly Cys Ala Gly Ala Gly Cys
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Ala Ala Cys Ala Ala Cys Ala Ala Gly Thr Ala Cys Gly Cys Cys Gly
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Cys Cys Ala Gly Cys Ala Gly Cys Thr Ala Cys Cys Thr Gly Ala Gly
545 550 555 560

Cys Cys Thr Cys Ala Cys Cys Cys Cys Cys Gly Ala Gly Cys Ala Gly
565 570 575

Thr Gly Gly Ala Ala Gly Ala Gly Cys Cys Ala Cys Cys Gly Gly Ala
580 585 590

Gly Cys Thr Ala Cys Ala Gly Cys Thr Gly Cys Cys Ala Gly Gly Thr
595 600 605

Gly Ala Cys Cys Cys Ala Cys Gly Ala Gly Gly Gly Cys Ala Gly Cys
610 615 620

Ala Cys Cys Gly Thr Gly Gly Ala Gly Ala Ala Gly Ala Cys Cys Gly
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Thr Gly Gly Cys Cys Cys Cys Cys Ala Cys Cys Gly Ala Gly Thr Gly
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Cys Ala Gly Cys
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Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Gly Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser

50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
65 70 75 80

Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Gly Thr Trp Asp Ser Ser Leu
85 90 95

Ser Ala Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

Ala Ala Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
115 120 125

Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile
130 135 140

Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser
145 150 155 160

Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser
165 170 175

Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln
180 185 190

Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser
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Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
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Ser Arg Ser Leu Asp Val
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Lys Ser Ser Gln Ser Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr Leu
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Ala

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Trp Ala Ser Thr Arg Glu Ser
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Ser Tyr Ala Ile Ser
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Gly Ile Ile Pro Ile Phe Gly Thr Thr Lys Tyr Ala Pro Lys Phe Gln
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Gly

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His Met Gly Tyr Gln Val Arg Glu Thr Met Asp Val
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Ser Gly Ser Thr Phe Asn Ile Gly Ser Asn Ala Val Asp
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Ser Asn Asn Gln Arg Pro Ser

1 5

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Ala Ala Trp Asp Asp Ile Leu Asn Val Pro Val
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Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
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Glu Val Ser Asn Arg Pro Ser
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Ser Ser Tyr Thr Ser Ser Ser Thr Tyr
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Lys Asn Thr Gln Arg Pro Ser
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Val Ala Trp Asp Asp Ser Val Asp Gly Tyr Val
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Ser Gly Ser Ser Ser Asn Ile Gly Asn Asp Tyr Val Ser
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Asp Asn Asn Lys Arg Pro Ser
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Ala Thr Trp Asp Arg Arg Pro Thr Ala Tyr Val Val
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Gly Ser Ala Ile Ser
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Gly Ile Ser Pro Leu Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe Gln
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Gly Pro Lys Tyr Tyr Ser Glu Tyr Met Asp Val
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Arg Ala Ser Gln Gly Ile Ser Ser Tyr Leu Ala
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Asp Ala Ser Thr Leu Arg Ser
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Gln Arg Tyr Asn Ser Ala Pro Pro Ile
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Gly Ile Met Gly Met Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe Gln
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Gly

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Ser Ser Gly Tyr Tyr Pro Glu Tyr Phe Gln Asp
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Ser Gly His Lys Leu Gly Asp Lys Tyr Val Ser
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Gln Asp Asn Arg Arg Pro Ser
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Gln Ala Trp Asp Ser Ser Thr Ala
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Ser Tyr Ala Ile Thr
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Gly Ile Ile Gly Met Phe Gly Ser Thr Asn Tyr Ala Gln Asn Phe Gln
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Gly

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Ser Thr Gly Tyr Tyr Pro Ala Tyr Leu His His
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Ser Phe Ala Ile Ser
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Asp Val Ser Lys Arg Pro Ser
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Ser Ser Tyr Thr Ser Ser Ser Thr His Val
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Ser Tyr Tyr Met His
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Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe Gln
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Gly

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Glu Gly Lys Trp Gly Pro Gln Ala Ala Phe Asp Ile
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Ser Tyr Ala Ile Ser
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Asp Ala Ser Ser Arg Ala Thr
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Gln Gln Tyr Gly Ser Ser Leu Trp
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Ile Tyr Ala Met Ser
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Ala Ile Ser Ser Ser Gly Asp Ser Thr Tyr Tyr Ala Asp Ser Val Lys
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Gly

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Ala Tyr Gly Tyr Thr Phe Asp Pro
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Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
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Leu Gly Ser Asn Arg Ala Ser
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Met Gln Ala Leu Gln Thr Pro Leu
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Ser Tyr Ser Met Asn
1 5

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Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

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Gly Gly Gly Ser Tyr Gly Ala Tyr Glu Gly Phe Asp Tyr
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Arg Ala Ser Gln Arg Val Ser Ser Tyr Leu Ala
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Gly Ala Ser Thr Arg Ala Ala
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Gln Gln Tyr Gly Arg Thr Pro Leu Thr
1 5

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Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1 5 10

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Asp Asp Ser Asp Arg Pro Ser
1 5

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Gln Val Trp Asp Ser Ser Ser Asp His Ala Val
1 5 10

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Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Tyr Val Tyr
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Arg Asp Gly Gln Arg Pro Ser
1 5

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Ala Thr Trp Asp Asp Asn Leu Ser Gly Pro Val
1 5 10

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Ser Tyr Gly Ile Ser
1 5

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Asp Ile Ile Gly Met Phe Gly Ser Thr Asn Tyr Ala Gln Asn Phe Gln
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Gly

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Ser Ser Gly Tyr Tyr Pro Ala Tyr Leu Pro His
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Gly Tyr Tyr Ile His
1 5

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Gly Ala Ser Ser Arg Ala Thr
1 5

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Gln Gln Tyr Gly Ser Ser Pro Arg Thr
1 5

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Phe Tyr Ser Met Ser
1 5

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Gly Ile Ile Pro Met Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

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Gly Asp Lys Gly Ile Tyr Tyr Tyr Tyr Met Asp Val
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Ser Ser Tyr Thr Ser Ser Ser Thr Leu Val
1 5 10

<210> 637
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Thr His Ala Ile Ser
1 5

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Gly Ile Ile Ala Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
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Gly

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Gly Ser Gly Tyr His Ile Ser Thr Pro Phe Asp Asn
1 5 10

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Gly Gly Asn Asn Ile Gly Ser Lys Gly Val His
1 5 10

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Met Thr Ala Phe Thr
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Gln Val Trp Asp Ser Ser Ser Asp His Val Val
1 5 10

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Gly Tyr Ala Ile Ser
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Gly Ile Ile Pro Ile Phe Gly Thr Thr Asn Tyr Ala Gln Lys Phe Gln
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Gly

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Val Lys Asp Gly Tyr Cys Thr Leu Thr Ser Cys Pro Val Gly Trp Tyr
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Phe Asp Leu

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Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
1 5 10

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Met Thr Ala Phe Thr
1 5

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Gln Gln Tyr Gly Ser Ser Leu Thr
1 5

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Ser Asn Ser Ile Ser
1 5

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Gly Ile Phe Ala Leu Phe Gly Thr Thr Asp Tyr Ala Gln Lys Phe Gln
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Gly

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Gly Ser Gly Tyr Thr Thr Arg Asn Tyr Phe Asp Tyr

1 5 10

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Arg Ala Ser Gln Ser Val Ser Ser Asn Tyr Leu Gly
1 5 10

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Gly Ala Ser Ser Arg Ala Ser
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Gln Gln Tyr Gly Ser Ser Pro Leu Thr
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Gly Ile Ile Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
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Gly Asn Tyr Tyr Tyr Glu Ser Ser Leu Asp Tyr
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Gln Val Trp Asp Ser Ser Ser Asp His
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Asn Phe Ala Ile Asn
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<210> 659
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Gly Ile Ile Ala Val Phe Gly Thr Thr Lys Tyr Ala His Lys Phe Gln
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Gly

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Gly Pro His Tyr Tyr Ser Ser Tyr Met Asp Val
1 5 10

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Arg Ala Ser Gln Gly Ile Ser Thr Tyr Leu Ala
1 5 10

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Ala Ala Ser Thr Leu Gln Ser
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Gln Lys Tyr Asn Ser Ala Pro Ser
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Ser Asn Ala Val Ser
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Gly Ile Leu Gly Val Phe Gly Ser Pro Ser Tyr Ala Gln Lys Phe Gln
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Gly

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Gly Pro Thr Tyr Tyr Tyr Ser Tyr Met Asp Val
1 5 10

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Gly Gly Asn Asn Ile Gly Arg Asn Ser Val His
1 5 10

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Asp Asn Ala Ile Ser
1 5

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Gln Val Trp His Ser Ser Ser Asp His Tyr Val
1 5 10

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Ser Tyr Ala Ile Ser
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Gly Ile Phe Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

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Ser Ser Gly Tyr Tyr Pro Gln Tyr Phe Gln Asp
1 5 10

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<400> 673

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

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

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
35 40 45

Arg Ala Ser Gln Asn Ile Tyr Lys Tyr Leu Asn Trp Tyr Gln Gln Arg
50 55 60

Pro Gly Lys Ala Pro Lys Gly Leu Ile Ser Ala Ala Ser Gly Leu Gln
65 70 75 80

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
85 90 95

Thr Leu Thr Ile Thr Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
100 105 110

Cys Gln Gln Ser Tyr Ser Pro Pro Leu Thr Phe Gly Gly Gly Thr Arg
115 120 125

Val Asp Ile Lys Arg Thr
130

<210> 674
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Ala Ser Thr Met Asp Met Arg Val Leu Ala Gln Leu Leu Gly Leu Leu
1 5 10 15

Leu Leu Trp Leu Arg Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser
20 25 30

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
35 40 45

Arg Ala Ser Gln Asn Ile Tyr Lys Tyr Leu Asn Trp Tyr Gln Gln Arg
50 55 60

Pro Gly Lys Ala Pro Lys Gly Leu Ile Ser Ala Ala Ser Gly Leu Gln
65 70 75 80

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
85 90 95

Thr Leu Thr Ile Thr Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
100 105 110

Cys Gln Gln Ser Tyr Ser Pro Pro Leu Thr Phe Gly Gly Gly Thr Arg
115 120 125

Val Glu Ile Lys Arg Thr
130

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<400> 675

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

Leu Leu Trp Leu Arg Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser
20 25 30

Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys
35 40 45

Arg Thr Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys
50 55 60

Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln
65 70 75 80

Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
85 90 95

Thr Leu Thr Ile Ser Gly Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
100 105 110

Cys Gln Gln Ser Tyr Ser Met Pro Ala Phe Gly Gln Gly Thr Lys Leu
115 120 125

Glu Ile Lys Arg Thr
130

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Ala Ser Thr Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala
1 5 10 15

Pro Ser Trp Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly
20 25 30

Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly
35 40 45

Ser Ser Ile Ser Asn Tyr Tyr Trp Ser Trp Ile Arg Gln Ser Pro Gly
50 55 60

Lys Gly Leu Glu Trp Ile Gly Phe Ile Tyr Tyr Gly Gly Asn Thr Lys
65 70 75 80

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

Lys Ser Gln Val Ser Leu Thr Met Ser Ser Val Thr Ala Ala Glu Ser
100 105 110

Ala Val Tyr Phe Cys Ala Arg Ala Ser Cys Ser Gly Gly Tyr Cys Ile
115 120 125

Leu Asp Tyr Trp Gly Gln Thr Leu Val Thr Val Ser
130 135 140

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Ala Ser Thr Met Glu Leu Gly Leu Cys Trp Val Phe Leu Val Ala Ile
1 5 10 15

Leu Lys Gly Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
20 25 30

Leu Val Gln Pro Gly Gly Ser Leu Arg Ile Ser Cys Ala Ala Ser Gly
35 40 45

Phe Thr Val Ser Ser Asn Tyr Met Ser Trp Val Arg Gln Ala Pro Gly
50 55 60

Lys Gly Leu Glu Trp Val Ser Val Ile Tyr Ser Gly Gly Ser Thr Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Ser Phe Ser Arg Asp Asn Ser
85 90 95

Lys Asn Thr Val Phe Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Cys Leu Ser Arg Met Arg Gly Tyr Gly
115 120 125

Leu Asp Val Trp Gly Gln Thr Thr Val Thr Val Ser
130 135 140

<210> 678
<211> 140
<212> PRT
<213> Homo sapiens

<400> 678

Ala Ser Thr Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala
1 5 10 15

Pro Ser Trp Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly
20 25 30

Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly
35 40 45

Ser Ser Ile Ser Asn Tyr Tyr Trp Ser Trp Ile Arg Gln Ser Pro Gly
50 55 60

Lys Gly Leu Glu Trp Ile Gly Phe Ile Tyr Tyr Gly Gly Asn Thr Lys
65 70 75 80

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

Lys Ser Gln Val Ser Leu Thr Met Ser Ser Val Thr Ala Ala Glu Ser
100 105 110

Ala Val Tyr Phe Cys Ala Arg Ala Ser Cys Ser Gly Gly Tyr Cys Ile
115 120 125

Leu Asp Tyr Trp Gly Gln Thr Leu Val Thr Val Ser
130 135 140

<210> 679
<211> 24
<212> PRT
<213> Influenza A virus

<400> 679

Met Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Lys Asn Gly Trp Glu
1 5 10 15

Cys Lys Cys Asn Asp Ser Ser Asp
20

<210> 680
<211> 23
<212> PRT
<213> Influenza A virus

<400> 680

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly Cys
1 5 10 15

Arg Cys Asn Asp Ser Ser Asp
20

<210> 681
<211> 23
<212> PRT
<213> Influenza A virus

<400> 681

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

Arg Cys Asn Asp Ser Gly Asp
            20


<210>  682
<211>  23
<212>  PRT
<213>  Influenza A virus

<400>  682

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Glu Cys
1               5                   10                  15

Arg Cys Asn Gly Ser Ser Asp
            20


<210>  683
<211>  23
<212>  PRT
<213>  Influenza A virus

<400>  683

Ser Leu Pro Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly Cys
1               5                   10                  15

Arg Cys Asn Asp Ser Ser Asp
            20


<210>  684
<211>  23
<212>  PRT
<213>  Influenza A virus

<400>  684

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly Cys
1               5                   10                  15

Arg Cys Asn Gly Ser Ser Asp
            20


<210>  685
<211>  23
<212>  PRT
<213>  Influenza A virus

<400>  685

Ser Leu Leu Thr Glu Val Asp Thr Leu Thr Arg Asn Gly Trp Gly Cys
1               5                   10                  15

Arg Cys Ser Asp Ser Ser Asp
            20
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<210> 686
<211> 23
<212> PRT
<213> Influenza A virus

<400> 686

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Lys Glu Trp Gly Cys
1 5 10 15

Asn Cys Ser Asp Ser Ser Asp
20

<210> 687
<211> 23
<212> PRT
<213> Influenza A virus

<400> 687

Ser Leu Leu Thr Glu Val Glu Thr Leu Ile Arg Asn Gly Trp Gly Cys
1 5 10 15

Arg Cys Ser Asp Ser Ser Asp
20

<210> 688
<211> 23
<212> PRT
<213> Influenza A virus

<400> 688

Ser Leu Leu Thr Glu Val Glu Thr Leu Thr Lys Asn Gly Trp Gly Cys
1 5 10 15

Arg Cys Ser Asp Ser Ser Asp
20

<210> 689
<211> 23
<212> PRT
<213> Influenza A virus

<400> 689

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

Arg Tyr Asn Asp Ser Ser Asp
20

<210> 690
<211> 23
<212> PRT
<213> Influenza A virus

<400> 690

Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Glu Cys
1 5 10 15

Lys Cys Ser Asp Ser Ser Asp
20

<210> 691
<211> 23
<212> PRT
<213> Influenza A virus

<400> 691

Ser Leu Leu Thr Glu Val Glu Thr His Thr Arg Asn Gly Trp Glu Cys
1 5 10 15

Lys Cys Ser Asp Ser Ser Asp
20

<210> 692
<211> 23
<212> PRT
<213> Influenza A virus

<400> 692

Ser Leu Leu Thr Glu Val Glu Thr His Thr Arg Asn Gly Trp Glu Cys
1 5 10 15

Lys Cys Ser Asp Ser Ser Asp
20

<210> 693
<211> 23
<212> PRT
<213> Influenza A virus

<400> 693

Ser Leu Leu Thr Glu Val Lys Thr Pro Thr Arg Asn Gly Trp Glu Cys
1 5 10 15

Lys Cys Ser Asp Ser Ser Asp
20

<210> 694
<211> 23
<212> PRT
<213> Influenza A virus

<400> 694

Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asp Gly Trp Glu Cys
1 5 10 15

Lys Cys Ser Asp Ser Ser Asp
20

<210> 695
<211> 23
<212> PRT
<213> Influenza A virus

<400> 695

Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Gly Cys
1 5 10 15

Arg Cys Ser Asp Ser Ser Asp
20

<210> 696
<211> 23
<212> PRT
<213> Influenza A virus

<400> 696

Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Glu Cys
1 5 10 15

Lys Cys Asn Asp Ser Ser Asp
20

<210> 697
<211> 23
<212> PRT
<213> Influenza A virus

<400> 697

Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Glu Cys
1 5 10 15

Lys Cys Asn Asp Ser Ser Asp
20

<210> 698
<211> 23
<212> PRT
<213> Influenza A virus

<400> 698

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly Cys
1 5 10 15

Lys Cys Asn Asp Ser Ser Asp
20

<210> 699
<211> 23
<212> PRT
<213> Influenza A virus

<400> 699

Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Glu Cys

1 5 10 15

Arg Cys Asn Asp Ser Ser Asp
20

<210> 700
<211> 23
<212> PRT
<213> Influenza A virus

<400> 700

Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Glu Cys
1 5 10 15

Arg Cys Asn Asp Ser Ser Asp
20

<210> 701
<211> 23
<212> PRT
<213> Influenza A virus

<400> 701

Ser Leu Leu Thr Glu Val Glu Thr Pro Thr Arg Asn Gly Trp Glu Cys
1 5 10 15

Arg Cys Asn Asp Ser Ser Asp
20

<210> 702
<211> 23
<212> PRT
<213> Influenza A virus

<400> 702

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Lys Gly Trp Glu Cys
1 5 10 15

Asn Cys Ser Asp Ser Ser Asp
20

<210> 703
<211> 23
<212> PRT
<213> Influenza A virus

<400> 703

Ser Leu Leu Thr Gly Val Glu Thr His Thr Arg Asn Gly Trp Gly Cys
1 5 10 15

Lys Cys Ser Asp Ser Ser Asp
20

<210> 704

<211> 23
<212> PRT
<213> Influenza A virus

<400> 704

Ser Leu Leu Pro Glu Val Glu Thr His Thr Arg Asn Gly Trp Gly Cys
1 5 10 15

Arg Cys Ser Asp Ser Ser Asp
20

<210> 705
<211> 16
<212> PRT
<213> Influenza A virus

<400> 705

Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly Cys Arg
1 5 10 15

<210> 706
<211> 15
<212> PRT
<213> Influenza A virus

<400> 706

Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly Cys Arg
1 5 10 15

<210> 707
<211> 12
<212> PRT
<213> Influenza A virus

<400> 707

Val Glu Thr Pro Ile Arg Asn Glu Trp Gly Cys Arg
1 5 10

<210> 708
<211> 17
<212> PRT
<213> Influenza A virus

<400> 708

Glu Thr Pro Ile Arg Asn Glu Trp Gly Cys Arg Cys Asn Asp Ser Ser
1 5 10 15

Asp

<210> 709
<211> 16
<212> PRT
<213> Influenza A virus

<400> 709

Thr Pro Ile Arg Asn Glu Trp Gly Cys Arg Cys Asn Asp Ser Ser Asp
1 5 10 15

<210> 710
<211> 15
<212> PRT
<213> Influenza A virus

<400> 710

Pro Ile Arg Asn Glu Trp Gly Cys Arg Cys Asn Asp Ser Ser Asp
1 5 10 15

<210> 711
<211> 14
<212> PRT
<213> Influenza A virus

<400> 711

Ile Arg Asn Glu Trp Gly Cys Arg Cys Asn Asp Ser Ser Asp
1 5 10

<210> 712
<211> 13
<212> PRT
<213> Influenza A virus

<400> 712

Arg Asn Glu Trp Gly Cys Arg Cys Asn Asp Ser Ser Asp
1 5 10

<210> 713
<211> 12
<212> PRT
<213> Influenza A virus

<400> 713

Asn Glu Trp Gly Cys Arg Cys Asn Asp Ser Ser Asp
1 5 10

<210> 714
<211> 17
<212> PRT
<213> Influenza A virus

<400> 714

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly Cys
1 5 10 15

Arg

<210> 715
<211> 16
<212> PRT
<213> Influenza A virus

<400> 715

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly Cys
1 5 10 15

<210> 716
<211> 15
<212> PRT
<213> Influenza A virus

<400> 716

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp Gly
1 5 10 15

<210> 717
<211> 14
<212> PRT
<213> Influenza A virus

<400> 717

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu Trp
1 5 10

<210> 718
<211> 13
<212> PRT
<213> Influenza A virus

<400> 718

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn Glu
1 5 10

<210> 719
<211> 12
<212> PRT
<213> Influenza A virus

<400> 719

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg Asn
1 5 10

<210> 720
<211> 11
<212> PRT
<213> Influenza A virus

<400> 720

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile Arg
1 5 10

<210> 721
<211> 10
<212> PRT
<213> Influenza A virus

<400> 721

Ser Leu Leu Thr Glu Val Glu Thr Pro Ile
1 5 10

<210> 722
<211> 8
<212> PRT
<213> Influenza A virus

<400> 722

Ser Leu Leu Thr Glu Val Glu Thr
1 5

<210> 723
<211> 7
<212> PRT
<213> Influenza A virus

<400> 723

Ser Leu Leu Thr Glu Val Glu
1 5

<210> 724
<211> 9
<212> PRT
<213> Influenza A virus

<400> 724

Ser Leu Leu Thr Glu Val Glu Thr Pro
1 5

<210> 725
<211> 12
<212> PRT
<213> Homo sapiens

<400> 725

Gly Ser Thr Tyr Asp Phe Ser Ser Gly Leu Asp Tyr
1 5 10

<210> 726
<211> 60
<212> PRT
<213> Artificial Sequence

<220>
<223> Recombinant homotrimeric foldon HA protein

<400> 726

Ser Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile Pro
1 5 10 15

Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp
20 25 30

Val Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu Leu

35 40 45

Gly Leu Asp Ser Thr Gly His His His His His His
50 55 60

<210> 727
<211> 572
<212> PRT
<213> Influenza A virus

<400> 727

Asp Thr Leu Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Asp Thr Val
1 5 10 15

Asp Thr Val Leu Glu Lys Asn Val Thr Val Thr His Ser Val Asn Leu
20 25 30

Leu Glu Asp Lys His Asn Gly Lys Leu Cys Lys Leu Arg Gly Val Ala
35 40 45

Pro Leu His Leu Gly Lys Cys Asn Ile Ala Gly Trp Ile Leu Gly Asn
50 55 60

Pro Glu Cys Glu Ser Leu Ser Thr Ala Ser Ser Trp Ser Tyr Ile Val
65 70 75 80

Glu Thr Pro Ser Ser Asp Asn Gly Thr Cys Tyr Pro Gly Asp Phe Ile
85 90 95

Asp Tyr Glu Glu Leu Arg Glu Gln Leu Ser Ser Val Ser Ser Phe Glu
100 105 110

Arg Phe Glu Ile Phe Pro Lys Thr Ser Ser Trp Pro Asn His Asp Ser
115 120 125

Asn Lys Gly Val Thr Ala Ala Cys Pro His Ala Gly Ala Lys Ser Phe
130 135 140

Tyr Lys Asn Leu Ile Trp Leu Val Lys Lys Gly Asn Ser Tyr Pro Lys
145 150 155 160

Leu Ser Lys Ser Tyr Ile Asn Asp Lys Gly Lys Glu Val Leu Val Leu
165 170 175

Trp Gly Ile His His Pro Ser Thr Ser Ala Asp Gln Gln Ser Leu Tyr
180 185 190

Gln Asn Ala Asp Thr Tyr Val Phe Val Gly Ser Ser Arg Tyr Ser Lys
195 200 205

Lys Phe Lys Pro Glu Ile Ala Ile Arg Pro Lys Val Arg Asp Gln Glu
210 215 220

Gly Arg Met Asn Tyr Tyr Trp Thr Leu Val Glu Pro Gly Asp Lys Ile
225 230 235 240

Thr Phe Glu Ala Thr Gly Asn Leu Val Val Pro Arg Tyr Ala Phe Ala
245 250 255

Met Glu Arg Asn Ala Gly Ser Gly Ile Ile Ile Ser Asp Thr Pro Val
260 265 270

His Asp Cys Asn Thr Thr Cys Gln Thr Pro Lys Gly Ala Ile Asn Thr
275 280 285

Ser Leu Pro Phe Gln Asn Ile His Pro Ile Thr Ile Gly Lys Cys Pro
290 295 300

Lys Tyr Val Lys Ser Thr Lys Leu Arg Leu Ala Thr Gly Leu Arg Asn
305 310 315 320

Ile Pro Ser Ile Gln Ser Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe
325 330 335

Ile Glu Gly Gly Trp Thr Gly Met Val Asp Gly Trp Tyr Gly Tyr His
340 345 350

His Gln Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Leu Lys Ser Thr
355 360 365

Gln Asn Ala Ile Asp Glu Ile Thr Asn Lys Val Asn Ser Val Ile Glu
370 375 380

Lys Met Asn Thr Gln Phe Thr Ala Val Gly Lys Glu Phe Asn His Leu
385 390 395 400

Glu Lys Arg Ile Glu Asn Leu Asn Lys Lys Val Asp Asp Gly Phe Leu
405 410 415

Asp Ile Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Leu Glu Asn Glu
420 425 430

Arg Thr Leu Asp Tyr His Asp Ser Asn Val Lys Asn Leu Tyr Glu Lys
435 440 445

Val Arg Ser Gln Leu Lys Asn Asn Ala Lys Glu Ile Gly Asn Gly Cys
450 455 460

Phe Glu Phe Tyr His Lys Cys Asp Asn Thr Cys Met Glu Ser Val Lys
465 470 475 480

Asn Gly Thr Tyr Asp Tyr Pro Lys Tyr Ser Glu Glu Ala Lys Leu Asn
485 490 495

Arg Glu Glu Ile Asp Gly Val Lys Leu Glu Ser Thr Arg Ile Tyr Gln
500 505 510

Ser Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile Pro
515 520 525

Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp
530 535 540

Val Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu Leu
545 550 555 560

Gly Leu Asp Ser Thr Gly His His His His His His
565 570

<210> 728
<211> 571
<212> PRT
<213> Influenza A virus

<400> 728

Asp Thr Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Asp Thr Val
1 5 10 15

Asp Thr Val Leu Glu Lys Asn Val Thr Val Thr His Ser Val Asn Leu
20 25 30

Leu Glu Asp Ser His Asn Gly Lys Leu Cys Leu Leu Lys Gly Ile Ala
35 40 45

Pro Leu Gln Leu Gly Asn Cys Ser Val Ala Gly Trp Ile Leu Gly Asn
50 55 60

Pro Glu Cys Glu Leu Leu Ile Ser Arg Glu Ser Trp Ser Tyr Ile Val
65 70 75 80

Glu Lys Pro Asn Pro Glu Asn Gly Thr Cys Tyr Pro Gly His Phe Ala
85 90 95

Asp Tyr Glu Glu Leu Arg Glu Gln Leu Ser Ser Val Ser Ser Phe Glu
100 105 110

Arg Phe Glu Ile Phe Pro Lys Glu Ser Ser Trp Pro Asn His Thr Thr
115 120 125

Thr Gly Val Ser Ala Ser Cys Ser His Asn Gly Glu Ser Ser Phe Tyr
130 135 140

Lys Asn Leu Leu Trp Leu Thr Gly Lys Asn Gly Leu Tyr Pro Asn Leu
145 150 155 160

```
Ser Lys Ser Tyr Ala Asn Asn Lys Glu Lys Glu Val Leu Val Leu Trp
                165                 170                 175

Gly Val His His Pro Pro Asn Ile Gly Asp Gln Arg Ala Leu Tyr His
            180                 185                 190

Lys Glu Asn Ala Tyr Val Ser Val Val Ser Ser His Tyr Ser Arg Lys
        195                 200                 205

Phe Thr Pro Glu Ile Ala Lys Arg Pro Lys Val Arg Asp Gln Glu Gly
    210                 215                 220

Arg Ile Asn Tyr Tyr Trp Thr Leu Leu Glu Pro Gly Asp Thr Ile Ile
225                 230                 235                 240

Phe Glu Ala Asn Gly Asn Leu Ile Ala Pro Arg Tyr Ala Phe Ala Leu
                245                 250                 255

Ser Arg Gly Phe Gly Ser Gly Ile Ile Asn Ser Asn Ala Pro Met Asp
            260                 265                 270

Glu Cys Asp Ala Lys Cys Gln Thr Pro Gln Gly Ala Ile Asn Ser Ser
        275                 280                 285

Leu Pro Phe Gln Asn Val His Pro Val Thr Ile Gly Glu Cys Pro Lys
    290                 295                 300

Tyr Val Arg Ser Ala Lys Leu Arg Met Val Thr Gly Leu Arg Asn Ile
305                 310                 315                 320

Pro Ser Ile Gln Ser Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe Ile
                325                 330                 335

Glu Gly Gly Trp Thr Gly Met Val Asp Gly Trp Tyr Gly Tyr His His
            340                 345                 350

Gln Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser Thr Gln
        355                 360                 365

Asn Ala Ile Asn Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu Lys
    370                 375                 380

Met Asn Thr Gln Phe Thr Ala Val Gly Lys Glu Phe Asn Lys Leu Glu
385                 390                 395                 400

Arg Arg Met Glu Asn Leu Asn Lys Lys Val Asp Asp Gly Phe Ile Asp
                405                 410                 415

Ile Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Leu Glu Asn Glu Arg
            420                 425                 430
```

```
Thr Leu Asp Phe His Asp Ser Asn Val Lys Asn Leu Tyr Glu Lys Val
        435                 440                 445

Lys Ser Gln Leu Lys Asn Asn Ala Lys Glu Ile Gly Asn Gly Cys Phe
    450                 455                 460

Glu Phe Tyr His Lys Cys Asn Asp Glu Cys Met Glu Ser Val Lys Asn
465                 470                 475                 480

Gly Thr Tyr Asp Tyr Pro Lys Tyr Ser Glu Glu Ser Lys Leu Asn Arg
                485                 490                 495

Glu Lys Ile Asp Gly Val Lys Leu Glu Ser Met Gly Val Tyr Gln Ser
            500                 505                 510

Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile Pro Glu
        515                 520                 525

Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val
    530                 535                 540

Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly
545                 550                 555                 560

Leu Asp Ser Thr Gly His His His His His His
                565                 570
```

<210> 729
<211> 589
<212> PRT
<213> Influenza A virus

<400> 729

```
Met Glu Ala Arg Leu Leu Val Leu Leu Cys Ala Phe Ala Ala Thr Asn
1               5                   10                  15

Ala Asp Thr Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Asp Thr
            20                  25                  30

Val Asp Thr Val Leu Glu Lys Asn Val Thr Val Thr His Ser Val Asn
        35                  40                  45

Leu Leu Glu Asp Ser His Asn Gly Lys Leu Cys Lys Leu Lys Gly Ile
    50                  55                  60

Ala Pro Leu Gln Leu Gly Lys Cys Asn Ile Ala Gly Trp Leu Leu Gly
65                  70                  75                  80

Asn Pro Glu Cys Asp Leu Leu Leu Thr Ala Ser Ser Trp Ser Tyr Ile
                85                  90                  95
```

Val Glu Thr Ser Asn Ser Glu Asn Gly Thr Cys Tyr Pro Gly Asp Phe
100 105 110

Ile Asp Tyr Glu Glu Leu Arg Glu Gln Leu Ser Ser Val Ser Ser Phe
115 120 125

Glu Lys Phe Glu Ile Phe Pro Lys Thr Ser Ser Trp Pro Asn His Glu
130 135 140

Thr Thr Lys Gly Val Thr Ala Ala Cys Ser Tyr Ala Gly Ala Ser Ser
145 150 155 160

Phe Tyr Arg Asn Leu Leu Trp Leu Thr Lys Lys Gly Ser Ser Tyr Pro
165 170 175

Lys Leu Ser Lys Ser Tyr Val Asn Asn Lys Gly Lys Glu Val Leu Val
180 185 190

Leu Trp Gly Val His His Pro Pro Thr Gly Thr Asp Gln Gln Ser Leu
195 200 205

Tyr Gln Asn Ala Asp Ala Tyr Val Ser Val Gly Ser Ser Lys Tyr Asn
210 215 220

Arg Arg Phe Thr Pro Glu Ile Ala Ala Arg Pro Lys Val Arg Asp Gln
225 230 235 240

Ala Gly Arg Met Asn Tyr Tyr Trp Thr Leu Leu Glu Pro Gly Asp Thr
245 250 255

Ile Thr Phe Glu Ala Thr Gly Asn Leu Ile Ala Pro Trp Tyr Ala Phe
260 265 270

Ala Leu Asn Arg Gly Ser Gly Ser Gly Ile Ile Thr Ser Asp Ala Pro
275 280 285

Val His Asp Cys Asn Thr Lys Cys Gln Thr Pro His Gly Ala Ile Asn
290 295 300

Ser Ser Leu Pro Phe Gln Asn Ile His Pro Val Thr Ile Gly Glu Cys
305 310 315 320

Pro Lys Tyr Val Arg Ser Thr Lys Leu Arg Met Ala Thr Gly Leu Arg
325 330 335

Asn Ile Pro Ser Ile Gln Ser Arg Gly Leu Phe Gly Ala Ile Ala Gly
340 345 350

Phe Ile Glu Gly Gly Trp Thr Gly Met Ile Asp Gly Trp Tyr Gly Tyr
355 360 365

```
His His Gln Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Gln Lys Ser
    370                 375                 380

Thr Gln Asn Ala Ile Asp Gly Ile Thr Asn Lys Val Asn Ser Val Ile
385                 390                 395                 400

Glu Lys Met Asn Thr Gln Phe Thr Ala Val Gly Lys Glu Phe Asn Asn
                405                 410                 415

Leu Glu Arg Arg Ile Glu Asn Leu Asn Lys Lys Val Asp Asp Gly Phe
            420                 425                 430

Leu Asp Ile Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Leu Glu Asn
        435                 440                 445

Glu Arg Thr Leu Asp Phe His Asp Ser Asn Val Arg Asn Leu Tyr Glu
    450                 455                 460

Lys Val Lys Ser Gln Leu Lys Asn Asn Ala Lys Glu Ile Gly Asn Gly
465                 470                 475                 480

Cys Phe Glu Phe Tyr His Lys Cys Asp Asp Ala Cys Met Glu Ser Val
                485                 490                 495

Arg Asn Gly Thr Tyr Asp Tyr Pro Lys Tyr Ser Glu Glu Ser Lys Leu
            500                 505                 510

Asn Arg Glu Glu Ile Asp Gly Val Lys Leu Glu Ser Met Gly Val Tyr
        515                 520                 525

Gln Ser Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile
    530                 535                 540

Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu
545                 550                 555                 560

Trp Val Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu
                565                 570                 575

Leu Gly Leu Asp Ser Thr Gly His His His His His His
            580                 585
```

<210> 730
<211> 570
<212> PRT
<213> Influenza A virus

<400> 730

```
Asp Gln Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Glu Lys Val
1               5                   10                  15

Asp Thr Asn Leu Glu Arg Asn Val Thr Val Thr His Ala Lys Asp Ile
```

20 25 30

Leu Glu Lys Thr His Asn Gly Lys Leu Cys Lys Leu Asn Gly Ile Pro
35 40 45

Pro Leu Glu Leu Gly Asp Cys Ser Ile Ala Gly Trp Leu Leu Gly Asn
50 55 60

Pro Glu Cys Asp Arg Leu Leu Ser Val Pro Glu Trp Ser Tyr Ile Met
65 70 75 80

Glu Lys Glu Asn Pro Arg Asp Gly Leu Cys Tyr Pro Gly Ser Phe Asn
85 90 95

Asp Tyr Glu Glu Leu Lys His Leu Leu Ser Ser Val Lys His Phe Glu
100 105 110

Lys Val Lys Ile Leu Pro Lys Asp Arg Trp Thr Gln His Thr Thr Thr
115 120 125

Gly Gly Ser Arg Ala Cys Ala Val Ser Gly Asn Pro Ser Phe Phe Arg
130 135 140

Asn Met Val Trp Leu Thr Lys Glu Gly Ser Asp Tyr Pro Val Ala Lys
145 150 155 160

Gly Ser Tyr Asn Asn Thr Ser Gly Glu Gln Met Leu Ile Ile Trp Gly
165 170 175

Val His His Pro Ile Asp Glu Thr Glu Gln Arg Thr Leu Tyr Gln Asn
180 185 190

Val Gly Thr Tyr Val Ser Val Gly Thr Ser Thr Leu Asn Lys Arg Ser
195 200 205

Thr Pro Glu Ile Ala Thr Arg Pro Lys Val Asn Gly Gln Gly Gly Arg
210 215 220

Met Glu Phe Ser Trp Thr Leu Leu Asp Met Trp Asp Thr Ile Asn Phe
225 230 235 240

Glu Ser Thr Gly Asn Leu Ile Ala Pro Glu Tyr Gly Phe Lys Ile Ser
245 250 255

Lys Arg Gly Ser Ser Gly Ile Met Lys Thr Glu Gly Thr Leu Glu Asn
260 265 270

Cys Glu Thr Lys Cys Gln Thr Pro Leu Gly Ala Ile Asn Thr Thr Leu
275 280 285

Pro Phe His Asn Val His Pro Leu Thr Ile Gly Glu Cys Pro Lys Tyr

290 295 300

Val Lys Ser Glu Lys Leu Val Leu Ala Thr Gly Leu Arg Asn Val Pro
305 310 315 320

Gln Ile Glu Ser Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe Ile Glu
325 330 335

Gly Gly Trp Gln Gly Met Val Asp Gly Trp Tyr Gly Tyr His His Ser
340 345 350

Asn Asp Gln Gly Ser Gly Tyr Ala Ala Asp Lys Glu Ser Thr Gln Lys
355 360 365

Ala Phe Asp Gly Ile Thr Asn Lys Val Asn Ser Val Ile Glu Lys Met
370 375 380

Asn Thr Gln Phe Glu Ala Val Gly Lys Glu Phe Gly Asn Leu Glu Arg
385 390 395 400

Arg Leu Glu Asn Leu Asn Lys Arg Met Glu Asp Gly Phe Leu Asp Val
405 410 415

Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Met Glu Asn Glu Arg Thr
420 425 430

Leu Asp Phe His Asp Ser Asn Val Lys Asn Leu Tyr Asp Lys Val Arg
435 440 445

Met Gln Leu Arg Asp Asn Val Lys Glu Leu Gly Asn Gly Cys Phe Glu
450 455 460

Phe Tyr His Lys Cys Asp Asp Glu Cys Met Asn Ser Val Lys Asn Gly
465 470 475 480

Thr Tyr Asp Tyr Pro Lys Tyr Glu Glu Glu Ser Lys Leu Asn Arg Asn
485 490 495

Glu Ile Lys Gly Val Lys Leu Ser Ser Met Gly Val Tyr Gln Ser Gly
500 505 510

Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile Pro Glu Ala
515 520 525

Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu
530 535 540

Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu
545 550 555 560

Asp Ser Thr Gly His His His His His His

565 570

<210> 731
<211> 570
<212> PRT
<213> Influenza A virus

<400> 731

Gln Lys Leu Pro Gly Asn Asp Asn Ser Thr Ala Thr Leu Cys Leu Gly
1 5 10 15

His His Ala Val Pro Asn Gly Thr Ile Val Lys Thr Ile Thr Asn Asp
20 25 30

Gln Ile Glu Val Thr Asn Ala Thr Glu Leu Val Gln Ser Ser Ser Thr
35 40 45

Gly Gly Ile Cys Asp Ser Pro His Gln Ile Leu Asp Gly Glu Asn Cys
50 55 60

Thr Leu Ile Asp Ala Leu Leu Gly Asp Pro Gln Cys Asp Gly Phe Gln
65 70 75 80

Asn Lys Lys Trp Asp Leu Phe Val Glu Arg Ser Lys Ala Tyr Ser Asn
85 90 95

Cys Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser Leu Arg Ser Leu Val
100 105 110

Ala Ser Ser Gly Thr Leu Glu Phe Asn Asp Glu Ser Phe Asn Trp Thr
115 120 125

Gly Val Thr Gln Asn Gly Thr Ser Ser Ser Cys Lys Arg Arg Ser Asn
130 135 140

Asn Ser Phe Phe Ser Arg Leu Asn Trp Leu Thr Gln Leu Lys Phe Lys
145 150 155 160

Tyr Pro Ala Leu Asn Val Thr Met Pro Asn Asn Glu Lys Phe Asp Lys
165 170 175

Leu Tyr Ile Trp Gly Val His His Pro Val Thr Asp Asn Asp Gln Ile
180 185 190

Phe Leu Tyr Ala Gln Ala Ser Gly Arg Ile Thr Val Ser Thr Lys Arg
195 200 205

Ser Gln Gln Thr Val Ile Pro Asn Ile Gly Ser Arg Pro Arg Ile Arg
210 215 220

Asn Ile Pro Ser Arg Ile Ser Ile Tyr Trp Thr Ile Val Lys Pro Gly
225 230 235 240

```
Asp Ile Leu Leu Ile Asn Ser Thr Gly Asn Leu Ile Ala Pro Arg Gly
                245                 250                 255

Tyr Phe Lys Ile Arg Ser Gly Lys Ser Ser Ile Met Arg Ser Asp Ala
            260                 265                 270

Pro Ile Gly Lys Cys Asn Ser Glu Cys Ile Thr Pro Asn Gly Ser Ile
        275                 280                 285

Pro Asn Asp Lys Pro Phe Gln Asn Val Asn Arg Ile Thr Tyr Gly Ala
    290                 295                 300

Cys Pro Arg Tyr Val Lys Gln Asn Thr Leu Lys Leu Ala Thr Gly Met
305                 310                 315                 320

Arg Asn Val Pro Glu Lys Gln Thr Arg Gly Ile Phe Gly Ala Ile Ala
                325                 330                 335

Gly Phe Ile Glu Asn Gly Trp Glu Gly Met Val Asp Gly Trp Tyr Gly
            340                 345                 350

Phe Arg His Gln Asn Ser Glu Gly Ile Gly Gln Ala Ala Asp Leu Lys
        355                 360                 365

Ser Thr Gln Ala Ala Ile Asn Gln Ile Asn Gly Lys Leu Asn Arg Leu
    370                 375                 380

Ile Gly Lys Thr Asn Glu Lys Phe His Gln Ile Glu Lys Glu Phe Ser
385                 390                 395                 400

Glu Val Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr
                405                 410                 415

Lys Ile Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu
            420                 425                 430

Asn Gln His Thr Ile Asp Leu Thr Asp Ser Glu Met Asn Lys Leu Phe
        435                 440                 445

Glu Arg Thr Lys Lys Gln Leu Arg Glu Asn Ala Glu Asp Met Gly Asn
    450                 455                 460

Gly Cys Phe Lys Ile Tyr His Lys Cys Asp Asn Ala Cys Ile Gly Ser
465                 470                 475                 480

Ile Arg Asn Gly Thr Tyr Asp His Asp Val Tyr Arg Asp Glu Ala Leu
                485                 490                 495

Asn Asn Arg Phe Gln Ile Lys Gly Val Glu Leu Lys Ser Gly Ser Gly
            500                 505                 510
```

Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile Pro Glu Ala
515 520 525

Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu
530 535 540

Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu
545 550 555 560

Asp Ser Thr Gly His His His His His His
565 570

<210> 732
<211> 571
<212> PRT
<213> Influenza A virus

<400> 732

Gln Asn Tyr Thr Gly Asn Pro Val Ile Cys Leu Gly His His Ala Val
1 5 10 15

Ser Asn Gly Thr Met Val Lys Thr Leu Thr Asp Asp Gln Ile Glu Val
20 25 30

Val Thr Ala Gln Glu Leu Val Glu Ser Gln His Leu Pro Glu Leu Cys
35 40 45

Pro Ser Pro Leu Arg Leu Val Asp Gly Gln Thr Cys Asp Ile Val Asn
50 55 60

Gly Ala Leu Gly Ser Pro Gly Cys Asp His Leu Asn Gly Ala Glu Trp
65 70 75 80

Asp Val Phe Ile Glu Arg Pro Thr Ala Val Asp Thr Cys Tyr Pro Phe
85 90 95

Asp Val Pro Asp Tyr Gln Ser Leu Arg Ser Ile Leu Ala Asn Asn Gly
100 105 110

Lys Phe Glu Phe Ile Ala Glu Glu Phe Gln Trp Asn Thr Val Lys Gln
115 120 125

Asn Gly Lys Ser Gly Ala Cys Lys Arg Ala Asn Val Asn Asp Phe Phe
130 135 140

Asn Arg Leu Asn Trp Leu Thr Lys Ser Asp Gly Asn Ala Tyr Pro Leu
145 150 155 160

Gln Asn Leu Thr Lys Val Asn Asn Gly Asp Tyr Ala Arg Leu Tyr Ile
165 170 175

```
Trp Gly Val His His Pro Ser Thr Asp Thr Glu Gln Thr Asn Leu Tyr
                180                 185                 190

Lys Asn Asn Pro Gly Arg Val Thr Val Ser Thr Gln Thr Ser Gln Thr
            195                 200                 205

Ser Val Val Pro Asn Ile Gly Ser Arg Pro Trp Val Arg Gly Leu Ser
        210                 215                 220

Ser Arg Ile Ser Phe Tyr Trp Thr Ile Val Glu Pro Gly Asp Leu Ile
225                 230                 235                 240

Val Phe Asn Thr Ile Gly Asn Leu Ile Ala Pro Arg Gly His Tyr Lys
                245                 250                 255

Leu Asn Ser Gln Lys Lys Ser Thr Ile Leu Asn Thr Ala Val Pro Ile
            260                 265                 270

Gly Ser Cys Val Ser Lys Cys His Thr Asp Lys Gly Ser Ile Ser Thr
        275                 280                 285

Thr Lys Pro Phe Gln Asn Ile Ser Arg Ile Ser Ile Gly Asp Cys Pro
    290                 295                 300

Lys Tyr Val Lys Gln Gly Ser Leu Lys Leu Ala Thr Gly Met Arg Ser
305                 310                 315                 320

Ile Leu Glu Lys Ala Thr Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe
                325                 330                 335

Ile Glu Asn Gly Trp Gln Gly Leu Ile Asp Gly Trp Tyr Gly Phe Arg
            340                 345                 350

His Gln Asn Ala Glu Gly Thr Gly Thr Ala Ala Asp Leu Lys Ser Thr
        355                 360                 365

Gln Ala Ala Ile Asp Gln Ile Asn Gly Lys Leu Asn Arg Leu Ile Gly
    370                 375                 380

Lys Pro Asn Glu Lys Tyr His Gln Ile Glu Lys Glu Phe Glu Gln Val
385                 390                 395                 400

Glu Gly Arg Ile Gln Asp Leu Glu Lys Tyr Val Glu Asp Thr Lys Ile
                405                 410                 415

Asp Leu Trp Ser Tyr Asn Ala Glu Leu Leu Val Ala Leu Glu Asn Gln
            420                 425                 430

His Thr Ile Asp Val Thr Asp Ser Glu Met Asn Lys Leu Phe Glu Arg
        435                 440                 445
```

```
Val Arg His Gln Leu Arg Glu Asn Ala Glu Asp Lys Gly Asn Gly Cys
    450                 455                 460

Phe Glu Ile Phe His Gln Cys Asp Asn Ser Cys Ile Glu Ser Ile Arg
465                 470                 475                 480

Asn Gly Thr Tyr Asp His Asp Ile Tyr Arg Asp Glu Ala Ile Asn Asn
                485                 490                 495

Arg Phe Gln Ile Gln Gly Val Lys Leu Ile Gln Gly Tyr Lys Asp Ser
            500                 505                 510

Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile Pro Glu
        515                 520                 525

Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val
    530                 535                 540

Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly
545                 550                 555                 560

Leu Asp Ser Thr Gly His His His His His His
                565                 570
```

<210> 733
<211> 591
<212> PRT
<213> Influenza A virus

<400> 733

```
Met Glu Arg Thr Val Leu Leu Leu Ala Thr Val Ser Leu Val Lys Ser
1               5                   10                  15

Asp Gln Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Glu Gln Val
            20                  25                  30

Asp Thr Ile Met Glu Lys Asn Val Thr Val Thr His Ala Gln Asp Ile
        35                  40                  45

Leu Glu Arg Thr His Asn Gly Lys Leu Cys Asp Leu Asn Gly Val Lys
    50                  55                  60

Pro Leu Ile Leu Arg Asp Cys Ser Val Ala Gly Trp Leu Leu Gly Asn
65                  70                  75                  80

Pro Met Cys Asp Glu Phe Ile Asn Val Pro Glu Trp Ser Tyr Ile Val
                85                  90                  95

Glu Lys Ala Ser Pro Ala Asn Asp Leu Cys Tyr Pro Gly Asn Phe Asn
            100                 105                 110
```

Asp Tyr Glu Glu Leu Lys His Leu Leu Ser Arg Ile Asn His Phe Glu
115 120 125

Lys Ile Gln Ile Ile Pro Lys Ser Ser Trp Ser Asn His Asp Ala Ser
130 135 140

Ser Gly Val Ser Ser Ala Cys Pro Tyr Leu Gly Arg Ser Ser Phe Phe
145 150 155 160

Arg Asn Val Val Trp Leu Ile Lys Lys Asn Ser Ala Tyr Pro Thr Ile
165 170 175

Lys Arg Ser Tyr Asn Asn Thr Asn Gln Glu Asp Leu Leu Val Leu Trp
180 185 190

Gly Val His His Pro Asn Asp Ala Ala Glu Gln Thr Lys Leu Tyr Gln
195 200 205

Asn Pro Thr Thr Tyr Ile Ser Val Gly Thr Ser Thr Leu Asn Gln Arg
210 215 220

Leu Val Pro Glu Ile Ala Thr Arg Pro Lys Val Asn Gly Gln Ser Gly
225 230 235 240

Arg Met Glu Phe Phe Trp Thr Ile Leu Lys Pro Asn Asp Ala Ile Asn
245 250 255

Phe Glu Ser Asn Gly Asn Phe Ile Ala Pro Glu Tyr Ala Tyr Lys Ile
260 265 270

Val Lys Lys Gly Asp Ser Thr Ile Met Lys Ser Glu Leu Glu Tyr Gly
275 280 285

Asn Cys Asn Thr Lys Cys Gln Thr Pro Met Gly Ala Ile Asn Ser Ser
290 295 300

Met Pro Phe His Asn Ile His Pro Leu Thr Ile Gly Glu Cys Pro Lys
305 310 315 320

Tyr Val Lys Ser Asn Arg Leu Val Leu Ala Thr Gly Leu Arg Asn Thr
325 330 335

Pro Gln Arg Glu Arg Arg Arg Lys Lys Arg Gly Leu Phe Gly Ala Ile
340 345 350

Ala Gly Phe Ile Glu Gly Gly Trp Gln Gly Met Val Asp Gly Trp Tyr
355 360 365

Gly Tyr His His Ser Asn Glu Gln Gly Ser Cys Tyr Ser Ala Asp Lys
370 375 380

Glu Ser Thr Gln Lys Ala Ile Asp Gly Val Thr Asn Lys Val Asn Ser
385 390 395 400

Ile Ile Asn Lys Met Asn Thr Gln Phe Glu Ala Val Gly Arg Glu Phe
405 410 415

Asn Asn Leu Glu Arg Arg Ile Glu Asn Leu Asn Lys Lys Met Glu Asp
420 425 430

Gly Phe Leu Asp Val Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Met
435 440 445

Glu Asn Glu Arg Thr Leu Asp Phe His Asp Ser Asn Val Lys Asn Leu
450 455 460

Tyr Asp Lys Val Arg Leu Gln Leu Arg Asp Asn Ala Lys Glu Leu Gly
465 470 475 480

Asn Gly Cys Phe Glu Phe Tyr His Lys Cys Asp Asn Glu Cys Met Glu
485 490 495

Ser Val Lys Asn Gly Thr Tyr Asp Tyr Pro Gln Tyr Ser Glu Glu Ala
500 505 510

Arg Leu Asn Arg Glu Glu Ile Ser Gly Val Lys Leu Glu Ser Met Gly
515 520 525

Thr Tyr Gln Ser Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly
530 535 540

Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp
545 550 555 560

Gly Glu Trp Val Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn
565 570 575

Pro Leu Leu Gly Leu Asp Ser Thr Gly His His His His His His
580 585 590

<210> 734
<211> 575
<212> PRT
<213> Influenza A virus

<400> 734

Asp Gln Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Glu Gln Val
1 5 10 15

Asp Thr Ile Met Glu Lys Asn Val Thr Val Thr His Ala Gln Asp Ile
20 25 30

Leu Glu Lys Lys His Asn Gly Lys Leu Cys Asp Leu Asp Gly Val Lys

35 40 45

Pro Leu Ile Leu Arg Asp Cys Ser Val Ala Gly Trp Leu Leu Gly Asn
50 55 60

Pro Met Cys Asp Glu Phe Ile Asn Val Pro Glu Trp Ser Tyr Ile Val
65 70 75 80

Glu Lys Ala Asn Pro Val Asn Asp Leu Cys Tyr Pro Gly Asp Phe Asn
85 90 95

Asp Tyr Glu Glu Leu Lys His Leu Leu Ser Arg Ile Asn His Phe Glu
100 105 110

Lys Ile Gln Ile Ile Pro Lys Ser Ser Trp Ser Ser His Glu Ala Ser
115 120 125

Leu Gly Val Ser Ser Ala Cys Pro Tyr Gln Gly Lys Ser Ser Phe Phe
130 135 140

Arg Asn Val Val Trp Leu Ile Lys Lys Asn Ser Thr Tyr Pro Thr Ile
145 150 155 160

Lys Arg Ser Tyr Asn Asn Thr Asn Gln Glu Asp Leu Leu Val Leu Trp
165 170 175

Gly Ile His His Pro Asn Asp Ala Ala Glu Gln Thr Lys Leu Tyr Gln
180 185 190

Asn Pro Thr Thr Tyr Ile Ser Val Gly Thr Ser Thr Leu Asn Gln Arg
195 200 205

Leu Val Pro Arg Ile Ala Thr Arg Ser Lys Val Asn Gly Gln Ser Gly
210 215 220

Arg Met Glu Phe Phe Trp Thr Ile Leu Lys Pro Asn Asp Ala Ile Asn
225 230 235 240

Phe Glu Ser Asn Gly Asn Phe Ile Ala Pro Glu Tyr Ala Tyr Lys Ile
245 250 255

Val Lys Lys Gly Asp Ser Thr Ile Met Lys Ser Glu Leu Glu Tyr Gly
260 265 270

Asn Cys Asn Thr Lys Cys Gln Thr Pro Met Gly Ala Ile Asn Ser Ser
275 280 285

Met Pro Phe His Asn Ile His Pro Leu Thr Ile Gly Glu Cys Pro Lys
290 295 300

Tyr Val Lys Ser Asn Arg Leu Val Leu Ala Thr Gly Leu Arg Asn Ser

305 310 315 320

Pro Gln Arg Glu Arg Arg Arg Lys Lys Arg Gly Leu Phe Gly Ala Ile
325 330 335

Ala Gly Phe Ile Glu Gly Gly Trp Gln Gly Met Val Asp Gly Trp Tyr
340 345 350

Gly Tyr His His Ser Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Lys
355 360 365

Glu Ser Thr Gln Lys Ala Ile Asp Gly Val Thr Asn Lys Val Asn Ser
370 375 380

Ile Ile Asp Lys Met Asn Thr Gln Phe Glu Ala Val Gly Arg Glu Phe
385 390 395 400

Asn Asn Leu Glu Arg Arg Ile Glu Asn Leu Asn Lys Lys Met Glu Asp
405 410 415

Gly Phe Leu Asp Val Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Met
420 425 430

Glu Asn Glu Arg Thr Leu Asp Phe His Asp Ser Asn Val Lys Asn Leu
435 440 445

Tyr Asp Lys Val Arg Leu Gln Leu Arg Asp Asn Ala Lys Glu Leu Gly
450 455 460

Asn Gly Cys Phe Glu Phe Tyr His Lys Cys Asp Asn Glu Cys Met Glu
465 470 475 480

Ser Val Arg Asn Gly Thr Tyr Asp Tyr Pro Gln Tyr Ser Glu Glu Ala
485 490 495

Arg Leu Lys Arg Glu Glu Ile Ser Gly Val Lys Leu Glu Ser Ile Gly
500 505 510

Ile Tyr Gln Ser Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly
515 520 525

Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp
530 535 540

Gly Glu Trp Val Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn
545 550 555 560

Pro Leu Leu Gly Leu Asp Ser Thr Gly His His His His His His
565 570 575

<210> 735

<211> 575
<212> PRT
<213> Influenza A virus

<400> 735

Asp Gln Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Glu Gln Val
1 5 10 15

Asp Thr Ile Met Glu Lys Asn Val Thr Val Thr His Ala Gln Asp Ile
20 25 30

Leu Glu Lys Thr His Asn Gly Lys Leu Cys Asp Leu Asp Gly Val Lys
35 40 45

Pro Leu Ile Leu Arg Asp Cys Ser Val Ala Gly Trp Leu Leu Gly Asn
50 55 60

Pro Met Cys Asp Glu Phe Ile Asn Val Pro Glu Trp Ser Tyr Ile Val
65 70 75 80

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

Asp Tyr Glu Glu Leu Lys His Leu Leu Ser Arg Ile Asn His Phe Glu
100 105 110

Lys Ile Gln Ile Ile Pro Lys Ser Ser Trp Ser Asp His Glu Ala Ser
115 120 125

Ser Gly Val Ser Ser Ala Cys Pro Tyr Leu Gly Ser Pro Ser Phe Phe
130 135 140

Arg Asn Val Val Trp Leu Ile Lys Lys Asn Ser Thr Tyr Pro Thr Ile
145 150 155 160

Lys Lys Ser Tyr Asn Asn Thr Asn Gln Glu Asp Leu Leu Val Leu Trp
165 170 175

Gly Ile His His Pro Asn Asp Ala Ala Glu Gln Thr Arg Leu Tyr Gln
180 185 190

Asn Pro Thr Thr Tyr Ile Ser Ile Gly Thr Ser Thr Leu Asn Gln Arg
195 200 205

Leu Val Pro Lys Ile Ala Thr Arg Ser Lys Val Asn Gly Gln Ser Gly
210 215 220

Arg Met Glu Phe Phe Trp Thr Ile Leu Lys Pro Asn Asp Ala Ile Asn
225 230 235 240

Phe Glu Ser Asn Gly Asn Phe Ile Ala Pro Glu Tyr Ala Tyr Lys Ile
245 250 255

Val Lys Lys Gly Asp Ser Ala Ile Met Lys Ser Glu Leu Glu Tyr Gly
260 265 270

Asn Cys Asn Thr Lys Cys Gln Thr Pro Met Gly Ala Ile Asn Ser Ser
275 280 285

Met Pro Phe His Asn Ile His Pro Leu Thr Ile Gly Glu Cys Pro Lys
290 295 300

Tyr Val Lys Ser Asn Arg Leu Val Leu Ala Thr Gly Leu Arg Asn Ser
305 310 315 320

Pro Gln Arg Glu Ser Arg Arg Lys Lys Arg Gly Leu Phe Gly Ala Ile
325 330 335

Ala Gly Phe Ile Glu Gly Gly Trp Gln Gly Met Val Asp Gly Trp Tyr
340 345 350

Gly Tyr His His Ser Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Lys
355 360 365

Glu Ser Thr Gln Lys Ala Ile Asp Gly Val Thr Asn Lys Val Asn Ser
370 375 380

Ile Ile Asp Lys Met Asn Thr Gln Phe Glu Ala Val Gly Arg Glu Phe
385 390 395 400

Asn Asn Leu Glu Arg Arg Ile Glu Asn Leu Asn Lys Lys Met Glu Asp
405 410 415

Gly Phe Leu Asp Val Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Met
420 425 430

Glu Asn Glu Arg Thr Leu Asp Phe His Asp Ser Asn Val Lys Asn Leu
435 440 445

Tyr Asp Lys Val Arg Leu Gln Leu Arg Asp Asn Ala Lys Glu Leu Gly
450 455 460

Asn Gly Cys Phe Glu Phe Tyr His Lys Cys Asp Asn Glu Cys Met Glu
465 470 475 480

Ser Ile Arg Asn Gly Thr Tyr Asn Tyr Pro Gln Tyr Ser Glu Glu Ala
485 490 495

Arg Leu Lys Arg Glu Glu Ile Ser Gly Val Lys Leu Glu Ser Ile Gly
500 505 510

Thr Tyr Gln Ser Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly
515 520 525

```
Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp
    530                 535                 540

Gly Glu Trp Val Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn
545                 550                 555                 560

Pro Leu Leu Gly Leu Asp Ser Thr Gly His His His His His His
                565                 570                 575


<210>  736
<211>  575
<212>  PRT
<213>  Influenza A virus

<400>  736

Asp Gln Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Glu Gln Val
1               5                   10                  15

Asp Thr Ile Met Glu Lys Asn Val Thr Val Thr His Ala Gln Asp Ile
            20                  25                  30

Leu Glu Lys Thr His Asn Gly Lys Leu Cys Asp Leu Asp Gly Val Lys
        35                  40                  45

Pro Leu Ile Leu Arg Asp Cys Ser Val Ala Gly Trp Leu Leu Gly Asn
    50                  55                  60

Pro Met Cys Asp Glu Phe Leu Asn Val Ser Glu Trp Ser Tyr Ile Val
65                  70                  75                  80

Glu Lys Ile Asn Pro Ala Asn Asp Leu Cys Tyr Pro Gly Asn Phe Asn
                85                  90                  95

Asn Tyr Glu Glu Leu Lys His Leu Leu Ser Arg Ile Asn Arg Phe Glu
            100                 105                 110

Lys Ile Gln Ile Ile Pro Lys Ser Ser Trp Pro Asp His Glu Ala Ser
        115                 120                 125

Leu Gly Val Ser Ser Ala Cys Pro Tyr Gln Gly Gly Pro Ser Phe Tyr
    130                 135                 140

Arg Asn Val Val Trp Leu Ile Lys Lys Asn Asn Thr Tyr Pro Thr Ile
145                 150                 155                 160

Lys Lys Ser Tyr His Asn Thr Asn Gln Glu Asp Leu Leu Val Leu Trp
                165                 170                 175

Gly Ile His His Pro Asn Asp Glu Ala Glu Gln Thr Arg Ile Tyr Lys
            180                 185                 190
```

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Asn Pro Thr Thr Tyr Ile Ser Val Gly Thr Ser Thr Leu Asn Gln Arg
        195                 200                 205

Leu Val Pro Lys Ile Ala Thr Arg Ser Lys Val Asn Gly Gln Ser Gly
    210                 215                 220

Arg Val Glu Phe Phe Trp Thr Ile Leu Lys Ser Asn Asp Thr Ile Asn
225                 230                 235                 240

Phe Glu Ser Asn Gly Asn Phe Ile Ala Pro Glu Asn Ala Tyr Lys Ile
                245                 250                 255

Val Lys Lys Gly Asp Ser Thr Ile Met Lys Ser Glu Leu Glu Tyr Gly
            260                 265                 270

Asn Cys Asn Thr Lys Cys Gln Thr Pro Ile Gly Ala Ile Asn Ser Ser
        275                 280                 285

Met Pro Phe His Asn Ile His Pro Leu Thr Ile Gly Glu Cys Pro Lys
    290                 295                 300

Tyr Val Lys Ser Asn Arg Leu Val Leu Ala Thr Gly Leu Arg Asn Ser
305                 310                 315                 320

Pro Gln Gly Glu Arg Arg Arg Lys Lys Arg Gly Leu Phe Gly Ala Ile
                325                 330                 335

Ala Gly Phe Ile Glu Gly Gly Trp Gln Gly Met Val Asp Gly Trp Tyr
            340                 345                 350

Gly Tyr His His Ser Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Lys
        355                 360                 365

Glu Ser Thr Gln Lys Ala Ile Asp Gly Val Thr Asn Lys Val Asn Ser
    370                 375                 380

Ile Ile Asp Lys Met Asn Thr Gln Phe Glu Ala Val Gly Arg Glu Phe
385                 390                 395                 400

Asn Asn Leu Glu Arg Arg Ile Glu Asn Leu Asn Lys Lys Met Glu Asp
                405                 410                 415

Gly Phe Leu Asp Val Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Met
            420                 425                 430

Glu Asn Glu Arg Thr Leu Asp Phe His Asp Ser Asn Val Lys Asn Leu
        435                 440                 445

Tyr Asp Lys Val Arg Leu Gln Leu Arg Asp Asn Ala Lys Glu Leu Gly
    450                 455                 460
```

```
Asn Gly Cys Phe Glu Phe Tyr His Arg Cys Asp Asn Glu Cys Met Glu
465                 470                 475                 480

Ser Val Arg Asn Gly Thr Tyr Asp Tyr Pro Gln Tyr Ser Glu Glu Ala
                485                 490                 495

Arg Leu Lys Arg Glu Glu Ile Ser Gly Val Lys Leu Glu Ser Ile Gly
            500                 505                 510

Thr Tyr Gln Ser Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly
        515                 520                 525

Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp
    530                 535                 540

Gly Glu Trp Val Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn
545                 550                 555                 560

Pro Leu Leu Gly Leu Asp Ser Thr Gly His His His His His His
                565                 570                 575
```

<210> 737
<211> 574
<212> PRT
<213> Influenza A virus

<400> 737

```
Asp His Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Glu Gln Val
1               5                   10                  15

Asp Thr Ile Met Glu Lys Asn Val Thr Val Thr His Ala Gln Asp Ile
            20                  25                  30

Leu Glu Lys Thr His Asn Gly Lys Leu Cys Asp Leu Asn Gly Val Lys
        35                  40                  45

Pro Leu Ile Leu Lys Asp Cys Ser Val Ala Gly Trp Leu Leu Gly Asn
    50                  55                  60

Pro Met Cys Asp Glu Phe Ile Asn Val Pro Glu Trp Ser Tyr Ile Val
65                  70                  75                  80

Glu Lys Ala Asn Pro Ala Asn Asp Leu Cys Tyr Pro Gly Asn Phe Asn
                85                  90                  95

Asp Tyr Glu Glu Leu Lys His Leu Leu Ser Arg Ile Asn His Phe Glu
            100                 105                 110

Lys Ile Gln Ile Ile Pro Lys Asp Ser Trp Ser Asp His Glu Ala Ser
        115                 120                 125
```

Leu Gly Val Ser Ser Ala Cys Pro Tyr Gln Gly Asn Ser Ser Phe Phe
130 135 140

Arg Asn Val Val Trp Leu Ile Lys Lys Gly Asn Ala Tyr Pro Thr Ile
145 150 155 160

Lys Lys Ser Tyr Asn Asn Thr Asn Gln Glu Asp Leu Leu Val Leu Trp
165 170 175

Gly Ile His His Pro Asn Asp Glu Ala Glu Gln Thr Arg Leu Tyr Gln
180 185 190

Asn Pro Thr Thr Tyr Ile Ser Ile Gly Thr Ser Thr Leu Asn Gln Arg
195 200 205

Leu Val Pro Lys Ile Ala Thr Arg Ser Lys Val Asn Gly Gln Ser Gly
210 215 220

Arg Ile Asp Phe Phe Trp Thr Ile Leu Lys Pro Asn Asp Ala Ile Asn
225 230 235 240

Phe Glu Ser Asn Gly Asn Phe Ile Ala Pro Glu Tyr Ala Tyr Lys Ile
245 250 255

Val Lys Lys Gly Asp Ser Thr Ile Met Lys Ser Glu Val Glu Tyr Gly
260 265 270

Asn Cys Asn Thr Arg Cys Gln Thr Pro Met Gly Ala Ile Asn Ser Ser
275 280 285

Met Pro Phe His Asn Ile His Pro Leu Thr Ile Gly Glu Cys Pro Lys
290 295 300

Tyr Val Lys Ser Asn Lys Leu Val Leu Ala Thr Gly Leu Arg Asn Ser
305 310 315 320

Pro Gln Arg Glu Arg Arg Arg Lys Arg Gly Leu Phe Gly Ala Ile Ala
325 330 335

Gly Phe Ile Glu Gly Gly Trp Gln Gly Met Val Asp Gly Trp Tyr Gly
340 345 350

Tyr His His Ser Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Lys Glu
355 360 365

Ser Thr Gln Lys Ala Ile Asp Gly Val Thr Asn Lys Val Asn Ser Ile
370 375 380

Ile Asp Lys Met Asn Thr Gln Phe Glu Ala Val Gly Arg Glu Phe Asn
385 390 395 400

Asn Leu Glu Arg Arg Ile Glu Asn Leu Asn Lys Lys Met Glu Asp Gly
405 410 415

Phe Leu Asp Val Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Met Glu
420 425 430

Asn Glu Arg Thr Leu Asp Phe His Asp Ser Asn Val Lys Asn Leu Tyr
435 440 445

Asp Lys Val Arg Leu Gln Leu Arg Asp Asn Ala Lys Glu Leu Gly Asn
450 455 460

Gly Cys Phe Glu Phe Tyr His Lys Cys Asp Asn Glu Cys Met Glu Ser
465 470 475 480

Val Arg Asn Gly Thr Tyr Asp Tyr Pro Gln Tyr Ser Glu Glu Ala Arg
485 490 495

Leu Lys Arg Glu Glu Ile Ser Gly Val Lys Leu Glu Ser Ile Gly Thr
500 505 510

Tyr Gln Ser Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr
515 520 525

Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly
530 535 540

Glu Trp Val Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro
545 550 555 560

Leu Leu Gly Leu Asp Ser Thr Gly His His His His His His
565 570

<210> 738
<211> 574
<212> PRT
<213> Influenza A virus

<400> 738

Asp Gln Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Glu Gln Val
1 5 10 15

Asp Thr Ile Met Glu Lys Asn Val Thr Val Thr His Ala Gln Asp Ile
20 25 30

Leu Glu Lys Thr His Asn Gly Lys Leu Cys Asp Leu Asp Gly Val Lys
35 40 45

Pro Leu Ile Leu Arg Asp Cys Ser Val Ala Gly Trp Leu Leu Gly Asn
50 55 60

Pro Met Cys Asp Glu Phe Ile Asn Val Pro Glu Trp Ser Tyr Ile Val

65 70 75 80

Glu Lys Ala Asn Pro Ala Asn Asp Leu Cys Tyr Pro Gly Asn Phe Asn
85 90 95

Asp Tyr Glu Glu Leu Lys His Leu Leu Ser Arg Ile Asn His Phe Glu
100 105 110

Lys Ile Gln Ile Ile Pro Lys Ser Ser Trp Ser Asp His Glu Ala Ser
115 120 125

Ser Gly Val Ser Ser Ala Cys Pro Tyr Gln Gly Thr Pro Ser Phe Phe
130 135 140

Arg Asn Val Val Trp Leu Ile Lys Lys Asn Asn Thr Tyr Pro Thr Ile
145 150 155 160

Lys Arg Ser Tyr Asn Asn Thr Asn Gln Glu Asp Leu Leu Ile Leu Trp
165 170 175

Gly Ile His His Ser Asn Asp Ala Ala Glu Gln Thr Lys Leu Tyr Gln
180 185 190

Asn Pro Thr Thr Tyr Ile Ser Val Gly Thr Ser Thr Leu Asn Gln Arg
195 200 205

Leu Val Pro Lys Ile Ala Thr Arg Ser Lys Val Asn Gly Gln Ser Gly
210 215 220

Arg Met Asp Phe Phe Trp Thr Ile Leu Lys Pro Asn Asp Ala Ile Asn
225 230 235 240

Phe Glu Ser Asn Gly Asn Phe Ile Ala Pro Glu Tyr Ala Tyr Lys Ile
245 250 255

Val Lys Lys Gly Asp Ser Ala Ile Val Lys Ser Glu Val Glu Tyr Gly
260 265 270

Asn Cys Asn Thr Lys Cys Gln Thr Pro Ile Gly Ala Ile Asn Ser Ser
275 280 285

Met Pro Phe His Asn Ile His Pro Leu Thr Ile Gly Glu Cys Pro Lys
290 295 300

Tyr Val Lys Ser Asn Lys Leu Val Leu Ala Thr Gly Leu Arg Asn Ser
305 310 315 320

Pro Leu Arg Glu Arg Arg Arg Lys Arg Gly Leu Phe Gly Ala Ile Ala
325 330 335

Gly Phe Ile Glu Gly Gly Trp Gln Gly Met Val Asp Gly Trp Tyr Gly

340 345 350

Tyr His His Ser Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Lys Glu
355 360 365

Ser Thr Gln Lys Ala Ile Asp Gly Val Thr Asn Lys Val Asn Ser Ile
370 375 380

Ile Asp Lys Met Asn Thr Gln Phe Glu Ala Val Gly Arg Glu Phe Asn
385 390 395 400

Asn Leu Glu Arg Arg Ile Glu Asn Leu Asn Lys Lys Met Glu Asp Gly
405 410 415

Phe Leu Asp Val Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Met Glu
420 425 430

Asn Glu Arg Thr Leu Asp Phe His Asp Ser Asn Val Lys Asn Leu Tyr
435 440 445

Asp Lys Val Arg Leu Gln Leu Arg Asp Asn Ala Lys Glu Leu Gly Asn
450 455 460

Gly Cys Phe Glu Phe Tyr His Lys Cys Asp Asn Glu Cys Met Glu Ser
465 470 475 480

Val Arg Asn Gly Thr Tyr Asp Tyr Pro Gln Tyr Ser Glu Glu Ala Arg
485 490 495

Leu Lys Arg Glu Glu Ile Ser Gly Val Lys Leu Glu Ser Ile Gly Thr
500 505 510

Tyr Gln Ser Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr
515 520 525

Ile Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly
530 535 540

Glu Trp Val Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro
545 550 555 560

Leu Leu Gly Leu Asp Ser Thr Gly His His His His His His
565 570

<210> 739
<211> 571
<212> PRT
<213> Influenza A virus

<400> 739

Asp Gln Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Glu Gln Val
1 5 10 15

Asp Thr Ile Met Glu Lys Asn Val Thr Val Thr His Ala Gln Asp Ile
20 25 30

Leu Glu Lys Thr His Asn Gly Lys Leu Cys Asn Leu Asp Gly Val Lys
35 40 45

Pro Leu Ile Leu Lys Asp Cys Ser Val Ala Gly Trp Leu Leu Gly Asn
50 55 60

Pro Met Cys Asp Glu Phe Leu Asn Val Ser Glu Trp Ser Tyr Ile Val
65 70 75 80

Glu Lys Ala Ser Pro Ala Asn Gly Leu Cys Tyr Pro Gly Asp Phe Asn
85 90 95

Asp Tyr Glu Glu Leu Lys His Leu Leu Ser Arg Ile Asn His Leu Lys
100 105 110

Lys Ile Lys Ile Ile Pro Lys Ser Tyr Trp Ser Asn His Glu Ala Ser
115 120 125

Ser Gly Val Ser Ala Ala Cys Ser Tyr Leu Gly Glu Pro Ser Phe Phe
130 135 140

Arg Asn Val Val Trp Leu Ile Lys Lys Asn Asn Thr Tyr Pro Pro Ile
145 150 155 160

Lys Val Asn Tyr Thr Asn Thr Asn Gln Glu Asp Leu Leu Val Leu Trp
165 170 175

Gly Ile His His Pro Asn Asp Glu Lys Glu Gln Ile Arg Ile Tyr Gln
180 185 190

Asn Pro Asn Thr Ser Ile Ser Val Gly Thr Ser Thr Leu Asn Gln Arg
195 200 205

Leu Val Pro Lys Ile Ala Thr Arg Pro Lys Val Asn Gly Gln Ser Gly
210 215 220

Arg Met Glu Phe Phe Trp Thr Ile Leu Lys Pro Asn Asp Ser Ile Asn
225 230 235 240

Phe Asp Ser Asn Gly Asn Phe Ile Ala Pro Glu Tyr Ala Tyr Lys Ile
245 250 255

Ala Lys Lys Gly Asp Ser Val Ile Met Lys Ser Glu Leu Glu Tyr Gly
260 265 270

Asn Cys Asn Thr Lys Cys Gln Thr Pro Met Gly Ala Ile Asn Ser Ser
275 280 285

Met Pro Phe His Asn Ile His Pro Leu Thr Ile Gly Glu Cys Pro Lys
290 295 300

Tyr Val Lys Ser Asn Arg Leu Val Leu Ala Thr Gly Leu Arg Asn Ala
305 310 315 320

Pro Gln Thr Glu Thr Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe Ile
325 330 335

Glu Gly Gly Trp Gln Gly Met Val Asp Gly Trp Tyr Gly Tyr His His
340 345 350

Ser Asn Glu Gln Gly Ser Gly Tyr Ala Ala Asp Lys Glu Ser Thr Gln
355 360 365

Lys Ala Ile Asp Gly Ile Thr Asn Lys Val Asn Ser Ile Ile Asp Lys
370 375 380

Met Asn Thr Gln Phe Glu Ile Val Gly Arg Glu Phe Asn Asn Leu Glu
385 390 395 400

Arg Arg Ile Glu Asn Leu Asn Lys Lys Met Glu Asp Gly Phe Leu Asp
405 410 415

Val Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Met Glu Asn Glu Arg
420 425 430

Thr Leu Asp Phe His Asp Ser Asn Val Lys Asn Leu Tyr Glu Lys Val
435 440 445

Arg Leu Gln Leu Arg Asp Asn Ala Lys Glu Leu Gly Asn Gly Cys Phe
450 455 460

Glu Phe Tyr His Lys Cys Asp Asn Glu Cys Met Glu Ser Val Arg Asn
465 470 475 480

Gly Thr Tyr Asp Tyr Pro Gln Tyr Ser Glu Glu Ala Arg Leu Ser Arg
485 490 495

Glu Glu Ile Ser Gly Val Lys Met Glu Ser Met Val Thr Tyr Gln Ser
500 505 510

Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile Pro Glu
515 520 525

Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val
530 535 540

Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly
545 550 555 560

```
Leu Asp Ser Thr Gly His His His His His His
                565                 570


<210>  740
<211>  573
<212>  PRT
<213>  Influenza A virus

<400>  740

Asp Lys Ile Cys Ile Gly Tyr His Ala Asn Asn Ser Thr Thr Gln Val
1               5                  10                  15

Asp Thr Ile Leu Glu Lys Asn Val Thr Val Thr His Ser Val Glu Leu
            20                  25                  30

Leu Glu Asn Gln Lys Glu Glu Arg Phe Cys Lys Ile Leu Asn Lys Ala
        35                  40                  45

Pro Leu Asp Leu Arg Gly Cys Thr Ile Glu Gly Trp Ile Leu Gly Asn
    50                  55                  60

Pro Gln Cys Asp Leu Leu Leu Gly Asp Gln Ser Trp Ser Tyr Ile Val
65                  70                  75                  80

Glu Arg Pro Thr Ala Gln Asn Gly Ile Cys Tyr Pro Gly Ala Leu Asn
                85                  90                  95

Glu Val Glu Glu Leu Lys Ala Leu Ile Gly Ser Gly Glu Arg Val Glu
            100                 105                 110

Arg Phe Glu Met Phe Pro Lys Ser Thr Trp Thr Gly Val Asp Thr Ser
        115                 120                 125

Ser Gly Val Thr Lys Ala Cys Pro Tyr Asn Ser Gly Ser Ser Phe Tyr
    130                 135                 140

Arg Asn Leu Leu Trp Ile Ile Lys Thr Lys Ser Ala Ala Tyr Pro Val
145                 150                 155                 160

Ile Lys Gly Thr Tyr Asn Asn Thr Gly Ser Gln Pro Ile Leu Tyr Phe
                165                 170                 175

Trp Gly Val His His Pro Pro Asp Thr Asn Glu Gln Asn Thr Leu Tyr
            180                 185                 190

Gly Ser Gly Asp Arg Tyr Val Arg Met Gly Thr Glu Ser Met Asn Phe
        195                 200                 205

Ala Lys Ser Pro Glu Ile Ala Ala Arg Pro Ala Val Asn Gly Gln Arg
    210                 215                 220
```

Gly Arg Ile Asp Tyr Tyr Trp Ser Val Leu Lys Pro Gly Glu Thr Leu
225 230 235 240

Asn Val Glu Ser Asn Gly Asn Leu Ile Ala Pro Trp Tyr Ala Tyr Lys
245 250 255

Phe Val Ser Thr Asn Asn Lys Gly Ala Ile Phe Lys Ser Asn Leu Pro
260 265 270

Ile Glu Asn Cys Asp Ala Thr Cys Gln Thr Ile Ala Gly Val Leu Arg
275 280 285

Thr Asn Lys Thr Phe Gln Asn Val Ser Pro Leu Trp Ile Gly Glu Cys
290 295 300

Pro Lys Tyr Val Lys Ser Glu Ser Leu Arg Leu Ala Thr Gly Leu Arg
305 310 315 320

Asn Val Pro Gln Ile Glu Thr Arg Gly Leu Phe Gly Ala Ile Ala Gly
325 330 335

Phe Ile Glu Gly Gly Trp Thr Gly Met Ile Asp Gly Trp Tyr Gly Tyr
340 345 350

His His Glu Asn Ser Gln Gly Ser Gly Tyr Ala Ala Asp Lys Glu Ser
355 360 365

Thr Gln Lys Ala Ile Asp Gly Ile Thr Asn Lys Val Asn Ser Ile Ile
370 375 380

Asp Lys Met Asn Thr Gln Phe Glu Ala Val Asp His Glu Phe Ser Asn
385 390 395 400

Leu Glu Arg Arg Ile Asp Asn Leu Asn Lys Arg Met Glu Asp Gly Phe
405 410 415

Leu Asp Val Trp Thr Tyr Asn Ala Glu Leu Leu Val Leu Leu Glu Asn
420 425 430

Glu Arg Thr Leu Asp Leu His Asp Ala Asn Val Lys Asn Leu Tyr Glu
435 440 445

Lys Val Lys Ser Gln Leu Arg Asp Asn Ala Asn Asp Leu Gly Asn Gly
450 455 460

Cys Phe Glu Phe Trp His Lys Cys Asp Asn Glu Cys Ile Glu Ser Val
465 470 475 480

Lys Asn Gly Thr Tyr Asp Tyr Pro Lys Tyr Gln Asp Glu Ser Lys Leu
485 490 495

```
Asn Arg Gln Glu Ile Glu Ser Val Lys Leu Asp Asn Leu Gly Val Tyr
            500                 505                 510

Gln Ser Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile
        515                 520                 525

Pro Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu
    530                 535                 540

Trp Val Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu
545                 550                 555                 560

Leu Gly Leu Asp Ser Thr Gly His His His His His His
                565                 570
```

<210> 741
<211> 567
<212> PRT
<213> Influenza A virus

<400> 741

```
Asp Lys Ile Cys Leu Gly His His Ala Val Ser Asn Gly Thr Lys Val
1               5                   10                  15

Asn Thr Leu Thr Glu Arg Gly Val Glu Val Val Asn Ala Thr Glu Thr
            20                  25                  30

Val Glu Arg Thr Asn Val Pro Arg Ile Cys Ser Lys Gly Lys Arg Thr
        35                  40                  45

Val Asp Leu Gly Gln Cys Gly Leu Leu Gly Thr Ile Thr Gly Pro Pro
    50                  55                  60

Gln Cys Asp Gln Phe Leu Glu Phe Ser Ala Asp Leu Ile Ile Glu Arg
65                  70                  75                  80

Arg Glu Gly Ser Asp Val Cys Tyr Pro Gly Lys Phe Val Asn Glu Glu
                85                  90                  95

Ala Leu Arg Gln Ile Leu Arg Glu Ser Gly Gly Ile Asp Lys Glu Thr
            100                 105                 110

Met Gly Phe Thr Tyr Ser Gly Ile Arg Thr Asn Gly Thr Thr Ser Ala
        115                 120                 125

Cys Arg Arg Ser Gly Ser Ser Phe Tyr Ala Glu Met Lys Trp Leu Leu
    130                 135                 140

Ser Asn Thr Asp Asn Ala Ala Phe Pro Gln Met Thr Lys Ser Tyr Lys
145                 150                 155                 160
```

Asn Thr Arg Lys Asp Pro Ala Leu Ile Ile Trp Gly Ile His His Ser
165 170 175

Gly Ser Thr Thr Glu Gln Thr Lys Leu Tyr Gly Ser Gly Asn Lys Leu
180 185 190

Ile Thr Val Gly Ser Ser Asn Tyr Gln Gln Ser Phe Val Pro Ser Pro
195 200 205

Gly Ala Arg Pro Gln Val Asn Gly Gln Ser Gly Arg Ile Asp Phe His
210 215 220

Trp Leu Ile Leu Asn Pro Asn Asp Thr Val Thr Phe Ser Phe Asn Gly
225 230 235 240

Ala Phe Ile Ala Pro Asp Arg Ala Ser Phe Leu Arg Gly Lys Ser Met
245 250 255

Gly Ile Gln Ser Glu Val Gln Val Asp Ala Asn Cys Glu Gly Asp Cys
260 265 270

Tyr His Ser Gly Gly Thr Ile Ile Ser Asn Leu Pro Phe Gln Asn Ile
275 280 285

Asn Ser Arg Ala Val Gly Lys Cys Pro Arg Tyr Val Lys Gln Glu Ser
290 295 300

Leu Leu Leu Ala Thr Gly Met Lys Asn Val Pro Glu Ile Pro Lys Arg
305 310 315 320

Arg Arg Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe Ile Glu Asn Gly
325 330 335

Trp Glu Gly Leu Ile Asp Gly Trp Tyr Gly Phe Arg His Gln Asn Ala
340 345 350

Gln Gly Glu Gly Thr Ala Ala Asp Tyr Lys Ser Thr Gln Ser Ala Ile
355 360 365

Asp Gln Ile Thr Gly Lys Leu Asn Arg Leu Ile Glu Lys Thr Asn Gln
370 375 380

Gln Phe Glu Leu Ile Asp Asn Glu Phe Thr Glu Val Glu Arg Gln Ile
385 390 395 400

Gly Asn Val Ile Asn Trp Thr Arg Asp Ser Met Thr Glu Val Trp Ser
405 410 415

Tyr Asn Ala Glu Leu Leu Val Ala Met Glu Asn Gln His Thr Ile Asp
420 425 430

Leu Ala Asp Ser Glu Met Asn Lys Leu Tyr Glu Arg Val Lys Arg Gln
435 440 445

Leu Arg Glu Asn Ala Glu Glu Asp Gly Thr Gly Cys Phe Glu Ile Phe
450 455 460

His Lys Cys Asp Asp Asp Cys Met Ala Ser Ile Arg Asn Asn Thr Tyr
465 470 475 480

Asp His Ser Lys Tyr Arg Glu Glu Ala Ile Gln Asn Arg Ile Gln Ile
485 490 495

Asp Pro Val Lys Leu Ser Ser Gly Tyr Lys Asp Ser Gly Arg Leu Val
500 505 510

Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile Pro Glu Ala Pro Arg Asp
515 520 525

Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu Leu Ser Thr
530 535 540

Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser Thr
545 550 555 560

Gly His His His His His His
565

<210> 742
<211> 572
<212> PRT
<213> Influenza A virus

<400> 742

Asp Arg Ile Cys Ile Gly Tyr Gln Ser Asn Asn Ser Thr Asp Thr Val
1 5 10 15

Asn Thr Leu Ile Glu Gln Lys Val Pro Val Thr Gln Thr Met Glu Leu
20 25 30

Val Glu Thr Glu Lys His Pro Ala Tyr Cys Asn Thr Asp Leu Gly Ala
35 40 45

Pro Leu Glu Leu Arg Asp Cys Lys Ile Glu Ala Val Ile Tyr Gly Asn
50 55 60

Pro Lys Cys Asp Ile His Leu Lys Asp Gln Gly Trp Ser Tyr Ile Val
65 70 75 80

Glu Arg Pro Ser Ala Pro Glu Gly Met Cys Tyr Pro Gly Ser Val Glu
85 90 95

Asn Leu Glu Glu Leu Arg Phe Val Phe Ser Ser Ala Ala Ser Tyr Lys

100 105 110

Arg Ile Arg Leu Phe Asp Tyr Ser Arg Trp Asn Val Thr Ser Ser Gly
115 120 125

Thr Ser Lys Ala Cys Asn Ala Ser Thr Gly Gly Gln Ser Phe Tyr Arg
130 135 140

Ser Ile Asn Trp Leu Thr Lys Lys Lys Pro Asp Thr Tyr Asp Phe Asn
145 150 155 160

Glu Gly Thr Tyr Val Asn Asn Glu Asp Gly Asp Ile Ile Phe Leu Trp
165 170 175

Gly Ile His His Pro Pro Asp Thr Lys Glu Gln Thr Thr Leu Tyr Lys
180 185 190

Asn Ala Asn Thr Leu Ser Ser Val Thr Thr Asn Thr Ile Asn Arg Ser
195 200 205

Phe Gln Pro Asn Ile Gly Pro Arg Pro Leu Val Arg Gly Gln Gln Gly
210 215 220

Arg Met Asp Tyr Tyr Trp Gly Ile Leu Lys Arg Gly Glu Thr Leu Lys
225 230 235 240

Ile Arg Thr Asn Gly Asn Leu Ile Ala Pro Glu Phe Gly Tyr Leu Leu
245 250 255

Lys Gly Glu Ser His Gly Arg Thr Ile Gln Asn Glu Asp Ile Pro Ile
260 265 270

Gly Asn Cys Tyr Thr Lys Cys Gln Thr Tyr Ala Gly Ala Ile Asn Ser
275 280 285

Ser Lys Pro Phe Gln Asn Ala Ser Arg His Tyr Met Gly Glu Cys Pro
290 295 300

Lys Tyr Val Lys Lys Ala Ser Leu Arg Leu Ala Val Gly Leu Arg Asn
305 310 315 320

Thr Pro Ser Val Glu Pro Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe
325 330 335

Ile Glu Gly Gly Trp Ser Gly Met Ile Asp Gly Trp Tyr Gly Phe His
340 345 350

His Ser Asn Ser Glu Gly Thr Gly Met Ala Ala Asp Gln Lys Ser Thr
355 360 365

Gln Glu Ala Ile Asp Lys Ile Thr Asn Lys Val Asn Asn Ile Val Asp

370 375 380

Lys Met Asn Arg Glu Phe Glu Val Val Asn His Glu Phe Ser Glu Val
385 390 395 400

Glu Lys Arg Ile Asn Met Ile Asn Asp Lys Ile Asp Asp Gln Ile Glu
405 410 415

Asp Leu Trp Ala Tyr Asn Ala Glu Leu Leu Val Leu Leu Glu Asn Gln
420 425 430

Lys Thr Leu Asp Glu His Asp Ser Asn Val Lys Asn Leu Phe Asp Glu
435 440 445

Val Lys Arg Arg Leu Ser Ala Asn Ala Ile Asp Ala Gly Asn Gly Cys
450 455 460

Phe Asp Ile Leu His Lys Cys Asp Asn Glu Cys Met Glu Thr Ile Lys
465 470 475 480

Asn Gly Thr Tyr Asp His Lys Glu Tyr Glu Glu Glu Ala Lys Leu Glu
485 490 495

Arg Ser Lys Ile Asn Gly Val Lys Leu Glu Glu Asn Thr Thr Tyr Lys
500 505 510

Ser Gly Arg Leu Val Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile Pro
515 520 525

Glu Ala Pro Arg Asp Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp
530 535 540

Val Leu Leu Ser Thr Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu Leu
545 550 555 560

Gly Leu Asp Ser Thr Gly His His His His His His
565 570

<210> 743
<211> 565
<212> PRT
<213> Influenza A virus

<400> 743

Asp Lys Ile Cys Ile Gly Tyr Gln Ser Thr Asn Ser Thr Glu Thr Val
1 5 10 15

Asp Thr Leu Thr Lys Thr Asn Val Pro Val Thr Gln Ala Lys Glu Leu
20 25 30

Leu His Thr Glu His Asn Gly Met Leu Cys Ala Thr Asn Leu Gly His
35 40 45

Pro Leu Ile Leu Asp Thr Cys Thr Ile Glu Gly Leu Ile Tyr Gly Asn
50 55 60

Pro Ser Cys Asp Leu Leu Leu Gly Gly Arg Glu Trp Ser Tyr Ile Val
65 70 75 80

Glu Arg Pro Ser Ala Val Asn Gly Met Cys Tyr Pro Gly Asn Val Glu
85 90 95

Asn Leu Glu Glu Leu Arg Leu Leu Phe Ser Ser Ala Ser Ser Tyr Gln
100 105 110

Arg Val Gln Ile Phe Pro Asp Thr Ile Trp Asn Val Thr Tyr Ser Gly
115 120 125

Thr Ser Ser Ala Cys Ser Asn Ser Phe Tyr Arg Ser Met Arg Trp Leu
130 135 140

Thr Gln Lys Asp Asn Thr Tyr Pro Val Gln Asp Ala Gln Tyr Thr Asn
145 150 155 160

Asn Arg Gly Lys Ser Ile Leu Phe Met Trp Gly Ile Asn His Pro Pro
165 170 175

Thr Asp Thr Val Gln Thr Asn Leu Tyr Thr Arg Thr Asp Thr Thr Thr
180 185 190

Ser Val Thr Thr Glu Asp Ile Asn Arg Ala Phe Lys Pro Val Ile Gly
195 200 205

Pro Arg Pro Leu Val Asn Gly Leu Gln Gly Arg Ile Asp Tyr Tyr Trp
210 215 220

Ser Val Leu Lys Pro Gly Gln Thr Leu Arg Val Arg Ser Asn Gly Asn
225 230 235 240

Leu Ile Ala Pro Trp Tyr Gly His Ile Leu Ser Gly Glu Ser His Gly
245 250 255

Arg Ile Leu Lys Ser Asp Leu Asn Ser Gly Asn Cys Val Val Gln Cys
260 265 270

Gln Thr Glu Arg Gly Gly Leu Asn Thr Thr Leu Pro Phe His Asn Val
275 280 285

Ser Lys Tyr Ala Phe Gly Asn Cys Pro Lys Tyr Val Gly Val Lys Ser
290 295 300

Leu Lys Leu Ala Val Gly Met Arg Asn Val Pro Ala Arg Ser Ser Arg
305 310 315 320

Gly Leu Phe Gly Ala Ile Ala Gly Phe Ile Glu Gly Gly Trp Pro Gly
325 330 335

Leu Val Ala Gly Trp Tyr Gly Phe Gln His Ser Asn Asp Gln Gly Val
340 345 350

Gly Met Ala Ala Asp Arg Asp Ser Thr Gln Lys Ala Ile Asp Lys Ile
355 360 365

Thr Ser Lys Val Asn Asn Ile Val Asp Lys Met Asn Lys Gln Tyr Glu
370 375 380

Ile Ile Asp His Glu Phe Ser Glu Ile Glu Thr Arg Leu Asn Met Ile
385 390 395 400

Asn Asn Lys Ile Asp Asp Gln Ile Gln Asp Ile Trp Ala Tyr Asn Ala
405 410 415

Glu Leu Leu Val Leu Leu Glu Asn Gln Lys Thr Leu Asp Glu His Asp
420 425 430

Ala Asn Val Asn Asn Leu Tyr Asn Lys Val Lys Arg Ala Leu Gly Ser
435 440 445

Asn Ala Met Glu Asp Gly Lys Gly Cys Phe Glu Leu Tyr His Lys Cys
450 455 460

Asp Asp Arg Cys Met Glu Thr Ile Arg Asn Gly Thr Tyr Asn Arg Gly
465 470 475 480

Lys Tyr Lys Glu Glu Ser Arg Leu Glu Arg Gln Lys Ile Glu Gly Val
485 490 495

Lys Leu Glu Ser Glu Gly Thr Tyr Lys Ser Gly Arg Leu Val Pro Arg
500 505 510

Gly Ser Pro Gly Ser Gly Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln
515 520 525

Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu Leu Ser Thr Phe Leu
530 535 540

Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser Thr Gly His
545 550 555 560

His His His His His
565

<210> 744
<211> 583

<212> PRT
<213> Influenza A virus

<400> 744

Met Glu Thr Ile Ser Leu Ile Thr Ile Leu Leu Val Val Thr Ala Ser
1 5 10 15

Asn Ala Asp Lys Ile Cys Ile Gly His Gln Ser Thr Asn Ser Thr Glu
20 25 30

Thr Val Asp Thr Leu Thr Glu Thr Asn Val Pro Val Thr His Ala Lys
35 40 45

Glu Leu Leu His Thr Glu His Asn Gly Met Leu Cys Ala Thr Ser Leu
50 55 60

Gly His Pro Leu Ile Leu Asp Thr Cys Thr Ile Glu Gly Leu Val Tyr
65 70 75 80

Gly Asn Pro Ser Cys Asp Leu Leu Leu Gly Gly Arg Glu Trp Ser Tyr
85 90 95

Ile Val Glu Arg Ser Ser Ala Val Asn Gly Thr Cys Tyr Pro Gly Asn
100 105 110

Val Glu Asn Leu Glu Glu Leu Arg Thr Leu Phe Ser Ser Ala Ser Ser
115 120 125

Tyr Gln Arg Ile Gln Ile Phe Pro Asp Thr Thr Trp Asn Val Thr Tyr
130 135 140

Thr Gly Thr Ser Arg Ala Cys Ser Gly Ser Phe Tyr Arg Ser Met Arg
145 150 155 160

Trp Leu Thr Gln Lys Ser Gly Phe Tyr Pro Val Gln Asp Ala Gln Tyr
165 170 175

Thr Asn Asn Arg Gly Lys Ser Ile Leu Phe Val Trp Gly Ile His His
180 185 190

Pro Pro Thr Tyr Thr Glu Gln Thr Asn Leu Tyr Ile Arg Asn Asp Thr
195 200 205

Thr Thr Ser Val Thr Thr Glu Asp Leu Asn Arg Thr Phe Lys Pro Val
210 215 220

Ile Gly Pro Arg Pro Leu Val Asn Gly Leu Gln Gly Arg Ile Asp Tyr
225 230 235 240

Tyr Trp Ser Val Leu Lys Pro Gly Gln Thr Leu Arg Val Arg Ser Asn
245 250 255

Gly Asn Leu Ile Ala Pro Trp Tyr Gly His Val Leu Ser Gly Gly Ser
260 265 270

His Gly Arg Ile Leu Lys Thr Asp Leu Lys Gly Gly Asn Cys Val Val
275 280 285

Gln Cys Gln Thr Glu Lys Gly Gly Leu Asn Ser Thr Leu Pro Phe His
290 295 300

Asn Ile Ser Lys Tyr Ala Phe Gly Thr Cys Pro Lys Tyr Val Arg Val
305 310 315 320

Asn Ser Leu Lys Leu Ala Val Gly Leu Arg Asn Val Pro Ala Arg Ser
325 330 335

Ser Arg Gly Leu Phe Gly Ala Ile Ala Gly Phe Ile Glu Gly Gly Trp
340 345 350

Pro Gly Leu Val Ala Gly Trp Tyr Gly Phe Gln His Ser Asn Asp Gln
355 360 365

Gly Val Gly Met Ala Ala Asp Arg Asp Ser Thr Gln Lys Ala Ile Asp
370 375 380

Lys Ile Thr Ser Lys Val Asn Asn Ile Val Asp Lys Met Asn Lys Gln
385 390 395 400

Tyr Glu Ile Ile Asp His Glu Phe Ser Glu Val Glu Thr Arg Leu Asn
405 410 415

Met Ile Asn Asn Lys Ile Asp Asp Gln Ile Gln Asp Val Trp Ala Tyr
420 425 430

Asn Ala Glu Leu Leu Val Leu Leu Glu Asn Gln Lys Thr Leu Asp Glu
435 440 445

His Asp Ala Asn Val Asn Asn Leu Tyr Asn Lys Val Lys Arg Ala Leu
450 455 460

Gly Ser Asn Ala Met Glu Asp Gly Lys Gly Cys Phe Glu Leu Tyr His
465 470 475 480

Lys Cys Asp Asp Gln Cys Met Glu Thr Ile Arg Asn Gly Thr Tyr Asn
485 490 495

Arg Arg Lys Tyr Arg Glu Glu Ser Arg Leu Glu Arg Gln Lys Ile Glu
500 505 510

Gly Val Lys Leu Glu Ser Glu Gly Thr Tyr Lys Ser Gly Arg Leu Val
515 520 525

```
Pro Arg Gly Ser Pro Gly Ser Gly Tyr Ile Pro Glu Ala Pro Arg Asp
    530                 535                 540

Gly Gln Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu Leu Ser Thr
545                 550                 555                 560

Phe Leu Gly Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser Thr
                565                 570                 575

Gly His His His His His His
            580
```

<210> 745
<211> 372
<212> DNA
<213> Homo sapiens

<400> 745

```
caggtgcaac tgcaggagtc gggcccagga ctggtgaagc cctcggagac cctgtccctc      60

acttgcgctg tctctggtgt ctccatcagc aatattgatt tctactgggg ctggatccgc     120

cagccccag ggaaggggct agaatggatt ggcaatatct attatacggg gatcaccttc     180

tacaacccgt ccctcagcag tcgagtcgcc atatccattg acacctccaa gaaccagttc     240

tccctgactc tgacttctgt gaccgccgca gacacggcta tgtattactg tgcgagacat     300

tacggtgact ccgaggcaat aaacgatgcc tttgacatct ggggccaagg gacaatgctc     360

accgtctcga gc                                                        372
```

<210> 746
<211> 124
<212> PRT
<213> Homo sapiens

<400> 746

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

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

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

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

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

Ser Leu Thr Leu Thr Ser Val Thr Ala Ala Asp Thr Ala Met Tyr Tyr
                85                  90                  95
```

```
Cys Ala Arg His Tyr Gly Asp Ser Glu Ala Ile Asn Asp Ala Phe Asp
            100                 105                 110


Ile Trp Gly Gln Gly Thr Met Leu Thr Val Ser Ser
        115                 120


<210>  747
<211>  7
<212>  PRT
<213>  Homo sapiens

<400>  747

Asn Ile Asp Phe Tyr Trp Gly
1               5


<210>  748
<211>  16
<212>  PRT
<213>  Homo sapiens

<400>  748

Asn Ile Tyr Tyr Thr Gly Ile Thr Phe Tyr Asn Pro Ser Leu Ser Ser
1               5                   10                  15


<210>  749
<211>  14
<212>  PRT
<213>  Homo sapiens

<400>  749

His Tyr Gly Asp Ser Glu Ala Ile Asn Asp Ala Phe Asp Ile
1               5                   10


<210>  750
<211>  6
<212>  PRT
<213>  Homo sapiens

<400>  750

Gly Val Ser Ile Ser Asn
1               5


<210>  751
<211>  9
<212>  PRT
<213>  Homo sapiens

<400>  751

Asn Ile Tyr Tyr Thr Gly Ile Thr Phe
1               5


<210>  752
<211>  324
<212>  DNA
<213>  Homo sapiens
```

<400> 752
gagatagtga tgacgcagtc tccagccacc ctgtctgtgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gagtgttggc aatagtttag cctggtacca gcagagacct 120

ggccaggctc ccaggctcct catctacggt gcatccacca gggccactgg tatcccaccc 180

aggttcagtg gcagtgggtc tgggacagaa ttcactctca ccatcagcag cctgcagact 240

gaagattttg cagtttatta ctgtcaacaa tatattaact ggcgtccgct cagttttggc 300

ggagggacca aggtggagat caaa 324

<210> 753
<211> 108
<212> PRT
<213> Homo sapiens

<400> 753

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Asn Ser
20 25 30

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

Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Pro Arg Phe Ser Gly
50 55 60

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

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Ile Asn Trp Arg Pro
85 90 95

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

<210> 754
<211> 11
<212> PRT
<213> Homo sapiens

<400> 754

Arg Ala Ser Gln Ser Val Gly Asn Ser Leu Ala
1 5 10

<210> 755
<211> 7
<212> PRT
<213> Homo sapiens

<400> 755

Gly Ala Ser Thr Arg Ala Thr
1 5

<210> 756
<211> 10
<212> PRT
<213> Homo sapiens

<400> 756

Gln Gln Tyr Ile Asn Trp Arg Pro Leu Ser
1 5 10

<210> 757
<211> 13
<212> PRT
<213> Influenza A virus

<400> 757

Thr Gly Ser Ser Ser Met Asn Ile Gly Asn Tyr Val Ala
1 5 10

<210> 758
<211> 366
<212> DNA
<213> Homo sapiens

<400> 758
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gcctgtgtag tctctgggtt caccgtcacc agcaattata taacttgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagtt atttatagtc atggtcgcgc atattattca 180

gcctccgtga atggccgatt caccatctcc agacacactt ccaagaacac agtttatctt 240

gaaatgaaca gcctgagacc tgaggacacg gccgtctatt actgtgcggg cgggggccta 300

gtcggtggct acgacgaata tttctttgac tattggggcc agggaaccct ggccaccgtc 360

tcctca 366

<210> 759
<211> 122
<212> PRT
<213> Homo sapiens

<400> 759

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

Ser Leu Arg Leu Ala Cys Val Val Ser Gly Phe Thr Val Thr Ser Asn
20 25 30

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

Ser Val Ile Tyr Ser His Gly Arg Ala Tyr Tyr Ser Ala Ser Val Asn
50 55 60

```
Gly Arg Phe Thr Ile Ser Arg His Thr Ser Lys Asn Thr Val Tyr Leu
65                  70                  75                  80

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

Gly Gly Gly Leu Val Gly Gly Tyr Asp Glu Tyr Phe Phe Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Leu Ala Thr Val Ser Ser
        115                 120
```

<210> 760
<211> 5
<212> PRT
<213> Homo sapiens

<400> 760

```
Ser Asn Tyr Ile Thr
1               5
```

<210> 761
<211> 16
<212> PRT
<213> Homo sapiens

<400> 761

```
Val Ile Tyr Ser His Gly Arg Ala Tyr Tyr Ser Ala Ser Val Asn Gly
1               5                   10                  15
```

<210> 762
<211> 14
<212> PRT
<213> Homo sapiens

<400> 762

```
Gly Gly Leu Val Gly Gly Tyr Asp Glu Tyr Phe Phe Asp Tyr
1               5                   10
```

<210> 763
<211> 6
<212> PRT
<213> Homo sapiens

<400> 763

```
Gly Phe Thr Val Thr Ser
1               5
```

<210> 764
<211> 9
<212> PRT
<213> Homo sapiens

<400> 764

Val Ile Tyr Ser His Gly Arg Ala Tyr
1 5

<210> 765
<211> 324
<212> DNA
<213> Homo sapiens

<400> 765
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ctctcctgca gagtcggtca gagtgttagc ggcagccact tagcctggta ccaacagaaa 120

cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180

gacaggttcg gtggcagtgt gtctgggaca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ctgcagttta ttactgtcag cagtatggtg actcacgata cacttttggc 300

caggggacca agctggagat caaa 324

<210> 766
<211> 108
<212> PRT
<213> Homo sapiens

<400> 766

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

Glu Arg Ala Thr Leu Ser Cys Arg Val Gly Gln Ser Val Ser Gly Ser
20 25 30

His 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 Gly
50 55 60

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

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

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

<210> 767
<211> 12
<212> PRT
<213> Homo sapiens

<400> 767

Arg Val Gly Gln Ser Val Ser Gly Ser His Leu Ala
1 5 10

<210> 768
<211> 7
<212> PRT
<213> Homo sapiens

<400> 768

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 769
<211> 9
<212> PRT
<213> Homo sapiens

<400> 769

Gln Gln Tyr Gly Asp Ser Arg Tyr Thr
1 5

<210> 770
<211> 381
<212> DNA
<213> Homo sapiens

<400> 770
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acctgcactg tgtctggggg gtccctcact gattactctt ggaactggat ccgccagccc 120

ccagggaagg ggctggagtg gatcggtgac accttcata atggctacac caactacaac 180

ccgtccctca ggggtcgagt ttccatctca atagacacgt ccaagaacca ggtctcactc 240

aggctgacct ctgtgaccgc cgcggacacg gctctttatt actgtgcgag aggctcaggt 300

ggatatggtg gcttcgatta ttttggcaag ctccggacat gggacttctg gggccaggga 360

acgctggtca ccgtctcctc a 381

<210> 771
<211> 127
<212> PRT
<213> Homo sapiens

<400> 771

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

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Leu Thr Asp Tyr
20 25 30

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

Gly Asp Thr Leu His Asn Gly Tyr Thr Asn Tyr Asn Pro Ser Leu Arg
50 55 60

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

Arg Leu Thr Ser Val Thr Ala Ala Asp Thr Ala Leu Tyr Tyr Cys Ala
85 90 95

Arg Gly Ser Gly Gly Tyr Gly Gly Phe Asp Tyr Phe Gly Lys Leu Arg
100 105 110

Thr Trp Asp Phe Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 772
<211> 5
<212> PRT
<213> Homo sapiens

<400> 772

Asp Tyr Ser Trp Asn
1 5

<210> 773
<211> 16
<212> PRT
<213> Homo sapiens

<400> 773

Asp Thr Leu His Asn Gly Tyr Thr Asn Tyr Asn Pro Ser Leu Arg Gly
1 5 10 15

<210> 774
<211> 19
<212> PRT
<213> Homo sapiens

<400> 774

Gly Ser Gly Gly Tyr Gly Gly Phe Asp Tyr Phe Gly Lys Leu Arg Thr
1 5 10 15

Trp Asp Phe

<210> 775
<211> 6
<212> PRT
<213> Homo sapiens

<400> 775

Gly Gly Ser Leu Thr Asp
1 5

<210> 776
<211> 9
<212> PRT
<213> Homo sapiens

<400> 776

Asp Thr Leu His Asn Gly Tyr Thr Asn
1 5

<210> 777
<211> 321
<212> DNA
<213> Homo sapiens

<400> 777
gacattcagt tgacccagtc tccatcctcc ctgtctgcat ctgtgggaga cagagtcacc 60

atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcaaaaacca 120

gggaacgccc ctaagcgcct gatctttggt gcatccagtt tgcaaagtgg ggtcccatca 180

aggttcagcg gcagtggatc tgggacagag ttcactctca caatcagcag cctgcagcct 240

gaggactttg caacttatta ctgtctacag cataatagtt acccgtacac ttttggccag 300

gggaccaagc tggagatcaa g 321

<210> 778
<211> 107
<212> PRT
<213> Homo sapiens

<400> 778

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

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

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

Phe Gly 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 Tyr
85 90 95

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

<210> 779
<211> 11
<212> PRT
<213> Homo sapiens

<400> 779

Arg Ala Ser Gln Gly Ile Arg Asn Asp Leu Gly
1 5 10

<210> 780
<211> 7
<212> PRT
<213> Homo sapiens

<400> 780

Gly Ala Ser Ser Leu Gln Ser
1 5

<210> 781
<211> 9
<212> PRT
<213> Homo sapiens

<400> 781

Leu Gln His Asn Ser Tyr Pro Tyr Thr
1 5

<210> 782
<211> 354
<212> DNA
<213> Homo sapiens

<400> 782
caggtgcaac tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg cagcttcagc aactatgcct tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg accatccctc tacttggtac aacaaactac 180

gcacagaagt tccagggcag agtcacgatt tccgcggacc aattcacgag cacagcctac 240

atggagctgg gcagcctgag atctgaagac acggccgtgt attactgtac gagacggaaa 300

atgactacgg cttttgactc tggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 783
<211> 118
<212> PRT
<213> Homo sapiens

<400> 783

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

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

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

Gly Gly Thr Ile Pro Leu Leu Gly Thr Thr Asn Tyr Ala Gln Lys Phe
50 55 60

```
Gln Gly Arg Val Thr Ile Ser Ala Asp Gln Phe Thr Ser Thr Ala Tyr
65                  70                  75                  80

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

Thr Arg Arg Lys Met Thr Thr Ala Phe Asp Ser Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser
        115
```

<210> 784
<211> 5
<212> PRT
<213> Homo sapiens

<400> 784

```
Asn Tyr Ala Phe Ser
1               5
```

<210> 785
<211> 17
<212> PRT
<213> Homo sapiens

<400> 785

```
Gly Thr Ile Pro Leu Leu Gly Thr Thr Asn Tyr Ala Gln Lys Phe Gln
1               5                   10                  15

Gly
```

<210> 786
<211> 9
<212> PRT
<213> Homo sapiens

<400> 786

```
Arg Lys Met Thr Thr Ala Phe Asp Ser
1               5
```

<210> 787
<211> 6
<212> PRT
<213> Homo sapiens

<400> 787

```
Gly Gly Ser Phe Ser Asn
1               5
```

<210> 788
<211> 10
<212> PRT
<213> Homo sapiens

<400> 788

Gly Thr Ile Pro Leu Leu Gly Thr Thr Asn
1 5 10

<210> 789
<211> 354
<212> DNA
<213> Homo sapiens

<400> 789
cagcctgttc tgactcagcc accttctgca tcagcctccc tgggagcctc ggtcacactc 60

acctgcaccc tgagcagcgc ctacagtaat tataaagtgg actggtacca gcagagacca 120

gggaagggcc cccgctttgt gatgcgagtg ggcactggtg ggattgtggg atccaagggg 180

gatggcatcc ctgatcgctt ctcagtcttg ggctcaggcc tgaatcggta cctgaccatc 240

aagaacatcc aggaagagga tgagagtgac taccactgtg gggcagacca tggcagtggg 300

agcaacttcg tgtcccctta cgtattcggc ggagggacca agctgaccgt tcta 354

<210> 790
<211> 118
<212> PRT
<213> Homo sapiens

<400> 790

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

Ser Val Thr Leu Thr Cys Thr Leu Ser Ser Ala Tyr Ser Asn Tyr Lys
20 25 30

Val Asp Trp Tyr Gln Gln Arg Pro Gly Lys Gly Pro Arg Phe Val Met
35 40 45

Arg Val Gly Thr Gly Gly Ile Val Gly Ser Lys Gly Asp Gly Ile Pro
50 55 60

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

Lys Asn Ile Gln Glu Glu Asp Glu Ser Asp Tyr His Cys Gly Ala Asp
85 90 95

His Gly Ser Gly Ser Asn Phe Val Ser Pro Tyr Val Phe Gly Gly Gly
100 105 110

Thr Lys Leu Thr Val Leu
115

<210> 791
<211> 12
<212> PRT

<213> Homo sapiens

<400> 791

Thr Leu Ser Ser Ala Tyr Ser Asn Tyr Lys Val Asp
1 5 10

<210> 792
<211> 12
<212> PRT
<213> Homo sapiens

<400> 792

Val Gly Thr Gly Gly Ile Val Gly Ser Lys Gly Asp
1 5 10

<210> 793
<211> 15
<212> PRT
<213> Homo sapiens

<400> 793

Gly Ala Asp His Gly Ser Gly Ser Asn Phe Val Ser Pro Tyr Val
1 5 10 15

<210> 794
<211> 369
<212> DNA
<213> Homo sapiens

<400> 794
caggtgcagc tggcgcagtc tggggctgag gtgaagaggc ctgggtcctc ggtgaaagtc 60

tcatgcacgg cttctggagg catcttcagg aagaatgcaa tcagctgggt gcgacaggcc 120

cctggacaag gccttgagtg gatgggaggg atcatcgcag tctttaacac agcaaattac 180

gcgcagaagt ttcagggcag agtcaaaatt accgcagacg aatccgggaa tacagcctac 240

atggagctga gcagcctgag atctgacgac acggccgtgt attactgtgc gagtcaccca 300

aaatatttct atggttcggg gagttatccg gacttctggg gccagggaac cctggtcacc 360

gtctcgagc 369

<210> 795
<211> 123
<212> PRT
<213> Homo sapiens

<400> 795

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

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Gly Ile Phe Arg Lys Asn
20 25 30

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

```
Gly Gly Ile Ile Ala Val Phe Asn Thr Ala Asn Tyr Ala Gln Lys Phe
    50                  55                  60

Gln Gly Arg Val Lys Ile Thr Ala Asp Glu Ser Gly Asn Thr Ala Tyr
65                  70                  75                  80

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

Ala Ser His Pro Lys Tyr Phe Tyr Gly Ser Gly Ser Tyr Pro Asp Phe
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  796
<211>  5
<212>  PRT
<213>  Homo sapiens

<400>  796

Lys Asn Ala Ile Ser
1               5


<210>  797
<211>  17
<212>  PRT
<213>  Homo sapiens

<400>  797

Gly Ile Ile Ala Val Phe Asn Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1               5                   10                  15

Gly


<210>  798
<211>  14
<212>  PRT
<213>  Homo sapiens

<400>  798

His Pro Lys Tyr Phe Tyr Gly Ser Gly Ser Tyr Pro Asp Phe
1               5                   10


<210>  799
<211>  6
<212>  PRT
<213>  Homo sapiens

<400>  799

Gly Gly Ile Phe Arg Lys
1               5
```

<210> 800
<211> 10
<212> PRT
<213> Homo sapiens

<400> 800

Gly Ile Ile Ala Val Phe Asn Thr Ala Asn
1 5 10

<210> 801
<211> 330
<212> DNA
<213> Homo sapiens

<400> 801
caatctgccc tgactcagcc tcgctcagtg tccgggtctc ctggacagtc agtcaccatc 60

tcctgcactg gaagcagcag tgatgttggt gcttctaact ctgtctcctg gtaccaacaa 120

cacccaggca aagcccccaa actcgttatt tatgatgtca ctgagcgacc ctcaggggtc 180

cctcatcgct tctctggctc caagtctggc aacacggcct ccctgaccgt ctctgggctc 240

cagcctgagg acgaggctga ttatttctgc tgcgcatatg gaggcaaata tcttgtggtc 300

ttcggcggag ggaccaaggt gaccgtcctc 330

<210> 802
<211> 110
<212> PRT
<213> Homo sapiens

<400> 802

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

Ser Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asp Val Gly Ala Ser
20 25 30

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

Val Ile Tyr Asp Val Thr Glu Arg Pro Ser Gly Val Pro His Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65 70 75 80

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

Tyr Leu Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 803

<211> 14
<212> PRT
<213> Homo sapiens

<400> 803

Thr Gly Ser Ser Ser Asp Val Gly Ala Ser Asn Ser Val Ser
1 5 10

<210> 804
<211> 7
<212> PRT
<213> Homo sapiens

<400> 804

Asp Val Thr Glu Arg Pro Ser
1 5

<210> 805
<211> 10
<212> PRT
<213> Homo sapiens

<400> 805

Cys Ala Tyr Gly Gly Lys Tyr Leu Val Val
1 5 10

<210> 806
<211> 387
<212> DNA
<213> Homo sapiens

<400> 806
gaggtgctga tggtggagtc tgggggaggc ttggtccagc ctgggggtc cgtgagactc 60

tcctgtgtag cctctggatt cagtttcagt agtcattgga tgacctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtggccaac atagaggacg atggaggtga caagtactat 180

gtggactctg tgaagggccg attcattatc tccagagaca acgccaagaa ttcagtgtat 240

ctgcaaatga acagcctaag agccgaggac acggctgtgt attttctgtg gcgagaggtt cg 300

gggagctctg atagaagtga ttatgacccc cactactact actacttgga cgtctggggc 360

aaaggggcca cggtcaccgt ctcctca 387

<210> 807
<211> 129
<212> PRT
<213> Homo sapiens

<400> 807

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

Ser Val Arg Leu Ser Cys Val Ala Ser Gly Phe Ser Phe Ser Ser His
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 Glu Asp Asp Gly Gly Asp Lys Tyr Tyr Val Asp Ser Val
50 55 60

Lys Gly Arg Phe Ile Ile Ser Arg Asp Asn Ala Lys Asn Ser Val Tyr
65 70 75 80

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

Ala Arg Gly Ser Gly Ser Ser Asp Arg Ser Asp Tyr Asp Pro His Tyr
100 105 110

Tyr Tyr Tyr Leu Asp Val Trp Gly Lys Gly Ala Thr Val Thr Val Ser
115 120 125

Ser

<210> 808
<211> 5
<212> PRT
<213> Homo sapiens

<400> 808

Ser His Trp Met Thr
1 5

<210> 809
<211> 17
<212> PRT
<213> Homo sapiens

<400> 809

Asn Ile Glu Asp Asp Gly Gly Asp Lys Tyr Tyr Val Asp Ser Val Lys
1 5 10 15

Gly

<210> 810
<211> 20
<212> PRT
<213> Homo sapiens

<400> 810

Gly Ser Gly Ser Ser Asp Arg Ser Asp Tyr Asp Pro His Tyr Tyr Tyr
1 5 10 15

Tyr Leu Asp Val
20

<210> 811
<211> 6
<212> PRT
<213> Homo sapiens

<400> 811

Gly Phe Ser Phe Ser Ser
1 5

<210> 812
<211> 10
<212> PRT
<213> Homo sapiens

<400> 812

Asn Ile Glu Asp Asp Gly Gly Asp Lys Tyr
1 5 10

<210> 813
<211> 321
<212> DNA
<213> Homo sapiens

<400> 813
gacatccagc tgacccagtc tccatcttcc ctgtctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagt aggtatttaa attggtatca gcaaaaacca 120

gggaaagccc ctaagctcct gctgtttgct gcttctactt tgctagatgg ggtcccatca 180

agattcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg caacttacta ctgtcaacgg aatcacagtc cctcgtggac gttcggccaa 300

gggaccaggg tggaaatcaa a 321

<210> 814
<211> 107
<212> PRT
<213> Homo sapiens

<400> 814

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

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

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

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

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

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

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

<210> 815
<211> 11
<212> PRT
<213> Homo sapiens

<400> 815

Arg Ala Ser Gln Ser Ile Ser Arg Tyr Leu Asn
1 5 10

<210> 816
<211> 7
<212> PRT
<213> Homo sapiens

<400> 816

Ala Ala Ser Thr Leu Leu Asp
1 5

<210> 817
<211> 9
<212> PRT
<213> Homo sapiens

<400> 817

Gln Arg Asn His Ser Pro Ser Trp Thr
1 5

<210> 818
<211> 372
<212> DNA
<213> Homo sapiens

<400> 818
caggtgcagc tgcaagagtc gggcccggga ctggtgaagc cttcggagac cctgtccctc 60

aactgcgctg tctctggagg ctccatcagt aattactact ggagctggat ccggcagccc 120

cccgggaagg gactggagtg gattggctat atctcttaca atgggaggcc caagtacaac 180

ccctccctca cgagtcgagt caccatatcc gtcgacacgt ccaaggacca gttctccctg 240

gagctgcgct ctgtgaccgc tgcggacacg gccctttatt actgtgcgag agaaacgcgg 300

ttcggggagt tattatctcc ctatgatgct tttgaaatct ggggccaagg gacaatggtc 360

accgtctcct ca 372

<210> 819
<211> 124
<212> PRT
<213> Homo sapiens

<400> 819

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

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

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

Gly Tyr Ile Ser Tyr Asn Gly Arg Pro Lys Tyr Asn Pro Ser Leu Thr
50 55 60

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

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

Arg Glu Thr Arg Phe Gly Glu Leu Leu Ser Pro Tyr Asp Ala Phe Glu
100 105 110

Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 820
<211> 5
<212> PRT
<213> Homo sapiens

<400> 820

Asn Tyr Tyr Trp Ser
1 5

<210> 821
<211> 16
<212> PRT
<213> Homo sapiens

<400> 821

Tyr Ile Ser Tyr Asn Gly Arg Pro Lys Tyr Asn Pro Ser Leu Thr Ser
1 5 10 15

<210> 822
<211> 16
<212> PRT
<213> Homo sapiens

<400> 822

Glu Thr Arg Phe Gly Glu Leu Leu Ser Pro Tyr Asp Ala Phe Glu Ile
1 5 10 15

<210> 823

<211> 9
<212> PRT
<213> Homo sapiens

<400> 823

Tyr Ile Ser Tyr Asn Gly Arg Pro Lys
1 5

<210> 824
<211> 6
<212> PRT
<213> Homo sapiens

<400> 824

Gly Gly Ser Ile Ser Asn
1 5

<210> 825
<211> 321
<212> DNA
<213> Homo sapiens

<400> 825
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atgacttgcc gggcaagtca gaacattaga agctatttaa attggtatca gcagagacca 120

gggacagccc ctaaactcct gatctatgct gcatccactt tacacagtgg ggtcccatca 180

aggttcagtg gcggtgggtc tgggacagat ttcactctca ccatcaataa tctgcaacct 240

gaagatttg catcttacta ctgtcaacag agttacgata accctcagac gttcggccaa 300

gggaccaagg tggaaatcaa a 321

<210> 826
<211> 107
<212> PRT
<213> Homo sapiens

<400> 826

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

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

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

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

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

Glu Asp Phe Ala Ser Tyr Tyr Cys Gln Gln Ser Tyr Asp Asn Pro Gln

85 90 95

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

<210> 827
<211> 11
<212> PRT
<213> Homo sapiens

<400> 827

Arg Ala Ser Gln Asn Ile Arg Ser Tyr Leu Asn
1 5 10

<210> 828
<211> 7
<212> PRT
<213> Homo sapiens

<400> 828

Ala Ala Ser Thr Leu His Ser
1 5

<210> 829
<211> 9
<212> PRT
<213> Homo sapiens

<400> 829

Gln Gln Ser Tyr Asp Asn Pro Gln Thr
1 5

<210> 830
<211> 399
<212> DNA
<213> Homo sapiens

<400> 830
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tcctgcaagg cttctggata caccttcacc aattatgaca tcaactggat tcgacaggcc 120

cctggtcaag gacttgagtg gatgggctgg ataaatccca acagtggaac cacgggctct 180

gcacagaggt tccagggcag agtcaccata accgtggaca cctccataac cacagtctac 240

atggaactga gcagcctgag atctgacgac acggccattt actactgcgc gagaggccgt 300

gagctcctcc ggcttcaaca ttttttgact gactcccagt ccgagaggag ggactgcttc 360

gacccctggg gccagggaac cctggtcacc gtctcctca 399

<210> 831
<211> 133
<212> PRT
<213> Homo sapiens

<400> 831

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

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

Asp Ile Asn Trp Ile Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Thr Thr Gly Ser Ala Gln Arg Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Val Asp Thr Ser Ile Thr Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

Ala Arg Gly Arg Glu Leu Leu Arg Leu Gln His Phe Leu Thr Asp Ser
100 105 110

Gln Ser Glu Arg Arg Asp Cys Phe Asp Pro Trp Gly Gln Gly Thr Leu
115 120 125

Val Thr Val Ser Ser
130

<210> 832
<211> 5
<212> PRT
<213> Homo sapiens

<400> 832

Asn Tyr Asp Ile Asn
1 5

<210> 833
<211> 17
<212> PRT
<213> Homo sapiens

<400> 833

Trp Ile Asn Pro Asn Ser Gly Thr Thr Gly Ser Ala Gln Arg Phe Gln
1 5 10 15

Gly

<210> 834
<211> 24
<212> PRT
<213> Homo sapiens

<400> 834

Gly Arg Glu Leu Leu Arg Leu Gln His Phe Leu Thr Asp Ser Gln Ser
1 5 10 15

Glu Arg Arg Asp Cys Phe Asp Pro
20

<210> 835
<211> 6
<212> PRT
<213> Homo sapiens

<400> 835

Gly Tyr Thr Phe Thr Asn
1 5

<210> 836
<211> 10
<212> PRT
<213> Homo sapiens

<400> 836

Trp Ile Asn Pro Asn Ser Gly Thr Thr Gly
1 5 10

<210> 837
<211> 321
<212> DNA
<213> Homo sapiens

<400> 837
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atcacttgcc gggcaaatca agacattggc atttatttaa attggtatca acagaatcca 120

gggaaagtcc ctaaactcct gctccatggt gcgtccagtt tgcagggcgg ggtcccatca 180

aggttcagtg ccagtggatc tgggacagat ttcactctca ccattcacag tctacaacct 240

gaagatttag caacctacta ctgtcaacag agtcgccgtc taccgtacac ttttggccag 300

gggaccaggg tggaactcaa a 321

<210> 838
<211> 107
<212> PRT
<213> Homo sapiens

<400> 838

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 Asn Gln Asp Ile Gly Ile Tyr
20 25 30

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

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

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

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

Thr Phe Gly Gln Gly Thr Arg Val Glu Leu Lys
            100                 105
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<210> 839
<211> 11
<212> PRT
<213> Homo sapiens

<400> 839

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Arg Ala Asn Gln Asp Ile Gly Ile Tyr Leu Asn
1               5                   10
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<210> 840
<211> 7
<212> PRT
<213> Homo sapiens

<400> 840

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Gly Ala Ser Ser Leu Gln Gly
1               5
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<210> 841
<211> 9
<212> PRT
<213> Homo sapiens

<400> 841

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Gln Gln Ser Arg Arg Leu Pro Tyr Thr
1               5
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<210> 842
<211> 360
<212> DNA
<213> Homo sapiens

<400> 842

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acctgcacct tctctgggtt ttcactcagc actaatggag tgaatgtggg ctggatccgt  120

cagccccag gaaaggccct ggagtggctt gcactcattt actgggatga tgataagcgc  180

tacagtccgt ctctgaagag aaggctcacc atcaccaagg acacctccaa aaaccaagtg  240

gtccttacac tgaccaacat ggaccctgta gatacagcca catattactg tgcacacaga  300

cccgacttct atggtgactt cgagtactgg ggcccgggaa ccctggtcac cgtctcctca  360
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<210> 843
<211> 120
<212> PRT
<213> Homo sapiens

<400> 843

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

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Asn
20 25 30

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

Trp Leu Ala Leu Ile Tyr Trp Asp Asp Asp Lys Arg Tyr Ser Pro Ser
50 55 60

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

Val Leu Thr Leu Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

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

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 844
<211> 7
<212> PRT
<213> Homo sapiens

<400> 844

Thr Asn Gly Val Asn Val Gly
1 5

<210> 845
<211> 16
<212> PRT
<213> Homo sapiens

<400> 845

Leu Ile Tyr Trp Asp Asp Asp Lys Arg Tyr Ser Pro Ser Leu Lys Arg
1 5 10 15

<210> 846
<211> 10
<212> PRT
<213> Homo sapiens

<400> 846

Arg Pro Asp Phe Tyr Gly Asp Phe Glu Tyr
1 5 10

<210> 847
<211> 8
<212> PRT
<213> Homo sapiens

<400> 847

Gly Phe Ser Leu Ser Thr Asn Gly
1 5

<210> 848
<211> 9
<212> PRT
<213> Homo sapiens

<400> 848

Leu Ile Tyr Trp Asp Asp Asp Lys Arg
1 5

<210> 849
<211> 330
<212> DNA
<213> Homo sapiens

<400> 849
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tcctgcactg gaagcagcag tgacattggt ggttataact atgtctcctg gtaccaacaa 120

cacccaggca aggcccccaa actcatgatt tacgatgtca ataatcggcc ctcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgactat ctctgggctc 240

cagactgacg acgaggctga ttattactgc ggctcatata caggcagtcc tcattatgtc 300

ttcggaactg ggaccaaggt caccgtccta 330

<210> 850
<211> 110
<212> PRT
<213> Homo sapiens

<400> 850

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

Ser Ile Thr Ile Ser Cys Thr Gly Ser Ser Ser Asp Ile Gly Gly Tyr
20 25 30

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

Met Ile Tyr Asp Val Asn Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Thr Asp Asp Glu Ala Asp Tyr Tyr Cys Gly Ser Tyr Thr Gly Ser
85 90 95

Pro His Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 851
<211> 14
<212> PRT
<213> Homo sapiens

<400> 851

Thr Gly Ser Ser Ser Asp Ile Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> 852
<211> 7
<212> PRT
<213> Homo sapiens

<400> 852

Asp Val Asn Asn Arg Pro Ser
1 5

<210> 853
<211> 10
<212> PRT
<213> Homo sapiens

<400> 853

Gly Ser Tyr Thr Gly Ser Pro His Tyr Val
1 5 10

<210> 854
<211> 363
<212> DNA
<213> Homo sapiens

<400> 854
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tcctgcaagg cttctggagg ccccttcatg agttatgcta tcggctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcaaccctg tgtttggtag accgcactac 180

gcacagaagt tccagggcag agtcaccatc gccacggacg actccacgaa gacatcgtac 240

atggaactga gtagcctgac gtctgaggac acgggcatgt attactgtgc gagtaggtat 300

agtaggtcgt ccccagggac ctttgagtcc tggggccagg gaaccctggt caccgtctcg 360

agc 363

<210> 855

<211> 121
<212> PRT
<213> Homo sapiens

<400> 855

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Met Ser Tyr
20 25 30

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

Gly Gly Ile Asn Pro Val Phe Gly Arg Pro His Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Ala Thr Asp Asp Ser Thr Lys Thr Ser Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr Gly Met Tyr Tyr Cys
85 90 95

Ala Ser Arg Tyr Ser Arg Ser Ser Pro Gly Thr Phe Glu Ser Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 856
<211> 5
<212> PRT
<213> Homo sapiens

<400> 856

Ser Tyr Ala Ile Gly
1 5

<210> 857
<211> 17
<212> PRT
<213> Homo sapiens

<400> 857

Gly Ile Asn Pro Val Phe Gly Arg Pro His Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 858
<211> 12
<212> PRT
<213> Homo sapiens

<400> 858

Arg Tyr Ser Arg Ser Ser Pro Gly Thr Phe Glu Ser
1 5 10

<210> 859
<211> 6
<212> PRT
<213> Homo sapiens

<400> 859

Gly Gly Pro Phe Met Ser
1 5

<210> 860
<211> 10
<212> PRT
<213> Homo sapiens

<400> 860

Gly Ile Asn Pro Val Phe Gly Arg Pro His
1 5 10

<210> 861
<211> 327
<212> DNA
<213> Homo sapiens

<400> 861
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ctctcctgta gggccagtca gagtgttagc aacaatttag cctggtacca gcaaaaacct 120

ggccagcctc ccaggctcct catctatgat gcatctacca gggccacggg tgtcccagcc 180

aagttcagtg gcactgggtc tggcacagag ttcactctca gcatcagcag cctgcagtcc 240

gaagattttg cagtttatta ctgtcagcag tatcacaact ggcctccctc gtacagtttt 300

ggcctgggga ccaagctgga gatcaaa 327

<210> 862
<211> 109
<212> PRT
<213> Homo sapiens

<400> 862

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

Glu Arg Val Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Asn Asn
20 25 30

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

Tyr Asp Ala Ser Thr Arg Ala Thr Gly Val Pro Ala Lys Phe Ser Gly

50 55 60

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

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr His Asn Trp Pro Pro
85 90 95

Ser Tyr Ser Phe Gly Leu Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 863
<211> 11
<212> PRT
<213> Homo sapiens

<400> 863

Arg Ala Ser Gln Ser Val Ser Asn Asn Leu Ala
1 5 10

<210> 864
<211> 7
<212> PRT
<213> Homo sapiens

<400> 864

Asp Ala Ser Thr Arg Ala Thr
1 5

<210> 865
<211> 11
<212> PRT
<213> Homo sapiens

<400> 865

Gln Gln Tyr His Asn Trp Pro Pro Ser Tyr Ser
1 5 10

<210> 866
<211> 387
<212> DNA
<213> Homo sapiens

<400> 866
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tcctgcacag gttctggatt cacctttggt gattatggtg tgacctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtaggtttc attagaacca gaccttgggg tgggacagca 180

gataccgccg cgtctgtgaa aggcagattc actatttcaa gagatgattc caaaagtctc 240

gcctatctgc aaatgaacag cctgaaaacc gaggacacag ccgtgtatta ctgttgtaga 300

gatgcccctc caaatgtgga agtggcttct atgaccaact ggtacttcga tctctggggc 360

cgtggcaccc tggtcaccgt ctcctca 387

<210> 867
<211> 129
<212> PRT
<213> Homo sapiens

<400> 867

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

Ser Leu Lys Leu Ser Cys Thr Gly Ser Gly Phe Thr Phe Gly Asp Tyr
20 25 30

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

Gly Phe Ile Arg Thr Arg Pro Trp Gly Gly Thr Ala Asp Thr Ala Ala
50 55 60

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

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

Tyr Cys Cys Arg Asp Ala Pro Pro Asn Val Glu Val Ala Ser Met Thr
100 105 110

Asn Trp Tyr Phe Asp Leu Trp Gly Arg Gly Thr Leu Val Thr Val Ser
115 120 125

Ser

<210> 868
<211> 5
<212> PRT
<213> Homo sapiens

<400> 868

Asp Tyr Gly Val Thr
1 5

<210> 869
<211> 19
<212> PRT
<213> Homo sapiens

<400> 869

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

Val Lys Gly

<210> 870
<211> 18
<212> PRT
<213> Homo sapiens

<400> 870

Asp Ala Pro Pro Asn Val Glu Val Ala Ser Met Thr Asn Trp Tyr Phe
1 5 10 15

Asp Leu

<210> 871
<211> 6
<212> PRT
<213> Homo sapiens

<400> 871

Gly Phe Thr Phe Gly Asp
1 5

<210> 872
<211> 12
<212> PRT
<213> Homo sapiens

<400> 872

Phe Ile Arg Thr Arg Pro Trp Gly Gly Thr Ala Asp
1 5 10

<210> 873
<211> 318
<212> DNA
<213> Homo sapiens

<400> 873
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atcacttgcc gggcgagtca gggcattctc aattgtttag cctggtatca gcagaaaccg 120

gggaaagttc ctaacctcct gatgtatgct gcatccacat tgcagtcagg ggtcccatct 180

cggttcagcg gcagtggatt tgggacagat ttcactctca ccatcagcag cctgcagcct 240

gaagatgttg caacttatta ctgtcaaacg tatggcggtg tctctacttt cggcggaggg 300

accaaggtgg agatcaga 318

<210> 874
<211> 106
<212> PRT
<213> Homo sapiens

<400> 874

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Leu Asn Cys
20 25 30

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

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

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

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

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

<210> 875
<211> 11
<212> PRT
<213> Homo sapiens

<400> 875

Arg Ala Ser Gln Gly Ile Leu Asn Cys Leu Ala
1 5 10

<210> 876
<211> 7
<212> PRT
<213> Homo sapiens

<400> 876

Ala Ala Ser Thr Leu Gln Ser
1 5

<210> 877
<211> 8
<212> PRT
<213> Homo sapiens

<400> 877

Gln Thr Tyr Gly Gly Val Ser Thr
1 5

<210> 878
<211> 372
<212> DNA
<213> Homo sapiens

<400> 878
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acctgcactg tctctggtgg ctccgtcagc agtgagactt actactggag ctggatccgg 120

cagcccccag ggaagggact agagtggatt ggatatatct attacattgg gaacaccgac 180

tacaggccct ccctcaagag tcgagtcacc atatcactgg acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gaccgctgcg gacacggccg tttattactg tgcgagaggc 300

gcttattatg atagtagtgg ttacccggct ttttatatct ggggccaagg gacaatggtc 360

accgtctcct ca 372

<210> 879
<211> 124
<212> PRT
<213> Homo sapiens

<400> 879

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

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

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

Trp Ile Gly Tyr Ile Tyr Tyr Ile Gly Asn Thr Asp Tyr Arg Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Leu 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 Gly Ala Tyr Tyr Asp Ser Ser Gly Tyr Pro Ala Phe Tyr
100 105 110

Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 880
<211> 7
<212> PRT
<213> Homo sapiens

<400> 880

Ser Glu Thr Tyr Tyr Trp Ser
1 5

<210> 881
<211> 16
<212> PRT
<213> Homo sapiens

<400> 881

Tyr Ile Tyr Tyr Ile Gly Asn Thr Asp Tyr Arg Pro Ser Leu Lys Ser
1 5 10 15

<210> 882
<211> 14
<212> PRT
<213> Homo sapiens

<400> 882

Gly Ala Tyr Tyr Asp Ser Ser Gly Tyr Pro Ala Phe Tyr Ile
1 5 10

<210> 883
<211> 8
<212> PRT
<213> Homo sapiens

<400> 883

Gly Gly Ser Val Ser Ser Glu Thr
1 5

<210> 884
<211> 9
<212> PRT
<213> Homo sapiens

<400> 884

Tyr Ile Tyr Tyr Ile Gly Asn Thr Asp
1 5

<210> 885
<211> 336
<212> DNA
<213> Homo sapiens

<400> 885
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tcctgcactg ggagcagctc caacatcggg tcagattatg atgtgcactg gtacaagcaa 120

cttccaggaa cagccccaa actcctcatc tttggtaaca gcaatcggcc ctcaggggtc 180

cctgaccgat tctctggctc caagtctggc acctcagcct ccctggccat cactgggctc 240

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catgtcttcg gaagtgggac caaggtcacc gtccta 336

<210> 886
<211> 112
<212> PRT
<213> Homo sapiens

<400> 886

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

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ser Asp

20 25 30

Tyr Asp Val His Trp Tyr Lys Gln Leu Pro Gly Thr Ala Pro Lys Leu
35 40 45

Leu Ile Phe Gly Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
85 90 95

Leu Ser Gly Phe His Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 887
<211> 14
<212> PRT
<213> Homo sapiens

<400> 887

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

<210> 888
<211> 7
<212> PRT
<213> Homo sapiens

<400> 888

Gly Asn Ser Asn Arg Pro Ser
1 5

<210> 889
<211> 12
<212> PRT
<213> Homo sapiens

<400> 889

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

<210> 890
<211> 354
<212> DNA
<213> Homo sapiens

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cctggacaag ggcttgagtg gatgggggga atcatccctc tcattaatgc accgaactac 180

gcaccgaagt tccagggcag agtgacgatt accgcggaca tgttctcgaa tatagtctcc 240

ttgcagttga ccagcctgag aactgacgac acggccgtgt attattgtgc gagacgaaaa 300

atgactacgg ctattgacta ttggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 891
<211> 118
<212> PRT
<213> Homo sapiens

<400> 891

Gln Val Gln Leu Val Gln Ser Gly Ala Asp Val Lys Lys Pro Gly Ser
1 5 10 15

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

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

Gly Gly Ile Ile Pro Leu Ile Asn Ala Pro Asn Tyr Ala Pro Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Met Phe Ser Asn Ile Val Ser
65 70 75 80

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

Ala Arg Arg Lys Met Thr Thr Ala Ile Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 892
<211> 5
<212> PRT
<213> Homo sapiens

<400> 892

Asn Tyr Gly Ile Asn
1 5

<210> 893
<211> 17
<212> PRT
<213> Homo sapiens

<400> 893

Gly Ile Ile Pro Leu Ile Asn Ala Pro Asn Tyr Ala Pro Lys Phe Gln
1 5 10 15

Gly

<210> 894
<211> 9
<212> PRT
<213> Homo sapiens

<400> 894

Arg Lys Met Thr Thr Ala Ile Asp Tyr
1 5

<210> 895
<211> 10
<212> PRT
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<400> 895

Gly Ile Ile Pro Leu Ile Asn Ala Pro Asn
1 5 10

<210> 896
<211> 354
<212> DNA
<213> Homo sapiens

<400> 896
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gggaagggcc cccgctttgt gatgcgggtg ggcaatggtg ggaatgtggc ttccaagggg 180

gatggcattc ctgatcgttt ctcagtctcg ggctcaggcc tgaatcggta cctgaccatc 240

aagaacatcc aggaagacga tgagagtgac tattattgtg gggcagacca tggcagtggg 300

aacaacttcg tgtcccctta tgtgtttggc ggagggacca agctgaccgt tcta 354

<210> 897
<211> 118
<212> PRT
<213> Homo sapiens

<400> 897

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

Ser Val Thr Leu Thr Cys Thr Leu Ser Ser Gly Phe Asp Asn Tyr Gln
20 25 30

Val Ala Trp Tyr Gln Gln Arg Pro Gly Lys Gly Pro Arg Phe Val Met
35 40 45

Arg Val Gly Asn Gly Gly Asn Val Ala Ser Lys Gly Asp Gly Ile Pro
50 55 60

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

Lys Asn Ile Gln Glu Asp Asp Glu Ser Asp Tyr Tyr Cys Gly Ala Asp
85 90 95

His Gly Ser Gly Asn Asn Phe Val Ser Pro Tyr Val Phe Gly Gly Gly
100 105 110

Thr Lys Leu Thr Val Leu
115

<210> 898
<211> 12
<212> PRT
<213> Homo sapiens

<400> 898

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

<210> 899
<211> 12
<212> PRT
<213> Homo sapiens

<400> 899

Val Gly Asn Gly Gly Asn Val Ala Ser Lys Gly Asp
1 5 10

<210> 900
<211> 15
<212> PRT
<213> Homo sapiens

<400> 900

Gly Ala Asp His Gly Ser Gly Asn Asn Phe Val Ser Pro Tyr Val
1 5 10 15

<210> 901
<211> 354
<212> DNA
<213> Homo sapiens

<400> 901
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tcctgcaggg aatctggagg caccttcaac ggctacacta tcacctgggt gcgacaggcc 120

cctgggcaag gcctgagtgg atgggaggg atcatccct a tgatggggac agtcaactac 180

gcacagaagt tgcagggcag agtcaccatt accacggact atttcacgaa aacagcctac 240

atggatctga acaatttaag atctgaagac acggccatgt attattgtgt gaaaatcaga 300

tatactgggc agcagctgct ctggggccag ggaaccctgg tcaccgtctc ctca 354

<210> 902
<211> 118
<212> PRT
<213> Homo sapiens

<400> 902

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

Ser Val Lys Val Ser Cys Arg Glu Ser Gly Gly Thr Phe Asn Gly Tyr
20 25 30

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

Gly Gly Ile Ile Pro Met Met Gly Thr Val Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Val Thr Ile Thr Thr Asp Tyr Phe Thr Lys Thr Ala Tyr
65 70 75 80

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

Val Lys Ile Arg Tyr Thr Gly Gln Gln Leu Leu Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 903
<211> 5
<212> PRT
<213> Homo sapiens

<400> 903

Gly Tyr Thr Ile Thr
1 5

<210> 904
<211> 17
<212> PRT
<213> Homo sapiens

<400> 904

Gly Ile Ile Pro Met Met Gly Thr Val Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

Gly

<210> 905
<211> 9
<212> PRT

<213> Homo sapiens

<400> 905

Ile Arg Tyr Thr Gly Gln Gln Leu Leu
1 5

<210> 906
<211> 6
<212> PRT
<213> Homo sapiens

<400> 906

Gly Gly Thr Phe Asn Gly
1 5

<210> 907
<211> 10
<212> PRT
<213> Homo sapiens

<400> 907

Gly Ile Ile Pro Met Met Gly Thr Val Asn
1 5 10

<210> 908
<211> 321
<212> DNA
<213> Homo sapiens

<400> 908
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atcacttgcc gggccagtca gagtattgca agttggttgg cctggtatca gcaaaaacca 120

gggaaagccc ctaagctcct gatctatgag gcagttaatt tagaaagtgg ggtcccatca 180

aggttcagcg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagccc 240

gatgattttg caacttattt ctgccaacat tatggtacta tttctcagac cttcggcgga 300

gggaccaagg tggagatcaa a 321

<210> 909
<211> 107
<212> PRT
<213> Homo sapiens

<400> 909

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ala 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 Glu Ala Val Asn Leu Glu 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

Asp Asp Phe Ala Thr Tyr Phe Cys Gln His Tyr Gly Thr Ile Ser Gln
85 90 95

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

<210> 910
<211> 11
<212> PRT
<213> Homo sapiens

<400> 910

Arg Ala Ser Gln Ser Ile Ala Ser Trp Leu Ala
1 5 10

<210> 911
<211> 7
<212> PRT
<213> Homo sapiens

<400> 911

Glu Ala Val Asn Leu Glu Ser
1 5

<210> 912
<211> 9
<212> PRT
<213> Homo sapiens

<400> 912

Gln His Tyr Gly Thr Ile Ser Gln Thr
1 5

<210> 913
<211> 360
<212> DNA
<213> Homo sapiens

<400> 913
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tcctgcacgg cctctggaag tgtcttcacc aatt atggaa ttagttgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatccctc tctttggcgc agccaagtac 180

gcacagaaat tccagggcag agtcaccatc acagcggacg aatccacgaa gacagtctac 240

atggagctga gcaggctgac atctaaagac acggccatat attttctgtg cgaaggcccc 300

cgtgtctacg agtactactt tgatcagtgg ggccagggaa ccccagtcac cgtctcctca 360

<210> 914
<211> 120
<212> PRT
<213> Homo sapiens

<400> 914

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

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

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

Gly Gly Ile Ile Pro Leu Phe Gly Ala Ala Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Lys Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Thr Ser Lys Asp Thr Ala Ile Tyr Phe Cys
85 90 95

Ala Lys Ala Pro Arg Val Tyr Glu Tyr Tyr Phe Asp Gln Trp Gly Gln
100 105 110

Gly Thr Pro Val Thr Val Ser Ser
115 120

<210> 915
<211> 5
<212> PRT
<213> Homo sapiens

<400> 915

Asn Tyr Gly Ile Ser
1 5

<210> 916
<211> 17
<212> PRT
<213> Homo sapiens

<400> 916

Gly Ile Ile Pro Leu Phe Gly Ala Ala Lys Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 917
<211> 11
<212> PRT

<213> Homo sapiens

<400> 917

Ala Pro Arg Val Tyr Glu Tyr Tyr Phe Asp Gln
1 5 10

<210> 918
<211> 6
<212> PRT
<213> Homo sapiens

<400> 918

Gly Ser Val Phe Thr Asn
1 5

<210> 919
<211> 10
<212> PRT
<213> Homo sapiens

<400> 919

Gly Ile Ile Pro Leu Phe Gly Ala Ala Lys
1 5 10

<210> 920
<211> 324
<212> DNA
<213> Homo sapiens

<400> 920
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ctctcctgca gggccagtca gagtgttagc agcagtcaat tagcctggta ccagcaaaaa 120

cctggccagg ctcccaggct catcatctat ggtgcgtcca ccagggccac tggcatccca 180

gacaggttca gtggaagtgg gtctgggaca gacttcactc tcaccatcgg cagactggag 240

cctgaagatt ttgcagtgtt tttctgtcag cagtatagta cctcacctcc gacgttcggc 300

caagggacca aggtggattt caaa 324

<210> 921
<211> 108
<212> PRT
<213> Homo sapiens

<400> 921

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

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

Ile Tyr Gly Ala 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 Gly Arg Leu Glu
65 70 75 80

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

Pro Thr Phe Gly Gln Gly Thr Lys Val Asp Phe Lys
100 105

<210> 922
<211> 12
<212> PRT
<213> Homo sapiens

<400> 922

Arg Ala Ser Gln Ser Val Ser Ser Ser Gln Leu Ala
1 5 10

<210> 923
<211> 9
<212> PRT
<213> Homo sapiens

<400> 923

Gln Gln Tyr Ser Thr Ser Pro Pro Thr
1 5

<210> 924
<211> 390
<212> DNA
<213> Homo sapiens

<400> 924
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acctgcgctg tctatggtgg gtccttcagt gtcagtggtt actactggag ctggatccgc 120

cagccccag ggaggggggct ggagtggatt ggggaaatca gtcatggtgg aagcaccaac 180

tacaacccgt ccctcaagag tcgagtcacc atatcagtgg acacgaccaa gaaccagttc 240

tccctgagac tgagctctgt gaccgccgcg gacacggccg tctattactg tgcgagaggg 300

acagaccctg acacggaagt attattgtcgt gttggtaact gcgcggcctt tgactactgg 360

ggccagggaa gcctggtcac cgtctcctca 390

<210> 925
<211> 130
<212> PRT
<213> Homo sapiens

<400> 925

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

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

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

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

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Thr 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 Gly Thr Asp Pro Asp Thr Glu Val Tyr Cys Arg Val Gly
            100                 105                 110

Asn Cys Ala Ala Phe Asp Tyr Trp Gly Gln Gly Ser Leu Val Thr Val
        115                 120                 125

Ser Ser
    130
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<210> 926
<211> 7
<212> PRT
<213> Homo sapiens

<400> 926

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Val Ser Gly Tyr Tyr Trp Ser
1               5
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<210> 927
<211> 16
<212> PRT
<213> Homo sapiens

<400> 927

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Glu Ile Ser His Gly Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1               5                   10                  15
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<210> 928
<211> 20
<212> PRT
<213> Homo sapiens

<400> 928

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Gly Thr Asp Pro Asp Thr Glu Val Tyr Cys Arg Val Gly Asn Cys Ala
1               5                   10                  15

Ala Phe Asp Tyr
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20

<210> 929
<211> 8
<212> PRT
<213> Homo sapiens

<400> 929

Gly Gly Ser Phe Ser Val Ser Gly
1 5

<210> 930
<211> 9
<212> PRT
<213> Homo sapiens

<400> 930

Glu Ile Ser His Gly Gly Ser Thr Asn
1 5

<210> 931
<211> 327
<212> DNA
<213> Homo sapiens

<400> 931
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ctctcctgca gggccagcca gtttgttagc accagatccc tggcctggta ccagcagaga 120

cctggccagg ctcccagact cctcatctat ggtgcatcca gcagggccac tggcatccca 180

gacaggttca gtggcagtgg gtctgggaca gacttcacgc tcaccatcag cagactggag 240

cctgaagatt ttgcagtgta ttactgtcag cactatggtt actcacctag gtacgctttt 300

ggccaggggt ccaaggttga gatcaaa 327

<210> 932
<211> 109
<212> PRT
<213> Homo sapiens

<400> 932

Glu Ile Ile Leu Ala 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 Phe Val Ser Thr Arg
20 25 30

Ser Leu Ala Trp Tyr Gln Gln Arg 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 His Tyr Gly Tyr Ser Pro
85 90 95

Arg Tyr Ala Phe Gly Gln Gly Ser Lys Val Glu Ile Lys
100 105

<210> 933
<211> 12
<212> PRT
<213> Homo sapiens

<400> 933

Arg Ala Ser Gln Phe Val Ser Thr Arg Ser Leu Ala
1 5 10

<210> 934
<211> 10
<212> PRT
<213> Homo sapiens

<400> 934

Gln His Tyr Gly Tyr Ser Pro Arg Tyr Ala
1 5 10

<210> 935
<211> 384
<212> DNA
<213> Homo sapiens

<400> 935
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acctgcgctg tctatggtgg gtccttcaga gatgactact ggacctggat tcgccagccc 120

ccaggcaagg ggctggagtg gattggggaa atcaatcata gtggaagaac caactacaac 180

ccgtccctca agagtcgagt caccatatca gtagacacgt ccctgaaaca gttctccttg 240

aaggtgattt ctgtgaccgc cgcggacacg gctgtttatt actgtgcgag agggacgagc 300

catgttttcc ggtattttga ttggttacca cccaccaact ggttcgaccc ctggggccag 360

ggaacccagg tcaccgtctc gagc 384

<210> 936
<211> 128
<212> PRT
<213> Homo sapiens

<400> 936

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

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

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

Gly Glu Ile Asn His Ser Gly Arg Thr Asn Tyr Asn Pro Ser Leu Lys
    50                  55                  60

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

Lys Val Ile Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Gly Thr Ser His Val Ser Arg Tyr Phe Asp Trp Leu Pro Pro Thr
            100                 105                 110

Asn Trp Phe Asp Pro Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser
        115                 120                 125


<210>  937
<211>  5
<212>  PRT
<213>  Homo sapiens

<400>  937

Asp Asp Tyr Trp Thr
1               5


<210>  938
<211>  16
<212>  PRT
<213>  Homo sapiens

<400>  938

Glu Ile Asn His Ser Gly Arg Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1               5                   10                  15


<210>  939
<211>  20
<212>  PRT
<213>  Homo sapiens

<400>  939

Gly Thr Ser His Val Ser Arg Tyr Phe Asp Trp Leu Pro Pro Thr Asn
1               5                   10                  15

Trp Phe Asp Pro
            20


<210>  940
<211>  6
<212>  PRT
<213>  Homo sapiens

<400>  940
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Gly Gly Ser Phe Arg Asp
1 5

<210> 941
<211> 9
<212> PRT
<213> Homo sapiens

<400> 941

Glu Ile Asn His Ser Gly Arg Thr Asn
1 5

<210> 942
<211> 324
<212> DNA
<213> Homo sapiens

<400> 942
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ctctcctgca gggccagtca gagtgttagc agcagctact tagcctggta ccagcagaaa 120

cctggccagg ctcccaggct cgtcatgtat ggtgcagcca ccagggccac tggcatccca 180

gacaggttca gtggcagtgg gtctgggcca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ttgcaatgta tttactgtca cagtatggta actcaccgat caccttcggc 300

caagggacac gactggagat caaa 324

<210> 943
<211> 108
<212> PRT
<213> Homo sapiens

<400> 943

Asp 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 Val
35 40 45

Met Tyr Gly Ala Ala Thr 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 Ser Arg Leu Glu
65 70 75 80

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

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

<210> 944
<211> 12
<212> PRT
<213> Homo sapiens

<400> 944

Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
1 5 10

<210> 945
<211> 7
<212> PRT
<213> Homo sapiens

<400> 945

Gly Ala Ala Thr Arg Ala Thr
1 5

<210> 946
<211> 9
<212> PRT
<213> Homo sapiens

<400> 946

Gln Gln Tyr Gly Asn Ser Pro Ile Thr
1 5

<210> 947
<211> 396
<212> DNA
<213> Homo sapiens

<400> 947
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acctgcgtct tctctgggtt ctcactcagc attactggag tgcgtgtggg ctggatccgt 120

cagccccag gaaaggccct ggagtggctt gcactcattt cttgggatga tgaaaagcac 180

tacagcccat ctctgcagag taggctcacc atcaccaagg acacctccaa aaaccaggtg 240

gtccttacaa tgaccaacct ggaccctgtc gacacagcca catattactg tgcacggtca 300

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gtctggggcc aagggacaat ggtcaccgtc tcgagc 396

<210> 948
<211> 132
<212> PRT
<213> Homo sapiens

<400> 948

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

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

20 25 30

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

Trp Leu Ala Leu Ile Ser Trp Asp Asp Glu Lys His Tyr Ser Pro Ser
50 55 60

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

Val Leu Thr Met Thr Asn Leu Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

Cys Ala Arg Ser Thr Asp Arg Gly His Val Leu Arg Tyr Phe Gly Trp
100 105 110

Met Leu Pro Gly Asp Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val
115 120 125

Thr Val Ser Ser
130

<210> 949
<211> 7
<212> PRT
<213> Homo sapiens

<400> 949

Ile Thr Gly Val Arg Val Gly
1 5

<210> 950
<211> 16
<212> PRT
<213> Homo sapiens

<400> 950

Leu Ile Ser Trp Asp Asp Glu Lys His Tyr Ser Pro Ser Leu Gln Ser
1 5 10 15

<210> 951
<211> 22
<212> PRT
<213> Homo sapiens

<400> 951

Ser Thr Asp Arg Gly His Val Leu Arg Tyr Phe Gly Trp Met Leu Pro
1 5 10 15

Gly Asp Ala Phe Asp Val
20

<210> 952
<211> 8
<212> PRT
<213> Homo sapiens

<400> 952

Gly Phe Ser Leu Ser Ile Thr Gly
1 5

<210> 953
<211> 9
<212> PRT
<213> Homo sapiens

<400> 953

Leu Ile Ser Trp Asp Asp Glu Lys His
1 5

<210> 954
<211> 339
<212> DNA
<213> Homo sapiens

<400> 954
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atcaactgca agtccagcca gagagttttа tacagctcca acaataaaaa ctacttagct 120

tggtaccagc tgaaaccagg gcagcctcct aagttgatca tttattgggc atctacccgg 180

gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagaatt cactctcacc 240

atcagcagcc tgcaggctga agatgtggca gtttattact gtcaacaata ttatagtcgt 300

ccgtacactt ttggccaggg gaccaagctc gagatcaaa 339

<210> 955
<211> 113
<212> PRT
<213> Homo sapiens

<400> 955

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

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Arg Val Leu Tyr Ser
20 25 30

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

Pro Pro Lys Leu Ile 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 Glu 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 Arg Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile
100 105 110

Lys

<210> 956
<211> 17
<212> PRT
<213> Homo sapiens

<400> 956

Lys Ser Ser Gln Arg Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr Leu
1 5 10 15

Ala

<210> 957
<211> 7
<212> PRT
<213> Homo sapiens

<400> 957

Trp Ala Ser Thr Arg Glu Ser
1 5

<210> 958
<211> 9
<212> PRT
<213> Homo sapiens

<400> 958

Gln Gln Tyr Tyr Ser Arg Pro Tyr Thr
1 5

<210> 959
<211> 375
<212> DNA
<213> Homo sapiens

<400> 959
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tcctgtgcag cctctgaaat cacctt cat t acctatgcta tgcactgggt ccgccaggcc 120

ccaggcaagg ggctggagtg ggtggcactt atatcagatg atggaagcaa taaatt ctac 180

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agctgaggac acggctgctt attactgtgc gagagaaggg 300

gttt actttg attcggggac ttataggggc tactttgact actggggcca ggaaaccctg 360

gtcaccgtct cgagc 375

<210> 960
<211> 125
<212> PRT
<213> Homo sapiens

<400> 960

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 Glu Ile Thr Phe Ile Thr Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Leu Ile Ser Asp Asp Gly Ser Asn Lys Phe 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 Ala Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Val Tyr Phe Asp Ser Gly Thr Tyr Arg Gly Tyr Phe
100 105 110

Asp Tyr Trp Gly Gln Glu Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 961
<211> 5
<212> PRT
<213> Homo sapiens

<400> 961

Thr Tyr Ala Met His
1 5

<210> 962
<211> 17
<212> PRT
<213> Homo sapiens

<400> 962

Leu Ile Ser Asp Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 963

<211> 16
<212> PRT
<213> Homo sapiens

<400> 963

Glu Gly Val Tyr Phe Asp Ser Gly Thr Tyr Arg Gly Tyr Phe Asp Tyr
1 5 10 15

<210> 964
<211> 6
<212> PRT
<213> Homo sapiens

<400> 964

Glu Ile Thr Phe Ile Thr
1 5

<210> 965
<211> 10
<212> PRT
<213> Homo sapiens

<400> 965

Leu Ile Ser Asp Asp Gly Ser Asn Lys Phe
1 5 10

<210> 966
<211> 324
<212> DNA
<213> Homo sapiens

<400> 966
gaaattgtgt tgacacagtc tccagccacc ctgtctttgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gagtgttagc agcttacttag cctggtacca acagaaacct 120

ggccaggctc ccaggctcct catctatgat gcatccaaca gggccactgg catcccagcc 180

aggttcagtg gcagtgggtc tgggacagac ttcactctca ccatcagcag cctagagcct 240

gaagattttg cagtttatta ctgtcagcag cgtagccact ggcctccgat caccttcggc 300

caagggacac gactggagat caaa 324

<210> 967
<211> 108
<212> PRT
<213> Homo sapiens

<400> 967

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 His Trp Pro Pro
                85                  90                  95

Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100                 105
```

<210> 968
<211> 11
<212> PRT
<213> Homo sapiens

<400> 968

```
Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1               5                   10
```

<210> 969
<211> 7
<212> PRT
<213> Homo sapiens

<400> 969

```
Asp Ala Ser Asn Arg Ala Thr
1               5
```

<210> 970
<211> 10
<212> PRT
<213> Homo sapiens

<400> 970

```
Gln Gln Arg Ser His Trp Pro Pro Ile Thr
1               5                   10
```

<210> 971
<211> 363
<212> DNA
<213> Homo sapiens

<400> 971

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tcctgtgcag cctctggatt cacctttcagt agctacgcca tgcactgggt ccgccaggct     120

ccaggcaagg ggctggagtg ggtggctatt atatcatacg acggaaatga tcaatactat      180

acagactccg tgaagggccg attcaccatc tccagagaca gctccaaagt gtatctccaa      240

atgcacaggc tgagacctga ggacacggct gttttattact gtgcgaaaga atttgaaact      300

agtggttatt ttcatgggag ttttgactac tggggccagg gaatcctggt caccgtctcg      360
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agc 363

<210> 972
<211> 121
<212> PRT
<213> Homo sapiens

<400> 972

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

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ile Ile Ser Tyr Asp Gly Asn Asp Gln Tyr Tyr Thr Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Ser Ser Lys Val Tyr Leu Gln
65 70 75 80

Met His Arg Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys
85 90 95

Glu Phe Glu Thr Ser Gly Tyr Phe His Gly Ser Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Ile Leu Val Thr Val Ser Ser
115 120

<210> 973
<211> 5
<212> PRT
<213> Homo sapiens

<400> 973

Ser Tyr Ala Met His
1 5

<210> 974
<211> 17
<212> PRT
<213> Homo sapiens

<400> 974

Ile Ile Ser Tyr Asp Gly Asn Asp Gln Tyr Tyr Thr Asp Ser Val Lys
1 5 10 15

Gly

<210> 975
<211> 14
<212> PRT
<213> Homo sapiens

<400> 975

Glu Phe Glu Thr Ser Gly Tyr Phe His Gly Ser Phe Asp Tyr
1 5 10

<210> 976
<211> 6
<212> PRT
<213> Homo sapiens

<400> 976

Gly Phe Thr Phe Ser Ser
1 5

<210> 977
<211> 10
<212> PRT
<213> Homo sapiens

<400> 977

Ile Ile Ser Tyr Asp Gly Asn Asp Gln Tyr
1 5 10

<210> 978
<211> 330
<212> DNA
<213> Homo sapiens

<400> 978
cagtctgccc tgactcagcc tgcctccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtaccaacaa 120

cacccaggca aagcccccaa actcttgatt tatgaggtca ctaattggcc tcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgacaat ctctgggctc 240

caggctgagg acgaggctga ctattactgc agctcatatg cgggcagcag cacttgggtg 300

ttcggcggag ggaccagggt gaccgttcta 330

<210> 979
<211> 110
<212> PRT
<213> Homo sapiens

<400> 979

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

```
Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35                  40                  45

Leu Ile Tyr Glu Val Thr Asn Trp Pro Ser Gly Val Ser Asn Arg Phe
    50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser
                85                  90                  95

Ser Thr Trp Val Phe Gly Gly Gly Thr Arg Val Thr Val Leu
            100                 105                 110


<210>  980
<211>  14
<212>  PRT
<213>  Homo sapiens

<400>  980

Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1               5                   10


<210>  981
<211>  7
<212>  PRT
<213>  Homo sapiens

<400>  981

Glu Val Thr Asn Trp Pro Ser
1               5


<210>  982
<211>  10
<212>  PRT
<213>  Homo sapiens

<400>  982

Ser Ser Tyr Ala Gly Ser Ser Thr Trp Val
1               5                   10


<210>  983
<211>  378
<212>  DNA
<213>  Homo sapiens

<400>  983
caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcggagac cctgtccctc      60

acctgcactg tctctggtgg ctccatcaat agttactact ggaactggat ccggcagccc     120

ccagggaagg gactggagtg gattggctat atctatcaca gtgggagcac caactacaac     180

ccctccctca agagtcgagt caccatttcg gtagacacgt ccaagaacca gttctccctg     240

cagctgagct ctgtgaccgc cgcagacacg gccgtgtatt actgtgcgag actccggacg     300
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gactacggtg accccgactc ggtatactac tacggtatgg acgtctgggg ccaagggacc 360

acggtcaccg tctcgagc 378

<210> 984
<211> 126
<212> PRT
<213> Homo sapiens

<400> 984

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Asn Ser Tyr
20 25 30

Tyr Trp Asn Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Tyr His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Gln Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Leu Arg Thr Asp Tyr Gly Asp Pro Asp Ser Val Tyr Tyr Tyr Gly
100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 985
<211> 5
<212> PRT
<213> Homo sapiens

<400> 985

Ser Tyr Tyr Trp Asn
1 5

<210> 986
<211> 16
<212> PRT
<213> Homo sapiens

<400> 986

Tyr Ile Tyr His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 987

<211> 18
<212> PRT
<213> Homo sapiens

<400> 987

Leu Arg Thr Asp Tyr Gly Asp Pro Asp Ser Val Tyr Tyr Tyr Gly Met
1 5 10 15

Asp Val

<210> 988
<211> 6
<212> PRT
<213> Homo sapiens

<400> 988

Gly Gly Ser Ile Asn Ser
1 5

<210> 989
<211> 9
<212> PRT
<213> Homo sapiens

<400> 989

Tyr Ile Tyr His Ser Gly Ser Thr Asn
1 5

<210> 990
<211> 324
<212> DNA
<213> Homo sapiens

<400> 990
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acctgctctg gagatgcatt gccaaagcaa aatgcttatt ggtaccagca gaagccaggc 120

caggcccctg tgctgctgat atataaagac agtgagaggc cctcagggat ccctgagcga 180

ttctctggct ccagctcagg gacaacagtc acgttgacca tcagtggagt ccaggcagag 240

gacgaggctg actattactg tcaatcagca gacagcagtg gtacttcttg ggtgttcggc 300

ggagggacca aactgaccgt ctta 324

<210> 991
<211> 108
<212> PRT
<213> Homo sapiens

<400> 991

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Ser Gly Asp Ala Leu Pro Lys Gln Asn Ala
20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Leu Ile Tyr
35 40 45

Lys Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Ser Ser Gly Thr Thr Val Thr Leu Thr Ile Ser Gly Val Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Ala Asp Ser Ser Gly Thr Ser
85 90 95

Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 992
<211> 375
<212> DNA
<213> Homo sapiens

<400> 992
caggtgcagc tgcaggagtc gggcccagga ctggtgaagc cttcacagac cctgtccctc 60

acctgcactg tctctggtgg ctccatcagc agtggtaatt actactggaa ctgggtccgc 120

cagcacccag ggaagggcct ggagtggatt gggtacatct attacagagg gagcacctac 180

tacaacccgt ccctcaagag tcgagtgacc atatcaatag acacgtctaa gaaccagttc 240

tccctgaggc tgagctctgt gacggccgcg gacacggccg tgtattactg tgcgaaggat 300

acaaggtcga gcctagacaa ttaccagtac ggtatggacg tctggggcca agggaccacg 360

gtcaccgtct cgagc 375

<210> 993
<211> 125
<212> PRT
<213> Homo sapiens

<400> 993

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

Asn Tyr Tyr Trp Asn Trp Val Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Arg Gly Ser Thr Phe Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Ile 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 Lys Asp Thr Arg Ser Ser Leu Asp Asn Tyr Gln Tyr Gly Met
            100                 105                 110

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120                 125


<210>  994
<211>  11
<212>  PRT
<213>  Homo sapiens

<400>  994

Ser Gly Asp Ala Leu Pro Lys Gln Asn Ala Tyr
1               5                   10


<210>  995
<211>  7
<212>  PRT
<213>  Homo sapiens

<400>  995

Lys Asp Ser Glu Arg Pro Ser
1               5


<210>  996
<211>  11
<212>  PRT
<213>  Homo sapiens

<400>  996

Gln Ser Ala Asp Ser Ser Gly Thr Ser Trp Val
1               5                   10


<210>  997
<211>  7
<212>  PRT
<213>  Homo sapiens

<400>  997

Ser Gly Asn Tyr Tyr Trp Asn
1               5


<210>  998
<211>  16
<212>  PRT
<213>  Homo sapiens

<400>  998

Tyr Ile Tyr Tyr Arg Gly Ser Thr Phe Tyr Asn Pro Ser Leu Lys Ser
1               5                   10                  15
```

<210> 999
<211> 15
<212> PRT
<213> Homo sapiens

<400> 999

Asp Thr Arg Ser Ser Leu Asp Asn Tyr Gln Tyr Gly Met Asp Val
1 5 10 15

<210> 1000
<211> 8
<212> PRT
<213> Homo sapiens

<400> 1000

Gly Gly Ser Ile Ser Ser Gly Asn
1 5

<210> 1001
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1001

Tyr Ile Tyr Tyr Arg Gly Ser Thr Phe
1 5

<210> 1002
<211> 330
<212> DNA
<213> Homo sapiens

<400> 1002
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acctgtgctt ccagcactgg agcagtcacc agtagttact ttccaaactg gttccagcag 120

aaacctggac aagcgcccag gccactgatt tatagtacaa ctatcagaca ctcctggacc 180

ccggcccgat tctcaggctc cctccttggg ggcaaagctg ccctgacact gtcaggtgtg 240

cagcctgagg acgaggctga ctattactgc ctgctctact ctggtggtga tccagtggct 300

ttcggcggag ggaccaaact gaccgttcta 330

<210> 1003
<211> 110
<212> PRT
<213> Homo sapiens

<400> 1003

Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Ala Ser Ser Thr Gly Ala Val Thr Ser Ser
20 25 30

Tyr Phe Pro Asn Trp Phe Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro
35 40 45

Leu Ile Tyr Ser Thr Thr Ile Arg His Ser Trp Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Leu Leu Tyr Ser Gly Gly
85 90 95

Asp Pro Val Ala Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 1004
<211> 14
<212> PRT
<213> Homo sapiens

<400> 1004

Ala Ser Ser Thr Gly Ala Val Thr Ser Ser Tyr Phe Pro Asn
1 5 10

<210> 1005
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1005

Ser Thr Thr Ile Arg His Ser
1 5

<210> 1006
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1006

Leu Leu Tyr Ser Gly Gly Asp Pro Val Ala
1 5 10

<210> 1007
<211> 378
<212> DNA
<213> Homo sapiens

<400> 1007
caggttcatc tggtgcagtc tggagctgag gtgaggaagc ctggggactc agtgaaggtc 60

tcctgtaaga cttctggtta cacctttcc acctatcctg tcgcctgggt gcgacaggtc 120

cccggacaag ggcttgagtg gatgggatgg atcagcactt acaatggaaa cacaaacttt 180

gcacagaact tccagggcag agtcaccctg accacagaca caaccacgaa cacagcctac 240

atggaagtga ggagcctgaa atttgacgac acggccgtct attactgtgc gagagtggaa 300

ggctcgtaca gggatttttg gaataatcaa aacagattcg acccctgggg ccagggaacc 360

ctggtcaccg tctcgagc 378

<210> 1008
<211> 126
<212> PRT
<213> Homo sapiens

<400> 1008

Gln Val His Leu Val Gln Ser Gly Ala Glu Val Arg Lys Pro Gly Asp
1 5 10 15

Ser Val Lys Val Ser Cys Lys Thr Ser Gly Tyr Thr Phe Ser Thr Tyr
20 25 30

Pro Val Ala Trp Val Arg Gln Val Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Thr Tyr Asn Gly Asn Thr Asn Phe Ala Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Leu Thr Thr Asp Thr Thr Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Val Arg Ser Leu Lys Phe Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Glu Gly Ser Tyr Arg Asp Phe Trp Asn Asn Gln Asn Arg
100 105 110

Phe Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 1009
<211> 5
<212> PRT
<213> Homo sapiens

<400> 1009

Thr Tyr Pro Val Ala
1 5

<210> 1010
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1010

Trp Ile Ser Thr Tyr Asn Gly Asn Thr Asn Phe Ala Gln Asn Phe Gln
1 5 10 15

Gly

<210> 1011
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1011

Val Glu Gly Ser Tyr Arg Asp Phe Trp Asn Asn Gln Asn Arg Phe Asp
1 5 10 15

Pro

<210> 1012
<211> 6
<212> PRT
<213> Homo sapiens

<400> 1012

Gly Tyr Thr Phe Ser Thr
1 5

<210> 1013
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1013

Trp Ile Ser Thr Tyr Asn Gly Asn Thr Asn
1 5 10

<210> 1014
<211> 318
<212> DNA
<213> Homo sapiens

<400> 1014
tcctatgtac tgactcagcc accctcggtg tcagtggccc caggacagac ggccaggatt 60

tcctgtgggg gaagcaacat tggagggaaa agtgtgcact ggtaccagca gaagccaggc 120

caggcccctg tgctggtcgt ctatgatgat agcggccggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg ggacacggcc accctgacca tcagcagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gataatttcg ggggagtctt cggaactggg 300

accaaggtca ccgttcta 318

<210> 1015
<211> 106
<212> PRT
<213> Homo sapiens

<400> 1015

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Ser Cys Gly Gly Ser Asn Ile Gly Gly Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Gly Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asp Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Phe Cys Gln Val Trp Asp Asn Phe Gly Gly Val
85 90 95

Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105

<210> 1016
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1016

Gly Gly Ser Asn Ile Gly Gly Lys Ser Val His
1 5 10

<210> 1017
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1017

Asp Asp Ser Gly Arg Pro Ser
1 5

<210> 1018
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1018

Gln Val Trp Asp Asn Phe Gly Gly Val
1 5

<210> 1019
<211> 369
<212> DNA
<213> Homo sapiens

<400> 1019
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acctgcactg tctctcgtgg ctccatcggt cattacttct ggagctggat ccggcagccc 120

ccagggaagg gactggagtg gattggttat atctcttaca gtgggagcac caagtacaac 180

ccctccctca ggagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg 240

aatctgaact ctgtcaccgc tacggacacg gccctatatt actgtgcgag agaggattac 300

gatattttga ctggggcggg acccggtatg gaggtctggg gccaagggac cacggtcacc 360

gtctcgagc 369

<210> 1020
<211> 123
<212> PRT
<213> Homo sapiens

<400> 1020

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Arg Gly Ser Ile Gly His Tyr
20 25 30

Phe Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Ser Tyr Ser Gly Ser Thr Lys Tyr Asn Pro Ser Leu Arg
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Asn Leu Asn Ser Val Thr Ala Thr Asp Thr Ala Leu Tyr Tyr Cys Ala
85 90 95

Arg Glu Asp Tyr Asp Ile Leu Thr Gly Ala Gly Pro Gly Met Glu Val
100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1021
<211> 5
<212> PRT
<213> Homo sapiens

<400> 1021

His Tyr Phe Trp Ser
1 5

<210> 1022
<211> 16
<212> PRT
<213> Homo sapiens

<400> 1022

Tyr Ile Ser Tyr Ser Gly Ser Thr Lys Tyr Asn Pro Ser Leu Arg Ser
1 5 10 15

<210> 1023
<211> 15
<212> PRT
<213> Homo sapiens

<400> 1023

Glu Asp Tyr Asp Ile Leu Thr Gly Ala Gly Pro Gly Met Glu Val
1 5 10 15

<210> 1024
<211> 6
<212> PRT
<213> Homo sapiens

<400> 1024

Arg Gly Ser Ile Gly His
1 5

<210> 1025
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1025

Tyr Ile Ser Tyr Ser Gly Ser Thr Lys
1 5

<210> 1026
<211> 333
<212> DNA
<213> Homo sapiens

<400> 1026
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ccaggaacgg cccccaaact cctcatctac agaaatgatc tgcggccctc aggggtccct 180

gaccgattct ctggctccaa gtctggcacc tcagcctccc tggccatcag tgggctccag 240

tctgaggatg aggctgatta ttactgtgca acatgggatg acagcctgaa tggttttat 300

gtcttcggaa ctgggaccaa agtcaccgtt cta 333

<210> 1027
<211> 111
<212> PRT
<213> Homo sapiens

<400> 1027

Gln Ser Met Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Thr Val Asn Trp Phe Lys His Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Arg Asn Asp Leu Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Asp Ser Leu
85 90 95

Asn Gly Phe Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 1028
<211> 13
<212> PRT
<213> Homo sapiens

<400> 1028

Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Val Asn
1 5 10

<210> 1029
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1029

Arg Asn Asp Leu Arg Pro Ser
1 5

<210> 1030
<211> 12
<212> PRT
<213> Homo sapiens

<400> 1030

Ala Thr Trp Asp Asp Ser Leu Asn Gly Phe Tyr Val
1 5 10

<210> 1031
<211> 384
<212> DNA
<213> Homo sapiens

<400> 1031
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tcctgcgctg tctttggtgg gtccttcagt gattactact ggacctggat acgccagccc 120

ccagggaagg ggctggagtg gattggcgaa atcaaacata gtggaagaac caactacaac 180

ccgtcccttg agagtcgagt caccatatca gtggacacgt ccaagaacca gttttccctg 240

aaactgagtt ctgtgaccgc cgcggacacg gctatatatt attgtgcgag agggacagac 300

cctgacacgg agggatattg tcgtagtggt agctgctcgg cctttgactt ctggggccag 360

ggaaccctgg tcaccgtctc gagc 384

<210> 1032
<211> 128
<212> PRT
<213> Homo sapiens

<400> 1032

Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Ser Cys Ala Val Phe Gly Gly Ser Phe Ser Asp Tyr
20 25 30

Tyr Trp Thr Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Lys His Ser Gly Arg Thr Asn Tyr Asn Pro Ser Leu Glu
50 55 60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Ile Tyr Tyr Cys Ala
85 90 95

Arg Gly Thr Asp Pro Asp Thr Glu Gly Tyr Cys Arg Ser Gly Ser Cys
100 105 110

Ser Ala Phe Asp Phe Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 1033
<211> 5
<212> PRT
<213> Homo sapiens

<400> 1033

Asp Tyr Tyr Trp Thr
1 5

<210> 1034
<211> 16
<212> PRT
<213> Homo sapiens

<400> 1034

Glu Ile Lys His Ser Gly Arg Thr Asn Tyr Asn Pro Ser Leu Glu Ser

1 5 10 15

<210> 1035
<211> 20
<212> PRT
<213> Homo sapiens

<400> 1035

Gly Thr Asp Pro Asp Thr Glu Gly Tyr Cys Arg Ser Gly Ser Cys Ser
1 5 10 15

Ala Phe Asp Phe
20

<210> 1036
<211> 6
<212> PRT
<213> Homo sapiens

<400> 1036

Gly Gly Ser Phe Ser Asp
1 5

<210> 1037
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1037

Glu Ile Lys His Ser Gly Arg Thr Asn
1 5

<210> 1038
<211> 327
<212> DNA
<213> Homo sapiens

<400> 1038
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ctctcctgca gggccagtca ctttgtgaac tacaggtcct tagcctggta ccagcagaca 120

cctggccagg ttcccaggct cctcatctat ggtgcgtcca ccagggccac tggcatccca 180

gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ttgcagtgta tttctgtcag cagtatggtg gctcacctag gtacactttt 300

ggccagggga ccaggctgga gatcaaa 327

<210> 1039
<211> 109
<212> PRT
<213> Homo sapiens

<400> 1039

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 His Phe Val Asn Tyr Arg
20 25 30

Ser Leu Ala Trp Tyr Gln Gln Thr Pro Gly Gln Val Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala 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 Phe Cys Gln Gln Tyr Gly Gly Ser Pro
85 90 95

Arg Tyr Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 1040
<211> 12
<212> PRT
<213> Homo sapiens

<400> 1040

Arg Ala Ser His Phe Val Asn Tyr Arg Ser Leu Ala
1 5 10

<210> 1041
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1041

Gln Gln Tyr Gly Gly Ser Pro Arg Tyr Thr
1 5 10

<210> 1042
<211> 384
<212> DNA
<213> Homo sapiens

<400> 1042
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acctgcggtg tctatggtgg gtccctcagt gattactact ggagctggat ccgccagccc 120

ccagggaagg ggctggagtg gattggagaa atcaatcata gtggaggcac caactacaat 180

ccgtccctca agagacgagt caccatatca gtagacacgt caaagaagca attctccctg 240

aagatgaact ctgtgaccgc cgcggacacg gctgtatatt actgtgcgag agggacagac 300

cctgacacgg aagtattatg tcgtgctggt aactgcgcgg cctttgactt ctggggccag 360

ggaaccctgg tcaccgtctc gagc 384

<210> 1043
<211> 128
<212> PRT
<213> Homo sapiens

<400> 1043

Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Gly Val Tyr Gly Gly Ser Leu Ser Asp Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile Asn His Ser Gly Gly Thr Asn Tyr Asn Pro Ser Leu Lys
50 55 60

Arg Arg Val Thr Ile Ser Val Asp Thr Ser Lys Lys Gln Phe Ser Leu
65 70 75 80

Lys Met Asn Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Gly Thr Asp Pro Asp Thr Glu Val Tyr Cys Arg Ala Gly Asn Cys
100 105 110

Ala Ala Phe Asp Phe Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 1044
<211> 5
<212> PRT
<213> Homo sapiens

<400> 1044

Asp Tyr Tyr Trp Ser
1 5

<210> 1045
<211> 16
<212> PRT
<213> Homo sapiens

<400> 1045

Glu Ile Asn His Ser Gly Gly Thr Asn Tyr Asn Pro Ser Leu Lys Arg
1 5 10 15

<210> 1046
<211> 20
<212> PRT
<213> Homo sapiens

<400> 1046

Gly Thr Asp Pro Asp Thr Glu Val Tyr Cys Arg Ala Gly Asn Cys Ala
1 5 10 15

Ala Phe Asp Phe
20

<210> 1047
<211> 6
<212> PRT
<213> Homo sapiens

<400> 1047

Gly Gly Ser Leu Ser Asp
1 5

<210> 1048
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1048

Glu Ile Asn His Ser Gly Gly Thr Asn
1 5

<210> 1049
<211> 327
<212> DNA
<213> Homo sapiens

<400> 1049
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ctctcctgcc gggccagtca ctttgttata ggcagggctg tagcctggta ccagcagaaa 120

cctggccagg ctcccaggct cctcatctac ggtgcatcca gcagggccac tggcatcccg 180

gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240

actgaagatt ttgctgtgtt ttactgtcag cactatggta gctcacctag gtacgctttt 300

ggccagggga ccaagctgga gatcaaa 327

<210> 1050
<211> 109
<212> PRT
<213> Homo sapiens

<400> 1050

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 His Phe Val Ile Gly Arg
20 25 30

Ala Val 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

Thr Glu Asp Phe Ala Val Phe Tyr Cys Gln His Tyr Gly Ser Ser Pro
85 90 95

Arg Tyr Ala Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 1051
<211> 12
<212> PRT
<213> Homo sapiens

<400> 1051

Arg Ala Ser His Phe Val Ile Gly Arg Ala Val Ala
1 5 10

<210> 1052
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1052

Gln His Tyr Gly Ser Ser Pro Arg Tyr Ala Phe
1 5 10

<210> 1053
<211> 384
<212> DNA
<213> Homo sapiens

<400> 1053
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acctgcactg tctctggtga ctccattagt agtgttgatc actactggag ctggatccgc 120

caacacccag tgaagggcct ggagtggatt gggttcatgt attacagtgc gagcacctat 180

tacaacccgt ccctcaagag tcgagttacc atatcaacgg acacgtctaa gaaccagttc 240

tccctgaggc tgagttctgt gactgccgcg gacacggccg tatattactg tgcgagaggc 300

acttgtgctg gtgactgctc ccttcactac tactactacg gtttggacgt ctggggccaa 360

gggaggacgg tcaccgtctc gagc 384

<210> 1054
<211> 128
<212> PRT
<213> Homo sapiens

<400> 1054

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 Asp Ser Ile Ser Ser Val
20 25 30

Asp His Tyr Trp Ser Trp Ile Arg Gln His Pro Val Lys Gly Leu Glu
35 40 45

Trp Ile Gly Phe Met Tyr Tyr Ser Ala Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Thr 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 Gly Thr Cys Ala Gly Asp Cys Ser Leu His Tyr Tyr Tyr
100 105 110

Tyr Gly Leu Asp Val Trp Gly Gln Gly Arg Thr Val Thr Val Ser Ser
115 120 125

<210> 1055
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1055

Ser Val Asp His Tyr Trp Ser
1 5

<210> 1056
<211> 16
<212> PRT
<213> Homo sapiens

<400> 1056

Phe Met Tyr Tyr Ser Ala Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 1057
<211> 18
<212> PRT
<213> Homo sapiens

<400> 1057

Gly Thr Cys Ala Gly Asp Cys Ser Leu His Tyr Tyr Tyr Tyr Gly Leu
1 5 10 15

Asp Val

<210> 1058
<211> 8
<212> PRT
<213> Homo sapiens

<400> 1058

Gly Asp Ser Ile Ser Ser Val Asp
1 5

<210> 1059
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1059

Phe Met Tyr Tyr Ser Ala Ser Thr Tyr
1 5

<210> 1060
<211> 321
<212> DNA
<213> Homo sapiens

<400> 1060
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atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcacaaacca 120

gggaaagccc ctaaggtcct gatgtatgct gtatccattt tgcaaagtgg ggtcccatca 180

aggttcagtg gcagtggatc tggggcagat ttcactctca ccatcagcag tctgcaacct 240

gaagattttg caacttacta ctgtcaacag agttacagtt ccccgctcac tttcggcgga 300

gggaccaagg tggagatcaa a 321

<210> 1061
<211> 107
<212> PRT
<213> Homo sapiens

<400> 1061

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln His Lys Pro Gly Lys Ala Pro Lys Val Leu Met
35 40 45

Tyr Ala Val Ser Ile Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Ser Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1062
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1062

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 1063
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1063

Ala Val Ser Ile Leu Gln Ser
1 5

<210> 1064
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1064

Gln Gln Ser Tyr Ser Ser Pro Leu Thr
1 5

<210> 1065
<211> 396
<212> DNA
<213> Homo sapiens

<400> 1065
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acctgcactg tctctagtgg ccccatgagt gattattact ggagctggat ccggcagccc 120

ccagggaagg gactggagtg gattgggcat gtctctgtct ctcacggagg gaggaccaaa 180

tccaatccct ccgtcatgag tcgagtcacc atttcagtag aaacgtccaa gaaccaattc 240

tccctgaaac tgacctccgt gaccgctgcg gacacggccg tttattactg tgcgagatta 300

aattactatg atagaagtgg ttatcattcg cctgacggcc cctcgaacaa ctggttcgac 360

ccctggggcc agggaaccct ggtcaccgtc tcgagc 396

<210> 1066
<211> 132
<212> PRT
<213> Homo sapiens

<400> 1066

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Ser Gly Pro Met Ser Asp Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly His Val Ser Val Ser His Gly Gly Arg Thr Lys Ser Asn Pro Ser
50 55 60

Val Met Ser Arg Val Thr Ile Ser Val Glu Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Thr Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Leu Asn Tyr Tyr Asp Arg Ser Gly Tyr His Ser Pro Asp
100 105 110

Gly Pro Ser Asn Asn Trp Phe Asp Pro Trp Gly Gln Gly Thr Leu Val
115 120 125

Thr Val Ser Ser
130

<210> 1067
<211> 18
<212> PRT
<213> Homo sapiens

<400> 1067

His Val Ser Val Ser His Gly Gly Arg Thr Lys Ser Asn Pro Ser Val
1 5 10 15

Met Ser

<210> 1068
<211> 22
<212> PRT
<213> Homo sapiens

<400> 1068

Leu Asn Tyr Tyr Asp Arg Ser Gly Tyr His Ser Pro Asp Gly Pro Ser
1 5 10 15

Asn Asn Trp Phe Asp Pro
20

<210> 1069

<211> 6
<212> PRT
<213> Homo sapiens

<400> 1069

Ser Gly Pro Met Ser Asp
1 5

<210> 1070
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1070

His Val Ser Val Ser His Gly Gly Arg Thr Lys
1 5 10

<210> 1071
<211> 339
<212> DNA
<213> Homo sapiens

<400> 1071
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atcaactgca agtccagcca gagtgttta tacagctcca acaataagaa ctacttagct 120

tggtaccagc agaaaccagg acagcctcct aagctgctca tttactgggc atctacccgg 180

gaatccgggg tccctgaccg aatcagcggc agcgggtctg gggcagattt cactctcacc 240

atcagcagcc tgcaggctga agatgtggca gtttattact gtcagcagta ttttgctact 300

cctcggacgt tcggccaagg gaccaaggtg gaaatcaaa 339

<210> 1072
<211> 113
<212> PRT
<213> Homo sapiens

<400> 1072

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 Ile Ser Gly Ser Gly Ser Gly Ala 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 Phe Ala Thr Pro Arg Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
100 105 110

Lys

<210> 1073
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1073

Lys Ser Ser Gln Ser Val Leu Tyr Ser Ser Asn Asn Lys Asn Tyr Leu
1 5 10 15

Ala

<210> 1074
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1074

Gln Gln Tyr Phe Ala Thr Pro Arg Thr
1 5

<210> 1075
<211> 366
<212> DNA
<213> Homo sapiens

<400> 1075
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tcctgcaagg cttctggata cacctcacc ggctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaaccct a acagtggtga cacaaactat 180

gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcac cacagcctac 240

atggagctga gcagcctgag atctgacgac acggccgtgt attactgtgc gagagattcc 300

ccctatagca gcagctggtc cttctttgac tactggggcc agggaccct ggtcaccgtc 360

tcgagc 366

<210> 1076
<211> 122
<212> PRT
<213> Homo sapiens

<400> 1076

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

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Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20                  25                  30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Trp Ile Asn Pro Asn Ser Gly Asp 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 Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Ser Pro Tyr Ser Ser Ser Trp Ser Phe Phe Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Pro Leu Val Thr Val Ser Ser
        115                 120


<210>  1077
<211>  5
<212>  PRT
<213>  Homo sapiens

<400>  1077

Gly Tyr Tyr Met His
1               5


<210>  1078
<211>  17
<212>  PRT
<213>  Homo sapiens

<400>  1078

Trp Ile Asn Pro Asn Ser Gly Asp Thr Asn Tyr Ala Gln Lys Phe Gln
1               5                   10                  15

Gly


<210>  1079
<211>  13
<212>  PRT
<213>  Homo sapiens

<400>  1079

Asp Ser Pro Tyr Ser Ser Ser Trp Ser Phe Phe Asp Tyr
1               5                   10


<210>  1080
<211>  6
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<212> PRT
<213> Homo sapiens

<400> 1080

Gly Tyr Thr Phe Thr Gly
1 5

<210> 1081
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1081

Trp Ile Asn Pro Asn Ser Gly Asp Thr Asn
1 5 10

<210> 1082
<211> 339
<212> DNA
<213> Homo sapiens

<400> 1082
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atcaactgca agtccagcca gagtgttta tacagctcca acaataagag ccacttagct 120

tggtaccagc agaaaccagg acagcctcct aagttgctca tttactgggc atctacccgg 180

gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt caccctcatc 240

atcagcagcc tgcaggctga ggatgtggca gtttattact gtcagcaata ttatttttct 300

ccctcacttt tcggcggagg gaccaaggtg gagatcaaa 339

<210> 1083
<211> 113
<212> PRT
<213> Homo sapiens

<400> 1083

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 Ser His 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 Ile
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 Phe Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
100 105 110

Lys

<210> 1084
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1084

Lys Ser Ser Gln Ser Val Leu Tyr Ser Ser Asn Asn Lys Ser His Leu
1 5 10 15

Ala

<210> 1085
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1085

Gln Gln Tyr Tyr Phe Ser Pro Leu Thr
1 5

<210> 1086
<211> 369
<212> DNA
<213> Homo sapiens

<400> 1086
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acctgcactg tctctggtgc ctccatcaat agtcactact ggagctggat ccggcagccc 120

ccagggaagg gactggagtg gattgggtat gtctattaca gtgggagcac cacctacaac 180

ccctccctca agagtcgagt caccttatca gtagatacgt ccaagaacca gttctccctg 240

aacctgagct ctgtgaccgc cgcagacacg gccttctatt actgtgcgag acatccctac 300

gatgttttga ctggttccgg ggactggttc gacccctggg gccagggaac cctggtcacc 360

gtctcgagc 369

<210> 1087
<211> 123
<212> PRT
<213> Homo sapiens

<400> 1087

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Ile Asn Ser His
            20                  25                  30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Gly Tyr Val Tyr Tyr Ser Gly Ser Thr Thr Tyr Asn Pro Ser Leu Lys
    50                  55                  60

Ser Arg Val Thr Leu Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80

Asn Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Phe Tyr Tyr Cys Ala
                85                  90                  95

Arg His Pro Tyr Asp Val Leu Thr Gly Ser Gly Asp Trp Phe Asp Pro
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  1088
<211>  5
<212>  PRT
<213>  Homo sapiens

<400>  1088

Ser His Tyr Trp Ser
1               5


<210>  1089
<211>  16
<212>  PRT
<213>  Homo sapiens

<400>  1089

Tyr Val Tyr Tyr Ser Gly Ser Thr Thr Tyr Asn Pro Ser Leu Lys Ser
1               5                   10                  15


<210>  1090
<211>  15
<212>  PRT
<213>  Homo sapiens

<400>  1090

His Pro Tyr Asp Val Leu Thr Gly Ser Gly Asp Trp Phe Asp Pro
1               5                   10                  15


<210>  1091
<211>  7
<212>  PRT
<213>  Homo sapiens

<400>  1091
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Gly Ala Ser Ile Asn Ser His
1 5

<210> 1092
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1092

Tyr Val Tyr Tyr Ser Gly Ser Thr Thr
1 5

<210> 1093
<211> 324
<212> DNA
<213> Homo sapiens

<400> 1093
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acctgtgggg gaaatgccat tggaagtaaa aaagttcact ggtaccagca caaggcaggc 120

caggcccctg tactcgtcgt ctatgatgat acagaccggc cctcagggat ccctgagcga 180

ttctctggct ccaactcttg gagcacggcc accctgacca tcaacagggt cgaagccggg 240

gatgaggccg actattactg tcaggtgtgg gattttacca ttgatcatgt ggtcttcggc 300

ggagggacca agctgaccgt ctta 324

<210> 1094
<211> 108
<212> PRT
<213> Homo sapiens

<400> 1094

Ser Tyr Val Leu Thr Gln Ala Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Ala Ile Gly Ser Lys Lys Val
20 25 30

His Trp Tyr Gln His Lys Ala Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Thr Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Trp Ser Thr Ala Thr Leu Thr Ile Asn Arg Val Glu Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Phe Thr Ile Asp His
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 1095
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1095

Gly Gly Asn Ala Ile Gly Ser Lys Lys Val His
1 5 10

<210> 1096
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1096

Asp Asp Thr Asp Arg Pro Ser
1 5

<210> 1097
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1097

Gln Val Trp Asp Phe Thr Ile Asp His Val Val
1 5 10

<210> 1098
<211> 387
<212> DNA
<213> Homo sapiens

<400> 1098
gaggtgcaac tggttcagtc tggatcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggcta cagctttagc aactactgga tcggctgggt gcgccacatg 120

cccgggaaag gcctggaatg gatggggatc atttatcctg gtgactctga taccagatac 180

agcccgtcct tccaaggcca ggtcaccatg tcagccgaca agtccagcag caccgtctac 240

ctgcagtgga gcagcctgaa ggcctcggac accgccattt atttattgtg cgagacgggc 300

ggacatagtt ttggatatgg gtcgggggg gacacgcaca gtgaattcga ctcctggggc 360

cagggaaccc tggtcaccgt ctcgagc 387

<210> 1099
<211> 129
<212> PRT
<213> Homo sapiens

<400> 1099

Glu Val Gln Leu Val Gln Ser Gly Ser Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Ser Asn Tyr
20 25 30

Trp Ile Gly Trp Val Arg His Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Met Ser Ala Asp Lys Ser Ser Ser Thr Val Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

Ala Arg Arg Gly Gly His Ser Phe Gly Tyr Gly Ser Gly Gly Asp Thr
100 105 110

His Ser Glu Phe Asp Ser Trp Gly Gln Gly Thr Leu Val Thr Val Ser
115 120 125

Ser

<210> 1100
<211> 5
<212> PRT
<213> Homo sapiens

<400> 1100

Asn Tyr Trp Ile Gly
1 5

<210> 1101
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1101

Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe Gln
1 5 10 15

Gly

<210> 1102
<211> 20
<212> PRT
<213> Homo sapiens

<400> 1102

Arg Gly Gly His Ser Phe Gly Tyr Gly Ser Gly Gly Asp Thr His Ser
1 5 10 15

Glu Phe Asp Ser

20

<210> 1103
<211> 6
<212> PRT
<213> Homo sapiens

<400> 1103

Gly Tyr Ser Phe Ser Asn
1 5

<210> 1104
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1104

Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg
1 5 10

<210> 1105
<211> 330
<212> DNA
<213> Homo sapiens

<400> 1105
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tcctgctctg gaagcgactc caacattggt gattattttg tatgttggta ccagcacctc 120

ccaggaaaac ccccccaact cctcatctat gaaaataata agcgaccctc agggattcct 180

gaccgattct ctggctccaa gtctggcacg tcagccaccc tgggcatcac cggaatccag 240

accggggacg aggccgatta ctactgcgca acttgggatg gcagcctgag tgcttgggtg 300

ttcggcggag gaccaagct gaccgttcta 330

<210> 1106
<211> 110
<212> PRT
<213> Homo sapiens

<400> 1106

Gln Ser Val Leu Thr Gln Ser Pro Ser Val Ser Ala Ala Pro Gly Gln
1 5 10 15

Lys Val Thr Ile Ser Cys Ser Gly Ser Asp Ser Asn Ile Gly Asp Tyr
20 25 30

Phe Val Cys Trp Tyr Gln His Leu Pro Gly Lys Pro Pro Gln Leu Leu
35 40 45

Ile Tyr Glu Asn Asn Lys Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Ile Gln

65 70 75 80

Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Gly Ser Leu
85 90 95

Ser Ala Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 1107
<211> 13
<212> PRT
<213> Homo sapiens

<400> 1107

Ser Gly Ser Asp Ser Asn Ile Gly Asp Tyr Phe Val Cys
1 5 10

<210> 1108
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1108

Glu Asn Asn Lys Arg Pro Ser
1 5

<210> 1109
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1109

Ala Thr Trp Asp Gly Ser Leu Ser Ala Trp Val
1 5 10

<210> 1110
<211> 363
<212> DNA
<213> Homo sapiens

<400> 1110
caggtccaag tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgagggtc 60

tcctgccagg cttctggagg caccttcatg aattatgcta tcatttgggt gcgacgggcc 120

cctggacaag gccttgagtg gatgggaggg atcatccctg tctttcctac accaaactac 180

gcacagatgt tccagggcag agtcacgatt tccacggacg aatccaggag cacatccttc 240

ttggaactga ccaacctgag atatgaggac acggccgttt attactgtgc gaggcgaatt 300

tatcacggtg gtaactccgg ctttgacttc tggggccagg gaaccctggt caccgtctcg 360

agc 363

<210> 1111
<211> 121
<212> PRT

<213> Homo sapiens

<400> 1111

Gln Val Gln Val Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Arg Val Ser Cys Gln Ala Ser Gly Gly Thr Phe Met Asn Tyr
20 25 30

Ala Ile Ile Trp Val Arg Arg Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Val Phe Pro Thr Pro Asn Tyr Ala Gln Met Phe
50 55 60

Gln Gly Arg Val Thr Ile Ser Thr Asp Glu Ser Arg Ser Thr Ser Phe
65 70 75 80

Leu Glu Leu Thr Asn Leu Arg Tyr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Ile Tyr His Gly Gly Asn Ser Gly Phe Asp Phe Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 1112
<211> 5
<212> PRT
<213> Homo sapiens

<400> 1112

Asn Tyr Ala Ile Ile
1 5

<210> 1113
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1113

Gly Ile Ile Pro Val Phe Pro Thr Pro Asn Tyr Ala Gln Met Phe Gln
1 5 10 15

Gly

<210> 1114
<211> 12
<212> PRT
<213> Homo sapiens

<400> 1114

Arg Ile Tyr His Gly Gly Asn Ser Gly Phe Asp Phe
1 5 10

<210> 1115
<211> 6
<212> PRT
<213> Homo sapiens

<400> 1115

Gly Gly Thr Phe Met Asn
1 5

<210> 1116
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1116

Gly Ile Ile Pro Val Phe Pro Thr Pro Asn
1 5 10

<210> 1117
<211> 327
<212> DNA
<213> Homo sapiens

<400> 1117
gaaattgtgt tgacacagtc tccagccacc ctgtctttgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gagtgttggc aactacttag cctggtacca acagaaacct 120

ggccaggctc ccaggctcct catctatgat tcatccaaca gggcccctgg catcccagcc 180

aggttcagtg gcagtgggtc tgggacagac ttcactctca ccatcagcag cctcgcgcct 240

gaagattttg cagtttatta ctgtcagcag cgtagcaagt ggcctcccat gtacagtttt 300

ggccatggga ccaagctgga gatcaaa 327

<210> 1118
<211> 109
<212> PRT
<213> Homo sapiens

<400> 1118

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 Gly Asn 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 Ser Ser Asn Arg Ala Pro 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 Ala Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Lys Trp Pro Pro
85 90 95

Met Tyr Ser Phe Gly His Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 1119
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1119

Arg Ala Ser Gln Ser Val Gly Asn Tyr Leu Ala
1 5 10

<210> 1120
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1120

Asp Ser Ser Asn Arg Ala Pro
1 5

<210> 1121
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1121

Gln Gln Arg Ser Lys Trp Pro Pro Met Tyr Ser
1 5 10

<210> 1122
<211> 357
<212> DNA
<213> Homo sapiens

<400> 1122
caggtccagg tggtgcagtc tgggactgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgccaga cttctggagg caggttcatg agttatgcta tcacctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggc atcgtccctg tcttcggaac agcaaactac 180

gctcagaagt tccagggcag agtcacgatc accacggacg attccacgcg cacagcctat 240

atggagttga gcagcctgag aagtgaggac acggccgttt attactgtgg gttccgatac 300

ggctctggtt acgggttiga ctcctggggc cagggaaccc tggtcaccgt ctcgagc 357

<210> 1123
<211> 119
<212> PRT

<213> Homo sapiens

<400> 1123

Gln Val Gln Val Val Gln Ser Gly Thr Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Gln Thr Ser Gly Gly Arg Phe Met Ser Tyr
20 25 30

Ala Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Val Pro Val Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Thr Asp Asp Ser Thr Arg 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

Gly Phe Arg Tyr Gly Ser Gly Tyr Gly Phe Asp Ser Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 1124
<211> 5
<212> PRT
<213> Homo sapiens

<400> 1124

Ser Tyr Ala Ile Thr
1 5

<210> 1125
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1125

Gly Ile Val Pro Val Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1126
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1126

Arg Tyr Gly Ser Gly Tyr Gly Phe Asp Ser
1 5 10

<210> 1127
<211> 6
<212> PRT
<213> Homo sapiens

<400> 1127

Gly Gly Arg Phe Met Ser
1 5

<210> 1128
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1128

Gly Ile Val Pro Val Phe Gly Thr Ala Asn
1 5 10

<210> 1129
<211> 324
<212> DNA
<213> Homo sapiens

<400> 1129
gaaattgtat tgacgcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gagtgttagt agcagctact tagcctggta tcagaagaaa 120

cctggccagg ctcccaggct cctcatctat ggtgcttcca ctagggccac tggcatcccg 180

gaccggttca ctggcagtgg gtctgggaca gacttcactc tcagcatcag tagactggag 240

cctgaagatt ttgcagtgta ttactgtcag cacttttggta cctcagtctt cacttttcggc 300

ggagggacca aggttgagat caaa 324

<210> 1130
<211> 108
<212> PRT
<213> Homo sapiens

<400> 1130

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 Lys Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Thr
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Phe Gly Thr Ser Val
85 90 95

Phe Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1131
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1131

Gln His Phe Gly Thr Ser Val Phe Thr
1 5

<210> 1132
<211> 360
<212> DNA
<213> Homo sapiens

<400> 1132
caggtgcagc tggtgcagtc tggggctgat ctgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggata caccttcacc gactactata ttcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaaccctg aaagtggtga cacaaagtat 180

gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcac cacagcctac 240

atggagctgg gtaggctgag atccgacgac acggccgtgt attactgtgc gagagatgta 300

agtacgacct ggagctggtt cgccccctgg ggccagggaa ccctggtcac cgtctcgagc 360

<210> 1133
<211> 120
<212> PRT
<213> Homo sapiens

<400> 1133

Gln Val Gln Leu Val Gln Ser Gly Ala Asp Leu Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp 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 Glu Ser Gly Asp Thr Lys 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 Gly Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Val Ser Thr Thr Trp Ser Trp Phe Ala Pro Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210>  1134
<211>  5
<212>  PRT
<213>  Homo sapiens

<400>  1134

Asp Tyr Tyr Ile His
1               5


<210>  1135
<211>  17
<212>  PRT
<213>  Homo sapiens

<400>  1135

Trp Ile Asn Pro Glu Ser Gly Asp Thr Lys Tyr Ala Gln Lys Phe Gln
1               5                   10                  15

Gly


<210>  1136
<211>  11
<212>  PRT
<213>  Homo sapiens

<400>  1136

Asp Val Ser Thr Thr Trp Ser Trp Phe Ala Pro
1               5                   10


<210>  1137
<211>  6
<212>  PRT
<213>  Homo sapiens

<400>  1137

Gly Tyr Thr Phe Thr Asp
1               5


<210>  1138
<211>  10
<212>  PRT
<213>  Homo sapiens

<400>  1138
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Trp Ile Asn Pro Glu Ser Gly Asp Thr Lys
1               5                  10


<210>  1139
<211>  339
<212>  DNA
<213>  Homo sapiens

<400>  1139
gacatcgtga tgacccagtc tccagactcc ctggcagtgt ctctgggcga gagggccacc      60

atcaactgca ggtccagcca gagtattttc cacaactcca acaatgagaa ctacttagct     120

tggtaccagc agaaaccagg acagcctcct aagctgctca tttactgggc atctacccgg     180

gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc     240

atcagcagcc tgcaggctga agatgtggcg gtttattttc tgtcagcaat attataatgct     300

ccgctcactt tcggcggagg gaccaaggtg gagatcaaa                             339


<210>  1140
<211>  113
<212>  PRT
<213>  Homo sapiens

<400>  1140

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 Arg Ser Ser Gln Ser Ile Phe His Asn
            20                  25                  30

Ser Asn Asn Glu 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 Asn Ala Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
            100                 105                 110

Lys


<210>  1141
<211>  17
<212>  PRT
<213>  Homo sapiens
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<400> 1141

Arg Ser Ser Gln Ser Ile Phe His Asn Ser Asn Asn Glu Asn Tyr Leu
1 5 10 15

Ala

<210> 1142
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1142

Gln Gln Tyr Tyr Asn Ala Pro Leu Thr
1 5

<210> 1143
<211> 369
<212> DNA
<213> Homo sapiens

<400> 1143
caggtgcagc tggtgcagtc tggggctgag gtgaagaggc ctgggtcctc ggtgaaggtc 60

tcatgcacgg cttctggagg catcttcagg aagaatgcaa tcagctgggt gcgacaggcc 120

cctggacaag gccttgagtg gatgggaggg atcatcgcag tctttaacac agcaaattac 180

gcgcagaagt tccagaacag agtcaaaatt accgcagacg agtcaggcaa tacggcctac 240

atggagctga gcagcctgac atctgacgac acggccgtgt attactgtgc gagtcaccca 300

aaatatttct atggttcggg gagttatccg gacttctggg gccagggaac cctggtcacc 360

gtctcgagc 369

<210> 1144
<211> 123
<212> PRT
<213> Homo sapiens

<400> 1144

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Arg Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Thr Ala Ser Gly Gly Ile Phe Arg Lys Asn
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Ala Val Phe Asn Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Asn Arg Val Lys Ile Thr Ala Asp Glu Ser Gly Asn Thr Ala Tyr
65 70 75 80

```
Met Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Ser His Pro Lys Tyr Phe Tyr Gly Ser Gly Ser Tyr Pro Asp Phe
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
        115                 120
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<210> 1145
<211> 330
<212> DNA
<213> Homo sapiens

<400> 1145
caatctgccc tgactcagcc tcgctcagtg tccgggtctc ctggacagtc aatcaccatc 60

tcctgtactg gtggcagcag tgatattggt gcttctaact ctgtctcctg gtaccaacaa 120

cacccaggca aagcccccaa actcgttatt tttgatgtca ctgagcgacc ctcaggggtc 180

ccgcatcggt tctctggctc caagtctggc aacacggcct ccctgaccgt ctctgggctc 240

cagcctgacg acgaggctga ttatttctgc tgcgcatatg gaggcaaata tcttgtggtc 300

ttcggcggag ggaccaaggt gaccgttcta 330

<210> 1146
<211> 110
<212> PRT
<213> Homo sapiens

<400> 1146

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Gln Ser Ala Leu Thr Gln Pro Arg Ser Val Ser Gly Ser Pro Gly Gln
1               5                   10                  15

Ser Ile Thr Ile Ser Cys Thr Gly Gly Ser Ser Asp Ile Gly Ala Ser
            20                  25                  30

Asn Ser Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35                  40                  45

Val Ile Phe Asp Val Thr Glu Arg Pro Ser Gly Val Pro His Arg Phe
    50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65                  70                  75                  80

Gln Pro Asp Asp Glu Ala Asp Tyr Phe Cys Cys Ala Tyr Gly Gly Lys
                85                  90                  95

Tyr Leu Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
            100                 105                 110
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<210> 1147

<211> 14
<212> PRT
<213> Homo sapiens

<400> 1147

Thr Gly Gly Ser Ser Asp Ile Gly Ala Ser Asn Ser Val Ser
1 5 10

<210> 1148
<211> 381
<212> DNA
<213> Homo sapiens

<400> 1148
caggtgcagc tggtgcagtc tggggctgag gtgaagaaac ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggata cacctttatc ggctatgata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaacgcta aaagaggtgg cacaaactat 180

gcacaaaagt ttcagggcag ggtcaccatg accagggaca cgtctatcag cacagcctac 240

atggagctga acagcctgag atctgacgac acggccgtgt attactgtgc gagaggggtg 300

gggtcacgaa ctacgatttt tggagttctc aacccggaat ttgactactg gggccaggga 360

accctggtca ccgtctcgag c 381

<210> 1149
<211> 127
<212> PRT
<213> Homo sapiens

<400> 1149

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 Ile Gly Tyr
20 25 30

Asp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Ala Lys Arg 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 Asn Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Val Gly Ser Arg Thr Thr Ile Phe Gly Val Leu Asn Pro
100 105 110

Glu Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 1150
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<212> PRT
<213> Homo sapiens

<400> 1150

Gly Tyr Asp Met His
1 5

<210> 1151
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1151

Trp Ile Asn Ala Lys Arg Gly Gly Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1152
<211> 18
<212> PRT
<213> Homo sapiens

<400> 1152

Gly Val Gly Ser Arg Thr Thr Ile Phe Gly Val Leu Asn Pro Glu Phe
1 5 10 15

Asp Tyr

<210> 1153
<211> 6
<212> PRT
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<400> 1153

Gly Tyr Thr Phe Ile Gly
1 5

<210> 1154
<211> 10
<212> PRT
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<400> 1154

Trp Ile Asn Ala Lys Arg Gly Gly Thr Asn
1 5 10

<210> 1155
<211> 330
<212> DNA

<213> Homo sapiens

<400> 1155
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cacccaggca aagcccccaa actcctgatt tatgaggtca ctaagcggcc tcaggggtc 180

cctgatcgct tctctggctc caagtctggc aacacggcct ccctgaccgt ctctgggctc 240

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ttcggacctg ggaccaaggt caccgttcta 330

<210> 1156
<211> 110
<212> PRT
<213> Homo sapiens

<400> 1156

Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asp Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Leu Ile Tyr Glu Val Thr Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Asn
85 90 95

Tyr Asn His Val Phe Gly Pro Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 1157
<211> 14
<212> PRT
<213> Homo sapiens

<400> 1157

Thr Gly Ser Ser Ser Asp Val Gly Gly Tyr Asp Tyr Val Ser
1 5 10

<210> 1158
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1158

Glu Val Thr Lys Arg Pro Ser
1 5

<210> 1159
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1159

Ser Ser Tyr Ala Gly Asn Tyr Asn His Val
1 5 10

<210> 1160
<211> 354
<212> DNA
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<400> 1160
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tcctgcaagg cttctggaca caccttcacc ggctactaca tacactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaaccctg acagtggtgc caccagttct 180

gcacagaact ttcagggcag ggtcaccatg accggggaca cgtcctctag cacagcctac 240

atggagctga gtaggctgag ttttgacgac acggccgtct attactgtgc gagagtactg 300

tttaccagtc cttttgactt ctggggtgag ggaaccctgg tcaccgtctc gagc 354

<210> 1161
<211> 118
<212> PRT
<213> Homo sapiens

<400> 1161

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 His 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 Asp Ser Gly Ala Thr Ser Ser Ala Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Gly Asp Thr Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Ser Phe Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Leu Phe Thr Ser Pro Phe Asp Phe Trp Gly Glu Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 1162
<211> 5
<212> PRT
<213> Homo sapiens

<400> 1162

Gly Tyr Tyr Ile His
1 5

<210> 1163
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1163

Trp Ile Asn Pro Asp Ser Gly Ala Thr Ser Ser Ala Gln Asn Phe Gln
1 5 10 15

Gly

<210> 1164
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1164

Val Leu Phe Thr Ser Pro Phe Asp Phe
1 5

<210> 1165
<211> 6
<212> PRT
<213> Homo sapiens

<400> 1165

Gly His Thr Phe Thr Gly
1 5

<210> 1166
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1166

Trp Ile Asn Pro Asp Ser Gly Ala Thr Ser
1 5 10

<210> 1167
<211> 330
<212> DNA

<213> Homo sapiens

<400> 1167
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acctgtggct ccagcactgg agctgtcacc aggggtcatt atccctattg gttccagcag 120

aagcctggcc aagcccccag ggcactcatt tatgatagtg caggcaacag acactcctgg 180

actcccgccc gattctcagg ctccctcctt gggggcaaag ctgccctgac cctttcgggt 240

gcgcagcctg aggatgaggc tgagtattac tgcttgctct cctatagtgg tgtctgggtg 300

ttcggcggag ggacgaagct gaccgttcta 330

<210> 1168
<211> 110
<212> PRT
<213> Homo sapiens

<400> 1168

Gln Ala Val Val Thr Gln Glu Pro Ser Leu Ala Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Arg Gly
20 25 30

His Tyr Pro Tyr Trp Phe Gln Gln Lys Pro Gly Gln Ala Pro Arg Ala
35 40 45

Leu Ile Tyr Asp Ser Ala Gly Asn Arg His Ser Trp Thr Pro Ala Arg
50 55 60

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly
65 70 75 80

Ala Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Leu Leu Ser Tyr Ser
85 90 95

Gly Val Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 1169
<211> 14
<212> PRT
<213> Homo sapiens

<400> 1169

Gly Ser Ser Thr Gly Ala Val Thr Arg Gly His Tyr Pro Tyr
1 5 10

<210> 1170
<211> 8
<212> PRT
<213> Homo sapiens

<400> 1170

Asp Ser Ala Gly Asn Arg His Ser
1 5

<210> 1171
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1171

Leu Leu Ser Tyr Ser Gly Val Trp Val
1 5

<210> 1172
<211> 360
<212> DNA
<213> Homo sapiens

<400> 1172
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tcctgcacgg cctctggaag tgtcttcacc aatt atggaa ttagttgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatccctc tctttggcgc agccaagtac 180

gcacagaaat tccagggcag agtcaccatc acagcggacg aatccacgaa gacagtctac 240

atggagctga gcaggctgac atctaaagac acggccatat attttctgtg cgaaggcccc 300

cgtgtctacg agtactactt tgatcagtgg ggccagggaa ccccagtcac cgtctcctca 360

<210> 1173
<211> 327
<212> DNA
<213> Homo sapiens

<400> 1173
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ctctcctgta gggccagtca gagtgttagc aacaatttag cctggtacca gcaaaaacct 120

ggccagcctc ccaggctcct catctatgat gcatctacca gggccacggg tgtcccagcc 180

aagttcagtg gcactgggtc tggcacagag ttcactctca gcatcagcag cctgcagtcc 240

gaagattttg cagtttatta ctgtcagcag tatcacaact ggcctccctc gtacagtttt 300

ggcctgggga ccaagctgga gatcaaa 327

<210> 1174
<211> 351
<212> DNA
<213> Homo sapiens

<400> 1174
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tcctgcaagg cttctagaaa gtccttcatt ggctactatg tacactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagccctg acagtgatgc cacaaagtac 180

gcacagaagt ttcagggctc cgtcatcatg accagggaca cgtccgtcag cacagtgtac 240

atggagctga gtaggctgac atctgacgac acggcccttt attactgtct ccttttttcga 300

ggtggaaact ccctctcctg gggccaggga accctggtca ccgtctcgag c 351

<210> 1175
<211> 117
<212> PRT
<213> Homo sapiens

<400> 1175

Gln Glu 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 Arg Lys Ser Phe Ile Gly Tyr
20 25 30

Tyr Val His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Pro Asp Ser Asp Ala Thr Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Ser Val Ile Met Thr Arg Asp Thr Ser Val Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Thr Ser Asp Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Leu Leu Phe Arg Gly Gly Asn Ser Leu Ser Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 1176
<211> 5
<212> PRT
<213> Homo sapiens

<400> 1176

Gly Tyr Tyr Val His
1 5

<210> 1177
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1177

Trp Ile Ser Pro Asp Ser Asp Ala Thr Lys Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1178
<211> 8
<212> PRT
<213> Homo sapiens

<400> 1178

Phe Arg Gly Gly Asn Ser Leu Ser
1 5

<210> 1179
<211> 6
<212> PRT
<213> Homo sapiens

<400> 1179

Arg Lys Ser Phe Ile Gly
1 5

<210> 1180
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1180

Trp Ile Ser Pro Asp Ser Asp Ala Thr Lys
1 5 10

<210> 1181
<211> 327
<212> DNA
<213> Homo sapiens

<400> 1181
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acctgtggct ccagcactgg acctgtcacc agtggtcatt atccctactg gttccagcag 120

aagcctggcc aagcccccag gacattgatt tctgctacat ccaacacaca ctcctggaca 180

cctgcccgct tctcaggctc cctccttggg ggcagagctg ccctgaccct ttcgggtgcg 240

cagcctgagg atgaggctga ctattattgc tttctctcct acagtggtgc ttgggtgttc 300

ggcggaggga ccacgctgac cgttcta 327

<210> 1182
<211> 109
<212> PRT
<213> Homo sapiens

<400> 1182

Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Pro Val Thr Ser Gly
20 25 30

His Tyr Pro Tyr Trp Phe Gln Gln Lys Pro Gly Gln Ala Pro Arg Thr
35 40 45

Leu Ile Ser Ala Thr Ser Asn Thr His Ser Trp Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Arg Ala Ala Leu Thr Leu Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Phe Leu Ser Tyr Ser Gly
85 90 95

Ala Trp Val Phe Gly Gly Gly Thr Thr Leu Thr Val Leu
100 105

<210> 1183
<211> 14
<212> PRT
<213> Homo sapiens

<400> 1183

Gly Ser Ser Thr Gly Pro Val Thr Ser Gly His Tyr Pro Tyr
1 5 10

<210> 1184
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1184

Ala Thr Ser Asn Thr His Ser
1 5

<210> 1185
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1185

Phe Leu Ser Tyr Ser Gly Ala Trp Val
1 5

<210> 1186
<211> 366
<212> DNA
<213> Homo sapiens

<400> 1186
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tcctgtgcag cctctggatt tatctttaga aatttactgga tgagctgggt ccggcaggct 120

ccagggaagg ggctggagtg ggtggccaac ataaaacaag atggaagaga gaagtactat 180

gtggactctc tgaggggccg agtcaacatc tccagagaca acgccgagaa ctcattgtat 240

ctgcacatga acagcctgag agtcgaggac acggctgttt atttctgtgc gagagctcgg 300

atggtggtgg ttactggcga tggttttgat gtctggggcc atgggacaat ggtcaccgtc 360

tcgagc 366

<210> 1187
<211> 122
<212> PRT
<213> Homo sapiens

<400> 1187

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ile Phe Arg Asn Tyr
20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Asn Ile Lys Gln Asp Gly Arg Glu Lys Tyr Tyr Val Asp Ser Leu
50 55 60

Arg Gly Arg Val Asn Ile Ser Arg Asp Asn Ala Glu Asn Ser Leu Tyr
65 70 75 80

Leu His Met Asn Ser Leu Arg Val Glu Asp Thr Ala Val Tyr Phe Cys
85 90 95

Ala Arg Ala Arg Met Val Val Val Thr Gly Asp Gly Phe Asp Val Trp
100 105 110

Gly His Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 1188
<211> 5
<212> PRT
<213> Homo sapiens

<400> 1188

Asn Tyr Trp Met Ser
1 5

<210> 1189
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1189

Asn Ile Lys Gln Asp Gly Arg Glu Lys Tyr Tyr Val Asp Ser Leu Arg
1 5 10 15

Gly

<210> 1190
<211> 13
<212> PRT
<213> Homo sapiens

<400> 1190

Ala Arg Met Val Val Val Thr Gly Asp Gly Phe Asp Val
1 5 10

<210> 1191
<211> 6
<212> PRT
<213> Homo sapiens

<400> 1191

Gly Phe Ile Phe Arg Asn
1 5

<210> 1192
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1192

Asn Ile Lys Gln Asp Gly Arg Glu Lys Tyr
1 5 10

<210> 1193
<211> 321
<212> DNA
<213> Homo sapiens

<400> 1193
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atcacttgcc gggcaagtca gaatattaag aggtatttca attggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctatgct gcatccaatt tagaaaatgg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag tctgcaacct 240

gaggattttg cgacttatta ctgtcagcag agttttcagt aatcgtggac attcggccaa 300

gggaccaacg tggacatcaa a 321

<210> 1194
<211> 107
<212> PRT
<213> Homo sapiens

<400> 1194

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 Asn Ile Lys Arg Tyr

20 25 30

Phe Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Asn Leu Glu Asn Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Phe Ser Lys Ser Trp
85 90 95

Thr Phe Gly Gln Gly Thr Asn Val Asp Ile Lys
100 105

<210> 1195
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1195

Arg Ala Ser Gln Asn Ile Lys Arg Tyr Phe Asn
1 5 10

<210> 1196
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1196

Ala Ala Ser Asn Leu Glu Asn
1 5

<210> 1197
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1197

Gln Gln Ser Phe Ser Lys Ser Trp Thr
1 5

<210> 1198
<211> 296
<212> DNA
<213> Homo sapiens

<400> 1198
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tcctgcaagg cttctggtta cacctttacc agctatggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagaga 296

<210> 1199
<211> 296
<212> DNA
<213> Homo sapiens

<400> 1199
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tcctgcaagg cttctggata cacctcacc ggctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtggtgg cacaaactat 180

gcacagaagt ttcagggcag ggtcaccatg accagggaca cgtccatcag cacagcctac 240

atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gagaga 296

<210> 1200
<211> 294
<212> DNA
<213> Homo sapiens

<400> 1200
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tcctgcaagg cttctggata cacctcacc ggctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtggtgg cacaaactat 180

gcacagaagt ttcagggctg ggtcaccatg accagggaca cgtccatcag cacagcctac 240

atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gaga 294

<210> 1201
<211> 296
<212> DNA
<213> Homo sapiens

<400> 1201
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tcctgcaagg cttctggagg cacctcagc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttggtac agcaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagaga 296

<210> 1202
<211> 294
<212> DNA
<213> Homo sapiens

<400> 1202
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tcctgcaagg cttctggagg cacctcagc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttggtac agcaaactac 180

gcacagaagt tccagggcag agtcacgatt accacggacg aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gaga 294

<210> 1203
<211> 296
<212> DNA
<213> Homo sapiens

<400> 1203
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cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttggtac agcaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggaca aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagaga 296

<210> 1204
<211> 296
<212> DNA
<213> Homo sapiens

<400> 1204
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tcctgcaagg cttctggagg caccttcagc agctatgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcccta tctttggtac agcaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatccacgag cacagcctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagaga 296

<210> 1205
<211> 296
<212> PRT
<213> Homo sapiens

<400> 1205

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Ala Gly Thr Cys Thr Gly Gly Gly Gly Cys Thr Gly Ala Gly Gly Thr
20 25 30

Gly Ala Ala Gly Ala Ala Gly Cys Cys Thr Gly Gly Gly Gly Cys Cys
35 40 45

Thr Cys Ala Gly Thr Gly Ala Ala Gly Gly Thr Cys Thr Cys Cys Thr
50 55 60

Gly Cys Ala Ala Gly Gly Cys Thr Thr Cys Thr Gly Gly Ala Thr Ala
65 70 75 80

Cys Ala Cys Cys Thr Thr Cys Ala Cys Cys Ala Gly Thr Thr Ala Thr
85 90 95

Gly Ala Thr Ala Thr Cys Ala Ala Cys Thr Gly Gly Gly Thr Gly Cys
100 105 110

Gly Ala Cys Ala Gly Gly Cys Cys Ala Cys Thr Gly Gly Ala Cys Ala
115 120 125

Ala Gly Gly Gly Cys Thr Thr Gly Ala Gly Thr Gly Gly Ala Thr Gly
130 135 140

Gly Gly Ala Thr Gly Gly Ala Thr Gly Ala Ala Cys Cys Cys Thr Ala
145 150 155 160

Ala Cys Ala Gly Thr Gly Gly Thr Ala Ala Cys Ala Cys Ala Gly Gly
165 170 175

Cys Thr Ala Thr Gly Cys Ala Cys Ala Gly Ala Ala Gly Thr Thr Cys
180 185 190

Cys Ala Gly Gly Gly Cys Ala Gly Ala Gly Thr Cys Ala Cys Cys Ala
195 200 205

Thr Gly Ala Cys Cys Ala Gly Gly Ala Ala Cys Ala Cys Cys Thr Cys
210 215 220

Cys Ala Thr Ala Ala Gly Cys Ala Cys Ala Gly Cys Cys Thr Ala Cys
225 230 235 240

Ala Thr Gly Gly Ala Gly Cys Thr Gly Ala Gly Cys Ala Gly Cys Cys
245 250 255

Thr Gly Ala Gly Ala Thr Cys Thr Gly Ala Gly Gly Ala Cys Ala Cys
260 265 270

Gly Gly Cys Cys Gly Thr Gly Thr Ala Thr Thr Ala Cys Thr Gly Thr
275 280 285

Gly Cys Gly Ala Gly Ala Gly Gly
290 295

<210> 1206
<211> 297
<212> DNA
<213> Homo sapiens

<400> 1206
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acctgcacct tctctgggtt ctcactcagc actagtggag tgggtgtggg ctggatccgt 120

cagccccag gaaaggccct ggagtggctt gcactcattt attgggatga tgataagcgc 180

tacagcccat ctctgaagag caggctcacc atcaccaagg acacctccaa aaaccaggtg 240

gtccttacaa tgaccaacat ggaccctgtg gacacagcca catattactg tgcacgg 297

<210> 1207
<211> 294
<212> DNA
<213> Homo sapiens

<400> 1207
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tcctgtgcag cctctggatt cacctttagt agctatgcta tgcactgggt ccgccaggct 120

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gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gaga 294

<210> 1208
<211> 296
<212> DNA
<213> Homo sapiens

<400> 1208
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gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240

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<213> Homo sapiens

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ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtaa taaatactat 180

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240

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<210> 1210
<211> 296
<212> PRT
<213> Homo sapiens

<400> 1210

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1 5 10 15

Ala Gly Thr Cys Thr Gly Gly Gly Gly Gly Ala Gly Gly Cys Gly Thr
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35 40 45

Thr Cys Cys Cys Thr Gly Ala Gly Ala Cys Thr Cys Thr Cys Cys Thr
50 55 60

Gly Thr Gly Cys Ala Gly Cys Gly Thr Cys Thr Gly Gly Ala Thr Thr
65 70 75 80

Cys Ala Cys Cys Thr Thr Cys Ala Gly Thr Ala Gly Cys Thr Ala Thr
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Gly Gly Cys Ala Thr Gly Cys Ala Cys Thr Gly Gly Gly Thr Cys Cys
100 105 110

Gly Cys Cys Ala Gly Gly Cys Thr Cys Cys Ala Gly Gly Cys Ala Ala
115 120 125

Gly Gly Gly Gly Cys Thr Gly Gly Ala Gly Thr Gly Gly Gly Thr Gly
130 135 140

Gly Cys Ala Gly Thr Thr Ala Thr Ala Thr Cys Ala Thr Ala Thr Gly
145 150 155 160

Ala Thr Gly Gly Ala Ala Gly Thr Ala Ala Thr Ala Ala Ala Thr Ala
165 170 175

Cys Thr Ala Thr Gly Cys Ala Gly Ala Cys Thr Cys Cys Gly Thr Gly
180 185 190

Ala Ala Gly Gly Gly Cys Cys Gly Ala Thr Thr Cys Ala Cys Cys Ala
195 200 205

Thr Cys Thr Cys Cys Ala Gly Ala Gly Ala Cys Ala Ala Thr Thr Cys
210 215 220

Cys Ala Ala Gly Ala Ala Cys Ala Cys Gly Cys Thr Gly Thr Ala Thr
225 230 235 240

Cys Thr Gly Cys Ala Ala Ala Thr Gly Ala Ala Cys Ala Gly Cys Cys
245 250 255

Thr Gly Ala Gly Ala Gly Cys Cys Gly Ala Gly Gly Ala Cys Ala Cys
260 265 270

Gly Gly Cys Thr Gly Thr Gly Thr Ala Thr Thr Ala Cys Thr Gly Thr
275 280 285

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290 295

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<211> 302
<212> DNA
<213> Homo sapiens

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ccagggaagg ggctggagtg ggtaggttt c attagaagca aagcttatgg tgggacaaca 180

gaatacgccg cgtctgtgaa aggcagattc accatctcaa gagatgattc caaaagcatc 240

gcctatctgc aaatgaacag cctgaaaacc gaggacacag ccgtgtatta ctgtactaga 300

ga 302

<210> 1212
<211> 293
<212> DNA
<213> Homo sapiens

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tcctgtgcag cctctgggtt caccgtcagt agcaactaca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagtt attttatagcg gtggtagcac atactacgca 180

gactccgtga agggccgatt caccatctcc agagacaatt ccaagaacac gctgtatctt 240

caaatgaaca gcctgagagc cgaggacacg gccgtgtatt actgtgcgag aga 293

<210> 1213
<211> 296
<212> DNA
<213> Homo sapiens

<400> 1213
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cctggacaag ggcttgagtg gatgggatgg ttcaacacct acactgggaa cccaacatat 180

gcccagggct tcacaggacg gttttgtctt tccatggaca cctctgccag cacagcatac 240

ctgcagatca gcagcctaaa ggctgaggac atggccatgt attactgtgc gagata 296

<210> 1214
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<212> DNA
<213> Homo sapiens

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tcctgtgcag cctctggatt caccttt agt agctattgga tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtggccaac ataaagcaag atggaagtga gaaatactat 180

gtggactctg tgaagggccg attcaccatc tccagagaca acgccaagaa ctcactgtat 240

ctgcaaatga acagcctgag agccgaggac acggctgtgt attactgtgc gagaga 296

<210> 1215
<211> 299
<212> DNA
<213> Homo sapiens

<400> 1215
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cagcacccag ggaagggcct ggagtggatt gggtacatct attacagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagttacc atatcagtag acacgtctaa gaaccagttc 240

tccctgaagc tgagctctgt gactgccgcg gacacggccg tgtattactg tgcgagaga 299

<210> 1216
<211> 290
<212> DNA
<213> Homo sapiens

<400> 1216
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cagcacccag ggaagggcct ggagtggatt gggtacatct attacagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagttacc atatcagtag acacgtctaa gaaccagttc 240

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<210> 1217
<211> 299
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<213> Homo sapiens

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acctgcactg tctctggtgg ctccatcagc agtagtagtt actactgggg ctggatccgc 120

cagcccccag ggaaggggct ggagtggatt gggagtatct attatagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gaccgccgca gacacggctg tgtattactg tgcgagaca 299

<210> 1218
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<213> Homo sapiens

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acctgcgctg tctatggtgg gtcctttagt ggttactact ggagctggat ccgccagccc 120

ccagggaagg ggctggagtg gattggggaa atcaatcata gtggaagcac caactacaac 180

ccgtccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg 240

aagctgagct ctgtgaccgc cgcggacacg gctgtgtatt actgtgcgag agg 293

<210> 1219
<211> 284
<212> DNA
<213> Homo sapiens

<400> 1219
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acctgcgctg tctatggtgg gtcctcagt ggttactact ggagctggat ccgccagccc 120

ccagggaagg ggctggagtg gattggggaa atcaatcata gtggaagcac caactacaac 180

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aagctgagct ctgtgaccgc cgcggacacg gccgtgtatt actg 284

<210> 1220
<211> 291
<212> DNA
<213> Homo sapiens

<400> 1220
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acctgcgctg tctatggtgg gtcctcagt ggttactact ggagctggat ccgccagccc 120

ccagggaagg ggctggagtg gattggggaa atcatttcat agtggaagcac caactacaac 180

ccgtccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg 240

aagctgagct ctgtgaccgc cgcggacacg gctgtgtatt actgtgcgag a 291

<210> 1221
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<212> DNA
<213> Homo sapiens

<400> 1221
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acctgcactg tctctggtgg ctccatcagc agtagtagtt actactgggg ctggatccgc 120

cagccccag ggaaggggct ggagtggatt gggagtatct attatagtgg gagcacctac 180

tacaacccgt ccctcaagag tcgagtcacc atatccgtag acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gaccgccgca gacacggctg tgtattactg tgcgagaca 299

<210> 1222
<211> 297
<212> DNA
<213> Homo sapiens

<400> 1222
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ctcctgtgca gcctctggat tcaccttcag tagctctgct atgcactggg tccaccaggc 120

tccaggaaag ggttttggagt gggtctcagt tattagtaca agtggtgata ccgtactcta 180

cacagactct gtgaagggct gattcaccat ctctagagac aatgcccaga attcactgta 240

tctgcaaatg aacagcctga gagccgacga catggctgtg ttattactgt gtgaaaga 297

<210> 1223
<211> 288
<212> DNA
<213> Homo sapiens

<400> 1223
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ccagggaagg gactggagtg gattgggtat atctattaca gtgggagcac caactacaac 180

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aagctgagct ctgtgaccgc tgcggacacg gccgtgtatt actgtgcg 288

<210> 1224
<211> 299
<212> DNA
<213> Homo sapiens

<400> 1224
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acctgcactg tctctggtgg ctccgtcagc agtggtagtt actactggag ctggatccgg 120

cagccccag ggaagggact ggagtggatt gggtatatct attacagtgg gagcaccaac 180

tacaacccct ccctcaagag tcgagtcacc atatcagtag acacgtccaa gaaccagttc 240

tccctgaagc tgagctctgt gaccgctgcg gacacggccg tgtattactg tgcgagaga 299

<210> 1225
<211> 296
<212> DNA
<213> Homo sapiens

<400> 1225
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tcctgcaagg cttctggtta cagtttcacc acctatggta tgaattgggt gccacaggcc 120

cctggacaag ggcttgagtg gatgggatgg ttcaacacct acactgggaa cccaacatat 180

gcccagggct tcacaggacg gttttgtctt tccatggaca cctctgccag cacagcatac 240

ctgcagatca gcagcctaaa ggctgaggac atggccatgt attactgtgc gagata 296

<210> 1226
<211> 296
<212> DNA
<213> Homo sapiens

<400> 1226
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tcctgtaagg gttctggata cagctttacc agctactgga tcggctgggt gcgccagatg 120

cccgggaaag gcctggagtg gatggggatc atctatcctg gtgactctga taccagatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag caccgcctac 240

ctgcagtgga gcagcctgaa ggcctcggac accgccatgt attactgtgc gagaca 296

<210> 1227
<211> 287
<212> DNA
<213> Homo sapiens

<400> 1227
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atcacttgcc gggcaagtca gggcattaga aatgatttag gctggtatca gcagaaacca 120

gggaaagccc ctaagcgcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180

aggttcagcg gcagtggatc tgggacagaa ttcactctca caatcagcag cctgcagcct 240

gaagatttg caacttatta ctgtctacag cataatagtt acccctcc 287

<210> 1228
<211> 287
<212> DNA
<213> Homo sapiens

<400> 1228
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atcacttgcc gggcgagtca gggcattagc aattatttag cctggtatca gcagaaacca 120

gggaaagttc ctaagctcct gatctatgct gcatccactt tgcaatcagg ggtcccatct 180

cggttcagtg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct 240

gaagatgttg caacttatta ctgtcaaaag tataacagtg ccctcc 287

<210> 1229
<211> 287
<212> DNA
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<400> 1229
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atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180

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gaagatttg caacttacta ctgtcaacag agttacagta ccctcc 287

<210> 1230
<211> 287
<212> DNA
<213> Homo sapiens

<400> 1230
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gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagtgg ggtcccatca 180

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gaagattttg caacttacta ctgtcaacag agttacagta ccctcc 287

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<211> 287
<212> DNA
<213> Homo sapiens

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gggaaagccc ctaagctcct gatctatgag gcgtctagtt tagaaagtgg ggtcccatca 180

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gatgattttg caacttatta ctgccaacag tataatagtt attctcc 287

<210> 1232
<211> 302
<212> DNA
<213> Homo sapiens

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atctcctgca ggtctagtca aagcctcgta cacagtgatg gaaacacctа ctgaattgg 120

tttcagcaga ggccaggcca atctccaagg cgcctaattt ataaggtttc taaccgggac 180

tctggggtcc cagacagatt cagcggcagt gggtcaggca ctgatttcac actgaaaatc 240

agcagggtgg aggctgagga tgttggggtt tattactgca tgcaaggtac acactggcct 300

cc 302

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<212> DNA
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ggccaggctc ccaggctcct catctatgat gcatccaaca gggccactgg catcccagcc 180

aggttcagtg gcagtgggtc tgggacagac ttcactctca ccatcagcag cctagagcct 240

gaagattttg cagtttatta ctgtcagcag cgtagcaact ggcctcc 287

<210> 1234
<211> 287
<212> DNA
<213> Homo sapiens

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ggccaggctc ccaggctcct catctatggt gcatccacca gggccactgg tatcccagcc 180

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gaagatttg cagttattac tgtcagcag tataataact ggcctcc 287

<210> 1235
<211> 290
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<213> Homo sapiens

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cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180

gacaggttca gtggcagtgg gtctgggaca gacttcactc tcaccatcag cagactggag 240

cctgaagatt ttgcagtgta ttactgtcag cagtatggta gctcacctcc 290

<210> 1236
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<212> DNA
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atcaactgca agtccagcca gagtgttttа tacagctcca acaataagaa ctacttagct 120

tggtaccagc agaaaccagg acagcctcct aagctgctca tttactgggc atctacccgg 180

gaatccgggg tccctgaccg attcagtggc agcgggtctg ggacagattt cactctcacc 240

atcagcagcc tgcaggctga agatgtggca gttattactg tcagcaatat ttatagtact 300

cctcc 305

<210> 1237
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<212> DNA
<213> Homo sapiens

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tcctgcactg ggagcagctc caacatcggg gcaggttatg atgtacactg gtaccagcag 120

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<210> 1238
<211> 296
<212> DNA
<213> Homo sapiens

<400> 1238
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tctgaggatg aggctgatta ttactgtgca gcatgggatg acagcctgaa tggtcc 296

<210> 1239
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<212> DNA
<213> Homo sapiens

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ccaggaacag cccccaaact cctcatctat gaaaataata agcgaccctc agggattcct 180

gaccgattct ctggctccaa gtctggcacg tcagccaccc tgggcatcac cggactccag 240

actggggacg aggccgatta ttactgcgga acatgggata gcagcctgag tgctgg 296

<210> 1240
<211> 297
<212> DNA
<213> Homo sapiens

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tcctgcactg gaaccagcag tgatgttggt ggttataact atgtctcctg gtaccaacag 120

cacccaggca aagcccccaa actcatgatt tatgatgtca gtaagcggcc ctcaggggtc 180

cctgatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

caggctgagg atgaggctga ttattactgc tgctcatatg caggcagcta cacttttc 297

<210> 1241
<211> 297
<212> DNA
<213> Homo sapiens

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tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtaccaacag 120

cacccaggca aagcccccaa actcatgatt tatgaggtca gtaatcggcc ctcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc 240

caggctgagg acgaggctga ttattactgc agctcatata caagcagcag cactctc 297

<210> 1242
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<212> DNA
<213> Homo sapiens

<400> 1242
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tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtaccaacag 120

cacccaggca aagcccccaa actcatgatt tatgaggtca gtaagcggcc ctcaggggtc 180

cctgatcgct tctctggctc caagtctggc aacacggcct ccctgaccgt ctctgggctc 240

caggctgagg atgaggctga ttattactgc agctcatatg caggcagcaa caatttc 297

<210> 1243
<211> 284
<212> DNA
<213> Homo sapiens

<400> 1243
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caggcccctg agttggtgat atacgaagat agtgagcggt accctggaat ccctgaacga 180

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<210> 1244
<211> 282
<212> DNA
<213> Homo sapiens

<400> 1244
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acctgctctg gagatgcatt gccaaagcaa tatgcttatt ggtaccagca gaagccaggc 120

caggcccctg tgctggtgat atatgaaagac agtgagaggc cctcagggat ccctgagcga 180

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gacgaggctg actattactg tcaatcagca gacagcagtg gt 282

<210> 1245
<211> 294
<212> DNA
<213> Homo sapiens

<400> 1245
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aaacctggac aagcacccag ggcactgatt tatagtacaa gcaacaaaca ctcctggacc 180

cctgcccggt tctcaggctc cctcctttgg ggcaaagctg ccctgacact gtcaggtgtg 240

cagcctgagg acgaggctga gtattactgc ctgctctact atggtggtgc tcag 294

<210> 1246
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<212> DNA
<213> Homo sapiens

<400> 1246
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aagcctggcc aagcccccag gacactgatt tatgatacaa gcaacaaaca ctcctggaca 180

cctgcccggt tctcaggctc cctcctttgg ggcaaagctg ccctgaccct ttcgggtgcg 240

cagcctgagg atgaggctga gtattactgc ttgctctcct atagtggtgc tcgg 294

<210> 1247
<211> 294
<212> DNA
<213> Homo sapiens

<400> 1247
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acctgtggct ccagcactgg agctgtcacc agtggtcatt atccctactg gttccagcag 120

aagcctggcc aagcccccag gacactgatt tatgatacaa gcaacaaaca ctcctggaca 180

cctgcccggt tctcaggctc cctcctttgg ggcaaagctg ccctgaccct tttgggtgcg 240

cagcctgagg atgaggctga gtattactgc ttgctctcct atagtggtgc tcgg 294

<210> 1248
<211> 317
<212> DNA
<213> Homo sapiens

<400> 1248
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acctgcaccc tgagcagcgg ctacagtaat tatataagtg gactggtacca gcagagacca 120

gggaagggcc cccggttttgt gatgcgagtg ggcactggtg ggattgtggg atccaagggg 180

gatggcatcc ctgatcgctt ctcagtcttg ggctcaggcc tgaatcggta cctgaccatc 240

aagaacatcc aggaagagga tgagagtgac taccactgtg gggcagacca tggcagtggg 300

agcaacttcg tgtaacc 317

<210> 1249
<211> 317
<212> DNA
<213> Homo sapiens

<400> 1249
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acctgcaccc tgagcagcgg ctacagtaat tatataagtg gactggtacca gcagagacca 120

gggaagggcc cccgatttgt gatgcgagtg ggcactggtg ggattgtggg atccaagggg 180

gatggcatcc ctgatcgctt ctcagtcttg ggctcaggcc tgaatcggta cctgaccatc 240

aagaacatcc aggaagagga tgagagtgac taccactgtg gggcagacca tggcagtggg 300

agcaacttcg tgtaacc 317

<210> 1250
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<212> PRT
<213> Influenza A virus

<400> 1250

Pro Gln Arg Glu Gly Gly Arg Arg Arg Lys Arg
1 5 10

<210> 1251
<211> 6
<212> PRT
<213> Influenza A virus

<400> 1251

Pro Gln Thr Glu Thr Arg
1 5

<210> 1252
<211> 13
<212> PRT
<213> Homo sapiens

<400> 1252

Thr Gly Ser Ser Ser Asn Ile Ala Ala Asn Tyr Val Gln
1 5 10

<210> 1253
<211> 14
<212> PRT
<213> Homo sapiens

<400> 1253

Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Ser Val Ser
1 5 10

<210> 1254
<211> 13
<212> PRT
<213> Homo sapiens

<400> 1254

Thr Gly Asn Ser Asn Asn Val Gly Asn Gln Gly Ala Ala
1 5 10

<210> 1255
<211> 13
<212> PRT
<213> Homo sapiens

<400> 1255

Thr Gly Asn Ser Asn Asn Val Gly His Gln Gly Thr Ala
1 5 10

<210> 1256
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1256

Gly Gly Asn Asn Ile Gly Gly Tyr Ser Val His

1 5 10

<210> 1257
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1257

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1 5 10

<210> 1258
<211> 12
<212> PRT
<213> Homo sapiens

<400> 1258

Arg Ala Ser Gln Ser Leu Ser Ser Lys Tyr Leu Ala
1 5 10

<210> 1259
<211> 13
<212> PRT
<213> Homo sapiens

<400> 1259

Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Val Asn
1 5 10

<210> 1260
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1260

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 1261
<211> 13
<212> PRT
<213> Homo sapiens

<400> 1261

Ser Gly Gly Thr Ser Asn Ile Gly Arg Asn His Val Asn
1 5 10

<210> 1262
<211> 12
<212> PRT
<213> Homo sapiens

<400> 1262

Thr Leu Ser Ser Gly His Ser Asn Tyr Ile Ile Ala
1 5 10

<210> 1263
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1263

Gly Ile Ile Pro Met Phe Gly Thr Pro Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1264
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<212> PRT
<213> Homo sapiens

<400> 1264

Gly Val Ile Pro Leu Phe Arg Thr Ala Ser Tyr Ala Gln Asn Val Gln
1 5 10 15

Asn

<210> 1265
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<212> PRT
<213> Homo sapiens

<400> 1265

Gly Ile Thr Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1266
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1266

Gly Ile Ser Pro Met Phe Gly Thr Pro Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1267
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1267

Gly Ile Ile Gly Val Phe Gly Val Pro Lys Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1268
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1268

Trp Ile Asn Pro Met Thr Gly Gly Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Val

<210> 1269
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1269

Gly Ile Ser Pro Ile Phe Arg Thr Pro Lys Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1270
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1270

Gly Ile Ser Pro Ile Phe Arg Thr Pro Lys Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1271
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1271

Gly Ile Ile Pro Ile Phe Gly Lys Pro Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 1272
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1272

Ser Asn Ser Asp Arg Pro Ser
1 5

<210> 1273
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1273

Glu Asp Asp Arg Arg Pro Ser
1 5

<210> 1274
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1274

Glu Val Thr Lys Arg Pro Ser
1 5

<210> 1275
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1275

Arg Asn Asn Asp Arg Pro Ser
1 5

<210> 1276
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1276

Arg Asn Gly Asn Arg Pro Ser
1 5

<210> 1277
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1277

Asp Asp Lys Asp Arg Pro Ser
1 5

<210> 1278
<211> 7

<212> PRT
<213> Homo sapiens

<400> 1278

Asp Ala Ser Asn Arg Ala Thr
1 5

<210> 1279
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1279

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 1280
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1280

Ser Asn Asn Gln Arg Pro Ser
1 5

<210> 1281
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1281

Ala Ala Ser Ser Leu Gln Arg
1 5

<210> 1282
<211> 7
<212> PRT
<213> Homo sapiens

<400> 1282

Ser Asn Glu Gln Arg Pro Ser
1 5

<210> 1283
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1283

Val Asn Ser Asp Gly Ser His Thr Lys Gly Asp
1 5 10

<210> 1284
<211> 12
<212> PRT
<213> Homo sapiens

<400> 1284

Ser Ser Gly Tyr Tyr Tyr Gly Gly Gly Phe Asp Val
1 5 10

<210> 1285
<211> 13
<212> PRT
<213> Homo sapiens

<400> 1285

Ser Ser Gly Tyr His Phe Gly Arg Ser His Phe Asp Ser
1 5 10

<210> 1286
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1286

Gly Leu Tyr Tyr Tyr Glu Ser Ser Leu Asp Tyr
1 5 10

<210> 1287
<211> 15
<212> PRT
<213> Homo sapiens

<400> 1287

Ser Pro Ser Tyr Ile Cys Ser Gly Gly Thr Cys Val Phe Asp His
1 5 10 15

<210> 1288
<211> 12
<212> PRT
<213> Homo sapiens

<400> 1288

Glu Pro Gly Tyr Tyr Gly Lys Asn Gly Phe Asp Val
1 5 10

<210> 1289
<211> 17
<212> PRT
<213> Homo sapiens

<400> 1289

Gly Ala Ser Val Leu Arg Tyr Phe Asp Trp Gln Pro Glu Ala Leu Asp
1 5 10 15

Ile

<210> 1290
<211> 14

<212> PRT
<213> Homo sapiens

<400> 1290

Thr Leu Ser Ser Tyr Gln Pro Asn Asn Asp Ala Phe Ala Ile
1 5 10

<210> 1291
<211> 14
<212> PRT
<213> Homo sapiens

<400> 1291

Thr Leu Ser Ser Tyr Gln Pro Asn Asn Asp Ala Phe Ala Ile
1 5 10

<210> 1292
<211> 14
<212> PRT
<213> Homo sapiens

<400> 1292

Asp Ser Asp Ala Tyr Tyr Tyr Gly Ser Gly Gly Met Asp Val
1 5 10

<210> 1293
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1293

Gln Ser Tyr Asp Ser Leu Ser Ala Tyr Val
1 5 10

<210> 1294
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1294

Gln Thr Tyr Asp Thr Asn Asn His Ala Val
1 5 10

<210> 1295
<211> 10
<212> PRT
<213> Homo sapiens

<400> 1295

Cys Ser Tyr Ala Gly His Ser Ala Tyr Val
1 5 10

<210> 1296
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1296

Ser Thr Trp Asp Ser Ser Leu Ser Ala Val Val
1 5 10

<210> 1297
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1297

Ser Val Trp Asp Ser Ser Leu Ser Ala Trp Val
1 5 10

<210> 1298
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1298

Gln Val Trp Asp Ser Gly Asn Asp Arg Pro Leu
1 5 10

<210> 1299
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1299

Gln Gln Tyr Gly Ser Ser Pro Gln Phe
1 5

<210> 1300
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1300

Gln Gln Tyr Asp Gly Val Pro Arg Thr
1 5

<210> 1301
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1301

Gln Ser Tyr Asp Ser Arg Leu Ser Ala Ser Leu
1 5 10

<210> 1302
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1302

Gln Gln Tyr Asp Ser Ser Pro Tyr Thr
1 5

<210> 1303
<211> 11
<212> PRT
<213> Homo sapiens

<400> 1303

Ala Ser Trp Asp Asp Asn Leu Ser Gly Trp Val
1 5 10

<210> 1304
<211> 9
<212> PRT
<213> Homo sapiens

<400> 1304

Glu Thr Trp Asp Thr Lys Ile His Val
1 5

<210> 1305
<211> 369
<212> DNA
<213> Homo sapiens

<400> 1305
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tcctgcaagg cttctggagg caccttcagt gacaatgcta tcagctgggt gcgacaggcc 120

ccaggacaag ggcttgagtg gatgggggggc atcattccta tctttggaaa accaaactac 180

gcacagaagt tccagggcag agtcacgatt actgcggacg aatccacgag cacagcctac 240

atggacctga ggagcctgag atctgaggac acggccgttt attactgtgc gagagattca 300

gacgcgtatt actatggttc ggggggtatg gacgtctggg gccaaggcac cctggtcacc 360

gtctcctca 369

<210> 1306
<211> 335
<212> DNA
<213> Homo sapiens

<400> 1306
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acctgcactc tgagcagtgg gcatagtaac tacatcatcg catggcatca acagcagcca 120

gggaaggccc ctcggtactt gatgaaggtt aatagtgatg gcagccacac caagggggac 180

gggatccctg atcgcttctc aggctccagc tctggggctg accgctacct caccatctcc 240

aacctccagt ctgaggatga ggctagttat ttctgtgaga cctgggacac taagattcat 300

gtcttcggaa ctgggaccaa ggtctccgtc ctcag 335

<210> 1307

<211> 123
<212> PRT
<213> Homo sapiens

<400> 1307

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Asp Asn
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Lys Pro Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Asp Leu Arg Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Ser Asp Ala Tyr Tyr Tyr Gly Ser Gly Gly Met Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 1308
<211> 111
<212> PRT
<213> Homo sapiens

<400> 1308

Leu Pro Val Leu Thr Gln Ser Ser Ser Ala Ser Ala Ser Leu Gly Ser
1 5 10 15

Ser Val Lys Leu Thr Cys Thr Leu Ser Ser Gly His Ser Asn Tyr Ile
20 25 30

Ile Ala Trp His Gln Gln Gln Pro Gly Lys Ala Pro Arg Tyr Leu Met
35 40 45

Lys Val Asn Ser Asp Gly Ser His Thr Lys Gly Asp Gly Ile Pro Asp
50 55 60

Arg Phe Ser Gly Ser Ser Ser Gly Ala Asp Arg Tyr Leu Thr Ile Ser
65 70 75 80

Asn Leu Gln Ser Glu Asp Glu Ala Ser Tyr Phe Cys Glu Thr Trp Asp
85 90 95

Thr Lys Ile His Val Phe Gly Thr Gly Thr Lys Val Ser Val Leu
100 105 110

<210> 1309
<211> 363
<212> DNA
<213> Homo sapiens

<400> 1309
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tcctgcaagg ctcctggagg tatcttcaac accaatgctt tcagctgggt ccgacaggcc 120

cctggacaag gtcttgagtg ggtgggaggg gtcatccctt tgtttcgaac agcaagctac 180

gcacagaacg tccagggcag agtcaccatt accgcggacg aatccacgaa cacagcctac 240

atggagctta ccagcctgag atctgcggac acggccgtgt attactgtgc gagaagtagt 300

ggttaccatt ttaggagtca ctttgactcc tggggcctgg gaaccctggt caccgtctcc 360

tca 363

<210> 1310
<211> 333
<212> DNA
<213> Homo sapiens

<400> 1310
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tcctgcaccg gcagcagtgg caacattgcc gccaactatg tgcagtggta ccaacaacgt 120

ccgggcagtg cccccactac tgtgatctat gaggatgacc gaagaccctc tggggtccct 180

gatcggttct ctggctccat cgacaggtcc tccaactctg cctccctcac catctcagga 240

ctgaagactg aggacgaggc tgactactac tgtcagactt atgataccaa caatcatgct 300

gtgttcggag gaggcaccca cctgaccgtc ctc 333

<210> 1311
<211> 363
<212> PRT
<213> Homo sapiens

<400> 1311

Cys Ala Gly Gly Thr Gly Cys Ala Gly Cys Thr Gly Gly Thr Gly Cys
1 5 10 15

Ala Ala Thr Cys Thr Gly Gly Gly Gly Cys Thr Gly Ala Gly Gly Thr
20 25 30

Gly Ala Ala Gly Ala Ala Gly Cys Cys Thr Gly Gly Gly Thr Cys Cys
35 40 45

Thr Cys Gly Gly Thr Gly Ala Ala Gly Gly Thr Cys Thr Cys Cys Thr
50 55 60

Gly Cys Ala Ala Gly Gly Cys Thr Cys Cys Thr Gly Gly Ala Gly Gly
65 70 75 80

Thr Ala Thr Cys Thr Thr Cys Ala Ala Cys Ala Cys Cys Ala Ala Thr
85 90 95

Gly Cys Thr Thr Thr Cys Ala Gly Cys Thr Gly Gly Gly Thr Cys Cys
100 105 110

Gly Ala Cys Ala Gly Gly Cys Cys Cys Cys Thr Gly Gly Ala Cys Ala
115 120 125

Ala Gly Gly Thr Cys Thr Thr Gly Ala Gly Thr Gly Gly Gly Thr Gly
130 135 140

Gly Gly Ala Gly Gly Gly Gly Thr Cys Ala Thr Cys Cys Cys Thr Thr
145 150 155 160

Thr Gly Thr Thr Thr Cys Gly Ala Ala Cys Ala Gly Cys Ala Ala Gly
165 170 175

Cys Thr Ala Cys Gly Cys Ala Cys Ala Gly Ala Ala Cys Gly Thr Cys
180 185 190

Cys Ala Gly Gly Gly Cys Ala Gly Ala Gly Thr Cys Ala Cys Cys Ala
195 200 205

Thr Thr Ala Cys Cys Gly Cys Gly Gly Ala Cys Gly Ala Ala Thr Cys
210 215 220

Cys Ala Cys Gly Ala Ala Cys Ala Cys Ala Gly Cys Cys Thr Ala Cys
225 230 235 240

Ala Thr Gly Gly Ala Gly Cys Thr Thr Ala Cys Cys Ala Gly Cys Cys
245 250 255

Thr Gly Ala Gly Ala Thr Cys Thr Gly Cys Gly Gly Ala Cys Ala Cys
260 265 270

Gly Gly Cys Cys Gly Thr Gly Thr Ala Thr Thr Ala Cys Thr Gly Thr
275 280 285

Gly Cys Gly Ala Gly Ala Ala Gly Thr Ala Gly Thr Gly Gly Thr Thr
290 295 300

Ala Cys Cys Ala Thr Thr Thr Thr Ala Gly Gly Ala Gly Thr Cys Ala
305 310 315 320

Cys Thr Thr Thr Gly Ala Cys Thr Cys Cys Thr Gly Gly Gly Gly Cys
325 330 335

Cys Thr Gly Gly Gly Ala Ala Cys Cys Cys Thr Gly Gly Thr Cys Ala
340 345 350

Cys Cys Gly Thr Cys Thr Cys Cys Thr Cys Ala
355 360

<210> 1312
<211> 330
<212> DNA
<213> Homo sapiens

<400> 1312
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tcttgttctg gaggcacctc caacatcgga cgtaatcatg ttaactggta ccagcaactc 120

ccaggaacgg cccccaaact cctcatctat agtaatgaac agcggccctc aggggtccct 180

gaccgattct ctggctccaa atctggcacc tccgcctccc tggccgtgag tgggctccag 240

tctgaggatg aggctgatta ttactgtgca tcatgggatg acaacttgag tggttgggtg 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> 1313
<211> 121
<212> PRT
<213> Homo sapiens

<400> 1313

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Pro Gly Gly Ile Phe Asn Thr Asn
20 25 30

Ala Phe Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Val
35 40 45

Gly Gly Val Ile Pro Leu Phe Arg Thr Ala Ser Tyr Ala Gln Asn Val
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Leu Thr Ser Leu Arg Ser Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Ser Gly Tyr His Phe Arg Ser His Phe Asp Ser Trp Gly
100 105 110

Leu Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 1314
<211> 111

<212> PRT
<213> Homo sapiens

<400> 1314

Asn Phe Met Leu Thr Gln Pro His Ser Val Ser Ala Ser Pro Gly Lys
1 5 10 15

Thr Val Thr Ile Ser Cys Thr Gly Ser Ser Gly Asn Ile Ala Ala Asn
20 25 30

Tyr Val Gln Trp Tyr Gln Gln Arg Pro Gly Ser Ala Pro Thr Thr Val
35 40 45

Ile Tyr Glu Asp Asp Arg Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Ile Asp Arg Ser Ser Asn Ser Ala Ser Leu Thr Ile Ser Gly
65 70 75 80

Leu Lys Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Thr Tyr Asp Thr
85 90 95

Asn Asn His Ala Val Phe Gly Gly Gly Thr His Leu Thr Val Leu
100 105 110

<210> 1315
<211> 110
<212> PRT
<213> Homo sapiens

<400> 1315

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Ala Ser Gly Lys His Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Gly Thr Ser Asn Ile Gly Arg Asn
20 25 30

His Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Asn Glu Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Val Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Trp Asp Asp Asn Leu
85 90 95

Ser Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 1316
<211> 361
<212> DNA
<213> Homo sapiens

<400> 1316
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tcctgcaagg cttctggagg caccttcagc gcttatgctt tcacctgggt gcggcaggcc 120

cctggacaag ggcttgagtg gatgggaggc atcaccggaa tgttggcac agcaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aactcacgag cacagcctac 240

atggagttga gctccctgac atctgaagac acggccctt attattgtgc gagaggattg 300

tattactatg agagtagtct tgacttttgg ggccagggaa ccctggtcac cgtctcctca 360

g 361

<210> 1317
<211> 330
<212> DNA
<213> Homo sapiens

<400> 1317
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tcctgcactg gaaccagcag tgacgttggt ggttatAACT ctgtctcctg gtaccaacag 120

cacccaggca aagcccccaa actcatgatt tatgaggtca ctaagcggcc tcaggggtc 180

cctgatcgct tctctggctc caagtctggc aacacggcct ccctgaccgt ctctgggctc 240

caggctgagg atgaggctga ttattactgc tgctcatatg caggccacag tgcttatgtc 300

ttcggaactg ggaccaaggt caccgtcctg 330

<210> 1318
<211> 361
<212> DNA
<213> Homo sapiens

<400> 1318
caggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaggg cttctggagg caccttcagc gcttatgctt tcacctgggt gcggcaggcc 120

cctggacaag ggcttgagtg gatgggaggc atcaccggaa tgttggcac agcaaactac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aactcacgag cacagcctac 240

atggagttga gctccctgac atctgaagac acggccctt attattgtgc gagaggattg 300

tattactatg agagtagtct tgacttttgg ggccagggaa ccctggtcac cgtctcctca 360

g 361

<210> 1319
<211> 324
<212> DNA
<213> Homo sapiens

<400> 1319
gaaattgtgc tgactcagtc tccaggcacc ctgtctttgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gagtcttagc agcaagtact tagcctggta tcagcagaaa 120

cctggccagg ctcccaggct cctcatctat ggtgcatcca gcagggccac tggcatccca 180

gacaggttca gtggcagtgg gtctgggaca gacttcaccc tcaccatcag tagactggag 240

cctgaagatt ttgcagtgta ttcctgtcag cagtatgatg gcgtacctcg gacgttcggc 300

caagggacca cggtggaaat caaa 324

<210> 1320
<211> 120
<212> PRT
<213> Homo sapiens

<400> 1320

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ala Tyr
20 25 30

Ala Phe Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Thr Gly Met Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Leu Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ala Arg Gly Leu Tyr Tyr Tyr Glu Ser Ser Leu Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 1321
<211> 110
<212> PRT
<213> Homo sapiens

<400> 1321

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Ser Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Thr Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Ala Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Phe Cys Cys Ser Tyr Ala Gly His
85 90 95

Ser Ala Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 1322
<211> 108
<212> PRT
<213> Homo sapiens

<400> 1322

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 Leu Ser Ser Lys
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 Ser Cys Gln Gln Tyr Asp Gly Val Pro
85 90 95

Arg Thr Phe Gly Gln Gly Thr Thr Val Glu Ile Lys
100 105

<210> 1323
<211> 372
<212> DNA
<213> Homo sapiens

<400> 1323
caggtgcagc tggtgcagtc aggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcacgt cctctgaagt caccttcagt agttttgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gctgggaggg atcagcccta tgttttggaac acctaattac 180

gcgcagaagt tccaaggcag agtcaccatt accgcggacc agtccacgag gacagcctac 240

atggacctga ggagcctgag atctgaggac acggccgtgt attattgtgc gagatctcct 300

tcttacattt gttctggtgg aacctgcgtc tttgaccatt ggggccaggg aaccctggtc 360

accgtctcct ca 372

<210> 1324
<211> 330
<212> DNA
<213> Homo sapiens

<400> 1324
cagcctgggc tgactcagcc accctcggtg tccaagggct tgagacagac cgccacactc 60

acctgcactg ggaacagcaa caatgttggc aaccaaggag cagcttggct gcagcagcac 120

cagggccacc ctcccaaact cctatcctac aggaataatg accggccctc agggatctca 180

gagagattct ctgcatccag gtcaggaaac acagcctccc tgaccattac tggactccag 240

cctgaggacg aggctgacta ttactgctca acatgggaca gcagcctcag tgctgtggta 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> 1325
<211> 372
<212> DNA
<213> Homo sapiens

<400> 1325
caggtacagc tgcagcagtc aggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcacgt cctctgaagt caccttcagt agttttgcta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gctgggaggg atcagcccta tgttttggaac acctaattac 180

gcgcagaagt tccaaggcag agtcaccatt accgcggacc agtccacgag gacagcctac 240

atggacctga ggagcctgag atctgaggac acggccgtgt attattgtgc gagatctcct 300

tcttacattt gttctggtgg aacctgcgtc tttgaccatt ggggccaggg aaccctggtc 360

accgtctcct ca 372

<210> 1326
<211> 321
<212> DNA
<213> Homo sapiens

<400> 1326
gacatccaga tgacccagtc tccatcctcc ctgtctctgcat ctgtaggaga cagagtcacc 60

atcacttgcc gggcaagtca gagcattagc agctatttaa attggtatca gcagaaacca 120

gggaaagccc ctaagctcct gatctatgct gcatccagtt tgcaaagagg ggtcccatca 180

aggttcagtg gcagtggatc tgggacagac ttcactctca ccattagcag cctgcagcct 240

gaagatttttg cagtgtatta ctgtcagcag tatgatagtt caccgtacac ttttggccag 300

gggaccaagg tagagatcaa a 321

<210> 1327
<211> 124
<212> PRT

<213> Homo sapiens

<400> 1327

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Thr Ser Ser Glu Val Thr Phe Ser Ser Phe
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Leu
35 40 45

Gly Gly Ile Ser Pro Met Phe Gly Thr Pro Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Gln Ser Thr Arg Thr Ala Tyr
65 70 75 80

Met Asp Leu Arg Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Ser Tyr Ile Cys Ser Gly Gly Thr Cys Val Phe Asp
100 105 110

His Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 1328
<211> 110
<212> PRT
<213> Homo sapiens

<400> 1328

Gln Pro Gly Leu Thr Gln Pro Pro Ser Val Ser Lys Gly Leu Arg Gln
1 5 10 15

Thr Ala Thr Leu Thr Cys Thr Gly Asn Ser Asn Asn Val Gly Asn Gln
20 25 30

Gly Ala Ala Trp Leu Gln Gln His Gln Gly His Pro Pro Lys Leu Leu
35 40 45

Ser Tyr Arg Asn Asn Asp Arg Pro Ser Gly Ile Ser Glu Arg Phe Ser
50 55 60

Ala Ser Arg Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Leu Gln
65 70 75 80

Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Thr Trp Asp Ser Ser Leu
85 90 95

Ser Ala Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu

100 105 110

<210> 1329
<211> 107
<212> PRT
<213> Homo sapiens

<400> 1329

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Arg 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 Val Tyr Tyr Cys Gln Gln Tyr Asp Ser Ser Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1330
<211> 366
<212> DNA
<213> Homo sapiens

<400> 1330
caggtgcagc tggtgcaatc tggggctgaa gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaaga cttctggagt caccttcagc agctatgcta tcagttgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaggg atcatcggtg tctttggtgt accaaagtac 180

gcgcagaact tccagggcag agtcacaatt accgcggaca aaccgacgag tacagtctac 240

atggagctga acagcctgag agctgaggac acggccgtgt attactgtgc gagagagccc 300

gggtactacg taggaaagaa tggttttgat gtctggggcc aagggacaat ggtcaccgtc 360

tcttca 366

<210> 1331
<211> 330
<212> DNA
<213> Homo sapiens

<400> 1331
tcctatgagc tgactcagcc accctcggtg tccaagggct tgagacagac cgccatactc 60

acctgcactg gagacagcaa caatgttggc caccaaggta cagcttggct gcaacaacac 120

cagggccacc ctcccaaact cctatcctac aggaatggca accggccctc agggatctca 180

gagagattct ctgcatccag gtcaggaaat acagcctccc tgaccattat tggactccag 240

cctgaggacg aggctgacta ctactgctca gtatgggaca gcagcctcag tgcctgggtg 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> 1332
<211> 122
<212> PRT
<213> Homo sapiens

<400> 1332

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 Thr Ser Gly Val Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Gly Val Phe Gly Val Pro Lys Tyr Ala Gln Asn Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Pro Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Pro Gly Tyr Tyr Val Gly Lys Asn Gly Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 1333
<211> 110
<212> PRT
<213> Homo sapiens

<400> 1333

Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val Ser Lys Gly Leu Arg Gln
1 5 10 15

Thr Ala Ile Leu Thr Cys Thr Gly Asp Ser Asn Asn Val Gly His Gln
20 25 30

Gly Thr Ala Trp Leu Gln Gln His Gln Gly His Pro Pro Lys Leu Leu
35 40 45

Ser Tyr Arg Asn Gly Asn Arg Pro Ser Gly Ile Ser Glu Arg Phe Ser
50 55 60

Ala Ser Arg Ser Gly Asn Thr Ala Ser Leu Thr Ile Ile Gly Leu Gln
65 70 75 80

Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Val Trp Asp Ser Ser Leu
85 90 95

Ser Ala Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 1334
<211> 378
<212> DNA
<213> Homo sapiens

<400> 1334
caggtgcagc tggtgcagtc tggggctgag gtgaggaagc ctggggcctc agtgaaggtc 60

tcatgtaagg cttctggata cacctcacc ggttattata ttcactgggt gcgacaggcc 120

cctggacaag gacttgagtg gatgggttgg atcaaccct a tgactggtgg cacaaactat 180

gcacagaagt ttcaggtctg ggtcaccatg acccgggaca cgtccatcaa cacagcctac 240

atggaggtga gcaggctgac atctgacgac acggccgtgt attactgtgc gagggggct 300

tccgtattac gatattttga ctggcagccc gaggctcttg atatctgggg cctcgggacc 360

acggtcaccg tctcctca 378

<210> 1335
<211> 324
<212> DNA
<213> Homo sapiens

<400> 1335
cagcctgtgc tgactcagcc accctcggtg tcagtggccc caggacagac ggccagcatt 60

ccctgtgggg ggaacaacat tggaggctac agtgtacact ggtaccaaca aaagccgggc 120

caggcccccc tcttggtcat ttatgacgat aaagaccggc cctcagggat ccctgagcga 180

ttctctggcg ccaactctgg gagcacggcc accctgacaa tcagcagggt cgaagccggg 240

gatgagggcg actactactg tcaggtgtgg gatagtggta atgatcgtcc gctgttcggc 300

ggagggacca agctgaccgt ccta 324

<210> 1336
<211> 126
<212> PRT
<213> Homo sapiens

<400> 1336

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Arg 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 Met Thr Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Val Trp Val Thr Met Thr Arg Asp Thr Ser Ile Asn Thr Ala Tyr
65 70 75 80

Met Glu Val Ser Arg Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Ala Ser Val Leu Arg Tyr Phe Asp Trp Gln Pro Glu Ala
100 105 110

Leu Asp Ile Trp Gly Leu Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 1337
<211> 108
<212> PRT
<213> Homo sapiens

<400> 1337

Gln Pro Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Ser Ile Pro Cys Gly Gly Asn Asn Ile Gly Gly Tyr Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Tyr
35 40 45

Asp Asp Lys Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ala
50 55 60

Asn Ser Gly Ser Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly
65 70 75 80

Asp Glu Gly Asp Tyr Tyr Cys Gln Val Trp Asp Ser Gly Asn Asp Arg
85 90 95

Pro Leu Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 1338
<211> 369
<212> DNA
<213> Homo sapiens

<400> 1338

caggtgcagc tggtgcagtc tggggctgaa gtgaagaagc ctggcctcctc ggtgaaggtt 60

tcctgcaagg cttctggagg cccctt cagc atgactgctt tcacctggct gcgacaggcc 120

cctggacaag ggcttgagtg gatgggtggg atcagccctta tctttcgtac accgaagtac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatccacgaa cacagccaac 240

atggagctga ccagcctgaa atctgaggac acggccgtgt attactgtgc gagaaccctt 300

tcctcctacc aaccgaataa tgatgctttt gctatctggg gccaagggac aatggtcacc 360

gtctcttca 369

<210> 1339
<211> 318
<212> DNA
<213> Homo sapiens

<400> 1339
gaaattgtgt tgacgcagtc tccagccacc ctgtctttgt ctccagggga aagagccacc 60

ctctcctgca gggccagtca gagtgttagc agcttacttag cctggtacca acagaaacct 120

ggccaggctc ccaggctcct catctatgat gcatccaaca gggccactgg catcccagcc 180

aggttcagtg gcagtgggtc tgggacagac ttcactctca ccatcagcag actggagcct 240

gaagattttg cagtctattt ctgtcagcag tatggtagct cacctcaatt cggccaaggg 300

acacgactgg agattaaa 318

<210> 1340
<211> 123
<212> PRT
<213> Homo sapiens

<400> 1340

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Ser Met Thr
20 25 30

Ala Phe Thr Trp Leu Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ser Pro Ile Phe Arg Thr Pro Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Asn
65 70 75 80

Met Glu Leu Thr Ser Leu Lys Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Thr Leu Ser Ser Tyr Gln Pro Asn Asn Asp Ala Phe Ala Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 1341
<211> 106
<212> PRT
<213> Homo sapiens

<400> 1341

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 Arg Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Tyr Gly Ser Ser Pro Gln
85 90 95

Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 1342
<211> 369
<212> DNA
<213> Homo sapiens

<400> 1342
caggtgcagc tggtgcagtc tggggctgaa gtgaagaagc ctggcctcct ggtgaaggtt 60

tcctgcaagg cttctggagg ccccttcagc atgactgctt tcacctggct gcgacaggcc 120

cctggacaag ggcttgagtg gatgggtggg atcagcccta tctttcgtac accgaagtac 180

gcacagaagt tccagggcag agtcacgatt accgcggacg aatccacgaa cacagccaac 240

atggagctga ccagcctgaa atctgaggac acggccgtgt attactgtgc gagaaccctt 300

tcctcctacc aaccgaataa tgatgctttt gctatctggg gccaagggac aatggtcacc 360

gtctcttca 369

<210> 1343
<211> 330
<212> DNA
<213> Homo sapiens

<400> 1343
ctgcctgtgc tgactcagcc accctcagcg tctgggaccc ccgggcagag ggtcaccatc 60

tcttgttctg gaagcagctc caacatcgga agtaatactg taaactggta ccagcagctc 120

ccaggaacgg cccccaaact cctcatctat agtaataatc agcggccctc aggggtccct 180

gaccgattct ctggctccag gtcaggcacc tcagcctccc tggccatcat tggactccgg 240

cctgaggatg aagctgatta ttactgtcag tcgtatgaca gcaggctcag tgcttctctc 300

ttcggaactg ggaccacggt caccgtcctc 330

<210> 1344
<211> 123
<212> PRT
<213> Homo sapiens

<400> 1344

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Pro Phe Ser Met Thr
20 25 30

Ala Phe Thr Trp Leu Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ser Pro Ile Phe Arg Thr Pro Lys Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Asn
65 70 75 80

Met Glu Leu Thr Ser Leu Lys Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Thr Leu Ser Ser Tyr Gln Pro Asn Asn Asp Ala Phe Ala Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 1345
<211> 110
<212> PRT
<213> Homo sapiens

<400> 1345

Leu Pro Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Arg Ser Gly Thr Ser Ala Ser Leu Ala Ile Ile Gly Leu Arg
65 70 75 80

Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Arg Leu
85 90 95

Ser Ala Ser Leu Phe Gly Thr Gly Thr Thr Val Thr Val Leu
100 105 110