(12) STANDARD PATENT (11) Application No. **AU 2017238168 B2**
(19) AUSTRALIAN PATENT OFFICE

(54) Title
DNA antibody constructs and method of using same

(51) International Patent Classification(s)
A61K 39/00 (2006.01) ***C12N 9/64*** (2006.01)
C12N 9/48 (2006.01)

(21) Application No: **2017238168** (22) Date of Filing: **2017.03.21**

(87) WIPO No: **WO17/165460**

(30) Priority Data

(31) Number	(32) Date	(33) Country
62/396,748	**2016.09.19**	**US**
62/396,750	**2016.09.19**	**US**
62/417,093	**2016.11.03**	**US**
62/332,381	**2016.05.05**	**US**
62/311,316	**2016.03.21**	**US**
62/376,162	**2016.08.17**	**US**
62/429,454	**2016.12.02**	**US**
62/429,473	**2016.12.02**	**US**

(43) Publication Date: **2017.09.28**
(44) Accepted Journal Date: **2024.06.13**

(71) Applicant(s)
David B. Weiner;Karuppiah Muthumani;Seleeke Flingai;Niranjan Sardesai;Sarah Elliott;Jian Yan;Ami Patel

(72) Inventor(s)
Weiner, David B.;Muthumani, Karuppiah;Flingai, Seleeke;Sardesai, Niranjan;Elliott, Sarah;Yan, Jian;Patel, Ami

(74) Agent / Attorney
FB Rice Pty Ltd, L 23 44 Market St, Sydney, NSW, 2000, AU

(56) Related Art
CN 1480215 A

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

CORRECTED VERSION

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
28 September 2017 (28.09.2017)

WIPO | PCT

(10) International Publication Number
WO 2017/165460 A9

(51) International Patent Classification:
A61K 39/00 (2006.01) *C12N 9/64* (2006.01)
C12N 9/48 (2006.01)

(21) International Application Number:
PCT/US2017/023479

(22) International Filing Date:
21 March 2017 (21.03.2017)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

62/311,316	21 March 2016 (21.03.2016)	US
62/332,381	05 May 2016 (05.05.2016)	US
62/376,162	17 August 2016 (17.08.2016)	US
62/396,748	19 September 2016 (19.09.2016)	US
62/396,750	19 September 2016 (19.09.2016)	US
62/417,093	03 November 2016 (03.11.2016)	US
62/429,454	02 December 2016 (02.12.2016)	US
62/429,473	02 December 2016 (02.12.2016)	US

(72) Inventors; and

(71) Applicants: **WEINER, David, B.** [US/US]; 717 Beacom Lane, Merion, PA 19066 (US). **MUTHUMANI, Karuppiah** [US/US]; 52 Ivy Lane, Cherry Hill, NJ 08002 (US). **FLINGAI, Seleeke** [US/US]; 1623 Penn Avenue North, Minneapolis, MN 55411 (US). **SARDESAI, Niranjan** [US/US]; 480 Mallard Circle, Blue Bell, PA 19422 (US). **ELLIOTT, Sarah** [US/US]; P.O. Box 301, Pullman, WA 99163 (US). **YAN, Jian** [US/US]; 503 Sheffield Drive, Wallingford, PA 19086 (US). **PATEL, Ami** [US/US]; 1 Rainey Court, Philadelphia, PA 19103 (US).

(74) Agent: **SLAUGHTER, Alison P.** et al.; Riverside Law, LLP, Glenhardie Corporate Center, 1285 Drummers Lane, Suite 202, Wayne, PA 19087 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*
— *with sequence listing part of description (Rule 5.2(a))*

(48) Date of publication of this corrected version:
09 November 2017 (09.11.2017)

(15) Information about Correction:
see Notice of 09 November 2017 (09.11.2017)

(54) Title: DNA ANTIBODY CONSTRUCTS AND METHOD OF USING SAME

(57) Abstract: Disclosed herein is a composition comprising the combination of a nucleic acid sequence encoding a desired polypeptide that elicits an immune response in a mammal and a nucleic acid sequence encoding an antibody, a fragment thereof, a variant thereof, or a combination thereof.

WO 2017/165460 A9

DNA ANTIBODY CONSTRUCTS AND METHOD OF USING SAME

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application claims priority to U.S. Provisional Application No. 62/311,316, filed March 21, 2016, U.S. Provisional Application No. 62/396,748, filed September 19, 2016, U.S. Provisional Application No. 62/396,750, filed September 19, 2016, U.S. Provisional Application No. 62/417,093, filed November 3, 2016, U.S. Provisional Application No 62/332,381, filed May 4, 2016, U.S. Provisional Application No 62/376,162, filed August 17, 2016, U.S. Provisional Application No 62/429,454, filed December 2, 2016, and U.S. Provisional Application No 62/429,473, filed December 2, 2016, each of which is hereby incorporated by reference in its entirety

TECHNICAL FIELD

[0002] The present invention relates to a combination of a DNA vaccine with a composition comprising a recombinant nucleic acid sequence for generating one or more synthetic antibodies, and functional fragments thereof, *in vivo.* The compositions of the invention provide improved methods for inducing immune responses, and for prophylactically and/or therapeutically immunizing individuals against an antigen.

BACKGROUND

[0003] The immunoglobulin molecule comprises two of each type of light (L) and heavy (H) chain, which are covalently linked by disulphide bonds (shown as S-S) between cysteine residues. The variable domains of the heavy chain (VH) and the light chain (VL) contribute to the binding site of the antibody molecule. The heavy-chain constant region is made up of three constant domains (CH1, CH2 and CH3) and the (flexible) hinge region. The light chain also has a constant domain (CL). The variable regions of the heavy and light chains comprise four framework regions (FRs; FR1, FR2, FR3 and FR4) and three complementarity-determining regions (CDRs; CDR1, CDR2 and CDR3). Accordingly, these are very complex genetic systems that have been difficult to assemble *in vivo.*

[0004] Targeted monoclonal antibodies (mAbs) represent one of the most important medical therapeutic advances of the last 25 years. This type of immune based therapy is now used routinely against a host of autoimmune diseases, treatment of cancer as well as infectious diseases. For malignancies, many of the immunoglobulin (Ig) based therapies currently used are in combination with cytotoxic chemotherapy regimens directed against tumors. This combination approach has significantly improved overall survival. Multiple mAb preparations are licensed for use against specific cancers, including Rituxan (Rituximab), a chimeric mAb targeting CD20 for the treatment of Non-Hodgkins lymphoma and Ipilimumab (Yervoy), a human mAb that blocks CTLA-4 and which has been used for the treatment of melanoma and other malignancies. Additionally, Bevacizumab (Avastin) is another prominent humanized mAb that targets VEGF and tumor neovascularization and has been used for the treatment of colorectal cancer. Perhaps the most high profile mAb for treatment of a malignancy is Trastuzumab (Herceptin), a humanized preparation targeting Her2/neu that has been demonstrated to have considerable efficacy against breast cancer in a subset of patients. Furthermore, a host of mAbs are in use for the treatment of autoimmune and specific blood disorders.

[0005] In addition to cancer treatments, passive transfer of polyclonal Igs mediate protective efficacy against a number of infectious diseases including diphtheria, hepatitis A and B, rabies, tetanus, chicken-pox and respiratory syncytial virus (RSV). In fact, several polyclonal Ig preparations provide temporary protection against specific infectious agents in individuals traveling to disease endemic areas in circumstances when there is insufficient time for protective Igs to be generated through active vaccination. Furthermore, in children with immune deficiency the Palivizumab (Synagis), a mAb, which targets RSV infection, has been demonstrated to clinically protect against RSV.

[0006] Currently available therapeutic antibodies that exist in the market are human IgG1 isotypes. These antibodies include glycoproteins bearing two N-linked biantennary complex-type oligosaccharides bound to the antibody constant region (Fc), in which a majority of the oligosaccharides are core-fucosylated. It exercises effector functions of antibody-dependent cellular toxicity (ADCC) and complement-dependent cytotoxicity (CDC) through the interaction of the Fc with either leukocyte receptors (FcγRs) or complement. There is a phenomena of reduced in vivo efficacy of therapeutic antibodies (versus in vitro), thus resulting in the need for large doses of therapeutic antibodies – sometimes weekly doses of several hundred milligrams.

This is mainly due to the competition between serum IgG and therapeutic antibodies for binding to FcγRIIIa on natural killer (NK) cells. Endogenous human serum IgG inhibits ADCC induced by therapeutic antibodies. Thus, there can be enhanced efficacy of non-fucosylated therapeutic antibodies in humans. Non-fucosylated therapeutic antibodies have much higher binding affinity for FcγRIIIa than fucosylated human serum IgG, which is a preferable character to conquer the interference by human plasma IgG.

[0007] Antibody based treatments are not without risks. One such risk is antibody-dependent enhancement (ADE), which occurs when non-neutralising antiviral proteins facilitate virus entry into host cells, leading to increased infectivity in the cells. Some cells do not have the usual receptors on their surfaces that viruses use to gain entry. The antiviral proteins (i.e., the antibodies) bind to antibody Fc receptors that some of these cells have in the plasma membrane. The viruses bind to the antigen binding site at the other end of the antibody. This virus can use this mechanism to infect human macrophages, causing a normally mild viral infection to become life-threatening. The most widely known example of ADE occurs in the setting of infection with the dengue virus (DENV). It is observed when a person who has previously been infected with one serotype of DENV becomes infected many months or years later with a different serotype. In such cases, the clinical course of the disease is more severe, and these people have higher viremia compared with those in whom ADE has not occurred. This explains the observation that while primary (first) infections cause mostly minor disease (DF) in children, secondary infection (re-infection at a later date) is more likely to be associated with severe disease (DHF and/or DSS) in both children and adults. There are four antigenically different serotypes of DENV (DENV-1 - DENV-4). Infection with DENV induces the production of neutralizing homotypic immunoglobulin G (IgG) antibodies which provide lifelong immunity against the infecting serotype. Infection with DENV also produces some degree of cross-protective immunity against the other three serotypes. In addition to inducing neutralizing heterotypic antibodies, infection with DENV can also induce heterotypic antibodies which neutralize the virus only partially or not at all. The production of such cross-reactive but non-neutralizing antibodies could be the reason for more severe secondary infections. Once inside the white blood cell, the virus replicates undetected, eventually generating very high virus titers which cause severe disease.

[0008] The clinical impact of mAb therapy is impressive. However, issues remain that limit the use and dissemination of this therapeutic approach. Some of these include the high cost of

production of these complex biologics that can limit their use in the broader population, particularly in the developing world where they could have a great impact. Furthermore, the frequent requirement for repeat administrations of the mAbs to attain and maintain efficacy can be an impediment in terms of logistics and patient compliance. New antibodies that would reduce or eliminate the low in vivo efficacy of therapeutic antibodies due to competition with serum IgGs are needed. New antibodies that can eliminate antibody dependent enhancement in viruses like Dengue, HIV, RSV and others are needed. Bispecific antibodies, bifunctional antibodies, and antibody cocktails are needed to perform several functions that could prove therapeutic or prophylactic. Combination therapies are needed as well that can utilize the synthetic antibodies described herein along with immunostimulating a host system through immunization with a vaccine, including a DNA based vaccine. Additionally, the long-term stability of these antibody formulations is frequently short and less than optimal. Thus, there remains a need in the art for a synthetic antibody molecule that can be delivered to a subject in a safe and cost effective manner.

SUMMARY

[0009] The present invention provides a combination of a composition that elicits an immune response in a mammal against an antigen with a composition comprising a recombinant nucleic acid sequence encoding an antibody, a fragment thereof, a variant thereof, or a combination thereof.

[0010] One aspect of the present invention provides nucleic acid constructs capable of expressing a polypeptide that elicits an immune response in a mammal against an antigen. The nucleic acid constructs are comprised of an encoding nucleotide sequence and a promoter operably linked to the encoding nucleotide sequence. The encoding nucleotide sequence expresses the polypeptide, wherein the polypeptide includes consensus antigens. The promoter regulates expression of the polypeptide in the mammal.

[0011] Another aspect of the present invention provides DNA plasmid vaccines that are capable of generating in a mammal an immune response against an antigen. The DNA plasmid vaccines are comprised of a DNA plasmid capable of expressing a consensus antigen in the

mammal and a pharmaceutically acceptable excipient. The DNA plasmid is comprised of a promoter operably linked to a coding sequence that encodes the consensus antigen.

[0012] Another aspect of the present invention provides methods of eliciting an immune response against an antigen in a mammal, comprising delivering a DNA plasmid vaccine to tissue of the mammal, the DNA plasmid vaccine comprising a DNA plasmid capable of expressing a consensus antigen in a cell of the mammal to elicit an immune response in the mammal, and electroporating cells of the tissue to permit entry of the DNA plasmids into the cells.

[0013] The present invention is directed to a method of generating a synthetic antibody in a subject. The method can comprise administering to the subject a composition comprising a recombinant nucleic acid sequence encoding an antibody or fragment thereof. The recombinant nucleic acid sequence can be expressed in the subject to generate the synthetic antibody.

[0014] The generated synthetic antibody may be defucosylated. The generated synthetic antibody may include two leucine to alanine mutations in a CH2 region of a Fc region.

[0015] The antibody can comprise a heavy chain polypeptide, or fragment thereof, and a light chain polypeptide, or fragment thereof. The heavy chain polypeptide, or fragment thereof, can be encoded by a first nucleic acid sequence and the light chain polypeptide, or fragment thereof, can be encoded by a second nucleic acid sequence. The recombinant nucleic acid sequence can comprise the first nucleic acid sequence and the second nucleic acid sequence. The recombinant nucleic acid sequence can further comprise a promoter for expressing the first nucleic acid sequence and the second nucleic acid sequence as a single transcript in the subject. The promoter can be a cytomegalovirus (CMV) promoter.

[0016] The recombinant nucleic acid sequence can further comprise a third nucleic acid sequence encoding a protease cleavage site. The third nucleic acid sequence can be located between the first nucleic acid sequence and second nucleic acid sequence. The protease of the subject can recognize and cleave the protease cleavage site.

[0017] The recombinant nucleic acid sequence can be expressed in the subject to generate an antibody polypeptide sequence. The antibody polypeptide sequence can comprise the heavy chain polypeptide, or fragment thereof, the protease cleavage site, and the light chain polypeptide, or fragment thereof. The protease produced by the subject can recognize and cleave the protease cleavage site of the antibody polypeptide sequence thereby generating a cleaved

heavy chain polypeptide and a cleaved light chain polypeptide. The synthetic antibody can be generated by the cleaved heavy chain polypeptide and the cleaved light chain polypeptide.

[0018] The recombinant nucleic acid sequence can comprise a first promoter for expressing the first nucleic acid sequence as a first transcript and a second promoter for expressing the second nucleic acid sequence as a second transcript. The first transcript can be translated to a first polypeptide and the second transcript can be translated into a second polypeptide. The synthetic antibody can be generated by the first and second polypeptide. The first promoter and the second promoter can be the same. The promoter can be a cytomegalovirus (CMV) promoter.

[0019] The heavy chain polypeptide can comprise a variable heavy region and a constant heavy region 1. The heavy chain polypeptide can comprise a variable heavy region, a constant heavy region 1, a hinge region, a constant heavy region 2 and a constant heavy region 3. The light chain polypeptide can comprise a variable light region and a constant light region.

[0020] The recombinant nucleic acid sequence can further comprise a Kozak sequence. The recombinant nucleic acid sequence can further comprise an immunoglobulin (Ig) signal peptide. The Ig signal peptide can comprise an IgE or IgG signal peptide.

[0021] The recombinant nucleic acid sequence can comprise a nucleic acid sequence encoding at least one amino acid sequence of SEQ ID NOs:1, 2, 5, 41, 43, 45, 46, 47, 48, 49, 51, 53, 55, 57, 59, 61, and 80. The recombinant nucleic acid sequence can comprise at least one nucleic acid sequence of SEQ ID NOs:3, 4, 6, 7, 40, 42, 44, 50, 52, 54, 56, 58, 60, 62, 63, and 79.

[0022] The present invention is also directed to a method of generating a synthetic antibody in a subject. The method can comprise administering to the subject a composition comprising a first recombinant nucleic acid sequence encoding a heavy chain polypeptide, or fragment thereof, and a second recombinant nucleic acid sequence encoding a light chain polypeptide, or fragment thereof. The first recombinant nucleic acid sequence can be expressed in the subject to generate a first polypeptide and the second recombinant nucleic acid can be expressed in the subject to generate a second polypeptide. The synthetic antibody can be generated by the first and second polypeptides.

[0023] The first recombinant nucleic acid sequence can further comprise a first promoter for expressing the first polypeptide in the subject. The second recombinant nucleic acid sequence can further comprise a second promoter for expressing the second polypeptide in the subject. The

first promoter and second promoter can be the same. The promoter can be a cytomegalovirus (CMV) promoter.

[0024] The heavy chain polypeptide can comprise a variable heavy region and a constant heavy region 1. The heavy chain polypeptide can comprise a variable heavy region, a constant heavy region 1, a hinge region, a constant heavy region 2 and a constant heavy region 3. The light chain polypeptide can comprise a variable light region and a constant light region.

[0025] The first recombinant nucleic acid sequence and the second recombinant nucleic acid sequence can further comprise a Kozak sequence. The first recombinant nucleic acid sequence and the second recombinant nucleic acid sequence can further comprise an immunoglobulin (Ig) signal peptide. The Ig signal peptide can comprise an IgE or IgG signal peptide.

[0026] The present invention is further directed to method of preventing or treating a disease in a subject. The method can comprise generating a synthetic antibody in a subject according to one of the above methods. The synthetic antibody can be specific for a foreign antigen. The foreign antigen can be derived from a virus. The virus can be Human immunodeficiency virus (HIV), Chikungunya virus (CHIKV) or Dengue virus.

[0027] The virus can be HIV. The recombinant nucleic acid sequence can comprise a nucleic acid sequence encoding at least one amino acid sequence of SEQ ID NOs:1, 2, 5, 46, 47, 48, 49, 51, 53, 55, and 57. The recombinant nucleic acid sequence can comprise at least one nucleic acid sequence of SEQ ID NOs: 3, 4, 6, 7, 50, 52, 55, 56, 62, and 63.

[0028] The virus can be CHIKV. The recombinant nucleic acid sequence can comprise a nucleic acid sequence encoding at least one amino acid sequence of SEQ ID NOs:59 and 61. The recombinant nucleic acid sequence can comprise at least one nucleic acid sequence of SEQ ID NOs: 58, 60, 97, 98, 99 and 100.

[0029] The virus can be Zika. The recombinant nucleic acid sequence can comprise a nucleic acid sequence encoding at least one amino acid sequence of SEQ ID NOs: 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 121, 122, 123, 125, 127, 129, 131, or 133. The recombinant nucleic acid sequence can comprise at least one nucleic acid sequence of SEQ ID NOs: 124, 126, 128, 130, or 132.

[0030] The virus can be Dengue virus. The recombinant nucleic acid sequence can comprise a nucleic acid sequence encoding at least one amino acid sequence of SEQ ID NO:45. The

recombinant nucleic acid sequence comprises at least one nucleic acid sequence of SEQ ID NO:44.

[0031] The synthetic antibody can be specific for a self-antigen. The self-antigen can be Her2. The recombinant nucleic acid sequence can comprise a nucleic acid sequence encoding at least one amino acid sequence of SEQ ID NOs:41 and 43. The recombinant nucleic acid sequence can comprise at least one nucleic acid sequence of SEQ ID NOs:40 and 42.

[0032] The synthetic antibody can be specific for a self-antigen. The self-antigen can be PSMA. The recombinant nucleic acid sequence can comprise a nucleic acid sequence encoding at least one amino acid sequence of SEQ ID NO:80. The recombinant nucleic acid sequence can comprise at least one nucleic acid sequence of SEQ ID NO:79.

[0033] The present invention is also directed to a product produced by any one of the above-described methods. The product can be a single DNA plasmid capable of expressing a functional antibody. The product can be comprised of two or more distinct DNA plasmids capable of expressing components of a functional antibody that combine in vivo to form a functional antibody.

[0034] The present invention is also directed to a method of treating a subject from infection by a pathogen, comprising: administering a nucleotide sequence encoding a synthetic antibody specific for the pathogen. The method can further comprise administering an antigen of the pathogen to generate an immune response in the subject.

[0035] The present invention is also directed to a method of treating a subject from cancer, comprising: administering a nucleotide sequence encoding a cancer marker to induce ADCC.

[0036] The present invention is also directed to a nucleic acid molecule encoding a synthetic antibody comprising a nucleic acid sequence having at least about 95% identity over an entire length of the nucleic acid sequence set forth in SEQ ID NO:79.

[0037] The present invention is also directed to a nucleic acid molecule encoding a synthetic antibody comprising a nucleic acid sequence as set forth in SEQ ID NO:79.

[0038] The present invention is also directed to a nucleic acid molecule encoding a synthetic antibody comprising a nucleic acid sequence encoding a protein having at least about 95% identity over an entire length of the amino acid sequence set forth in SEQ ID NO:80.

[0039] The present invention is also directed to a nucleic acid molecule encoding a synthetic antibody comprising a nucleic acid sequence encoding a protein comprising an amino acid sequence as set forth in SEQ ID NO:80.

[0040] Any one of the above-described nucleic acid molecules may comprise an expression vector.

[0041] The present invention is also directed to a composition comprising one or more of the above-described nucleic acid molecules. The composition may also include a pharmaceutically acceptable excipient.

BRIEF DESCRIPTION OF THE DRAWINGS

[0042] Figure 1, comprising Figure 1A through Figure 1D, depicts CVM1–immunoglobulin G (IgG) and CVM-1–Fab dMAb plasmid design and expression. Figure 1A depicts in vitro expression of CVM1-Fab. The CVM1-Fab, CVM1–variable heavy chain (VH), and CVM1–variable light chain (VL) constructs were transfected into 293T cells to determine in vitro expression through binding enzyme-linked immunosorbent assays (ELISAs). Samples were analyzed at 0, 24, and 48 hours post-transfection. Cells transfected with an empty backbone pVax1 plasmid served as a negative control. Figure 1B depicts In vitro expression of CVM1-IgG. The CVM1-IgG was transfected into 293T cells to determine in vitro expression through binding enzyme-linked immunosorbent assays (ELISAs). Samples were analyzed at 0, 24, and 48 hours post-transfection. Cells transfected with an empty backbone pVax1 plasmid served as a negative control. Figure 1C depicts in vivo expression of CVM1-IgG and CVM1-Fab. Mice (B6.Cg-Foxn1nu/J) aged 5–6 weeks received a single, 100-μg intramuscular injection of CVM1-IgG, CVM1-VH, CVM1-VL, or CVM1-Fab plasmids, followed by electroporation (5 mice per group). Injection of a pVax1 vector was used a negative control. Sera IgG levels were measured at various time points in mice injected intramuscularly. Figure 1D depicts experimental results demonstrating sera from CVM1-IgG–administered mice binds chikungunya virus (CHIKV) envelope protein (Env). ELISA plates were coated with recombinant CHIKV envelope or human immunodeficiency virus type 1 (HIV-1) (subtype B; MN) envelope protein, and sera obtained on day 15 from mice given a single injection of CVM1-IgG, CVM1-Fab, or pVax1 were tested.

[0043] Figure 2, comprising Figure 2A through Figure 2D, depicts binding analyses and neutralization activity of CVM1–immunoglobulin G (IgG) antibodies. Figure 2A depicts an immunofluorescence assay demonstrating that IgG generated from CVM1-IgG–administered mice was capable of binding to chikungunya virus (CHIKV) envelope protein (Env). CHIKV-infected Vero cells were fixed 24 hours after infection and evaluated by an immunofluorescence assay to detect CHIKV Env antigen expression (green). Cell nuclei were stained with DAPI (blue). Sera from control mice injected with pVax1 were used as a negative control. Figure 2B depicts binding affinity of sera from CVM1-IgG–injected mice (day 15) to target proteins. Binding was tested by Western blot, using cell lysates from CHIKV- or mock-infected cells. Protein transferred membranes were re-probed with antibody against β-actin as a loading control. The image presented here was cropped from an original image and is representative of several gels. Figure 2C depicts fluorescence-activated cell-sorting analysis of the binding of sera from plasmid-injected mice to CHIKV-infected cells. The x-axis indicates green fluorescent protein (GFP) staining, using the lentiviral GFP pseudovirus complemented with CHIKV Env. The y-axis demonstrates staining of infected cells by human IgG produced in mice 15 days after injection with CVM1-IgG. Staining with a control anti-CHIKV antibody (Env antibody) is also shown, as well as staining with no antibodies and pVax1. The presence and number of double-positive cells indicate presence and level of sera binding to the CHIKV-infected cells. Figure 2D depicts sera from mice injected with CVM1-IgG via electroporation possess neutralizing activity against multiple CHIKV strains (ie, Ross, LR2006-OPY1, IND-63-WB1, PC-08, DRDE-06, and SL-CH1). Neutralizing antibody titers are plotted, and 50% inhibitory concentrations (IC50 values; parenthesis) were calculated with Prism GraphPad software. Similar results were observed in 2 independent experiments with at least 10 mice per group for each experiment.

[0044] Figure 3, comprising Figure 3A through Figure 3D, depicts the characterization of in vivo immune protection conferred by CVM1-Fab and CVM1–immunoglobulin G (IgG). Figure 3A depicts BALB/c mice were injected with 100 μg of pVax1 (negative control), CVM1-IgG, CVM1–variable heavy chain, and CVM1–variable light chain on day 0 and challenged on day 2 with chikungunya virus (CHIKV). Mice were monitored daily, and survival rates were recorded for 20 days after viral challenge. Figure 3B depicts BALB/c mice were injected with 100 μg of pVax1 (negative control), CVM1-IgG, CVM1–variable heavy chain, and CVM1–variable light chain on day 0 and challenged on day 30 with chikungunya virus (CHIKV). Mice were

monitored daily, and survival rates were recorded for 20 days after viral challenge. Figure 3C depicts protection of mice from different routes of CHIKV challenge. Two groups of mice were injected with 100 μg of CVM1-IgG by the intramuscular route, followed by viral challenge on day 2 with subcutaneous inoculation. Mice were monitored daily, and survival rates were recorded for 20 days after the viral challenge. The black arrow indicates plasmid injections; the red arrow indicates the time of viral challenge. Each group consisted of 10 mice, and the results were representative of 2 independent experiments. Figure 3D depicts protection of mice from different routes of CHIKV challenge. Two groups of mice were injected with 100 μg of CVM1-IgG by the intramuscular route, followed by viral challenge on day 2 with intranasal inoculation. Mice were monitored daily, and survival rates were recorded for 20 days after the viral challenge. The black arrow indicates plasmid injections; the red arrow indicates the time of viral challenge. Each group consisted of 10 mice, and the results were representative of 2 independent experiments.

[0045] Figure 4, comprising Figure 4A through Figure 4D, depicts comparative and combination studies with CVM1–immunoglobulin G (IgG) and the chikungunya virus (CHIKV) envelope protein (Env) DNA vaccine. Figure 4A depicts a survival analysis of BALB/c mice were injected with 100 μg of CVM1-IgG, 100 μg of pVax1 (negative control), or 25 μg of CHIKV-Env DNA on day 0 and challenged on day 2 with CHIKV Del-03 (JN578247; 1×10^7 plaque-forming units in a total volume of 25 μL). Mice were monitored for 20 days after challenge, and survival rates were recorded. Figure 4B depicts a survival analysis of BALB/c mice were administered either a single injection of 100 μg of CVM1-IgG on day 0 or 3 immunizations of 25 μg of CHIKV Env DNA on day 0, day 14, and day 28 and then challenged on day 35 under the same conditions and with the same CHIKV isolate. Mice were monitored for 20 days after challenge, and survival rates were recorded. Figure 4C depicts a survival analysis of Groups of 20 BALB/c mice were administered a single 100 μg injection of CVM1-IgG on day 0 and 3 immunizations with CHIKV-Env DNA (25 μg) on day 0, day 14, and day 28. Half of the mice were then challenged on day 2, and the remaining half were challenged on day 35 under the same conditions and with the same CHIKV isolate challenge described above. The black arrow indicates plasmid injection, and the red arrow indicates the time of viral challenge. Mice were monitored for 20 days after challenge, and survival rates were recorded. Figure 4D depicts experimental results demonstrating induction of persistent and systemic anti-CHIKV Env

antibodies following a single CVM1-IgG (human anti-CHIKV Env) injection and CHIKV-Env immunization (mouse anti-CHIKV Env) 1 week after the second immunization in mice.

[0046] Figure 5, comprising Figure 5A through Figure 5C, depicts characterization of pathologic footpad swelling and changes in weight in viral-challenged mice vaccinated with CVM1–immunoglobulin G (IgG) and/or chikungunya virus (CHIKV) envelope protein (Env) DNA. Figure 5A depicts viral titers 1 week after CHIKV challenge in mice that received CVM1-IgG, CHIKV-Env, CVM1-IgG plus CHIKV-Env, or pVax1 (control). Each data point represents the average viral titers from 10 mice. Error bars indicate standard errors of the means. Figure 5B depicts mean daily weight gain (±standard deviation [SD]) after subcutaneous inoculation with the CHIKV isolate among mice that received CVM1-IgG, CHIKV-Env, CVM1-IgG plus CHIKV-Env, or pVax1. Mice were weighed on the specified days after inoculation. Results are presented as mean body weights (±SD). Figure 5C depicts swelling of the hind feet quantified using calipers on the specified days among mice that received CVM1-IgG, CHIKV-Env, CVM1-IgG plus CHIKV-Env, or pVax1. Data are mean values (±SD).

[0047] Figure 6, comprising Figure 6A and Figure 6B, depicts cellular immune analysis in viral challenged CVM1-IgG and/or CHIKV-Env DNA vaccinated mice. Figure 6A depicts concentrations of anti-CHIKV human IgG levels were measured from the mice that were injected with CVM1-IgG plus CHIKV-Env and then challenged on day 35 under the same conditions with the CHIKV isolate. Concentrations of anti-CHIKV human IgG levels were measured at indicated time points following injection. Figure 6B depicts T-cell responses in splenocytes of mice injected with CVM1-IgG plus CHIKV-Env after stimulation with CHIKV-specific peptides. IFN-γ ELISPOTs were performed on day 35 samples. The data indicated are representative of at least 2 separate experiments.

[0048] Figure 7 depicts characterization of serum pro-inflammatory cytokines levels from CHIKV infected mice. Cytokine (TNF-α, IL-1β and IL-6) levels were measured in mice at one week post-challenge by specific ELISA assays. Mice injected with CHIKV IgG and CHIKV-Env had similar and significantly lower sera levels of TNF-α, IL-1β and IL-6 levels. Data represent the average of 3 wells per mouse (n = 10 per group).

[0049] Figure 8 depicts experimental results demonstrating the induction of persistent and systemic anti-Zika virus-Env antibodies. Anti-ZIKV antibody responses are induced by ZIKV-prME +ZV-DMAb immunization. A129 mice (n=4) were immunized i.m. three times with 25 μg

of ZIKV-prME plasmid at 2-week intervals or one time with ZIKV-DMAb. Binding to recombinant ZIKV-Envelope was analyzed with sera from animals at different time points as indicated. Induction of persistent and systemic anti-ZIKV Env antibodies following a single ZV-IgG (human anti-ZIKV) injection and ZIKV-prME immunization (mouse anti-ZIKV Envelope). The data shown are representative of at least two separate experiments and mean OD450 values are shown ±SD.

[0050] Figure 9 depicts the structure of the ZIKV-E protein.

[0051] Figure 10 depicts the workflow for development and characterization of Zika dMABs.

[0052] Figure 11 depicts the binding ELISA for ZIKV-Env specific monoclonal antibodies.

[0053] Figure 12 depicts a western blot of ZV Env and ZV mAB. 2μg of rZV envelope protein loaded; 1:250 dilution were used for ZV monoclonal antibody.

[0054] Figure 13 depicts ZIKA mAb VH and VL alignments.

[0055] Figure 14 depicts ZIKA mAb VH and VL alignments and identity and RMSD matrices.

[0056] Figure 15 depicts mAb model superpositions.

[0057] Figure 16 depicts a comparison of model CDR regions

[0058] Figure 17 depicts mAB 1C2A6, 8D10F4, and 8A9F9 VH and VL alignments.

[0059] Figure 18 depicts a model of 1C2A6 Fv.

[0060] Figure 19 depicts a summary of Fv biophysical features for 8D10F4, 1C2A6, 8A9F9, 3F12E9, and 1D4G7.

[0061] Figure 20, comprising Figure 20A through Figure 20E depicts experimental results demonstrating the construction of the ZIKV-prME consensus DNA vaccine. Figure 20A depicts a diagrammatic representation of the ZIKV-prME DNA vaccine indicating the cloning of rME into the pVax1 mammalian expression vector. A consensus design strategy was adopted for the ZIKV-prME consensus sequence. Codon-optimized synthetic genes of the prME construct included a synthetic IgE leader sequence. The optimized gene construct was inserted into the BamH1 and Xho1 sites of a modified pVax1 vector under the control of the CMV promoter. Figure 20B depicts a model building of the ZIKV-E proteins demonstrates overlap of the vaccine target with potentially relevant epitope regions. Several changes made for vaccine design purpose are located in domains II and III (located within dashed lines of inset, middle left). Vaccine-specific residue changes in these regions are shown in violet CPK format on a ribbon

backbone representation of an E (envelope) protein dimer (each chain in light and dark green, respectively). Regions corresponding to the defined EDE are indicated in cyan, and the fusion loop is indicated in blue. Residue Ile156 (T156I) of the vaccine E protein, modelled as exposed on the surface of the 150 loop, is part of an N-linked glycosylation motif NXS/T in several other ZIKV strains as well as in multiple dengue virus strains. Figure 20C depicts expression analysis by SDS-PAGE of ZIKV-prME protein expression in 293T cells using western blot analysis. The 293T cells were transfected with the ZIKV-prME plasmid and the cell lysates and supernatants were analyzed for expression of the vaccine construct with pan-flavivirus immunized sera. Protein molecular weight markers (kDa); cell lysate and supernatant from ZIKV-prME transfected cells and rZIKV-E positive control were loaded as indicated. Figure 20D depicts expression analysis by SDS-PAGE of ZIKV-prME protein expression in 293T cells using western blot analysis. The 293T cells were transfected with the ZIKV-prME plasmid and the cell lysates and supernatants were analyzed for expression of the vaccine construct with ZIKV-prME immunized sera. Protein molecular weight markers (kDa); cell lysate and supernatant from ZIKV-prME transfected cells and rZIKV-E positive control were loaded as indicated. Figure 20E depicts Immunofluorescence assay (IFA) analysis for ZIKV-prME protein expression in 293T cells. The cells were transfected with 5 μg of the ZIKVprME plasmid. Twenty-four hours post transfection, immunofluorescence labelling was performed with the addition of sera (1:100) from ZIKV-prME immunized mice followed by the addition of the secondary anti-mouse IgG-AF488 antibody for detection. Staining with sera from ZIKV-prME and pVax1 immunized mice is shown. DAPI panels show control staining of cell nuclei. Overlay panels are combinations of antimouse IgG-AF488 and DAPI staining patterns. DAPI, 4',6-diamidino-2-phenylindole; ZIKV-prME, precursor membrane and envelope of Zika virus.

[0062] Figure 21, comprising Figure 21A through Figure 21D depicts experimental results demonstrating the characterization of cellular immune responses in mice following vaccination with the ZIKV-prME DNA vaccine. Figure 21A depicts a timeline of vaccine immunizations and immune analysis used in the study. Figure 21B depicts ELISpot analysis measuring IFN-γ secretion in splenocytes in response to ZIKV-prME immunization. C57BL/6 mice (n=4/group) were immunized i.m. three times with 25 μg of either pVax1 or the ZIKV-prME DNA vaccine followed by electroporation. IFN-γ generation, as an indication of induction of cellular immune responses, was measured by an IFN-γ ELISpot assay. The splenocytes harvested 1 week after the

third immunization were incubated in the presence of one of the six peptide pools spanning the entire prM and Envelope proteins. Results are shown in stacked bar graphs. The data represent the average numbers of SFU (spot-forming units) per million splenocytes with values representing the mean responses in each± s.e.m. Figure 21C depicts the epitope composition of the ZIKVprME- specific IFN-γ response as determined by stimulation with matrix peptide pools 1 week after the third immunization. The values represent mean responses in each group ±s.e.m. The experiments were performed independently at least three times with similar results. Figure 21D depicts flow cytometric analysis of T-cell responses. Immunisation with ZIKV-prME induces higher number of IFN-γ and TNF-α secreting cells when stimulated by ZIKV peptides. One week after the last immunization with the ZIKV-prME vaccine, splenocytes were cultured in the presence of pooled ZIKV peptides (5 μM) or R10 only. Frequencies of ZIKV peptide-specific IFN-γ and TNF-α secreting cells were measured by flow cytometry. Single function gates were set based on negative control (unstimulated) samples and were placed consistently across samples. The percentage of the total $CD8^+$ T-cell responses are shown. These data are representative of two independent immunization experiments. IFN, interferon; TNF, tumour necrosis factor; ZIKV-prME, precursor membrane and envelope of Zika virus.

[0063] Figure 22, comprising Figure 22A through Figure 22E depicts experimental results demonstrating that anti-ZIKV antibody responses are induced by ZIKV-prME vaccination. Figure 22A depicts ELISA analysis measuring binding antibody production (measured by OD450 values) in immunized mice. The C57BL/6 mice (n =4) were immunized i.m. three times with 25 μg of ZIKV-prME plasmid or pVax1 at 2-week intervals. Binding to rZIKV-E was analyzed with sera from animals at different time points (days 21, 35 and 50) post immunization at various dilutions. The data shown are representative of at least three separate experiments. Figure 22B depicts End point binding titer analysis. Differences in the anti-ZIKV end point titers produced in response to the ZIKV-prME immunogen were analyzed in sera from immunized animals after each boost. Figure 22C depicts Western blot analysis of rZIKV-E specific antibodies induced by ZIKV-prME immunization. The rZIKV-E protein was electrophoresed on a 12.5% SDS polyacrylamide gel and analyzed by western blot analysis with pooled sera from ZIKV-prME immunized mice (day 35). Binding to rZIKV-E is indicated by the arrowhead. Figure 22D depicts immunofluorescence analysis of ZIKV specific antibodies induced by ZIKV-prME immunization. The Vero cells infected with either ZIKV-MR766 or mock infected were

stained with pooled sera from ZIKV-prME immunized mice (day 35) followed by an anti-mouse-AF488 secondary antibody for detection. Figure 22E depicts plaque-reduction neutralization (PRNT) assay analysis of neutralizing antibodies induced by ZIKV-prME immunization. The serum samples from the ZIKV-prME immunized mice were tested for their ability to neutralize ZIKV infectivity in vitro. PRNT50 was defined as the serum dilution factor that could inhibit 50% of the input virus. The values in parentheses indicate the PRNT50. Control ZIKV-Cap (DNA vaccine expressing the ZIKV capsid protein) and pVax1 sera were used as negative controls. ZIKV-prME, precursor membrane and envelope of Zika virus.

[0064] Figure 23, comprising Figure 23A through Figure 23E depicts experimental results demonstrating Induction of ZIKV specific cellular immune responses following ZIKV-prME vaccination of non-human primates (NHPs). Figure 23A depicts ELISpot analysis measuring IFN-γ secretion in peripheral blood mononuclear cells (PBMCs) in response to ZIKV-prME immunization. Rhesus macaques were immunized intradermally with 2 mg of ZIKV-prME plasmid at weeks 0 and 4 administered as 1 mg at each of two sites, with immunization immediately followed by intradermal electroporation. PBMCs were isolated pre-immunization and at week 6 and were used for the ELISPOT assay to detect IFN-γ-secreting cells in response to stimulation with ZIKV-prME peptides as described in the 'Materials and Methods' section. The number of IFN-γ producing cells obtained per million PBMCs against six peptide pools encompassing the entire prME protein is shown. The values represent mean responses in each group (n=5) ±s.e.m. Figure 23B depicts the detection of ZIKV-prME-specific antibody responses following DNA vaccination. Anti-ZIKV IgG antibodies were measured pre-immunization and at week 6 by ELISA. Figure 23C depicts end point ELISA titers for anti ZIKV-envelope antibodies are shown following the first and second immunizations. Figure 23D depicts western blot analysis using week 6 RM immune sera demonstrated binding to recombinant envelope protein. Figure 23E depicts PRNT activity of serum from RM immunized with ZIKV-prME. Pre-immunization and week 6 immune sera from individual monkeys were tested by plaque-reduction neutralization (PRNT) assay for their ability to neutralize ZIKV infectivity in vitro. PRNT50 was defined as the serum dilution factor that could inhibit 50% of the input virus. Calculated (PRNT50) values are listed for each monkey. IFN, interferon; ZIKV-prME, precursor membrane and envelope of Zika virus.

[0065] Figure 24, comprising Figure 24A through Figure 24F depicts experimental results demonstrating survival data for immunized mice lacking the type I interferon α, β receptor following ZIKV infection. Figure 24A depicts survival of $IFNAR^{-/-}$ mice after ZIKV infection. Mice were immunized twice with 25 μg of the ZIKV-prME DNA vaccine at 2-week intervals and challenged with ZIKV-PR209 virus 1 week after the second immunization with 1×10^6 plaque-forming units Figure 24B depicts survival of $IFNAR^{-/-}$ mice after ZIKV infection. Mice were immunized twice with 25 μg of the ZIKV-prME DNA vaccine at 2-week intervals and challenged with ZIKV-PR209 virus 1 week after the second immunization with 2×10^6 plaque-forming units Figure 24C depicts the weight change of animals immunized with 1×10^6 plaque-forming units. Figure 24D depicts the weight change of animals immunized with 2×10^6 plaque-forming units. Figure 24E depicts the clinical scores of animals immunized with 1×10^6 plaque-forming units. Figure 24F depicts the clinical scores of animals immunized with 2×10^6 plaque-forming units. The designation for the clinical scores is as follows: 1: no disease, 2: decreased mobility; 3: hunched posture and decreased mobility; 4: hind limb knuckle walking (partial paralysis); 5: paralysis of one hind limb; and 6: paralysis of both hind limbs. The data reflect the results from two independent experiments with 10 mice per group per experiment. ZIKV-prME, precursor membrane and envelope of Zika virus.

[0066] Figure 25, comprising Figure 25A through Figure 25d depicts experimental results demonstrating single immunization with the ZIKV-prME vaccine provided protection against ZIKV challenge in mice lacking the type I interferon α, β receptor. The mice were immunized once and challenged with 2×10^6 plaque-forming units of ZIKV-PR209, 2 weeks after the single immunization. The survival curves depict 10 mice per group per experiment Figure 25A demonstrates that the ZIKV-prME vaccine prevented ZIKA-induced neurological abnormalities in the mouse brain Figure 25B depicts brain sections from pVax1 and ZIKV-prME vaccinated groups were collected 7–8 days after challenge and stained with H&E (haematoxylin and eosin) for histology. The sections taken from representative, unprotected pVax1 control animals shows pathology. (i): nuclear fragments within neuropils of the cerebral cortex (inset shows higher magnification and arrows to highlight nuclear fragments); (ii): perivascular cuffing of vessels within the cortex, lymphocyte infiltration and degenerating cells; (iii): perivascular cuffing, cellular degeneration and nuclear fragments within the cerebral cortex; and (iv): degenerating neurons within the hippocampus (arrows). An example of normal tissue from ZIKV-prME

vaccinated mice appeared to be within normal limits (v and vi). Figure 25C depicts levels of ZIKV RNA in the plasma samples from mice following vaccination and viral challenge at the indicated day post infection. The results are indicated as the genome equivalents per milliliter of plasma. Figure 25D depicts levels of ZIKV-RNA in the brain tissues were analyzed at day 28 post infection. The results are indicated as the genome equivalent per gram of tissue. ZIKV-prME, precursor membrane and envelope of Zika virus.

[0067] Figure 25, comprising Figure 26A and Figure 26B, depicts experimental results demonstrating protection of mice lacking the type I interferon α, β receptor following passive transfer of anti-ZIKV immune sera following ZIKV challenge. Pooled NHP anti-ZIKV immune sera, titred for anti-ZIKA virus IgG, was administered i.p. (150 µl/mouse) to mice 1 day after s.c. challenge with a ZIKA virus (10^6 plaque-forming units per mouse). As a control, normal monkey sera and phosphate-buffered saline (PBS) were administered (150 µl/mouse) to age-matched mice as controls. Figure 26A depicts the mouse weight change during the course of infection and treatment. Each point represents the mean and standard error of the calculated percent pre-challenge (day 0) weight for each mouse. Figure 26B depicts the survival of mice following administration of the NHP immune sera. ZIKV-prME, precursor membrane and envelope of Zika virus.

[0068] Figure 27, comprising Figure 27A through Figure 27D, depicts experimental results demonstrating the characterization of immune responses of ZIKV-prME-MR766 or ZIKV-prME Brazil vaccine in C57BL/6 mice. Figure 27A depicts ELISpot and ELISA analysis measuring cellular and antibody responses after vaccination with either ZIKV-prME-MR766 and ZIKV-prME-Brazil DNA vaccines. C57BL/6 mice (n = 4/group) were immunized intramuscularly three times with 25µg of ZIKV-prME-MR766 followed by in vivo EP. IFN-γ generation, as an indication of cellular immune response induction, was measured by IFN-γ ELISpot. Splenocytes harvested one week after the third immunization were incubated in the presence of one of six peptide pools spanning the entire prM and E proteins. Results are shown in stacked bar graphs. The data represent the average numbers of SFU (spot forming units) per million splenocytes with values representing the mean responses in each ± SEM. Figure 27B depicts ELISpot and ELISA analysis measuring cellular and antibody responses after vaccination with either ZIKV-prME-MR766 and ZIKV-prME-Brazil DNA vaccines. C57BL/6 mice (n = 4/group) were immunized intramuscularly three times with 25µg of ZIKV prME-Brazil followed by in vivo EP. IFN-γ

generation, as an indication of cellular immune response induction, was measured by IFN-γ ELISpot. Splenocytes harvested one week after the third immunization were incubated in the presence of one of six peptide pools spanning the entire prM and E proteins. Results are shown in stacked bar graphs. The data represent the average numbers of SFU (spot forming units) per million splenocytes with values representing the mean responses in each ± SEM. Figure 27C depicts ELISA analysis measuring binding antibody production in immunized C57BL/6 mice. Binding to rZIKV-E was analyzed with sera from mice at day 35 post immunization at various dilutions. Figure 27D depicts ELISA analysis measuring binding antibody production in immunized C57BL/6 mice. Binding to rZIKV-E was analyzed with sera from mice at day 35 post immunization at various dilutions.

[0069] Figure 28, comprising Figure 28A through Figure 28D, depicts experimental results demonstrating the expression, purification, and characterization of ZIKV-Envelope protein. Figure 28A depicts the cloning plasmid for rZIKV E expression. Figure 28B depicts the characterization of the recombinant ZIKV-E (rZIKV-E) protein by SDS-PAGE and Western blot analysis. Lane 1-BSA control; Lane 2- lysates from E. coli cultures transformed with pET-28a vector plasmid, was purified by nickel metal affinity resin columns and separated by SDS-PAGE after IPTG induction. Lane 3, 37 recombinant ZV-E purified protein was analyzed by Western blot with anti-His tag antibody. Lane M, Protein molecular weight marker. Figure 28C depicts the purified rZIKV-E protein was evaluated for its antigenicity. ELISA plates were coated with rZIKV-E and then incubated with various dilutions of immune sera from the mice immunized with ZIKV-prME vaccine or Pan-flavivirus antibody as positive control. Bound IgG was detected by the addition of peroxidase-conjugated anti-mouse antibody followed by tetramethylbenzidine substrate as described in Experimental Example. Figure 28D depicts western blot detection of purified rZIKV-E protein with immune sera from ZIKV prME immunized mice. Various concentrations of purified rZIKV-E protein were loaded onto an SDS-PAGE gel as described. A dilution of 1:100 immune sera, and goat anti-mouse at 1:15,000 were used for 1 hour at room temperature. After washing, the membranes were imaged on the Odyssey infrared imager. Odyssey protein molecular weight standards were used. The arrows indicate the position of rZIKV-E protein.

Figure 29, comprising Figure 29A through Figure 29C, depicts experimental results demonstrating the characterization of immune responses ZIKA-prME in $IFNAR^{-/-}$ mice.

ELISpot and ELISA analysis measuring cellular and antibody responses to ZIKV-prME in IFNAR$^{-/-}$ mice. Mice (n = 4/group) were immunized intramuscularly three times with 25 μg of ZIKV-prME followed by in vivo EP. Figure 29A depicts IFN-γ generation, as an indication of cellular immune response induction, was measured by IFN-γ ELISPOT. Figure 29B depicts ELISA analysis measuring binding antibody production in immunized IFNAR$^{-/-}$ mice. Binding to rZIKV-E was analyzed with sera from mice at various time points post immunization. Figure 29C depicts endpoint titer analysis of anti-ZIKV antibodies produced in immunized IFNAR$^{-/-}$ mice.

[0070] Figure 30, comprising Figure 30A through Figure 30D, depicts experimental results demonstrating the neutralization activity of immune sera from Rhesus Macaques immunized against ZIKV-prME. SK-N-SH and U87MG cells were mock infected or infected with MR766 at an MOI of 0.01 PFU/cell in the presence of pooled NHP sera immunized with ZIKV-prME vaccine (Wk 6). Zika viral infectivity were analyzed 4 days post infection by indirect immunofluorescence assay (IFA) using sera from ZIKV-prME vaccinated NHPs. Figure 30A depicts photographs of stained tissue sample slices taken with a 20x objective demonstrating inhibition of infection by ZIKV viruses MR766 and PR209 in Vero, SK-N-SH and U87MG Figure 30B depicts photographs of stained tissue sample slices taken with a 20x objective demonstrating inhibition of infection by ZIKV viruses SK-N-SH and U87MG in Vero, SK-N-SH and U87MG Figure 30C depicts a bar graph shows the percentage of infected (GFP positive cells) demonstrating the inhibition of infection by ZIKV viruses MR766 and PR209 in Vero, SK-N-SH and U87MG Figure 30D depicts a bar graph showing the percentage of infected (GFP positive cells) demonstrating the inhibition of infection by ZIKV viruses SK-N-SH and U87MG in Vero, SK-N-SH and U87MG

[0071] Figure 31, comprising Figure 31A through Figure 31D, depicts experimental results demonstrating ZIKV is virulent to IFNAR$^{-/-}$ mice. These data confirm that ZIKV is virulent in IFNAR$^{-/-}$ resulting in morbidity and mortality. Figure 31A depicts Kaplan-Meier survival curves of IFNAR$^{-/-}$ mice inoculated via intracranial with 10^6 pfu ZIKV-PR209 virus. Figure 31B depicts Kaplan-Meier survival curves of IFNAR$^{-/-}$ mice inoculated via intravenously with 10^6 pfu ZIKV-PR209 virus. Figure 31C depicts Kaplan-Meier survival curves of IFNAR$^{-/-}$ mice inoculated via intraperitoneal with 10^6 pfu ZIKV-PR209 virus. Figure 31D depicts Kaplan-Meier survival

curves of IFNAR$^{-/-}$ mice inoculated via subcutaneously with 10^6 pfu ZIKV-PR209 virus. Figure 31A depicts the mouse weight change during the course of infection for all the routes.

DETAILED DESCRIPTION

[0072] In one embodiment, the invention provides composition comprising one or more nucleotide sequences encoding one or more antigens and one or more nucleotide sequences encoding one or more antibodies or fragments thereof.

[0073] In one embodiment, the invention provides a composition comprising a combination of a composition that elicits an immune response in a mammal against a desired target and a composition comprising a recombinant nucleic acid sequence encoding an antibody, a fragment thereof, a variant thereof, or a combination thereof.

[0074] In one embodiment, the recombinant nucleic acid sequence encoding an antibody comprises sequences that encode a heavy chain and light chain. In particular, the heavy chain and light chain polypeptides expressed from the recombinant nucleic acid sequences can assemble into the synthetic antibody. The heavy chain polypeptide and the light chain polypeptide can interact with one another such that assembly results in the synthetic antibody being capable of binding the antigen, being more immunogenic as compared to an antibody not assembled as described herein, and being capable of eliciting or inducing an immune response against the antigen.

[0075] Additionally, these synthetic antibodies are generated more rapidly in the subject than antibodies that are produced in response to antigen induced immune response. The synthetic antibodies are able to effectively bind and neutralize a range of antigens. The synthetic antibodies are also able to effectively protect against and/or promote survival of disease.

[0076] Another aspect of the present invention provides DNA plasmid vaccines that are capable of generating in a mammal an immune response against a desired target (e.g. an antigen). The DNA plasmid vaccines are comprised of a DNA plasmid capable of expressing a consensus antigen in a mammal and a pharmaceutically acceptable excipient. The DNA plasmid is comprised of a promoter operably linked to a coding sequence that encodes the consensus antigen.

1. **Definitions**

[0077] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art. In case of conflict, the present document, including definitions, will control. Preferred methods and materials are described below, although methods and materials similar or equivalent to those described herein can be used in practice or testing of the present invention. All publications, patent applications, patents and other references mentioned herein are incorporated by reference in their entirety. The materials, methods, and examples disclosed herein are illustrative only and not intended to be limiting.

[0078] The terms "comprise(s)," "include(s)," "having," "has," "can," "contain(s)," and variants thereof, as used herein, are intended to be open-ended transitional phrases, terms, or words that do not preclude the possibility of additional acts or structures. The singular forms "a," "and" and "the" include plural references unless the context clearly dictates otherwise. The present disclosure also contemplates other embodiments "comprising," "consisting of" and "consisting essentially of," the embodiments or elements presented herein, whether explicitly set forth or not.

[0079] "Antibody" may mean an antibody of classes IgG, IgM, IgA, IgD or IgE, or fragments, fragments or derivatives thereof, including Fab, F(ab')2, Fd, and single chain antibodies, and derivatives thereof. The antibody may be an antibody isolated from the serum sample of mammal, a polyclonal antibody, affinity purified antibody, or mixtures thereof which exhibits sufficient binding specificity to a desired epitope or a sequence derived therefrom.

[0080] "Antibody fragment" or "fragment of an antibody" as used interchangeably herein refers to a portion of an intact antibody comprising the antigen-binding site or variable region. The portion does not include the constant heavy chain domains (i.e. CH2, CH3, or CH4, depending on the antibody isotype) of the Fc region of the intact antibody. Examples of antibody fragments include, but are not limited to, Fab fragments, Fab' fragments, Fab'-SH fragments, F(ab')2 fragments, Fd fragments, Fv fragments, diabodies, single-chain Fv (scFv) molecules, single-chain polypeptides containing only one light chain variable domain, single-chain polypeptides containing the three CDRs of the light-chain variable domain, single-chain polypeptides containing only one heavy chain variable region, and single-chain polypeptides containing the three CDRs of the heavy chain variable region.

[0081] "Antigen" refers to proteins that have the ability to generate an immune response in a host. An antigen may be recognized and bound by an antibody. An antigen may originate from within the body or from the external environment.

[0082] "Coding sequence" or "encoding nucleic acid" as used herein may mean refers to the nucleic acid (RNA or DNA molecule) that comprise a nucleotide sequence which encodes an antibody as set forth herein. The coding sequence may further include initiation and termination signals operably linked to regulatory elements including a promoter and polyadenylation signal capable of directing expression in the cells of an individual or mammal to whom the nucleic acid is administered. The coding sequence may further include sequences that encode signal peptides.

[0083] "Complement" or "complementary" as used herein may mean a nucleic acid may mean Watson-Crick (e.g., A-T/U and C-G) or Hoogsteen base pairing between nucleotides or nucleotide analogs of nucleic acid molecules.

[0084] "Constant current" as used herein to define a current that is received or experienced by a tissue, or cells defining said tissue, over the duration of an electrical pulse delivered to same tissue. The electrical pulse is delivered from the electroporation devices described herein. This current remains at a constant amperage in said tissue over the life of an electrical pulse because the electroporation device provided herein has a feedback element, preferably having instantaneous feedback. The feedback element can measure the resistance of the tissue (or cells) throughout the duration of the pulse and cause the electroporation device to alter its electrical energy output (e.g., increase voltage) so current in same tissue remains constant throughout the electrical pulse (on the order of microseconds), and from pulse to pulse. In some embodiments, the feedback element comprises a controller.

[0085] "Current feedback" or "feedback" as used herein may be used interchangeably and may mean the active response of the provided electroporation devices, which comprises measuring the current in tissue between electrodes and altering the energy output delivered by the EP device accordingly in order to maintain the current at a constant level. This constant level is preset by a user prior to initiation of a pulse sequence or electrical treatment. The feedback may be accomplished by the electroporation component, e.g., controller, of the electroporation device, as the electrical circuit therein is able to continuously monitor the current in tissue between electrodes and compare that monitored current (or current within tissue) to a preset

current and continuously make energy-output adjustments to maintain the monitored current at preset levels. The feedback loop may be instantaneous as it is an analog closed-loop feedback.

[0086] "Decentralized current" as used herein may mean the pattern of electrical currents delivered from the various needle electrode arrays of the electroporation devices described herein, wherein the patterns minimize, or preferably eliminate, the occurrence of electroporation related heat stress on any area of tissue being electroporated.

[0087] "Electroporation," "electro-permeabilization," or "electro-kinetic enhancement" ("EP") as used interchangeably herein may refer to the use of a transmembrane electric field pulse to induce microscopic pathways (pores) in a bio-membrane; their presence allows biomolecules such as plasmids, oligonucleotides, siRNA, drugs, ions, and water to pass from one side of the cellular membrane to the other.

[0088] "Endogenous antibody" as used herein may refer to an antibody that is generated in a subject that is administered an effective dose of an antigen for induction of a humoral immune response.

[0089] "Feedback mechanism" as used herein may refer to a process performed by either software or hardware (or firmware), which process receives and compares the impedance of the desired tissue (before, during, and/or after the delivery of pulse of energy) with a present value, preferably current, and adjusts the pulse of energy delivered to achieve the preset value. A feedback mechanism may be performed by an analog closed loop circuit.

[0090] "Fragment" may mean a polypeptide fragment of an antibody that is function, i.e., can bind to desired target and have the same intended effect as a full length antibody. A fragment of an antibody may be 100% identical to the full length except missing at least one amino acid from the N and/or C terminal, in each case with or without signal peptides and/or a methionine at position 1. Fragments may comprise 20% or more, 25% or more, 30% or more, 35% or more, 40% or more, 45% or more, 50% or more, 55% or more, 60% or more, 65% or more, 70% or more, 75% or more, 80% or more, 85% or more, 90% or more, 91% or more, 92% or more, 93% or more, 94% or more, 95% or more, 96% or more, 97% or more, 98% or more, 99% or more percent of the length of the particular full length antibody, excluding any heterologous signal peptide added. The fragment may comprise a fragment of a polypeptide that is 95% or more, 96% or more, 97% or more, 98% or more or 99% or more identical to the antibody and additionally comprise an N terminal methionine or heterologous signal peptide which is not

included when calculating percent identity. Fragments may further comprise an N terminal methionine and/or a signal peptide such as an immunoglobulin signal peptide, for example an IgE or IgG signal peptide. The N terminal methionine and/or signal peptide may be linked to a fragment of an antibody.

[0091] A fragment of a nucleic acid sequence that encodes an antibody may be 100% identical to the full length except missing at least one nucleotide from the 5' and/or 3' end, in each case with or without sequences encoding signal peptides and/or a methionine at position 1. Fragments may comprise 20% or more, 25% or more, 30% or more, 35% or more, 40% or more, 45% or more, 50% or more, 55% or more, 60% or more, 65% or more, 70% or more, 75% or more, 80% or more, 85% or more, 90% or more, 91% or more, 92% or more, 93% or more, 94% or more, 95% or more, 96% or more, 97% or more, 98% or more, 99% or more percent of the length of the particular full length coding sequence, excluding any heterologous signal peptide added. The fragment may comprise a fragment that encode a polypeptide that is 95% or more, 96% or more, 97% or more, 98% or more or 99% or more identical to the antibody and additionally optionally comprise sequence encoding an N terminal methionine or heterologous signal peptide which is not included when calculating percent identity. Fragments may further comprise coding sequences for an N terminal methionine and/or a signal peptide such as an immunoglobulin signal peptide, for example an IgE or IgG signal peptide. The coding sequence encoding the N terminal methionine and/or signal peptide may be linked to a fragment of coding sequence.

[0092] "Genetic construct" as used herein refers to the DNA or RNA molecules that comprise a nucleotide sequence which encodes a protein, such as an antibody. The coding sequence includes initiation and termination signals operably linked to regulatory elements including a promoter and polyadenylation signal capable of directing expression in the cells of the individual to whom the nucleic acid molecule is administered. As used herein, the term "expressible form" refers to gene constructs that contain the necessary regulatory elements operable linked to a coding sequence that encodes a protein such that when present in the cell of the individual, the coding sequence will be expressed.

[0093] "Identical" or "identity" as used herein in the context of two or more nucleic acids or polypeptide sequences, may mean that the sequences have a specified percentage of residues that are the same over a specified region. The percentage may be calculated by optimally aligning the

two sequences, comparing the two sequences over the specified region, determining the number of positions at which the identical residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the specified region, and multiplying the result by 100 to yield the percentage of sequence identity. In cases where the two sequences are of different lengths or the alignment produces one or more staggered ends and the specified region of comparison includes only a single sequence, the residues of single sequence are included in the denominator but not the numerator of the calculation. When comparing DNA and RNA, thymine (T) and uracil (U) may be considered equivalent. Identity may be performed manually or by using a computer sequence algorithm such as BLAST or BLAST 2.0.

[0094] "Impedance" as used herein may be used when discussing the feedback mechanism and can be converted to a current value according to Ohm's law, thus enabling comparisons with the preset current.

[0095] "Immune response" as used herein may mean the activation of a host's immune system, e.g., that of a mammal, in response to the introduction of one or more nucleic acids and/or peptides. The immune response can be in the form of a cellular or humoral response, or both.

[0096] "Nucleic acid" or "oligonucleotide" or "polynucleotide" as used herein may mean at least two nucleotides covalently linked together. The depiction of a single strand also defines the sequence of the complementary strand. Thus, a nucleic acid also encompasses the complementary strand of a depicted single strand. Many variants of a nucleic acid may be used for the same purpose as a given nucleic acid. Thus, a nucleic acid also encompasses substantially identical nucleic acids and complements thereof. A single strand provides a probe that may hybridize to a target sequence under stringent hybridization conditions. Thus, a nucleic acid also encompasses a probe that hybridizes under stringent hybridization conditions.

[0097] Nucleic acids may be single stranded or double stranded, or may contain portions of both double stranded and single stranded sequence. The nucleic acid may be DNA, both genomic and cDNA, RNA, or a hybrid, where the nucleic acid may contain combinations of deoxyribo- and ribo-nucleotides, and combinations of bases including uracil, adenine, thymine, cytosine, guanine, inosine, xanthine hypoxanthine, isocytosine and isoguanine. Nucleic acids may be obtained by chemical synthesis methods or by recombinant methods.

[0098] "Operably linked" as used herein may mean that expression of a gene is under the control of a promoter with which it is spatially connected. A promoter may be positioned 5' (upstream) or 3' (downstream) of a gene under its control. The distance between the promoter and a gene may be approximately the same as the distance between that promoter and the gene it controls in the gene from which the promoter is derived. As is known in the art, variation in this distance may be accommodated without loss of promoter function.

[0099] A "peptide," "protein," or "polypeptide" as used herein can mean a linked sequence of amino acids and can be natural, synthetic, or a modification or combination of natural and synthetic.

[00100] "Promoter" as used herein may mean a synthetic or naturally-derived molecule which is capable of conferring, activating or enhancing expression of a nucleic acid in a cell. A promoter may comprise one or more specific transcriptional regulatory sequences to further enhance expression and/or to alter the spatial expression and/or temporal expression of same. A promoter may also comprise distal enhancer or repressor elements, which can be located as much as several thousand base pairs from the start site of transcription. A promoter may be derived from sources including viral, bacterial, fungal, plants, insects, and animals. A promoter may regulate the expression of a gene component constitutively, or differentially with respect to cell, the tissue or organ in which expression occurs or, with respect to the developmental stage at which expression occurs, or in response to external stimuli such as physiological stresses, pathogens, metal ions, or inducing agents. Representative examples of promoters include the bacteriophage T7 promoter, bacteriophage T3 promoter, SP6 promoter, lac operator-promoter, tac promoter, SV40 late promoter, SV40 early promoter, RSV-LTR promoter, CMV IE promoter, SV40 early promoter or SV 40 late promoter and the CMV IE promoter.

[00101] "Signal peptide" and "leader sequence" are used interchangeably herein and refer to an amino acid sequence that can be linked at the amino terminus of a protein set forth herein. Signal peptides/leader sequences typically direct localization of a protein. Signal peptides/leader sequences used herein preferably facilitate secretion of the protein from the cell in which it is produced. Signal peptides/leader sequences are often cleaved from the remainder of the protein, often referred to as the mature protein, upon secretion from the cell. Signal peptides/leader sequences are linked at the N terminus of the protein.

[00102] "Stringent hybridization conditions" as used herein may mean conditions under which a first nucleic acid sequence (e.g., probe) will hybridize to a second nucleic acid sequence (e.g., target), such as in a complex mixture of nucleic acids. Stringent conditions are sequence dependent and will be different in different circumstances. Stringent conditions may be selected to be about 5-10°C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength pH. The T_m may be the temperature (under defined ionic strength, pH, and nucleic concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at T_m, 50% of the probes are occupied at equilibrium). Stringent conditions may be those in which the salt concentration is less than about 1.0 M sodium ion, such as about 0.01-1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes (e.g., about 10-50 nucleotides) and at least about 60°C for long probes (e.g., greater than about 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. For selective or specific hybridization, a positive signal may be at least 2 to 10 times background hybridization. Exemplary stringent hybridization conditions include the following: 50% formamide, 5x SSC, and 1% SDS, incubating at 42°C, or, 5x SSC, 1% SDS, incubating at 65°C, with wash in 0.2x SSC, and 0.1% SDS at 65°C.

[00103] "Subject" and "patient" as used herein interchangeably refers to any vertebrate, including, but not limited to, a mammal (e.g., cow, pig, camel, llama, horse, goat, rabbit, sheep, hamsters, guinea pig, cat, dog, rat, and mouse, a non-human primate (for example, a monkey, such as a cynomolgous or rhesus monkey, chimpanzee, etc) and a human). In some embodiments, the subject may be a human or a non-human. The subject or patient may be undergoing other forms of treatment.

[00104] "Substantially complementary" as used herein may mean that a first sequence is at least 60%, 65%, 70%, 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the complement of a second sequence over a region of 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100 or more nucleotides or amino acids, or that the two sequences hybridize under stringent hybridization conditions.

[00105] "Substantially identical" as used herein may mean that a first and second sequence are at least 60%, 65%, 70%, 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%,

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%,or 99% over a region of 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, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1100 or more nucleotides or amino acids, or with respect to nucleic acids, if the first sequence is substantially complementary to the complement of the second sequence.

[00106] "Synthetic antibody" as used herein refers to an antibody that is encoded by the recombinant nucleic acid sequence described herein and is generated in a subject.

[00107] "Treatment" or "treating," as used herein can mean protecting of a subject from a disease through means of preventing, suppressing, repressing, or completely eliminating the disease. Preventing the disease involves administering a vaccine of the present invention to a subject prior to onset of the disease. Suppressing the disease involves administering a vaccine of the present invention to a subject after induction of the disease but before its clinical appearance. Repressing the disease involves administering a vaccine of the present invention to a subject after clinical appearance of the disease.

[00108] "Variant" used herein with respect to a nucleic acid may mean (i) a portion or fragment of a referenced nucleotide sequence; (ii) the complement of a referenced nucleotide sequence or portion thereof; (iii) a nucleic acid that is substantially identical to a referenced nucleic acid or the complement thereof; or (iv) a nucleic acid that hybridizes under stringent conditions to the referenced nucleic acid, complement thereof, or a sequences substantially identical thereto.

[00109] "Variant" with respect to a peptide or polypeptide that differs in amino acid sequence by the insertion, deletion, or conservative substitution of amino acids, but retain at least one biological activity. Variant may also mean a protein with an amino acid sequence that is substantially identical to a referenced protein with an amino acid sequence that retains at least one biological activity. A conservative substitution of an amino acid, i.e., replacing an amino acid with a different amino acid of similar properties (e.g., hydrophilicity, degree and distribution of charged regions) is recognized in the art as typically involving a minor change. These minor changes can be identified, in part, by considering the hydropathic index of amino acids, as understood in the art. Kyte et al., J. Mol. Biol. 157:105-132 (1982). The hydropathic index of an amino acid is based on a consideration of its hydrophobicity and charge. It is known in the art that amino acids of similar hydropathic indexes can be substituted and still retain

protein function. In one aspect, amino acids having hydropathic indexes of ±2 are substituted. The hydrophilicity of amino acids can also be used to reveal substitutions that would result in proteins retaining biological function. A consideration of the hydrophilicity of amino acids in the context of a peptide permits calculation of the greatest local average hydrophilicity of that peptide, a useful measure that has been reported to correlate well with antigenicity and immunogenicity. U.S. Patent No. 4,554,101, incorporated fully herein by reference. Substitution of amino acids having similar hydrophilicity values can result in peptides retaining biological activity, for example immunogenicity, as is understood in the art. Substitutions may be performed with amino acids having hydrophilicity values within ±2 of each other. Both the hyrophobicity index and the hydrophilicity value of amino acids are influenced by the particular side chain of that amino acid. Consistent with that observation, amino acid substitutions that are compatible with biological function are understood to depend on the relative similarity of the amino acids, and particularly the side chains of those amino acids, as revealed by the hydrophobicity, hydrophilicity, charge, size, and other properties.

[00110] A variant may be a nucleic acid sequence that is substantially identical over the full length of the full gene sequence or a fragment thereof. The nucleic acid sequence may be 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical over the full length of the gene sequence or a fragment thereof. A variant may be an amino acid sequence that is substantially identical over the full length of the amino acid sequence or fragment thereof. The amino acid sequence may be 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical over the full length of the amino acid sequence or a fragment thereof.

[00111] "Vector" as used herein may mean a nucleic acid sequence containing an origin of replication. A vector may be a plasmid, bacteriophage, bacterial artificial chromosome or yeast artificial chromosome. A vector may be a DNA or RNA vector. A vector may be either a self-replicating extrachromosomal vector or a vector which integrates into a host genome.

[00112] For the recitation of numeric ranges herein, each intervening number there between with the same degree of precision is explicitly contemplated. For example, for the range of 6-9, the numbers 7 and 8 are contemplated in addition to 6 and 9, and for the range 6.0-7.0, the number 6.0, 6.1, 6.2, 6.3, 6.4, 6.5, 6.6, 6.7, 6.8, 6.9, and 7.0 are explicitly contemplated.

2. **Composition**

[00113] In one aspect, the present invention provides a combination of a composition that elicits an immune response in a mammal against an antigen with a composition comprising a recombinant nucleic acid sequence encoding an antibody, a fragment thereof, a variant thereof, or a combination thereof. The composition can be administered to a subject in need thereof to facilitate in vivo expression and formation of a synthetic antibody.

[00114] In one embodiment, the present invention relates to a combination of a first composition that elicits an immune response in a mammal against an antigen and a second composition comprising a recombinant nucleic acid sequence encoding an antibody, a fragment thereof, a variant thereof, or a combination thereof. In one embodiment, the first composition comprises a nucleic acid encoding one or more antigens. In one embodiment, the first composition comprises a DNA vaccine.

[00115] The present invention relates to a composition comprising a recombinant nucleic acid sequence encoding an antibody, a fragment thereof, a variant thereof, or a combination thereof. The composition, when administered to a subject in need thereof, can result in the generation of a synthetic antibody in the subject. The synthetic antibody can bind a target molecule (i.e., an antigen) present in the subject. Such binding can neutralize the antigen, block recognition of the antigen by another molecule, for example, a protein or nucleic acid, and elicit or induce an immune response to the antigen.

[00116] The synthetic antibody can treat, prevent, and/or protect against disease in the subject administered the composition. The synthetic antibody by binding the antigen can treat, prevent, and/or protect against disease in the subject administered the composition. The synthetic antibody can promote survival of the disease in the subject administered the composition. The synthetic antibody can provide at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% survival of the disease in the subject administered the composition. In other embodiments, the synthetic antibody can provide at least about 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, or 80% survival of the disease in the subject administered the composition.

[00117] The composition can result in the generation of the synthetic antibody in the subject within at least about 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, 8 hours, 9 hours,

10 hours, 11 hours, 12 hours, 13 hours, 14 hours, 15 hours, 20 hours, 25 hours, 30 hours, 35 hours, 40 hours, 45 hours, 50 hours, or 60 hours of administration of the composition to the subject. The composition can result in generation of the synthetic antibody in the subject within at least about 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, or 10 days of administration of the composition to the subject. The composition can result in generation of the synthetic antibody in the subject within about 1 hour to about 6 days, about 1 hour to about 5 days, about 1 hour to about 4 days, about 1 hour to about 3 days, about 1 hour to about 2 days, about 1 hour to about 1 day, about 1 hour to about 72 hours, about 1 hour to about 60 hours, about 1 hour to about 48 hours, about 1 hour to about 36 hours, about 1 hour to about 24 hours, about 1 hour to about 12 hours, or about 1 hour to about 6 hours of administration of the composition to the subject.

[00118] The composition, when administered to the subject in need thereof, can result in the generation of the synthetic antibody in the subject more quickly than the generation of an endogenous antibody in a subject who is administered an antigen to induce a humoral immune response. The composition can result in the generation of the synthetic antibody at least about 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, or 10 days before the generation of the endogenous antibody in the subject who was administered an antigen to induce a humoral immune response.

[00119] The composition of the present invention can have features required of effective compositions such as being safe so that the composition does not cause illness or death; being protective against illness; and providing ease of administration, few side effects, biological stability and low cost per dose.

[00120] Another aspect of the present invention provides DNA plasmid vaccines that are capable of generating in a mammal an immune response against an antigen. The DNA plasmid vaccines are comprised of a DNA plasmid capable of expressing a consensus antigen in the mammal and a pharmaceutically acceptable excipient. The DNA plasmid is comprised of a promoter operably linked to a coding sequence that encodes the consensus antigen.

[00121] In some embodiments, the DNA sequences herein can have removed from the 5' end the IgE leader sequence, and the protein sequences herein can have removed from the N-terminus the IgE leader sequence.

[00122] In some embodiments, the DNA plasmid includes and encoding sequence that encodes for a antigen minus an IgE leader sequence on the N-terminal end of the coding sequence. In some embodiments, the DNA plasmid further comprises an IgE leader sequence attached to an N-terminal end of the coding sequence and operably linked to the promoter.

[00123] The DNA plasmid can further include a polyadenylation sequence attached to the C-terminal end of the coding sequence. Preferably, the DNA plasmid is codon optimized.

[00124] In some embodiments, the pharmaceutically acceptable excipient is an adjuvant. Preferably, the adjuvant is selected from the group consisting of: IL-12 and IL-15. In some embodiments, the pharmaceutically acceptable excipient is a transfection facilitating agent. Preferably, the transfection facilitating agent is a polyanion, polycation, or lipid, and more preferably poly-L-glutamate. Preferably, the poly-L-glutamate is at a concentration less than 6 mg/ml. Preferably, the DNA plasmid vaccine has a concentration of total DNA plasmid of 1 mg/ml or greater.

[00125] In some embodiments, the DNA plasmid comprises a plurality of unique DNA plasmids, wherein each of the plurality of unique DNA plasmids encodes a polypeptide comprising a consensus antigen.

[00126] In some embodiments of the present invention, the DNA plasmid vaccines can further include an adjuvant. In some embodiments, the adjuvant is selected from the group consisting of: alpha-interferon, gamma-interferon, platelet derived growth factor (PDGF), TNFα, TNFβ, GM-CSF, epidermal growth factor (EGF), cutaneous T cell-attracting chemokine (CTACK), epithelial thymus-expressed chemokine (TECK), mucosae-associated epithelial chemokine (MEC), IL-12, IL-15, MHC, CD80,CD86 including IL-15 having the signal sequence deleted and optionally including the signal peptide from IgE. Other genes which may be useful adjuvants include those encoding: MCP-1, MIP-l-alpha, MIP-1p, IL-8, RANTES, L-selectin, P-selectin, E-selectin, CD34, GlyCAM-1, MadCAM-1, LFA-1, VLA-1, Mac-1, pl50.95, PECAM, ICAM-1, ICAM-2, ICAM-3, CD2, LFA-3, M-CSF, G-CSF, IL-4, mutant forms of IL-18, CD40, CD40L, vascular growth factor, fibroblast growth factor, IL-7, nerve growth factor, vascular endothelial growth factor, Fas, TNF receptor, Flt, Apo-1, p55, WSL-1, DR3, TRAMP, Apo-3, AIR, LARD, NGRF, DR4, DR5, KILLER, TRAIL-R2, TRICK2, DR6, Caspase ICE, Fos, c-jun, Sp-1, Ap-1, Ap-2, p38, p65Rel, MyD88, IRAK, TRAF6, IkB, Inactive NIK, SAP K, SAP-1, JNK, interferon response genes, NFkB, Bax, TRAIL, TRAILrec, TRAILrecDRC5, TRAIL-R3, TRAIL-R4,

RANK, RANK LIGAND, Ox40, Ox40 LIGAND, NKG2D, MICA, MICB, NKG2A, NKG2B, NKG2C, NKG2E, NKG2F, TAP1, TAP2 and functional fragments thereof. In some preferred embodiments, the adjuvant is selected from IL-12, IL-15, CTACK, TECK, or MEC.

[00127] In some embodiments, methods of eliciting an immune response in mammals against a consensus antigen include methods of inducing mucosal immune responses. Such methods include administering to the mammal one or more of CTACK protein, TECK protein, MEC protein and functional fragments thereof or expressible coding sequences thereof in combination with a DNA plasmid including a consensus antigen, described above. The one or more of CTACK protein, TECK protein, MEC protein and functional fragments thereof may be administered prior to, simultaneously with or after administration of the DNA plasmid vaccines provided herein. In some embodiments, an isolated nucleic acid molecule that encodes one or more proteins of selected from the group consisting of: CTACK, TECK, MEC and functional fragments thereof is administered to the mammal.

3. **DNA Vaccine**

[00128] As described above, the composition can comprise immunogenic compositions, such as vaccines, comprising one or more antigens. The vaccine can be used to protect against any number of antigens, thereby treating, preventing, and/or protecting against antigen based pathologies. The vaccine can significantly induce an immune response of a subject administered the vaccine, thereby protecting against and treating infection by the antigen.

[00129] The vaccine can be a DNA vaccine, a peptide vaccine, or a combination DNA and peptide vaccine. The DNA vaccine can include a nucleic acid sequence encoding the antigen. The nucleic acid sequence can be DNA, RNA, cDNA, a variant thereof, a fragment thereof, or a combination thereof. The nucleic acid sequence can also include additional sequences that encode linker, leader, or tag sequences that are linked to the antigen by a peptide bond. The peptide vaccine can include a antigenic peptide, a antigenic protein, a variant thereof, a fragment thereof, or a combination thereof. The combination DNA and peptide vaccine can include the above described nucleic acid sequence encoding the antigen and the antigenic peptide or protein, in which the antigenic peptide or protein and the encoded antigen have the same amino acid sequence.

[00130] The vaccine can induce a humoral immune response in the subject administered the vaccine. The induced humoral immune response can be specific for the antigen. The induced humoral immune response can be reactive with the antigen. The humoral immune response can be induced in the subject administered the vaccine by about 1.5-fold to about 16-fold, about 2-fold to about 12-fold, or about 3-fold to about 10-fold. The humoral immune response can be induced in the subject administered the vaccine by at least about 1.5-fold, at least about 2.0-fold, at least about 2.5-fold, at least about 3.0-fold, at least about 3.5-fold, at least about 4.0-fold, at least about 4.5-fold, at least about 5.0-fold, at least about 5.5-fold, at least about 6.0-fold, at least about 6.5-fold, at least about 7.0-fold, at least about 7.5-fold, at least about 8.0-fold, at least about 8.5-fold, at least about 9.0-fold, at least about 9.5-fold, at least about 10.0-fold, at least about 10.5-fold, at least about 11.0-fold, at least about 11.5-fold, at least about 12.0-fold, at least about 12.5-fold, at least about 13.0-fold, at least about 13.5-fold, at least about 14.0-fold, at least about 14.5-fold, at least about 15.0-fold, at least about 15.5-fold, or at least about 16.0-fold.

[00131] The humoral immune response induced by the vaccine can include an increased level of neutralizing antibodies associated with the subject administered the vaccine as compared to a subject not administered the vaccine. The neutralizing antibodies can be specific for the antigen. The neutralizing antibodies can be reactive with the antigen. The neutralizing antibodies can provide protection against and/or treatment of infection and its associated pathologies in the subject administered the vaccine.

[00132] The humoral immune response induced by the vaccine can include an increased level of IgG antibodies associated with the subject administered the vaccine as compared to a subject not administered the vaccine. These IgG antibodies can be specific for the antigen. These IgG antibodies can be reactive with the antigen. Preferably, the humoral response is cross-reactive against two or more strains of the antigen. The level of IgG antibody associated with the subject administered the vaccine can be increased by about 1.5-fold to about 16-fold, about 2-fold to about 12-fold, or about 3-fold to about 10-fold as compared to the subject not administered the vaccine. The level of IgG antibody associated with the subject administered the vaccine can be increased by at least about 1.5-fold, at least about 2.0-fold, at least about 2.5-fold, at least about 3.0-fold, at least about 3.5-fold, at least about 4.0-fold, at least about 4.5-fold, at least about 5.0-fold, at least about 5.5-fold, at least about 6.0-fold, at least about 6.5-fold, at least about 7.0-fold, at least about 7.5-fold, at least about 8.0-fold, at least about 8.5-fold, at least about 9.0-fold, at

least about 9.5-fold, at least about 10.0-fold, at least about 10.5-fold, at least about 11.0-fold, at least about 11.5-fold, at least about 12.0-fold, at least about 12.5-fold, at least about 13.0-fold, at least about 13.5-fold, at least about 14.0-fold, at least about 14.5-fold, at least about 15.0-fold, at least about 15.5-fold, or at least about 16.0-fold as compared to the subject not administered the vaccine.

[00133] The vaccine can induce a cellular immune response in the subject administered the vaccine. The induced cellular immune response can be specific for the antigen. The induced cellular immune response can be reactive to the antigen. Preferably, the cellular response is cross-reactive against two or more strains of the antigen. The induced cellular immune response can include eliciting a $CD8^+$ T cell response. The elicited $CD8^+$ T cell response can be reactive with the antigen. The elicited $CD8^+$ T cell response can be polyfunctional. The induced cellular immune response can include eliciting a $CD8^+$ T cell response, in which the $CD8^+$ T cells produce interferon-gamma (IFN-γ), tumor necrosis factor alpha (TNF-α), interleukin-2 (IL-2), or a combination of IFN-γ and TNF-α.

[00134] The induced cellular immune response can include an increased $CD8^+$ T cell response associated with the subject administered the vaccine as compared to the subject not administered the vaccine. The $CD8^+$ T cell response associated with the subject administered the vaccine can be increased by about 2-fold to about 30-fold, about 3-fold to about 25-fold, or about 4-fold to about 20-fold as compared to the subject not administered the vaccine. The $CD8^+$ T cell response associated with the subject administered the vaccine can be increased by at least about 1.5-fold, at least about 2.0-fold, at least about 3.0-fold, at least about 4.0-fold, at least about 5.0-fold, at least about 6.0-fold, at least about 6.5-fold, at least about 7.0-fold, at least about 7.5-fold, at least about 8.0-fold, at least about 8.5-fold, at least about 9.0-fold, at least about 9.5-fold, at least about 10.0-fold, at least about 10.5-fold, at least about 11.0-fold, at least about 11.5-fold, at least about 12.0-fold, at least about 12.5-fold, at least about 13.0-fold, at least about 13.5-fold, at least about 14.0-fold, at least about 14.5-fold, at least about 15.0-fold, at least about 16.0-fold, at least about 17.0-fold, at least about 18.0-fold, at least about 19.0-fold, at least about 20.0-fold, at least about 21.0-fold, at least about 22.0-fold, at least about 23.0-fold, at least about 24.0-fold, at least about 25.0-fold, at least about 26.0-fold, at least about 27.0-fold, at least about 28.0-fold, at least about 29.0-fold, or at least about 30.0-fold as compared to the subject not administered the vaccine.

[00135] The induced cellular immune response can include an increased frequency of $CD3^+CD8^+$ T cells that produce IFN-γ. The frequency of $CD3^+CD8^+IFN\text{-}\gamma^+$ T cells associated with the subject administered the vaccine can be increased by at least about 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 11-fold, 12-fold, 13-fold, 14-fold, 15-fold, 16-fold, 17-fold, 18-fold, 19-fold, or 20-fold as compared to the subject not administered the vaccine.

[00136] The induced cellular immune response can include an increased frequency of $CD3^+CD8^+$ T cells that produce TNF-α. The frequency of $CD3^+CD8^+TNF\text{-}\alpha^+$ T cells associated with the subject administered the vaccine can be increased by at least about 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 11-fold, 12-fold, 13-fold, or 14-fold as compared to the subject not administered the vaccine.

[00137] The induced cellular immune response can include an increased frequency of $CD3^+CD8^+$ T cells that produce IL-2. The frequency of $CD3^+CD8^+IL\text{-}2^+$ T cells associated with the subject administered the vaccine can be increased by at least about 0.5-fold, 1.0-fold, 1.5-fold, 2.0-fold, 2.5-fold, 3.0-fold, 3.5-fold, 4.0-fold, 4.5-fold, or 5.0-fold as compared to the subject not administered the vaccine.

[00138] The induced cellular immune response can include an increased frequency of $CD3^+CD8^+$ T cells that produce both IFN-γ and TNF-α. The frequency of $CD3^+CD8^+IFN\text{-}\gamma^+TNF\text{-}\alpha^+$ T cells associated with the subject administered the vaccine can be increased by at least about 25-fold, 30-fold, 35-fold, 40-fold, 45-fold, 50-fold, 55-fold, 60-fold, 65-fold, 70-fold, 75-fold, 80-fold, 85-fold, 90-fold, 95-fold, 100-fold, 110-fold, 120-fold, 130-fold, 140-fold, 150-fold, 160-fold, 170-fold, or 180-fold as compared to the subject not administered the vaccine.

[00139] The cellular immune response induced by the vaccine can include eliciting a $CD4^+$ T cell response. The elicited $CD4^+$ T cell response can be reactive with the desired antigen. The elicited $CD4^+$ T cell response can be polyfunctional. The induced cellular immune response can include eliciting a $CD4^+$ T cell response, in which the $CD4^+$ T cells produce IFN-γ, TNF-α, IL-2, or a combination of IFN-γ and TNF-α.

[00140] The induced cellular immune response can include an increased frequency of $CD3^+CD4^+$ T cells that produce IFN-γ. The frequency of $CD3^+CD4^+IFN\text{-}\gamma^+$ T cells associated with the subject administered the vaccine can be increased by at least about 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 11-fold, 12-fold, 13-fold, 14-fold, 15-fold, 16-fold, 17-fold, 18-fold, 19-fold, or 20-fold as compared to the subject not administered the vaccine.

[00141] The induced cellular immune response can include an increased frequency of $CD3^+CD4^+$ T cells that produce TNF-α. The frequency of $CD3^+CD4^+TNF\text{-}\alpha^+$ T cells associated with the subject administered the vaccine can be increased by at least about 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 11-fold, 12-fold, 13-fold, 14-fold, 15-fold, 16-fold, 17-fold, 18-fold, 19-fold, 20-fold, 21-fold, or 22-fold as compared to the subject not administered the vaccine.

[00142] The induced cellular immune response can include an increased frequency of $CD3^+CD4^+$ T cells that produce IL-2. The frequency of $CD3^+CD4^+IL\text{-}2^+$ T cells associated with the subject administered the vaccine can be increased by at least about 2-fold, 3-fold, 4-fold, 5-fold, 6-fold, 7-fold, 8-fold, 9-fold, 10-fold, 11-fold, 12-fold, 13-fold, 14-fold, 15-fold, 16-fold, 17-fold, 18-fold, 19-fold, 20-fold, 21-fold, 22-fold, 23-fold, 24-fold, 25-fold, 26-fold, 27-fold, 28-fold, 29-fold, 30-fold, 31-fold, 32-fold, 33-fold, 34-fold, 35-fold, 36-fold, 37-fold, 38-fold, 39-fold, 40-fold, 45-fold, 50-fold, 55-fold, or 60-fold as compared to the subject not administered the vaccine.

[00143] The induced cellular immune response can include an increased frequency of $CD3^+CD4^+$ T cells that produce both IFN-γ and TNF-α. The frequency of $CD3^+CD4^+IFN\text{-}\gamma^+TNF\text{-}\alpha^+$ associated with the subject administered the vaccine can be increased by at least about 2-fold, 2.5-fold, 3.0-fold, 3.5-fold, 4.0-fold, 4.5-fold, 5.0-fold, 5.5-fold, 6.0-fold, 6.5-fold, 7.0-fold, 7.5-fold, 8.0-fold, 8.5-fold, 9.0-fold, 9.5-fold, 10.0-fold, 10.5-fold, 11.0-fold, 11.5-fold, 12.0-fold, 12.5-fold, 13.0-fold, 13.5-fold, 14.0-fold, 14.5-fold, 15.0-fold, 15.5-fold, 16.0-fold, 16.5-fold, 17.0-fold, 17.5-fold, 18.0-fold, 18.5-fold, 19.0-fold, 19.5-fold, 20.0-fold, 21-fold, 22-fold, 23-fold 24-fold, 25-fold, 26-fold, 27-fold, 28-fold, 29-fold, 30-fold, 31-fold, 32-fold, 33-fold, 34-fold, or 35-fold as compared to the subject not administered the vaccine.

[00144] The vaccine of the present invention can have features required of effective vaccines such as being safe so the vaccine itself does not cause illness or death; is protective against illness resulting from exposure to live pathogens such as viruses or bacteria; induces neutralizing antibody to prevent invention of cells; induces protective T cells against intracellular pathogens; and provides ease of administration, few side effects, biological stability, and low cost per dose.

[00145] The vaccine can further induce an immune response when administered to different tissues such as the muscle or skin. The vaccine can further induce an immune response when administered via electroporation, or injection, or subcutaneously, or intramuscularly.

a. Vaccine Constructs and Plasmids

[00146] The vaccine can comprise nucleic acid constructs or plasmids that encode the one or more antigens. The nucleic acid constructs or plasmids can include or contain one or more heterologous nucleic acid sequences. Provided herein are genetic constructs that can comprise a nucleic acid sequence that encodes the antigens. The genetic construct can be present in the cell as a functioning extrachromosomal molecule. The genetic construct can be a linear minichromosome including centromere, telomeres or plasmids or cosmids. The genetic constructs can include or contain one or more heterologous nucleic acid sequences.

[00147] The genetic constructs can be in the form of plasmids expressing the antigen in any order.

[00148] The genetic construct can also be part of a genome of a recombinant viral vector, including recombinant adenovirus, recombinant adenovirus associated virus and recombinant vaccinia. The genetic construct can be part of the genetic material in attenuated live microorganisms or recombinant microbial vectors which live in cells.

[00149] The genetic constructs can comprise regulatory elements for gene expression of the coding sequences of the nucleic acid. The regulatory elements can be a promoter, an enhancer an initiation codon, a stop codon, or a polyadenylation signal.

[00150] The nucleic acid sequences can make up a genetic construct that can be a vector. The vector can be capable of expressing the antigen in the cell of a mammal in a quantity effective to elicit an immune response in the mammal. The vector can be recombinant. The vector can comprise heterologous nucleic acid encoding the antigen. The vector can be a plasmid. The vector can be useful for transfecting cells with nucleic acid encoding the antigen, which the transformed host cell is cultured and maintained under conditions wherein expression of the antigen takes place.

[00151] Coding sequences can be optimized for stability and high levels of expression. In some instances, codons are selected to reduce secondary structure formation of the RNA such as that formed due to intramolecular bonding.

[00152] The vector can comprise heterologous nucleic acid encoding the antigens and can further comprise an initiation codon, which can be upstream of the one or more cancer antigen coding sequence(s), and a stop codon, which can be downstream of the coding sequence(s) of the antigen. The initiation and termination codon can be in frame with the coding sequence(s) of the

antigen. The vector can also comprise a promoter that is operably linked to the coding sequence(s) of the antigen. The promoter operably linked to the coding sequence(s) of the antigen can be a promoter from simian virus 40 (SV40), a mouse mammary tumor virus (MMTV) promoter, a human immunodeficiency virus (HIV) promoter such as the bovine immunodeficiency virus (BIV) long terminal repeat (LTR) promoter, a Moloney virus promoter, an avian leukosis virus (ALV) promoter, a cytomegalovirus (CMV) promoter such as the CMV immediate early promoter, Epstein Barr virus (EBV) promoter, or a Rous sarcoma virus (RSV) promoter. The promoter can also be a promoter from a human gene such as human actin, human myosin, human hemoglobin, human muscle creatine, or human metalothionein. The promoter can also be a tissue specific promoter, such as a muscle or skin specific promoter, natural or synthetic. Examples of such promoters are described in US patent application publication no. US20040175727, the contents of which are incorporated herein in its entirety.

[00153] The vector can also comprise a polyadenylation signal, which can be downstream of the coding sequence(s) of the antigen. The polyadenylation signal can be a SV40 polyadenylation signal, LTR polyadenylation signal, bovine growth hormone (bGH) polyadenylation signal, human growth hormone (hGH) polyadenylation signal, or human β-globin polyadenylation signal. The SV40 polyadenylation signal can be a polyadenylation signal from a pCEP4 vector (Invitrogen, San Diego, CA).

[00154] The vector can also comprise an enhancer upstream of the antigen. The enhancer can be necessary for DNA expression. The enhancer can be human actin, human myosin, human hemoglobin, human muscle creatine or a viral enhancer such as one from CMV, HA, RSV or EBV. Polynucleotide function enhances are described in U.S. Patent Nos. 5,593,972, 5,962,428, and WO94/016737, the contents of each are fully incorporated by reference.

[00155] The vector can also comprise a mammalian origin of replication in order to maintain the vector extrachromosomally and produce multiple copies of the vector in a cell. The vector can be pVAX1, pCEP4 or pREP4 from Invitrogen (San Diego, CA), which can comprise the Epstein Barr virus origin of replication and nuclear antigen EBNA-1 coding region, which can produce high copy episomal replication without integration. The vector can be pVAX1 or a pVax1 variant with changes such as the variant plasmid described herein. The variant pVax1 plasmid is a 2998 basepair variant of the backbone vector plasmid pVAX1 (Invitrogen, Carlsbad CA). The CMV promoter is located at bases 137-724. The T7 promoter/priming site is at bases

664-683. Multiple cloning sites are at bases 696-811. Bovine GH polyadenylation signal is at bases 829-1053. The Kanamycin resistance gene is at bases 1226-2020. The pUC origin is at bases 2320-2993.

[00156] Based upon the sequence of pVAX1 available from Invitrogen, the following mutations were found in the sequence of pVAX1 that was used as the backbone for plasmids 1-6 set forth herein:

[00157] C>G241 in CMV promoter

[00158] C>T1942 backbone, downstream of the bovine growth hormone polyadenylation signal (bGHpolyA)

[00159] A> -2876 backbone, downstream of the Kanamycin gene

[00160] C>T3277 in pUC origin of replication (Ori) high copy number mutation (see Nucleic Acid Research 1985)

[00161] G>C 3753 in very end of pUC Ori upstream of RNASeH site

[00162] Base pairs 2, 3 and 4 are changed from ACT to CTG in backbone, upstream of CMV promoter.

[00163] The backbone of the vector can be pAV0242. The vector can be a replication defective adenovirus type 5 (Ad5) vector.

[00164] The vector can also comprise a regulatory sequence, which can be well suited for gene expression in a mammalian or human cell into which the vector is administered. The one or more cancer antigen sequences disclosed herein can comprise a codon, which can allow more efficient transcription of the coding sequence in the host cell.

[00165] The vector can be pSE420 (Invitrogen, San Diego, Calif.), which can be used for protein production in Escherichia coli (E. coli). The vector can also be pYES2 (Invitrogen, San Diego, Calif.), which can be used for protein production in Saccharomyces cerevisiae strains of yeast. The vector can also be of the MAXBAC™ complete baculovirus expression system (Invitrogen, San Diego, Calif.), which can be used for protein production in insect cells. The vector can also be pcDNA I or pcDNA3 (Invitrogen, San Diego, Calif.), which maybe used for protein production in mammalian cells such as Chinese hamster ovary (CHO) cells. The vector can be expression vectors or systems to produce protein by routine techniques and readily available starting materials including Sambrook et al., Molecular Cloning and Laboratory Manual, Second Ed., Cold Spring Harbor (1989), which is incorporated fully by reference.

4. **DNA encoded antibody**

[00166] As described above, the composition can comprise a recombinant nucleic acid sequence. The recombinant nucleic acid sequence can encode the antibody, a fragment thereof, a variant thereof, or a combination thereof. The antibody is described in more detail below.

[00167] The recombinant nucleic acid sequence can be a heterologous nucleic acid sequence. The recombinant nucleic acid sequence can include at least one heterologous nucleic acid sequence or one or more heterologous nucleic acid sequences.

[00168] The recombinant nucleic acid sequence can be an optimized nucleic acid sequence. Such optimization can increase or alter the immunogenicity of the antibody. Optimization can also improve transcription and/or translation. Optimization can include one or more of the following: low GC content leader sequence to increase transcription; mRNA stability and codon optimization; addition of a kozak sequence (e.g., GCC ACC) for increased translation; addition of an immunoglobulin (Ig) leader sequence encoding a signal peptide; and eliminating to the extent possible cis-acting sequence motifs (i.e., internal TATA boxes).

a. Recombinant Nucleic Acid Sequence Construct

[00169] The recombinant nucleic acid sequence can include one or more recombinant nucleic acid sequence constructs. The recombinant nucleic acid sequence construct can include one or more components, which are described in more detail below.

[00170] The recombinant nucleic acid sequence construct can include a heterologous nucleic acid sequence that encodes a heavy chain polypeptide, a fragment thereof, a variant thereof, or a combination thereof. The recombinant nucleic acid sequence construct can include a heterologous nucleic acid sequence that encodes a light chain polypeptide, a fragment thereof, a variant thereof, or a combination thereof. The recombinant nucleic acid sequence construct can also include a heterologous nucleic acid sequence that encodes a protease or peptidase cleavage site. The recombinant nucleic acid sequence construct can include one or more leader sequences, in which each leader sequence encodes a signal peptide. The recombinant nucleic acid sequence construct can include one or more promoters, one or more introns, one or more transcription termination regions, one or more initiation codons, one or more termination or stop codons,

and/or one or more polyadenylation signals. The recombinant nucleic acid sequence construct can also include one or more linker or tag sequences. The tag sequence can encode a hemagglutinin (HA) tag.

(1) Heavy Chain Polypeptide

[00171] The recombinant nucleic acid sequence construct can include the heterologous nucleic acid encoding the heavy chain polypeptide, a fragment thereof, a variant thereof, or a combination thereof. The heavy chain polypeptide can include a variable heavy chain (VH) region and/or at least one constant heavy chain (CH) region. The at least one constant heavy chain region can include a constant heavy chain region 1 (CH1), a constant heavy chain region 2 (CH2), and a constant heavy chain region 3 (CH3), and/or a hinge region.

[00172] In some embodiments, the heavy chain polypeptide can include a VH region and a CH1 region. In other embodiments, the heavy chain polypeptide can include a VH region, a CH1 region, a hinge region, a CH2 region, and a CH3 region.

[00173] The heavy chain polypeptide can include a complementarity determining region ("CDR") set. The CDR set can contain three hypervariable regions of the VH region. Proceeding from N-terminus of the heavy chain polypeptide, these CDRs are denoted "CDR1," "CDR2," and "CDR3," respectively. CDR1, CDR2, and CDR3 of the heavy chain polypeptide can contribute to binding or recognition of the antigen.

(2) Light Chain Polypeptide

[00174] The recombinant nucleic acid sequence construct can include the heterologous nucleic acid sequence encoding the light chain polypeptide, a fragment thereof, a variant thereof, or a combination thereof. The light chain polypeptide can include a variable light chain (VL) region and/or a constant light chain (CL) region.

[00175] The light chain polypeptide can include a complementarity determining region ("CDR") set. The CDR set can contain three hypervariable regions of the VL region. Proceeding from N-terminus of the light chain polypeptide, these CDRs are denoted "CDR1," "CDR2," and "CDR3," respectively. CDR1, CDR2, and CDR3 of the light chain polypeptide can contribute to binding or recognition of the antigen.

(3) Protease Cleavage Site

[00176] The recombinant nucleic acid sequence construct can include the heterologous nucleic acid sequence encoding the protease cleavage site. The protease cleavage site can be recognized by a protease or peptidase. The protease can be an endopeptidase or endoprotease, for example, but not limited to, furin, elastase, HtrA, calpain, trypsin, chymotrypsin, trypsin, and pepsin. The protease can be furin. In other embodiments, the protease can be a serine protease, a threonine protease, cysteine protease, aspartate protease, metalloprotease, glutamic acid protease, or any protease that cleaves an internal peptide bond (i.e., does not cleave the N-terminal or C-terminal peptide bond).

[00177] The protease cleavage site can include one or more amino acid sequences that promote or increase the efficiency of cleavage. The one or more amino acid sequences can promote or increase the efficiency of forming or generating discrete polypeptides. The one or more amino acids sequences can include a 2A peptide sequence.

(4) Linker Sequence

[00178] The recombinant nucleic acid sequence construct can include one or more linker sequences. The linker sequence can spatially separate or link the one or more components described herein. In other embodiments, the linker sequence can encode an amino acid sequence that spatially separates or links two or more polypeptides.

(5) Promoter

[00179] The recombinant nucleic acid sequence construct can include one or more promoters. The one or more promoters may be any promoter that is capable of driving gene expression and regulating gene expression. Such a promoter is a cis-acting sequence element required for transcription via a DNA dependent RNA polymerase. Selection of the promoter used to direct gene expression depends on the particular application. The promoter may be positioned about the same distance from the transcription start in the recombinant nucleic acid sequence construct as it is from the transcription start site in its natural setting. However, variation in this distance may be accommodated without loss of promoter function.

[00180] The promoter may be operably linked to the heterologous nucleic acid sequence encoding the heavy chain polypeptide and/or light chain polypeptide. The promoter may be a

promoter shown effective for expression in eukaryotic cells. The promoter operably linked to the coding sequence may be a CMV promoter, a promoter from simian virus 40 (SV40), such as SV40 early promoter and SV40 later promoter, a mouse mammary tumor virus (MMTV) promoter, a human immunodeficiency virus (HIV) promoter such as the bovine immunodeficiency virus (BIV) long terminal repeat (LTR) promoter, a Moloney virus promoter, an avian leukosis virus (ALV) promoter, a cytomegalovirus (CMV) promoter such as the CMV immediate early promoter, Epstein Barr virus (EBV) promoter, or a Rous sarcoma virus (RSV) promoter. The promoter may also be a promoter from a human gene such as human actin, human myosin, human hemoglobin, human muscle creatine, human polyhedrin, or human metalothionein.

[00181] The promoter can be a constitutive promoter or an inducible promoter, which initiates transcription only when the host cell is exposed to some particular external stimulus. In the case of a multicellular organism, the promoter can also be specific to a particular tissue or organ or stage of development. The promoter may also be a tissue specific promoter, such as a muscle or skin specific promoter, natural or synthetic. Examples of such promoters are described in US patent application publication no. US20040175727, the contents of which are incorporated herein in its entirety.

[00182] The promoter can be associated with an enhancer. The enhancer can be located upstream of the coding sequence. The enhancer may be human actin, human myosin, human hemoglobin, human muscle creatine or a viral enhancer such as one from CMV, FMDV, RSV or EBV. Polynucleotide function enhances are described in U.S. Patent Nos. 5,593,972, 5,962,428, and W094/016737, the contents of each are fully incorporated by reference.

(6) Intron

[00183] The recombinant nucleic acid sequence construct can include one or more introns. Each intron can include functional splice donor and acceptor sites. The intron can include an enhancer of splicing. The intron can include one or more signals required for efficient splicing.

(7) Transcription Termination Region

[00184] The recombinant nucleic acid sequence construct can include one or more transcription termination regions. The transcription termination region can be downstream of the

coding sequence to provide for efficient termination. The transcription termination region can be obtained from the same gene as the promoter described above or can be obtained from one or more different genes.

(8) Initiation Codon

[00185] The recombinant nucleic acid sequence construct can include one or more initiation codons. The initiation codon can be located upstream of the coding sequence. The initiation codon can be in frame with the coding sequence. The initiation codon can be associated with one or more signals required for efficient translation initiation, for example, but not limited to, a ribosome binding site.

(9) Termination Codon

[00186] The recombinant nucleic acid sequence construct can include one or more termination or stop codons. The termination codon can be downstream of the coding sequence. The termination codon can be in frame with the coding sequence. The termination codon can be associated with one or more signals required for efficient translation termination.

(10) Polyadenylation Signal

[00187] The recombinant nucleic acid sequence construct can include one or more polyadenylation signals. The polyadenylation signal can include one or more signals required for efficient polyadenylation of the transcript. The polyadenylation signal can be positioned downstream of the coding sequence. The polyadenylation signal may be a SV40 polyadenylation signal, LTR polyadenylation signal, bovine growth hormone (bGH) polyadenylation signal, human growth hormone (hGH) polyadenylation signal, or human β-globin polyadenylation signal. The SV40 polyadenylation signal may be a polyadenylation signal from a pCEP4 plasmid (Invitrogen, San Diego, CA).

(11) Leader Sequence

[00188] The recombinant nucleic acid sequence construct can include one or more leader sequences. The leader sequence can encode a signal peptide. The signal peptide can be an

immunoglobulin (Ig) signal peptide, for example, but not limited to, an IgG signal peptide and a IgE signal peptide.

b. Arrangement of the Recombinant Nucleic Acid Sequence Construct

[00189] As described above, the recombinant nucleic acid sequence can include one or more recombinant nucleic acid sequence constructs, in which each recombinant nucleic acid sequence construct can include one or more components. The one or more components are described in detail above. The one or more components, when included in the recombinant nucleic acid sequence construct, can be arranged in any order relative to one another. In some embodiments, the one or more components can be arranged in the recombinant nucleic acid sequence construct as described below.

(1) Arrangement 1

[00190] In one arrangement, a first recombinant nucleic acid sequence construct can include the heterologous nucleic acid sequence encoding the heavy chain polypeptide and a second recombinant nucleic acid sequence construct can include the heterologous nucleic acid sequence encoding the light chain polypeptide.

[00191] The first recombinant nucleic acid sequence construct can be placed in a vector. The second recombinant nucleic acid sequence construct can be placed in a second or separate vector. Placement of the recombinant nucleic acid sequence construct into the vector is described in more detail below.

[00192] The first recombinant nucleic acid sequence construct can also include the promoter, intron, transcription termination region, initiation codon, termination codon, and/or polyadenylation signal. The first recombinant nucleic acid sequence construct can further include the leader sequence, in which the leader sequence is located upstream (or 5') of the heterologous nucleic acid sequence encoding the heavy chain polypeptide. Accordingly, the signal peptide encoded by the leader sequence can be linked by a peptide bond to the heavy chain polypeptide.

[00193] The second recombinant nucleic acid sequence construct can also include the promoter, initiation codon, termination codon, and polyadenylation signal. The second recombinant nucleic acid sequence construct can further include the leader sequence, in which the leader sequence is located upstream (or 5') of the heterologous nucleic acid sequence

encoding the light chain polypeptide. Accordingly, the signal peptide encoded by the leader sequence can be linked by a peptide bond to the light chain polypeptide.

[00194] Accordingly, one example of arrangement 1 can include the first vector (and thus first recombinant nucleic acid sequence construct) encoding the heavy chain polypeptide that includes VH and CH1, and the second vector (and thus second recombinant nucleic acid sequence construct) encoding the light chain polypeptide that includes VL and CL. A second example of arrangement 1 can include the first vector (and thus first recombinant nucleic acid sequence construct) encoding the heavy chain polypeptide that includes VH, CH1, hinge region, CH2, and CH3, and the second vector (and thus second recombinant nucleic acid sequence construct) encoding the light chain polypeptide that includes VL and CL.

(2) Arrangement 2

[00195] In a second arrangement, the recombinant nucleic acid sequence construct can include the heterologous nucleic acid sequence encoding the heavy chain polypeptide and the heterologous nucleic acid sequence encoding the light chain polypeptide. The heterologous nucleic acid sequence encoding the heavy chain polypeptide can be positioned upstream (or 5') of the heterologous nucleic acid sequence encoding the light chain polypeptide. Alternatively, the heterologous nucleic acid sequence encoding the light chain polypeptide can be positioned upstream (or 5') of the heterologous nucleic acid sequence encoding the heavy chain polypeptide.

[00196] The recombinant nucleic acid sequence construct can be placed in the vector as described in more detail below.

[00197] The recombinant nucleic acid sequence construct can include the heterologous nucleic acid sequence encoding the protease cleavage site and/or the linker sequence. If included in the recombinant nucleic acid sequence construct, the heterologous nucleic acid sequence encoding the protease cleavage site can be positioned between the heterologous nucleic acid sequence encoding the heavy chain polypeptide and the heterologous nucleic acid sequence encoding the light chain polypeptide. Accordingly, the protease cleavage site allows for separation of the heavy chain polypeptide and the light chain polypeptide into distinct polypeptides upon expression. In other embodiments, if the linker sequence is included in the recombinant nucleic acid sequence construct, then the linker sequence can be positioned between the heterologous

nucleic acid sequence encoding the heavy chain polypeptide and the heterologous nucleic acid sequence encoding the light chain polypeptide.

[00198] The recombinant nucleic acid sequence construct can also include the promoter, intron, transcription termination region, initiation codon, termination codon, and/or polyadenylation signal. The recombinant nucleic acid sequence construct can include one or more promoters. The recombinant nucleic acid sequence construct can include two promoters such that one promoter can be associated with the heterologous nucleic acid sequence encoding the heavy chain polypeptide and the second promoter can be associated with the heterologous nucleic acid sequence encoding the light chain polypeptide. In still other embodiments, the recombinant nucleic acid sequence construct can include one promoter that is associated with the heterologous nucleic acid sequence encoding the heavy chain polypeptide and the heterologous nucleic acid sequence encoding the light chain polypeptide.

[00199] The recombinant nucleic acid sequence construct can further include two leader sequences, in which a first leader sequence is located upstream (or 5') of the heterologous nucleic acid sequence encoding the heavy chain polypeptide and a second leader sequence is located upstream (or 5') of the heterologous nucleic acid sequence encoding the light chain polypeptide. Accordingly, a first signal peptide encoded by the first leader sequence can be linked by a peptide bond to the heavy chain polypeptide and a second signal peptide encoded by the second leader sequence can be linked by a peptide bond to the light chain polypeptide.

[00200] Accordingly, one example of arrangement 2 can include the vector (and thus recombinant nucleic acid sequence construct) encoding the heavy chain polypeptide that includes VH and CH1, and the light chain polypeptide that includes VL and CL, in which the linker sequence is positioned between the heterologous nucleic acid sequence encoding the heavy chain polypeptide and the heterologous nucleic acid sequence encoding the light chain polypeptide.

[00201] A second example of arrangement of 2 can include the vector (and thus recombinant nucleic acid sequence construct) encoding the heavy chain polypeptide that includes VH and CH1, and the light chain polypeptide that includes VL and CL, in which the heterologous nucleic acid sequence encoding the protease cleavage site is positioned between the heterologous nucleic acid sequence encoding the heavy chain polypeptide and the heterologous nucleic acid sequence encoding the light chain polypeptide.

[00202] A third example of arrangement 2 can include the vector (and thus recombinant nucleic acid sequence construct) encoding the heavy chain polypeptide that includes VH, CH1, hinge region, CH2, and CH3, and the light chain polypeptide that includes VL and CL, in which the linker sequence is positioned between the heterologous nucleic acid sequence encoding the heavy chain polypeptide and the heterologous nucleic acid sequence encoding the light chain polypeptide.

[00203] A forth example of arrangement of 2 can include the vector (and thus recombinant nucleic acid sequence construct) encoding the heavy chain polypeptide that includes VH, CH1, hinge region, CH2, and CH3, and the light chain polypeptide that includes VL and CL, in which the heterologous nucleic acid sequence encoding the protease cleavage site is positioned between the heterologous nucleic acid sequence encoding the heavy chain polypeptide and the heterologous nucleic acid sequence encoding the light chain polypeptide.

c. Expression from the Recombinant Nucleic Acid Sequence Construct

[00204] As described above, the recombinant nucleic acid sequence construct can include, amongst the one or more components, the heterologous nucleic acid sequence encoding the heavy chain polypeptide and/or the heterologous nucleic acid sequence encoding the light chain polypeptide. Accordingly, the recombinant nucleic acid sequence construct can facilitate expression of the heavy chain polypeptide and/or the light chain polypeptide.

[00205] When arrangement 1 as described above is utilized, the first recombinant nucleic acid sequence construct can facilitate the expression of the heavy chain polypeptide and the second recombinant nucleic acid sequence construct can facilitate expression of the light chain polypeptide. When arrangement 2 as described above is utilized, the recombinant nucleic acid sequence construct can facilitate the expression of the heavy chain polypeptide and the light chain polypeptide.

[00206] Upon expression, for example, but not limited to, in a cell, organism, or mammal, the heavy chain polypeptide and the light chain polypeptide can assemble into the synthetic antibody. In particular, the heavy chain polypeptide and the light chain polypeptide can interact with one another such that assembly results in the synthetic antibody being capable of binding the antigen. In other embodiments, the heavy chain polypeptide and the light chain polypeptide can interact with one another such that assembly results in the synthetic antibody being more

immunogenic as compared to an antibody not assembled as described herein. In still other embodiments, the heavy chain polypeptide and the light chain polypeptide can interact with one another such that assembly results in the synthetic antibody being capable of eliciting or inducing an immune response against the antigen.

d. Vector

[00207] The recombinant nucleic acid sequence construct described above can be placed in one or more vectors. The one or more vectors can contain an origin of replication. The one or more vectors can be a plasmid, bacteriophage, bacterial artificial chromosome or yeast artificial chromosome. The one or more vectors can be either a self-replication extra chromosomal vector, or a vector which integrates into a host genome.

[00208] The one or more vectors can be a heterologous expression construct, which is generally a plasmid that is used to introduce a specific gene into a target cell. Once the expression vector is inside the cell, the heavy chain polypeptide and/or light chain polypeptide that are encoded by the recombinant nucleic acid sequence construct is produced by the cellular-transcription and translation machinery ribosomal complexes. The one or more vectors can express large amounts of stable messenger RNA, and therefore proteins.

(1) Expression Vector

[00209] The one or more vectors can be a circular plasmid or a linear nucleic acid. The circular plasmid and linear nucleic acid are capable of directing expression of a particular nucleotide sequence in an appropriate subject cell. The one or more vectors comprising the recombinant nucleic acid sequence construct may be chimeric, meaning that at least one of its components is heterologous with respect to at least one of its other components.

(2) Plasmid

[00210] The one or more vectors can be a plasmid. The plasmid may be useful for transfecting cells with the recombinant nucleic acid sequence construct. The plasmid may be useful for introducing the recombinant nucleic acid sequence construct into the subject. The plasmid may also comprise a regulatory sequence, which may be well suited for gene expression in a cell into which the plasmid is administered.

[00211] The plasmid may also comprise a mammalian origin of replication in order to maintain the plasmid extrachromosomally and produce multiple copies of the plasmid in a cell. The plasmid may be pVAXI, pCEP4 or pREP4 from Invitrogen (San Diego, CA), which may comprise the Epstein Barr virus origin of replication and nuclear antigen EBNA-1 coding region, which may produce high copy episomal replication without integration. The backbone of the plasmid may be pAV0242. The plasmid may be a replication defective adenovirus type 5 (Ad5) plasmid.

[00212] The plasmid may be pSE420 (Invitrogen, San Diego, Calif.), which may be used for protein production in *Escherichia coli* (E.coli). The plasmid may also be p YES2 (Invitrogen, San Diego, Calif.), which may be used for protein production in Saccharomyces cerevisiae strains of yeast. The plasmid may also be of the MAXBAC™ complete baculovirus expression system (Invitrogen, San Diego, Calif.), which may be used for protein production in insect cells. The plasmid may also be pcDNAI or pcDNA3 (Invitrogen, San Diego, Calif.), which may be used for protein production in mammalian cells such as Chinese hamster ovary (CHO) cells.

(3) Circular and Linear Vector

[00213] The one or more vectors may be circular plasmid, which may transform a target cell by integration into the cellular genome or exist extrachromosomally (e.g., autonomous replicating plasmid with an origin of replication). The vector can be pVAX, pcDNA3.0, or provax, or any other expression vector capable of expressing the heavy chain polypeptide and/or light chain polypeptide encoded by the recombinant nucleic acid sequence construct.

[00214] Also provided herein is a linear nucleic acid, or linear expression cassette ("LEC"), that is capable of being efficiently delivered to a subject via electroporation and expressing the heavy chain polypeptide and/or light chain polypeptide encoded by the recombinant nucleic acid sequence construct. The LEC may be any linear DNA devoid of any phosphate backbone. The LEC may not contain any antibiotic resistance genes and/or a phosphate backbone. The LEC may not contain other nucleic acid sequences unrelated to the desired gene expression.

[00215] The LEC may be derived from any plasmid capable of being linearized. The plasmid may be capable of expressing the heavy chain polypeptide and/or light chain polypeptide encoded by the recombinant nucleic acid sequence construct. The plasmid can be pNP (Puerto Rico/34) or pM2 (New Caledonia/99). The plasmid may be WLV009, pVAX, pcDNA3.0, or

provax, or any other expression vector capable of expressing the heavy chain polypeptide and/or light chain polypeptide encoded by the recombinant nucleic acid sequence construct.

[00216] The LEC can be pcrM2. The LEC can be pcrNP. pcrNP and pcrMR can be derived from pNP (Puerto Rico/34) and pM2 (New Caledonia/99), respectively.

(4) Method of Preparing the Vector

[00217] Provided herein is a method for preparing the one or more vectors in which the recombinant nucleic acid sequence construct has been placed. After the final subcloning step, the vector can be used to inoculate a cell culture in a large scale fermentation tank, using known methods in the art.

[00218] In other embodiments, after the final subcloning step, the vector can be used with one or more electroporation (EP) devices. The EP devices are described below in more detail.

[00219] The one or more vectors can be formulated or manufactured using a combination of known devices and techniques, but preferably they are manufactured using a plasmid manufacturing technique that is described in WO/2008/148010, published December 4, 2008. In some examples, the DNA plasmids described herein can be formulated at concentrations greater than or equal to 10 mg/mL. The manufacturing techniques also include or incorporate various devices and protocols that are commonly known to those of ordinary skill in the art, in addition to those described in U.S. Serial No. 60/939792, including those described in a licensed patent, US Patent No. 7,238,522, which issued on July 3, 2007. The above-referenced application and patent, US Serial No. 60/939,792 and US Patent No. 7,238,522, respectively, are hereby incorporated in their entirety.

5. Antibody

[00220] As described above, the recombinant nucleic acid sequence can encode the antibody, a fragment thereof, a variant thereof, or a combination thereof. The antibody can bind or react with the antigen, which is described in more detail below.

[00221] The antibody may comprise a heavy chain and a light chain complementarity determining region ("CDR") set, respectively interposed between a heavy chain and a light chain framework ("FR") set which provide support to the CDRs and define the spatial relationship of the CDRs relative to each other. The CDR set may contain three hypervariable regions of a

heavy or light chain V region. Proceeding from the N-terminus of a heavy or light chain, these regions are denoted as "CDR1," "CDR2," and "CDR3," respectively. An antigen-binding site, therefore, may include six CDRs, comprising the CDR set from each of a heavy and a light chain V region.

[00222] The proteolytic enzyme papain preferentially cleaves IgG molecules to yield several fragments, two of which (the F(ab) fragments) each comprise a covalent heterodimer that includes an intact antigen-binding site. The enzyme pepsin is able to cleave IgG molecules to provide several fragments, including the $F(ab')_2$ fragment, which comprises both antigen-binding sites. Accordingly, the antibody can be the Fab or $F(ab')_2$. The Fab can include the heavy chain polypeptide and the light chain polypeptide. The heavy chain polypeptide of the Fab can include the VH region and the CH1 region. The light chain of the Fab can include the VL region and CL region.

[00223] The antibody can be an immunoglobulin (Ig). The Ig can be, for example, IgA, IgM, IgD, IgE, and IgG. The immunoglobulin can include the heavy chain polypeptide and the light chain polypeptide. The heavy chain polypeptide of the immunoglobulin can include a VH region, a CH1 region, a hinge region, a CH2 region, and a CH3 region. The light chain polypeptide of the immunoglobulin can include a VL region and CL region.

[00224] The antibody can be a polyclonal or monoclonal antibody. The antibody can be a chimeric antibody, a single chain antibody, an affinity matured antibody, a human antibody, a humanized antibody, or a fully human antibody. The humanized antibody can be an antibody from a non-human species that binds the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and framework regions from a human immunoglobulin molecule.

[00225] The antibody can be a bispecific antibody as described below in more detail. The antibody can be a bifunctional antibody as also described below in more detail.

[00226] As described above, the antibody can be generated in the subject upon administration of the composition to the subject. The antibody may have a half-life within the subject. In some embodiments, the antibody may be modified to extend or shorten its half-life within the subject. Such modifications are described below in more detail.

[00227] The antibody can be defucosylated as described in more detail below.

[00228] The antibody may be modified to reduce or prevent antibody-dependent enhancement (ADE) of disease associated with the antigen as described in more detail below.

a. Bispecific Antibody

[00229] The recombinant nucleic acid sequence can encode a bispecific antibody, a fragment thereof, a variant thereof, or a combination thereof. The bispecific antibody can bind or react with two antigens, for example, two of the antigens described below in more detail. The bispecific antibody can be comprised of fragments of two of the antibodies described herein, thereby allowing the bispecific antibody to bind or react with two desired target molecules, which may include the antigen, which is described below in more detail, a ligand, including a ligand for a receptor, a receptor, including a ligand-binding site on the receptor, a ligand-receptor complex, and a marker, including a cancer marker.

b. Bifunctional Antibody

[00230] The recombinant nucleic acid sequence can encode a bifunctional antibody, a fragment thereof, a variant thereof, or a combination thereof. The bifunctional antibody can bind or react with the antigen described below. The bifunctional antibody can also be modified to impart an additional functionality to the antibody beyond recognition of and binding to the antigen. Such a modification can include, but is not limited to, coupling to factor H or a fragment thereof. Factor H is a soluble regulator of complement activation and thus, may contribute to an immune response via complement-mediated lysis (CML).

c. Extension of Antibody Half-Life

[00231] As described above, the antibody may be modified to extend or shorten the half-life of the antibody in the subject. The modification may extend or shorten the half-life of the antibody in the serum of the subject.

[00232] The modification may be present in a constant region of the antibody. The modification may be one or more amino acid substitutions in a constant region of the antibody that extend the half-life of the antibody as compared to a half-life of an antibody not containing the one or more amino acid substitutions. The modification may be one or more amino acid

substitutions in the CH2 domain of the antibody that extend the half-life of the antibody as compared to a half-life of an antibody not containing the one or more amino acid substitutions.

[00233] In some embodiments, the one or more amino acid substitutions in the constant region may include replacing a methionine residue in the constant region with a tyrosine residue, a serine residue in the constant region with a threonine residue, a threonine residue in the constant region with a glutamate residue, or any combination thereof, thereby extending the half-life of the antibody.

[00234] In other embodiments, the one or more amino acid substitutions in the constant region may include replacing a methionine residue in the CH2 domain with a tyrosine residue, a serine residue in the CH2 domain with a threonine residue, a threonine residue in the CH2 domain with a glutamate residue, or any combination thereof, thereby extending the half-life of the antibody.

d. Defucosylation

[00235] The recombinant nucleic acid sequence can encode an antibody that is not fucosylated (i.e., a defucosylated antibody or a non-fucosylated antibody), a fragment thereof, a variant thereof, or a combination thereof. Fucosylation includes the addition of the sugar fucose to a molecule, for example, the attachment of fucose to N-glycans, O-glycans and glycolipids. Accordingly, in a defucosylated antibody, fucose is not attached to the carbohydrate chains of the constant region. In turn, this lack of fucosylation may improve FcγRIIIa binding and antibody directed cellular cytotoxic (ADCC) activity by the antibody as compared to the fucosylated antibody. Therefore, in some embodiments, the non-fucosylated antibody may exhibit increased ADCC activity as compared to the fucosylated antibody.

[00236] The antibody may be modified so as to prevent or inhibit fucosylation of the antibody. In some embodiments, such a modified antibody may exhibit increased ADCC activity as compared to the unmodified antibody. The modification may be in the heavy chain, light chain, or a combination thereof. The modification may be one or more amino acid substitutions in the heavy chain, one or more amino acid substitutions in the light chain, or a combination thereof.

e. Reduced ADE Response

[00237] The antibody may be modified to reduce or prevent antibody-dependent enhancement (ADE) of disease associated with the antigen, but still neutralize the antigen. For example, the

antibody may be modified to reduce or prevent ADE of disease associated with DENV, which is described below in more detail, but still neutralize DENV.

[00238] In some embodiments, the antibody may be modified to include one or more amino acid substitutions that reduce or prevent binding of the antibody to FcyR1a. The one or more amino acid substitutions may be in the constant region of the antibody. The one or more amino acid substitutions may include replacing a leucine residue with an alanine residue in the constant region of the antibody, i.e., also known herein as LA, LA mutation or LA substitution. The one or more amino acid substitutions may include replacing two leucine residues, each with an alanine residue, in the constant region of the antibody and also known herein as LALA, LALA mutation, or LALA substitution. The presence of the LALA substitutions may prevent or block the antibody from binding to FcyR1a, and thus, the modified antibody does not enhance or cause ADE of disease associated with the antigen, but still neutralizes the antigen.

6. **Antigen**

[00239] The DNA plasmid vaccines encode an antigen or fragment or variant thereof. The synthetic antibody is directed to the antigen or fragment or variant thereof. The antigen can be a nucleic acid sequence, an amino acid sequence, or a combination thereof. The nucleic acid sequence can be DNA, RNA, cDNA, a variant thereof, a fragment thereof, or a combination thereof. The amino acid sequence can be a protein, a peptide, a variant thereof, a fragment thereof, or a combination thereof.

[00240] The antigen can be from any number of organisms, for example, a virus, a parasite, a bacterium, a fungus, or a mammal. The antigen can be associated with an autoimmune disease, allergy, or asthma. In other embodiments, the antigen can be associated with cancer, herpes, influenza, hepatitis B, hepatitis C, human papilloma virus (HPV), or human immunodeficiency virus (HIV).

[00241] In some embodiments, the antigen is foreign. In some embodiments, the antigen is a self-antigen.

a. Foreign Antigens

[00242] In some embodiments, the antigen is foreign. A foreign antigen is any non-self substance (i.e., originates external to the subject) that, when introduced into the body, is capable of stimulating an immune response.

(1) Viral Antigens

[00243] The foreign antigen can be a viral antigen, or fragment thereof, or variant thereof. The viral antigen can be from a virus from one of the following families: *Adenoviridae, Arenaviridae, Bunyaviridae, Caliciviridae, Coronaviridae, Filoviridae, Hepadnaviridae, Herpesviridae, Orthomyxoviridae, Papovaviridae, Paramyxoviridae, Parvoviridae, Picornaviridae, Poxviridae, Reoviridae, Retroviridae, Rhabdoviridae,* or *Togaviridae*. The viral antigen can be from human immunodeficiency virus (HIV), Chikungunya virus (CHIKV), dengue fever virus, papilloma viruses, for example, human papillomoa virus (HPV), polio virus, hepatitis viruses, for example, hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and hepatitis E virus (HEV), smallpox virus (Variola major and minor), vaccinia virus, influenza virus, rhinoviruses, equine encephalitis viruses, rubella virus, yellow fever virus, Norwalk virus, hepatitis A virus, human T-cell leukemia virus (HTLV-I), hairy cell leukemia virus (HTLV-II), California encephalitis virus, Hanta virus (hemorrhagic fever), rabies virus, Ebola fever virus, Marburg virus, measles virus, mumps virus, respiratory syncytial virus (RSV), herpes simplex 1 (oral herpes), herpes simplex 2 (genital herpes), herpes zoster (varicella-zoster, a.k.a., chickenpox), cytomegalovirus (CMV), for example human CMV, Epstein-Barr virus (EBV), flavivirus, foot and mouth disease virus, lassa virus, arenavirus, or cancer causing virus.

(a) Human Immunodeficiency Virus (HIV) Antigen

[00244] The viral antigen may be from Human Immunodeficiency Virus (HIV) virus. In some embodiments, the HIV antigen can be a subtype A envelope protein, subtype B envelope protein, subtype C envelope protein, subtype D envelope protein, subtype B Nef-Rev protein, Gag subtype A, B, C, or D protein, MPol protein, a nucleic acid or amino acid sequences of Env A, Env B, Env C, Env D, B Nef-Rev, Gag, or any combination thereof.

[00245] A synthetic antibody specific for HIV can include a Fab fragment comprising the amino acid sequence of SEQ ID NO:48, which is encoded by the nucleic acid sequence of SEQ

ID NO:3, and the amino acid sequence of SEQ ID NO:49, which is encoded by the nucleic acid sequence of SEQ ID NO:4. The synthetic antibody can comprise the amino acid sequence of SEQ ID NO:46, which is encoded by the nucleic acid sequence of SEQ ID NO:6, and the amino acid sequence of SEQ ID NO:47, which is encoded by the nucleic acid sequence of SEQ ID NO:7. The Fab fragment comprise the amino acid sequence of SEQ ID NO:51, which is encoded by the nucleic acid sequence of SEQ ID NO:50. The Fab can comprise the amino acid sequence of SEQ ID NO:53, which is encoded by the nucleic acid sequence of SEQ ID NO:52.

[00246] A synthetic antibody specific for HIV can include an Ig comprising the amino acid sequence of SEQ ID NO:5. The Ig can comprise the amino acid sequence of SEQ ID NO:1, which is encoded by the nucleic acid sequence of SEQ ID NO:62. The Ig can comprise the amino acid sequence of SEQ ID NO:2, which is encoded by the nucleic acid sequence of SEQ ID NO:63. The Ig can comprise the amino acid sequence of SEQ ID NO:55, which is encoded by the nucleic acid sequence of SEQ ID NO:54, and the amino acid sequence of SEQ ID NO:57, which is encoded by the nucleic acid sequence SEQ ID NO:56.

[00247] A DNA vaccine encoding an HIV antigen can include a vaccine encoding a subtype A envelope protein, subtype B envelope protein, subtype C envelope protein, subtype D envelope protein, subtype B Nef-Rev protein, Gag subtype A, B, C, or D protein, MPol protein, a nucleic acid or amino acid sequences of Env A, Env B, Env C, Env D, B Nef-Rev, Gag, or any combination thereof. Examples of DNA vaccines encoding HIV antigens include those described in U.S. Patent No. 8,168,769 and WO2015/073291, the contents of each are fully incorporated by reference.

(b) Chikungunya Virus

[00248] The viral antigen may be from Chikungunya virus. Chikungunya virus belongs to the alphavirus genus of the Togaviridae family. Chikungunya virus is transmitted to humans by the bite of infected mosquitoes, such as the genus *Aedes*.

[00249] A synthetic antibody specific for CHIKV can include a Fab fragment comprising the amino acid sequence of SEQ ID NO:59, which is encoded by the nucleic acid sequence of SEQ ID NO:58, and the amino acid sequence of SEQ ID NO:61, which is encoded by the nucleic acid sequence of SEQ ID NO:60. A synthetic antibody specific for CHIKV can include an Ig encoded by one of SEQ ID NOs: 97-100.

[00250] The DNA vaccine may encode a CHIKV antigen. Examples of DNA vaccines encoding CHIKV antigens include those described in U.S. Patent No. 8,852,609, the contents of which is fully incorporated by reference. A DNA vaccine encoding a CHIKV antigen may include a nucleic acid sequence encoding an amino acid sequence comprising one of SEQ ID NOs: 81-88. The DNA vaccine encoding a CHIKV antigen may include a nucleic acid sequence comprising the sequence SEQ ID NOs: 89-96.For Example, in one embodiment, the DNA vaccine encodes a CHIKV E1 consensus protein. In one embodiment, the CHIKV E1 consensus protein comprises an amino acid sequence of one of SEQ ID NOs: 81 or 84. In one embodiment, the DNA vaccine encoding a CHIKV E1 consensus protein comprises a nucleic acid sequence of SEQ ID NOs:89 or 92. In one embodiment, the DNA vaccine encodes a CHIKV E2 consensus protein. In one embodiment, the CHIKV E2 consensus protein comprises an amino acid sequence of one of SEQ ID NOs: 82 or 85. In one embodiment, the DNA vaccine encoding a CHIKV E2 consensus protein comprises a nucleic acid sequence of SEQ ID NOs: 90 or 93. In one embodiment, the DNA vaccine encodes a CHIKV Capsid consensus protein. In one embodiment, the CHIKV Capsid consensus protein comprises an amino acid sequence of one of SEQ ID NOs: 83 or 86. In one embodiment, the DNA vaccine encoding a CHIKV Capsid consensus protein comprises a nucleic acid sequence of SEQ ID NOs: 91 or 94. In one embodiment, the DNA vaccine encodes a CHIKV Env consensus protein. In one embodiment, the CHIKV Env consensus protein comprises an amino acid sequence of one of SEQ ID NOs: 87 or 88. In one embodiment, the DNA vaccine encoding a CHIKV Env consensus protein comprises a nucleic acid sequence of SEQ ID NOs: 95 or 96.

(c) Dengue Virus

[00251] The viral antigen may be from Dengue virus. The Dengue virus antigen may be one of three proteins or polypeptides (C, prM, and E) that form the virus particle. The Dengue virus antigen may be one of seven other proteins or polypeptides (NS1, NS2a, NS2b, NS3, NS4a, NS4b, NS5) which are involved in replication of the virus. The Dengue virus may be one of five strains or serotypes of the virus, including DENV-1, DENV-2, DENV-3 and DENV-4. The antigen may be any combination of a plurality of Dengue virus antigens.

[00252] A synthetic antibody specific for Dengue virus can include a Ig comprising the amino acid sequence of SEQ ID NO:45, which is encoded by the nucleic acid sequence of SEQ ID NO:44.

[00253] The DNA vaccine may encode a Dengue virus antigen. Examples of DNA vaccines encoding Dengue virus antigens include those described in U.S. Patent No. 8,835,620 and WO2014/144786, the contents of each are fully incorporated by reference.

(d) Hepatitis Antigen

[00254] The viral antigen may include a hepatitis virus antigen (i.e., hepatitis antigen), or a fragment thereof, or a variant thereof. The hepatitis antigen can be an antigen or immunogen from one or more of hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and/or hepatitis E virus (HEV).

[00255] The hepatitis antigen can be an antigen from HAV. The hepatitis antigen can be a HAV capsid protein, a HAV non-structural protein, a fragment thereof, a variant thereof, or a combination thereof.

[00256] The hepatitis antigen can be an antigen from HCV. The hepatitis antigen can be a HCV nucleocapsid protein (i.e., core protein), a HCV envelope protein (e.g., E1 and E2), a HCV non-structural protein (e.g., NS1, NS2, NS3, NS4a, NS4b, NS5a, and NS5b), a fragment thereof, a variant thereof, or a combination thereof.

[00257] The hepatitis antigen can be an antigen from HDV. The hepatitis antigen can be a HDV delta antigen, fragment thereof, or variant thereof.

[00258] The hepatitis antigen can be an antigen from HEV. The hepatitis antigen can be a HEV capsid protein, fragment thereof, or variant thereof.

[00259] The hepatitis antigen can be an antigen from HBV. The hepatitis antigen can be a HBV core protein, a HBV surface protein, a HBV DNA polymerase, a HBV protein encoded by gene X, fragment thereof, variant thereof, or combination thereof. The hepatitis antigen can be a HBV genotype A core protein, a HBV genotype B core protein, a HBV genotype C core protein, a HBV genotype D core protein, a HBV genotype E core protein, a HBV genotype F core protein, a HBV genotype G core protein, a HBV genotype H core protein, a HBV genotype A surface protein, a HBV genotype B surface protein, a HBV genotype C surface protein, a HBV genotype D surface protein, a HBV genotype E surface protein, a HBV genotype F surface

protein, a HBV genotype G surface protein, a HBV genotype H surface protein, fragment thereof, variant thereof, or combination thereof.

[00260] In some embodiments, the hepatitis antigen can be an antigen from HBV genotype A, HBV genotype B, HBV genotype C, HBV genotype D, HBV genotype E, HBV genotype F, HBV genotype G, or HBV genotype H.

[00261] The DNA vaccine may encode a hepatitis antigen. Examples of DNA vaccines encoding hepatitis antigens include those described in U.S. Patent Nos. 8,829,174, US 8,921,536, US 9,403,879, US 9,238,679, the contents of each are fully incorporated by reference.

(e) Human Papilloma Virus (HPV) Antigen

[00262] The viral antigen may comprise an antigen from HPV. The HPV antigen can be from HPV types 16, 18, 31, 33, 35, 45, 52, and 58 which cause cervical cancer, rectal cancer, and/or other cancers. The HPV antigen can be from HPV types 6 and 11, which cause genital warts, and are known to be causes of head and neck cancer.

[00263] The HPV antigens can be the HPV E6 or E7 domains from each HPV type. For example, for HPV type 16 (HPV16), the HPV16 antigen can include the HPV16 E6 antigen, the HPV16 E7 antigen, fragments, variants, or combinations thereof. Similarly, the HPV antigen can be HPV 6 E6 and/or E7, HPV 11 E6 and/or E7, HPV 18 E6 and/or E7, HPV 31 E6 and/or E7, HPV 33 E6 and/or E7, HPV 52 E6 and/or E7, or HPV 58 E6 and/or E7, fragments, variants, or combinations thereof.

[00264] The DNA vaccine may encode a HPV antigen. Examples of DNA vaccines encoding HPV antigens include those described in WO/2008/014521, published January 31, 2008; U.S. Patent Application Pub. No. 20160038584; U.S. Patent Nos. 8389706 and 9,050,287, the contents of each are fully incorporated by reference.

(f) RSV Antigen

[00265] The viral antigen may comprise a RSV antigen. The RSV antigen can be a human RSV fusion protein (also referred to herein as "RSV F," "RSV F protein," and "F protein"), or fragment or variant thereof. The human RSV fusion protein can be conserved between RSV subtypes A and B. The RSV antigen can be a RSV F protein, or fragment or variant thereof, from the RSV Long strain (GenBank AAX23994.1). The RSV antigen can be a RSV F protein from

the RSV A2 strain (GenBank AAB59858.1), or a fragment or variant thereof. The RSV antigen can be a monomer, a dimer, or trimer of the RSV F protein, or a fragment or variant thereof.

[00266] The RSV F protein can be in a prefusion form or a postfusion form. The postfusion form of RSV F elicits high titer neutralizing antibodies in immunized animals and protects the animals from RSV challenge.

[00267] The RSV antigen can also be human RSV attachment glycoprotein (also referred to herein as "RSV G," "RSV G protein," and "G protein"), or fragment or variant thereof. The human RSV G protein differs between RSV subtypes A and B. The antigen can be RSV G protein, or fragment or variant thereof, from the RSV Long strain (GenBank AAX23993). The RSV antigen can be RSV G protein from the RSV subtype B isolate H5601, the RSV subtype B isolate H1068, the RSV subtype B isolate H5598, the RSV subtype B isolate H1123, or a fragment or variant thereof.

[00268] In other embodiments, the RSV antigen can be human RSV non-structural protein 1 ("NS1 protein"), or fragment or variant thereof. For example, the RSV antigen can be RSV NS1 protein, or fragment or variant thereof, from the RSV Long strain (GenBank AAX23987.1). The RSV antigen human can also be RSV non-structural protein 2 ("NS2 protein"), or fragment or variant thereof. For example, the RSV antigen can be RSV NS2 protein, or fragment or variant thereof, from the RSV Long strain (GenBank AAX23988.1). The RSV antigen can further be human RSV nucleocapsid ("N") protein, or fragment or variant thereof. For example, the RSV antigen can be RSV N protein, or fragment or variant thereof, from the RSV Long strain (GenBank AAX23989.1). The RSV antigen can be human RSV Phosphoprotein ("P") protein, or fragment or variant thereof. For example, the RSV antigen can be RSV P protein, or fragment or variant thereof, from the RSV Long strain (GenBank AAX23990.1). The RSV antigen also can be human RSV Matrix protein ("M") protein, or fragment or variant thereof. For example, the RSV antigen can be RSV M protein, or fragment or variant thereof, from the RSV Long strain (GenBank AAX23991.1).

[00269] In still other embodiments, the RSV antigen can be human RSV small hydrophobic ("SH") protein, or fragment or variant thereof. For example, the RSV antigen can be RSV SH protein, or fragment or variant thereof, from the RSV Long strain (GenBank AAX23992.1). The RSV antigen can also be human RSV Matrix protein2-1 ("M2-1") protein, or fragment or variant thereof. For example, the RSV antigen can be RSV M2-1 protein, or fragment or variant thereof,

from the RSV Long strain (GenBank AAX23995.1). The RSV antigen can further be human RSV Matrix protein 2-2 ("M2-2") protein, or fragment or variant thereof. For example, the RSV antigen can be RSV M2-2 protein, or fragment or variant thereof, from the RSV Long strain (GenBank AAX23997.1). The RSV antigen human can be RSV Polymerase L ("L") protein, or fragment or variant thereof. For example, the RSV antigen can be RSV L protein, or fragment or variant thereof, from the RSV Long strain (GenBank AAX23996.1).

[00270] In further embodiments, the RSV antigen can have an optimized amino acid sequence of NS1, NS2, N, P, M, SH, M2-1, M2-2, or L protein. The RSV antigen can be a human RSV protein or recombinant antigen, such as any one of the proteins encoded by the human RSV genome.

[00271] In other embodiments, the RSV antigen can be, but is not limited to, the RSV F protein from the RSV Long strain, the RSV G protein from the RSV Long strain, the optimized amino acid RSV G amino acid sequence, the human RSV genome of the RSV Long strain, the optimized amino acid RSV F amino acid sequence, the RSV NS1 protein from the RSV Long strain, the RSV NS2 protein from the RSV Long strain, the RSV N protein from the RSV Long strain, the RSV P protein from the RSV Long strain, the RSV M protein from the RSV Long strain, the RSV SH protein from the RSV Long strain, the RSV M2-1 protein from the RSV Long strain, the RSV M2-2 protein from the RSV Long strain, the RSV L protein from the RSV Long strain, the RSV G protein from the RSV subtype B isolate H5601, the RSV G protein from the RSV subtype B isolate H1068, the RSV G protein from the RSV subtype B isolate H5598, the RSV G protein from the RSV subtype B isolate H1123, or fragment thereof, or variant thereof.

[00272] The DNA vaccine may encode a RSV antigen. Examples of DNA vaccines encoding RSV antigens include those described in U.S. Patent Application Pub. No. 20150079121, the content of which is incorporated by reference.

(g) Influenza Antigen

[00273] The viral antigen may comprise an antigen from influenza virus. The influenza antigens are those capable of eliciting an immune response in a mammal against one or more influenza serotypes. The antigen can comprise the full length translation product HA0, subunit HA1, subunit HA2, a variant thereof, a fragment thereof or a combination thereof. The influenza

hemagglutinin antigen can be derived from multiple strains of influenza A serotype H1, serotype H2, a hybrid sequence derived from different sets of multiple strains of influenza A serotype H1, or derived from multiple strains of influenza B. The influenza hemagglutinin antigen can be from influenza B.

[00274] The influenza antigen can also contain at least one antigenic epitope that can be effective against particular influenza immunogens against which an immune response can be induced. The antigen may provide an entire repertoire of immunogenic sites and epitopes present in an intact influenza virus. The antigen may be derived from hemagglutinin antigen sequences from a plurality of influenza A virus strains of one serotype such as a plurality of influenza A virus strains of serotype H1 or of serotype H2. The antigen may be a hybrid hemagglutinin antigen sequence derived from combining two different hemagglutinin antigen sequences or portions thereof. Each of two different hemagglutinin antigen sequences may be derived from a different set of a plurality of influenza A virus strains of one serotype such as a plurality of influenza A virus strains of serotype H1. The antigen may be a hemagglutinin antigen sequence derived from hemagglutinin antigen sequences from a plurality of influenza B virus strains.

[00275] In some embodiments, the influenza antigen can be H1 HA, H2 HA, H3 HA, H5 HA, or a BHA antigen.

[00276] A synthetic antibody specific for an influenza antigen can include an Ig comprising the amino acid sequence of one of SEQ ID NOs: 155-161. A synthetic antibody specific for an influenza antigen can be encoded by a nucleic acid molecule comprising a nucleic acid sequence of one of SEQ ID NOs:162-170.

[00277] The DNA vaccine may encode a influenza antigen. Examples of DNA vaccines encoding influenza antigens include those described in WO/2008/014521, published January 31, 2008; U.S. Patent Nos. 9,592,285, US 8,298,820; U.S. Patent Application Pub. Nos. 20160022806, US 20160175427, the contents of each are fully incorporated by reference.

(h) Ebola Virus

[00278] The viral antigen may be from Ebola virus. Ebola virus disease (EVD) or Ebola hemorrhagic fever (EHF) includes any of four of the five known Ebola viruses including Bundibugyo virus (BDBV), Ebola virus (EBOV), Sudan virus (SUDV), and Taï Forest virus (TAFV, also referred to as Côte d'Ivoire Ebola virus (Ivory Coast Ebolavirus, CIEBOV).

[00279] A synthetic antibody specific for an Ebola virus antigen. A synthetic antibody specific for Ebola virus can include a Ig comprising the amino acid sequence of SEQ ID NO: 135, SEQ ID NO: 137, SEQ ID NO: 139, SEQ ID NO: 141, SEQ ID NO:143, SEQ ID NO:145, or SEQ ID NO: 147. A synthetic antibody specific for Ebola virus can be encoded by a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 136, SEQ ID NO: 138, SEQ ID NO: 140, SEQ ID NO: 142, SEQ ID NO:144, SEQ ID NO:146, or SEQ ID NO: 148.

[00280] The DNA vaccine may encode an Ebola antigen. Examples of DNA vaccines encoding Ebola antigens include those described in U.S. Patent Application Pub. No. 20150335726, the content of which is incorporated by reference.

(i) Zika Virus

[00281] The viral antigen may be from Zika virus. Zika disease is caused by infection with the Zika virus and can be transmitted to humans through the bite of infected mosquitoes or sexually transmitted between humans. The Zika antigen can include a Zika Virus Envelope protein, Zika Virus NS1 protein, or a Zika Virus Capsid protein.

[00282] A synthetic antibody specific for a Zika antigen. A synthetic antibody specific for Zika Virus can include an Ig comprising the amino acid sequence of SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO: 104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:121, or SEQ ID NO:122.

[00283] The DNA vaccine may encode a Zika antigen. A DNA vaccine encoding a Zika antigen may include a nucleic acid sequence encoding an amino acid sequence comprising one of SEQ ID NO: 123, SEQ ID NO: 125, SEQ ID NO: 127, SEQ ID NO: 129, SEQ ID NO: 131, and SEQ ID NO: 133. A DNA vaccine encoding a Zika antigen may include a nucleic acid sequence comprising one of SEQ ID NO: 124, SEQ ID NO: 126, SEQ ID NO: 128, SEQ ID NO: 130, and SEQ ID NO: 132.

(j) Marburg Virus

[00284] The viral antigen may be from Marburg virus. Marburgvirus immunogens that can be used to induce broad immunity against multiple subtypes or serotypes of Marburgvirus. The antigen may be derived from a Marburg virus envelope glycoprotein.

[00285] The DNA vaccine may encode a Marburg antigen. Examples of DNA vaccines encoding Marburg antigens include those described in U.S. Patent Nos. 9,597,388, the contents of which are fully incorporated by reference. A DNA vaccine encoding a Marburg virus antigen may include a nucleic acid sequence encoding an amino acid sequence comprising one of SEQ ID NO: 150, SEQ ID NO: 152, and SEQ ID NO: 154. A DNA vaccine encoding a Marburg virus antigen may include a nucleic acid sequence comprising one of SEQ ID NO: 149, SEQ ID NO: 151, and SEQ ID NO: 153.

(2) Bacterial Antigens

[00286] The foreign antigen can be a bacterial antigen or fragment or variant thereof. The bacterium can be from any one of the following phyla: Acidobacteria, Actinobacteria, Aquificae, Bacteroidetes, Caldiserica, Chlamydiae, Chlorobi, Chloroflexi, Chrysiogenetes, Cyanobacteria, Deferribacteres, Deinococcus-Thermus, Dictyoglomi, Elusimicrobia, Fibrobacteres, Firmicutes, Fusobacteria, Gemmatimonadetes, Lentisphaerae, Nitrospira, Planctomycetes, Proteobacteria, Spirochaetes, Synergistetes, Tenericutes, Thermodesulfobacteria, Thermotogae, and Verrucomicrobia.

[00287] The bacterium can be a gram positive bacterium or a gram negative bacterium. The bacterium can be an aerobic bacterium or an anerobic bacterium. The bacterium can be an autotrophic bacterium or a heterotrophic bacterium. The bacterium can be a mesophile, a neutrophile, an extremophile, an acidophile, an alkaliphile, a thermophile, a psychrophile, an halophile, or an osmophile.

[00288] The bacterium can be an anthrax bacterium, an antibiotic resistant bacterium, a disease causing bacterium, a food poisoning bacterium, an infectious bacterium, Salmonella bacterium, Staphylococcus bacterium, Streptococcus bacterium, or tetanus bacterium. The bacterium can be a mycobacteria, *Clostridium tetani*, *Yersinia pestis*, *Bacillus anthracis*, methicillin-resistant

Staphylococcus aureus (MRSA), or *Clostridium difficile*. The bacterium can be *Mycobacterium tuberculosis*.

[00289] Examples of DNA vaccines encoding *Clostridium difficile* antigens include those described in U.S. Patent Application Pub. No. 20140341936, the content of which is incorporated by reference.

[00290] Examples of DNA vaccines encoding *MRSA* antigens include those described in U.S. Patent Application Pub. No. 20140341944, the content of which is incorporated by reference.

(a) Mycobacterium tuberculosis Antigens

[00291] The bacterial antigen may be a *Mycobacterium tuberculosis* antigen (i.e., TB antigen or TB immunogen), or fragment thereof, or variant thereof. The TB antigen can be from the Ag85 family of TB antigens, for example, Ag85A and Ag85B. The TB antigen can be from the Esx family of TB antigens, for example, EsxA, EsxB, EsxC, EsxD, EsxE, EsxF, EsxH, EsxO, EsxQ, EsxR, EsxS, EsxT, EsxU, EsxV, and EsxW.

[00292] The DNA vaccine may encode a *Mycobacterium tuberculosis* antigen. Examples of DNA vaccines encoding *Mycobacterium tuberculosis* antigens include those described in U.S. Patent Application Pub. No. 20160022796, the content of which is incorporated by reference.

(3) Parasitic Antigens

[00293] The foreign antigen can be a parasite antigen or fragment or variant thereof. The parasite can be a protozoa, helminth, or ectoparasite. The helminth (i.e., worm) can be a flatworm (e.g., flukes and tapeworms), a thorny-headed worm, or a round worm (e.g., pinworms). The ectoparasite can be lice, fleas, ticks, and mites.

[00294] The parasite can be any parasite causing any one of the following diseases: Acanthamoeba keratitis, Amoebiasis, Ascariasis, Babesiosis, Balantidiasis, Baylisascariasis, Chagas disease, Clonorchiasis, Cochliomyia, Cryptosporidiosis, Diphyllobothriasis, Dracunculiasis, Echinococcosis, Elephantiasis, Enterobiasis, Fascioliasis, Fasciolopsiasis, Filariasis, Giardiasis, Gnathostomiasis, Hymenolepiasis, Isosporiasis, Katayama fever, Leishmaniasis, Lyme disease, Malaria, Metagonimiasis, Myiasis, Onchocerciasis, Pediculosis, Scabies, Schistosomiasis, Sleeping sickness, Strongyloidiasis, Taeniasis, Toxocariasis, Toxoplasmosis, Trichinosis, and Trichuriasis.

[00295] The parasite can be Acanthamoeba, Anisakis, *Ascaris lumbricoides*, Botfly, *Balantidium coli*, Bedbug, *Cestoda* (tapeworm), Chiggers, *Cochliomyia hominivorax*, Entamoeba histolytica, *Fasciola hepatica*, *Giardia lamblia*, Hookworm, *Leishmania*, *Linguatula serrata*, Liver fluke, Loa loa, *Paragonimus* - lung fluke, Pinworm, *Plasmodium falciparum*, Schistosoma, *Strongyloides stercoralis*, Mite, Tapeworm, *Toxoplasma gondii*, *Trypanosoma*, Whipworm, or *Wuchereria bancrofti*.

(a) Malaria Antigen

[00296] The foreign antigen may be a malaria antigen (i.e., PF antigen or PF immunogen), or fragment thereof, or variant thereof. The antigen can be from a parasite causing malaria. The malaria causing parasite can be *Plasmodium falciparum*. The *Plasmodium falciparum* antigen can include the circumsporozoite (CS) antigen.

[00297] In some embodiments, the malaria antigen can be one of *P. falciparum* immunogens CS; LSA1; TRAP; CelTOS; and Ama1. The immunogens may be full length or immunogenic fragments of full length proteins.

[00298] In other embodiments, the malaria antigen can be TRAP, which is also referred to as SSP2. In still other embodiments, the malaria antigen can be CelTOS, which is also referred to as Ag2 and is a highly conserved *Plasmodium* antigen. In further embodiments, the malaria antigen can be Ama1, which is a highly conserved *Plasmodium* antigen. In some embodiments, the malaria antigen can be a CS antigen.

[00299] In other embodiments, the malaria antigen can be a fusion protein comprising a combination of two or more of the PF proteins set forth herein. For example, fusion proteins may comprise two or more of CS immunogen, ConLSA1 immunogen, ConTRAP immunogen, ConCelTOS immunogen, and ConAma1 immunogen linked directly adjacent to each other or linked with a spacer or one or more amino acids in between. In some embodiments, the fusion protein comprises two PF immunogens; in some embodiments the fusion protein comprises three PF immunogens, in some embodiments the fusion protein comprises four PF immunogens, and in some embodiments the fusion protein comprises five PF immunogens. Fusion proteins with two PF immunogens may comprise: CS and LSA1; CS and TRAP; CS and CelTOS; CS and Ama1; LSA1 and TRAP; LSA1 and CelTOS; LSA1 and Ama1; TRAP and CelTOS; TRAP and Ama1; or CelTOS and Ama1. Fusion proteins with three PF immunogens may comprise: CS,

LSA1 and TRAP; CS, LSA1 and CelTOS; CS, LSA1 and Ama1; LSA1, TRAP and CelTOS; LSA1, TRAP and Ama1; or TRAP, CelTOS and Ama1. Fusion proteins with four PF immunogens may comprise: CS, LSA1, TRAP and CelTOS; CS, LSA1, TRAP and Ama1; CS, LSA1, CelTOS and Ama1; CS, TRAP, CelTOS and Ama1; or LSA1, TRAP, CelTOS and Ama1. Fusion proteins with five PF immunogens may comprise CS or CS-alt, LSA1, TRAP, CelTOS and Ama1.

[00300] The DNA vaccine may encode a malaria antigen. Examples of DNA vaccines encoding malaria antigens include those described in U.S. Patent Application Pub. No. 20130273112, the content of which is incorporated by reference.

(4) Fungal Antigens

[00301] The foreign antigen can be a fungal antigen or fragment or variant thereof. The fungus can be Aspergillus species, Blastomyces dermatitidis, *Candida* yeasts (e.g., *Candida albicans), Coccidioides, Cryptococcus neoformans, Cryptococcus gattii, dermatophyte, Fusarium species, Histoplasma capsulatum, Mucoromycotina, Pneumocystis jirovecii, Sporothrix schenckii, Exserohilum, or Cladosporium.*

b. Self Antigens

[00302] In some embodiments, the antigen is a self antigen. A self antigen may be a constituent of the subject's own body that is capable of stimulating an immune response. In some embodiments, a self antigen does not provoke an immune response unless the subject is in a disease state, e.g., an autoimmune disease.

[00303] Self antigens may include, but are not limited to, cytokines, antibodies against viruses such as those listed above including HIV and Dengue, antigens affecting cancer progression or development, and cell surface receptors or transmembrane proteins.

(1) WT-1

[00304] The self-antigen antigen can be Wilm's tumor suppressor gene 1 (WT1), a fragment thereof, a variant thereof, or a combination thereof. WT1 is a transcription factor containing at the N-terminus, a proline/glutamine-rich DNA-binding domain and at the C-terminus, four zinc finger motifs. WT1 plays a role in the normal development of the urogenital system and interacts

with numerous factors, for example, p53, a known tumor suppressor and the serine protease HtrA2, which cleaves WT1 at multiple sites after treatment with a cytotoxic drug. Mutation of WT1 can lead to tumor or cancer formation, for example, Wilm's tumor or tumors expressing WT1.

[00305] The DNA vaccine may encode a WT-1 antigen. Examples of DNA vaccines encoding WT-1 antigens include those described in U.S. Patent Application Pub. Nos. 20150328298 and 20160030536, the contents each are incorporated by reference.

(2) EGFR

[00306] The self-antigen may include an epidermal growth factor receptor (EGFR) or a fragment or variation thereof. EGFR (also referred to as ErbB-1 and HER1) is the cell-surface receptor for members of the epidermal growth factor family (EGF-family) of extracellular protein ligands. EGFR is a member of the ErbB family of receptors, which includes four closely related receptor tyrosine kinases: EGFR (ErbB-1), HER2/c-neu (ErbB-2), Her 3 (ErbB-3), and Her 4 (ErbB-4). Mutations affecting EGFR expression or activity could result in cancer.

[00307] The antigen may include an ErbB-2 antigen. Erb-2 (human epidermal growth factor receptor 2) is also known as Neu, HER2, CD340 (cluster of differentiation 340), or p185 and is encoded by the ERBB2 gene. Amplification or over-expression of this gene has been shown to play a role in the development and progression of certain aggressive types of breast cancer. In approximately 25-30% of women with breast cancer, a genetic alteration occurs in the ERBB2 gene, resulting in the production of an increased amount of HER2 on the surface of tumor cells. This overexpression of HER2 promotes rapid cell division and thus, HER2 marks tumor cells.

[00308] A synthetic antibody specific for HER2 can include a Fab fragment comprising an amino acid sequence of SEQ ID NO:41, which is encoded by the nucleic acid sequence of SEQ ID NO:40, and an amino acid sequence of SEQ ID NO:43, which is encoded by the nucleic acid sequence of SEQ ID NO:42.

(3) Cocaine

[00309] The self-antigen may be a cocaine receptor antigen. Cocaine receptors include dopamine transporters.

(4) PD-1

[00310] The self-antigen may include programmed death 1 (PD-1). Programmed death 1 (PD-1) and its ligands, PD-L1 and PD-L2, deliver inhibitory signals that regulate the balance between T cell activation, tolerance, and immunopathology. PD-1 is a 288 amino acid cell surface protein molecule including an extracellular IgV domain followed by a transmembrane region and an intracellular tail.

[00311] The DNA vaccine may encode a PD-1 antigen. Examples of DNA vaccines encoding PD-1 antigens include those described in U.S. Patent Application Pub. No. 20170007693, the content of which is incorporated by reference.

(5) 4-1BB

[00312] The self-antigen may include 4-1BB ligand. 4-1BB ligand is a type 2 transmembrane glycoprotein belonging to the TNF superfamily. 4-1BB ligand may be expressed on activated T Lymphocytes. 4-1BB is an activation-induced T-cell costimulatory molecule. Signaling via 4-1BB upregulates survival genes, enhances cell division, induces cytokine production, and prevents activation-induced cell death in T cells.

(6) CTLA4

[00313] The self-antigen may include CTLA-4 (Cytotoxic T-Lymphocyte Antigen 4), also known as CD152 (Cluster of differentiation 152). CTLA-4 is a protein receptor found on the surface of T cells, which lead the cellular immune attack on antigens. The antigen may be a fragment of CTLA-4, such as an extracellular V domain, a transmembrane domain, and a cytoplasmic tail, or combination thereof.

(7) IL-6

[00314] The self-antigen may include interleukin 6 (IL-6). IL-6 stimulates the inflammatory and auto-immune processes in many diseases including, but not limited to, diabetes, atherosclerosis, depression, Alzheimer's Disease, systemic lupus erythematosus, multiple myeloma, cancer, Behçet's disease, and rheumatoid arthritis.

(8) MCP-1

[00315] The self-antigen may include monocyte chemotactic protein-1 (MCP-1). MCP-1 is also referred to as chemokine (C-C motif) ligand 2 (CCL2) or small inducible cytokine A2. MCP-1 is a cytokine that belongs to the CC chemokine family. MCP-1 recruits monocytes, memory T cells, and dendritic cells to the sites of inflammation produced by either tissue injury or infection.

(9) Amyloid beta

[00316] The self-antigen may include amyloid beta (Aβ) or a fragment or a variant thereof. The Aβ antigen can comprise an Aβ(X-Y) peptide, wherein the amino acid sequence from amino acid position X to amino acid Y of the human sequence Aβ protein including both X and Y, in particular to the amino acid sequence from amino acid position X to amino acid position Y of the amino acid sequence DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVI (SEQ ID NO: 171) (corresponding to amino acid positions 1 to 47; the human query sequence) or variants thereof. The Aβ antigen can comprise an Aβ polypeptide of Aβ(X-Y) polypeptide wherein X can be 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, or 32 and Y can be 47, 46, 45, 44, 43, 42, 41, 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, or 15. The Aβ polypeptide can comprise a fragment that is at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 30, at least 35, at least 36, at least 37, at least 38, at least 39, at least 40, at least 41, at least 42, at least 43, at least 44, at least 45, or at least 46 amino acids.

(10) IP-10

[00317] The self-antigen may include interferon (IFN)-gamma-induced protein 10 (IP-10). IP-10 is also known as small-inducible cytokine B10 or C-X-C motif chemokine 10 (CXCL10). CXCL10 is secreted by several cell types, such as monocytes, endothelial cells and fibroblasts, in response to IFN-γ.

(11) PSMA

[00318] The self-antigen may include prostate-specific membrane antigen (PSMA). PSMA is also known as glutamate carboxypeptidase II (GCPII), N-acetyl-L-aspartyl-L-glutamate peptidase I (NAALADase I), NAAG peptidase, or folate hydrolase (FOLH). PMSA is an integral membrane protein highly expressed by prostate cancer cells.

[00319] In some embodiments, the recombinant nucleic acid sequence encoding an antibody directed against PSMA (anti-PSMA antibody) may be a recombinant nucleic acid sequence including a recombinant nucleic acid sequence construct in arrangement 2.

[00320] In still other embodiments, the anti-PSMA antibody encoded by the recombinant nucleic acid sequence may be modified as described herein. One such modification is a defucosylated antibody, which as demonstrated in the Examples, exhibited increased ADCC activity as compared to commercial antibodies. The modification may be in the heavy chain, light chain, or a combination thereof. The modification may be one or more amino acid substitutions in the heavy chain, one or more amino acid substitutions in the light chain, or a combination thereof.

[00321] An antibody specific for PSMA and modified to not be fucosylated may be encoded by the nucleic acid sequence set forth in SEQ ID NO:79. SEQ ID NO:79 encodes the amino acid sequence set forth in SEQ ID NO:80.

[00322] The DNA vaccine may encode a PSMA antigen. Examples of DNA vaccines encoding PSMA antigens include those described in U.S. Patent Application Pub. No. 20130302361, the content of which is incorporated by reference.

c. Other Antigens

[00323] In some embodiments, the antigen is an antigen other than the foreign antigen and/or the self-antigen.

(a) HIV-1 VRC01

[00324] The other antigen can be HIV-1 VRC01. HIV-1 VCR01 is a neutralizing CD4-binding site-antibody for HIV. HIV-1 VCR01 contacts portions of HIV-1 including within the gp120 loop D, the CD4 binding loop, and the V5 region of HIV-1.

(b) HIV-1 PG9

[00325] The other antigen can be HIV-1 PG9. HIV-1 PG9 is the founder member of an expanding family of glycan-dependent human antibodies that preferentially bind the HIV (HIV-1) envelope (Env) glycoprotein (gp) trimer and broadly neutralize the virus.

(c) HIV-1 4E10

[00326] The other antigen can be HIV-1 4E10. HIV-1 4E10 is a neutralizing anti-HIV antibody. HIV-1 4E10 is directed against linear epitopes mapped to the membrane-proximal external region (MPER) of HIV-1, which is located at the C terminus of the gp41 ectodomain.

(d) DV-SF1

[00327] The other antigen can be DV-SF1. DV-SF1 is a neutralizing antibody that binds the envelope protein of the four Dengue virus serotypes.

(e) DV-SF2

[00328] The other antigen can be DV-SF2. DV-SF2 is a neutralizing antibody that binds an epitope of the Dengue virus. DV-SF2 can be specific for the DENV4 serotype.

(f) DV-SF3

[00329] The other antigen can be DV-SF3. DV-SF3 is a neutralizing antibody that binds the EDIII A strand of the Dengue virus envelope protein.

7. **Excipients and Other Components of the Composition**

[00330] The composition may further comprise a pharmaceutically acceptable excipient. The pharmaceutically acceptable excipient can be functional molecules such as vehicles, carriers, or diluents. The pharmaceutically acceptable excipient can be a transfection facilitating agent, which can include surface active agents, such as immune-stimulating complexes (ISCOMS), Freunds incomplete adjuvant, LPS analog including monophosphoryl lipid A, muramyl peptides, quinone analogs, vesicles such as squalene and squalene, hyaluronic acid, lipids, liposomes,

calcium ions, viral proteins, polyanions, polycations, or nanoparticles, or other known transfection facilitating agents.

[00331] The transfection facilitating agent is a polyanion, polycation, including poly-L-glutamate (LGS), or lipid. The transfection facilitating agent is poly-L-glutamate, and the poly-L-glutamate may be present in the composition at a concentration less than 6 mg/ml. The transfection facilitating agent may also include surface active agents such as immune-stimulating complexes (ISCOMS), Freunds incomplete adjuvant, LPS analog including monophosphoryl lipid A, muramyl peptides, quinone analogs and vesicles such as squalene and squalene, and hyaluronic acid may also be used administered in conjunction with the composition. The composition may also include a transfection facilitating agent such as lipids, liposomes, including lecithin liposomes or other liposomes known in the art, as a DNA-liposome mixture (see for example W09324640), calcium ions, viral proteins, polyanions, polycations, or nanoparticles, or other known transfection facilitating agents. The transfection facilitating agent is a polyanion, polycation, including poly-L-glutamate (LGS), or lipid. Concentration of the transfection agent in the vaccine is less than 4 mg/ml, less than 2 mg/ml, less than 1 mg/ml, less than 0.750 mg/ml, less than 0.500 mg/ml, less than 0.250 mg/ml, less than 0.100 mg/ml, less than 0.050 mg/ml, or less than 0.010 mg/ml.

[00332] The composition may further comprise a genetic facilitator agent.

[00333] The composition may comprise DNA at quantities of from about 1 nanogram to 100 milligrams; about 1 microgram to about 10 milligrams; or preferably about 0.1 microgram to about 10 milligrams; or more preferably about 1 milligram to about 2 milligram. In some preferred embodiments, composition according to the present invention comprises about 5 nanogram to about 1000 micrograms of DNA. In some preferred embodiments, composition can contain about 10 nanograms to about 800 micrograms of DNA. In some preferred embodiments, the composition can contain about 0.1 to about 500 micrograms of DNA. In some preferred embodiments, the composition can contain about 1 to about 350 micrograms of DNA. In some preferred embodiments, the composition can contain about 25 to about 250 micrograms, from about 100 to about 200 microgram, from about 1 nanogram to 100 milligrams; from about 1 microgram to about 10 milligrams; from about 0.1 microgram to about 10 milligrams; from about 1 milligram to about 2 milligram, from about 5 nanogram to about 1000 micrograms, from about 10 nanograms to about 800 micrograms, from about 0.1 to about 500 micrograms, from

about 1 to about 350 micrograms, from about 25 to about 250 micrograms, from about 100 to about 200 microgram of DNA.

[00334] The composition can be formulated according to the mode of administration to be used. An injectable pharmaceutical composition can be sterile, pyrogen free and particulate free. An isotonic formulation or solution can be used. Additives for isotonicity can include sodium chloride, dextrose, mannitol, sorbitol, and lactose. The composition can comprise a vasoconstriction agent. The isotonic solutions can include phosphate buffered saline. The composition can further comprise stabilizers including gelatin and albumin. The stabilizers can allow the formulation to be stable at room or ambient temperature for extended periods of time, including LGS or polycations or polyanions.

8. Method of Generating the Synthetic Antibody

[00335] The present invention also relates a method of generating the synthetic antibody. The method can include administering the composition to the subject in need thereof by using the method of delivery described in more detail below. Accordingly, the synthetic antibody is generated in the subject or in vivo upon administration of the composition to the subject.

[00336] The method can also include introducing the composition into one or more cells, and therefore, the synthetic antibody can be generated or produced in the one or more cells. The method can further include introducing the composition into one or more tissues, for example, but not limited to, skin and muscle, and therefore, the synthetic antibody can be generated or produced in the one or more tissues.

9. Method of Identifying or Screening for the Antibody

[00337] The present invention further relates to a method of identifying or screening for the antibody described above, which is reactive to or binds the antigen described above. The method of identifying or screening for the antibody can use the antigen in methodologies known in those skilled in art to identify or screen for the antibody. Such methodologies can include, but are not limited to, selection of the antibody from a library (e.g., phage display) and immunization of an animal followed by isolation and/or purification of the antibody.

10. **Method of Delivery of the Composition**

[00338] The present invention also relates to a method of delivering the composition to the subject in need thereof. The method of delivery can include, administering the composition to the subject. Administration can include, but is not limited to, DNA injection with and without in vivo electroporation, liposome mediated delivery, and nanoparticle facilitated delivery.

[00339] The mammal receiving delivery of the composition may be human, primate, non-human primate, cow, cattle, sheep, goat, antelope, bison, water buffalo, bison, bovids, deer, hedgehogs, elephants, llama, alpaca, mice, rats, and chicken.

[00340] The composition may be administered by different routes including orally, parenterally, sublingually, transdermally, rectally, transmucosally, topically, via inhalation, via buccal administration, intrapleurally, intravenous, intraarterial, intraperitoneal, subcutaneous, intramuscular, intranasal intrathecal, and intraarticular or combinations thereof. For veterinary use, the composition may be administered as a suitably acceptable formulation in accordance with normal veterinary practice. The veterinarian can readily determine the dosing regimen and route of administration that is most appropriate for a particular animal. The composition may be administered by traditional syringes, needleless injection devices, "microprojectile bombardment gone guns", or other physical methods such as electroporation ("EP"), "hydrodynamic method", or ultrasound.

a. Electroporation

[00341] Administration of the composition via electroporation may be accomplished using electroporation devices that can be configured to deliver to a desired tissue of a mammal, a pulse of energy effective to cause reversible pores to form in cell membranes, and preferable the pulse of energy is a constant current similar to a preset current input by a user. The electroporation device may comprise an electroporation component and an electrode assembly or handle assembly. The electroporation component may include and incorporate one or more of the various elements of the electroporation devices, including: controller, current waveform generator, impedance tester, waveform logger, input element, status reporting element, communication port, memory component, power source, and power switch. The electroporation may be accomplished using an in vivo electroporation device, for example CELLECTRA EP

system (Inovio Pharmaceuticals, Plymouth Meeting, PA) or Elgen electroporator (Inovio Pharmaceuticals, Plymouth Meeting, PA) to facilitate transfection of cells by the plasmid.

[00342] The electroporation component may function as one element of the electroporation devices, and the other elements are separate elements (or components) in communication with the electroporation component. The electroporation component may function as more than one element of the electroporation devices, which may be in communication with still other elements of the electroporation devices separate from the electroporation component. The elements of the electroporation devices existing as parts of one electromechanical or mechanical device may not limited as the elements can function as one device or as separate elements in communication with one another. The electroporation component may be capable of delivering the pulse of energy that produces the constant current in the desired tissue, and includes a feedback mechanism. The electrode assembly may include an electrode array having a plurality of electrodes in a spatial arrangement, wherein the electrode assembly receives the pulse of energy from the electroporation component and delivers same to the desired tissue through the electrodes. At least one of the plurality of electrodes is neutral during delivery of the pulse of energy and measures impedance in the desired tissue and communicates the impedance to the electroporation component. The feedback mechanism may receive the measured impedance and can adjust the pulse of energy delivered by the electroporation component to maintain the constant current.

[00343] A plurality of electrodes may deliver the pulse of energy in a decentralized pattern. The plurality of electrodes may deliver the pulse of energy in the decentralized pattern through the control of the electrodes under a programmed sequence, and the programmed sequence is input by a user to the electroporation component. The programmed sequence may comprise a plurality of pulses delivered in sequence, wherein each pulse of the plurality of pulses is delivered by at least two active electrodes with one neutral electrode that measures impedance, and wherein a subsequent pulse of the plurality of pulses is delivered by a different one of at least two active electrodes with one neutral electrode that measures impedance.

[00344] The feedback mechanism may be performed by either hardware or software. The feedback mechanism may be performed by an analog closed-loop circuit. The feedback occurs every 50 μs, 20 μs, 10 μs or 1 μs, but is preferably a real-time feedback or instantaneous (i.e., substantially instantaneous as determined by available techniques for determining response

time). The neutral electrode may measure the impedance in the desired tissue and communicates the impedance to the feedback mechanism, and the feedback mechanism responds to the impedance and adjusts the pulse of energy to maintain the constant current at a value similar to the preset current. The feedback mechanism may maintain the constant current continuously and instantaneously during the delivery of the pulse of energy.

[00345] Examples of electroporation devices and electroporation methods that may facilitate delivery of the composition of the present invention, include those described in U.S. Patent No. 7,245,963 by Draghia-Akli, et al., U.S. Patent Pub. 2005/0052630 submitted by Smith, et al., the contents of which are hereby incorporated by reference in their entirety. Other electroporation devices and electroporation methods that may be used for facilitating delivery of the composition include those provided in co-pending and co-owned U.S. Patent Application, Serial No. 11/874072, filed October 17, 2007, which claims the benefit under 35 USC 119(e) to U.S. Provisional Applications Ser. Nos. 60/852,149, filed October 17, 2006, and 60/978,982, filed October 10, 2007, all of which are hereby incorporated in their entirety.

[00346] U.S. Patent No. 7,245,963 by Draghia-Akli, et al. describes modular electrode systems and their use for facilitating the introduction of a biomolecule into cells of a selected tissue in a body or plant. The modular electrode systems may comprise a plurality of needle electrodes; a hypodermic needle; an electrical connector that provides a conductive link from a programmable constant-current pulse controller to the plurality of needle electrodes; and a power source. An operator can grasp the plurality of needle electrodes that are mounted on a support structure and firmly insert them into the selected tissue in a body or plant. The biomolecules are then delivered via the hypodermic needle into the selected tissue. The programmable constant-current pulse controller is activated and constant-current electrical pulse is applied to the plurality of needle electrodes. The applied constant-current electrical pulse facilitates the introduction of the biomolecule into the cell between the plurality of electrodes. The entire content of U.S. Patent No. 7,245,963 is hereby incorporated by reference.

[00347] U.S. Patent Pub. 2005/0052630 submitted by Smith, et al. describes an electroporation device which may be used to effectively facilitate the introduction of a biomolecule into cells of a selected tissue in a body or plant. The electroporation device comprises an electro-kinetic device ("EKD device") whose operation is specified by software or firmware. The EKD device produces a series of programmable constant-current pulse patterns between electrodes in an array

based on user control and input of the pulse parameters, and allows the storage and acquisition of current waveform data. The electroporation device also comprises a replaceable electrode disk having an array of needle electrodes, a central injection channel for an injection needle, and a removable guide disk. The entire content of U.S. Patent Pub. 2005/0052630 is hereby incorporated by reference.

[00348] The electrode arrays and methods described in U.S. Patent No. 7,245,963 and U.S. Patent Pub. 2005/0052630 may be adapted for deep penetration into not only tissues such as muscle, but also other tissues or organs. Because of the configuration of the electrode array, the injection needle (to deliver the biomolecule of choice) is also inserted completely into the target organ, and the injection is administered perpendicular to the target issue, in the area that is pre-delineated by the electrodes The electrodes described in U.S. Patent No. 7,245,963 and U.S. Patent Pub. 2005/005263 are preferably 20 mm long and 21 gauge.

[00349] Additionally, contemplated in some embodiments that incorporate electroporation devices and uses thereof, there are electroporation devices that are those described in the following patents: US Patent 5,273,525 issued December 28, 1993, US Patents 6,110,161 issued August 29, 2000, 6,261,281 issued July 17, 2001, and 6,958,060 issued October 25, 2005, and US patent 6,939,862 issued September 6, 2005. Furthermore, patents covering subject matter provided in US patent 6,697,669 issued February 24, 2004, which concerns delivery of DNA using any of a variety of devices, and US patent 7,328,064 issued February 5, 2008, drawn to method of injecting DNA are contemplated herein. The above-patents are incorporated by reference in their entirety.

11. **Method of Treatment**

[00350] Also provided herein is a method of treating, protecting against, and/or preventing disease in a subject in need thereof by generating the synthetic antibody in the subject. The method can include administering the composition to the subject. Administration of the composition to the subject can be done using the method of delivery described above.

[00351] Upon generation of the synthetic antibody in the subject, the synthetic antibody can bind to or react with the antigen. Such binding can neutralize the antigen, block recognition of the antigen by another molecule, for example, a protein or nucleic acid, and elicit or induce an

immune response to the antigen, thereby treating, protecting against, and/or preventing the disease associated with the antigen in the subject.

[00352] The method of delivering the vaccine or vaccination may be provided to induce a therapeutic and prophylactic immune response. The vaccination process may generate in the mammal an immune response against the antigen. The vaccine may be delivered to an individual to modulate the activity of the mammal's immune system and enhance the immune response. The delivery of the vaccine may be the transfection of the consensus antigen as a nucleic acid molecule that is expressed in the cell and delivered to the surface of the cell upon which the immune system recognized and induces a cellular, humoral, or cellular and humoral response. The delivery of the vaccine may be used to induce or elicit and immune response in mammals against the antigen by administering to the mammals the vaccine as discussed above.

[00353] The composition dose can be between 1 μg to 10 mg active component/kg body weight/time, and can be 20 μg to 10 mg component/kg body weight/time. The composition can be administered every 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, or 31 days. The number of composition doses for effective treatment can be 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

[00354] The composition can comprise 1 or more, 2 or more, 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, or 10 or more DNA vaccines encoding an antigen. The composition may comprise 1 or more, 2 or more, 3 or more, 4 or more, 5 or more, 6 or more, 7 or more, 8 or more, 9 or more, or 10 or more DNA encoded synthetic antibodies or fragments thereof.

[00355] The DNA vaccine and the DMAb may be administered at the same time or at different times. In one embodiment, the DNA vaccine and the DMAb are administered simultaneously. In one embodiment, the DNA vaccine is administered before the DMAb. In one embodiment, the DMAb is administered before the DNA vaccine.

[00356] In certain embodiments, the DNA vaccine is administered 1 or more days, 2 or more days, 3 or more days, 4 or more days, 5 or more days, 6 or more days, 7 or more days, 8 or more days, 9 or more days, 10 or more days, 11 or more days, 12 or more days, 13 or more days, or 14 or more days after the DMAb is administered. In certain embodiments, the DNA vaccine is administered 1 or more weeks, 2 or more weeks, 3 or more weeks, 4 or more weeks, 5 or more weeks, 6 or more weeks, 7 or more weeks, 8 or more weeks, 9 or more weeks, or 10 or more

weeks after the DMAb is administered. In certain embodiments, the DNA vaccine is administered 1 or more months, 2 or more months, 3 or more months, 4 or more months, 5 or more months, 6 or more months, 7 or more months, 8 or more months, 9 or more months, 10 or more months, 11 or more months, or 12 or more months after the DMAb is administered.

[00357] In certain embodiments, the DMAb is administered 1 or more days, 2 or more days, 3 or more days, 4 or more days, 5 or more days, 6 or more days, 7 or more days, 8 or more days, 9 or more days, 10 or more days, 11 or more days, 12 or more days, 13 or more days, or 14 or more days after the DNA vaccine is administered. In certain embodiments, the DMAb is administered 1 or more weeks, 2 or more weeks, 3 or more weeks, 4 or more weeks, 5 or more weeks, 6 or more weeks, 7 or more weeks, 8 or more weeks, 9 or more weeks, or 10 or more weeks after the DNA vaccine is administered. In certain embodiments, the DMAb is administered 1 or more months, 2 or more months, 3 or more months, 4 or more months, 5 or more months, 6 or more months, 7 or more months, 8 or more months, 9 or more months, 10 or more months, 11 or more months, or 12 or more months after the DNA vaccine is administered.

[00358] In certain embodiments, the DMAb and DNA vaccine are administered once. In certain embodiments, the DMAb and/or the DNA vaccine are administered more than once. In certain embodiments, administration of the DMAb and DNA vaccine provides a persistent and systemic immune response.

12. **Use in Combination with Antibiotics**

[00359] The present invention also provides a method of treating, protecting against, and/or preventing disease in a subject in need thereof by administering a combination of the synthetic antibody and a therapeutic antibiotic agent.

[00360] The synthetic antibody and an antibiotic agent may be administered using any suitable method such that a combination of the synthetic antibody and antibiotic agent are both present in the subject. In one embodiment, the method may comprise administration of a first composition comprising a synthetic antibody of the invention by any of the methods described in detail above and administration of a second composition comprising an antibiotic agent less than 1, less than 2, less than 3, less than 4, less than 5, less than 6, less than 7, less than 8, less than 9 or less than 10 days following administration of the synthetic antibody. In one embodiment, the method may comprise administration of a first composition comprising a synthetic antibody of the invention

by any of the methods described in detail above and administration of a second composition comprising an antibiotic agent more than 1, more than 2, more than 3, more than 4, more than 5, more than 6, more than 7, more than 8, more than 9 or more than 10 days following administration of the synthetic antibody. In one embodiment, the method may comprise administration of a first composition comprising an antibiotic agent and administration of a second composition comprising a synthetic antibody of the invention by any of the methods described in detail above less than 1, less than 2, less than 3, less than 4, less than 5, less than 6, less than 7, less than 8, less than 9 or less than 10 days following administration of the antibiotic agent. In one embodiment, the method may comprise administration of a first composition comprising an antibiotic agent and administration of a second composition comprising a synthetic antibody of the invention by any of the methods described in detail above more than 1, more than 2, more than 3, more than 4, more than 5, more than 6, more than 7, more than 8, more than 9 or more than 10 days following administration of the antibiotic agent. In one embodiment, the method may comprise administration of a first composition comprising a synthetic antibody of the invention by any of the methods described in detail above and a second composition comprising an antibiotic agent concurrently. In one embodiment, the method may comprise administration of a first composition comprising a synthetic antibody of the invention by any of the methods described in detail above and a second composition comprising an antibiotic agent concurrently. In one embodiment, the method may comprise administration of a single composition comprising a synthetic antibody of the invention and an antibiotic agent.

[00361] Non-limiting examples of antibiotics that can be used in combination with the synthetic antibody of the invention include aminoglycosides (e.g., gentamicin, amikacin, tobramycin), quinolones (e.g., ciprofloxacin, levofloxacin), cephalosporins (e.g., ceftazidime, cefepime, cefoperazone, cefpirome, ceftobiprole), antipseudomonal penicillins: carboxypenicillins (e.g., carbenicillin and ticarcillin) and ureidopenicillins (e.g., mezlocillin, azlocillin, and piperacillin), carbapenems (e.g., meropenem, imipenem, doripenem), polymyxins (e.g., polymyxin B and colistin) and monobactams (e.g., aztreonam).

[00362] The present invention has multiple aspects, illustrated by the following non-limiting examples.

13. **Examples**

[00363] The present invention is further illustrated in the following Examples. It should be understood that these Examples, while indicating preferred embodiments of the invention, are given by way of illustration only. From the above discussion and these Examples, one skilled in the art can ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions. Thus, various modifications of the invention in addition to those shown and described herein will be apparent to those skilled in the art from the foregoing description. Such modifications are also intended to fall within the scope of the appended claims.

Example 1

Rapid and long-term immunity elicited by DNA encoded antibody prophylaxis and DNA vaccination against Chikungunya virus

[00364] Vaccination is known to exhibit a lag phase before generation of immunity; thus, there is a gap of time during infection before an immune response is in effect. The following provides specific novel approaches that utilizes the benefit of vaccines and the native immune response along with a rapid generation of effective immunity using the DNA synthetic antibodies or dMabs.

[00365] An antibody-based prophylaxis/therapy entailing the electroporation mediated delivery of synthetic plasmids, encoding biologically active anti-Chikungunya virus envelope mAb (designated dMAb), was designed and evaluated for anti-viral efficacy as well as for the ability to overcome shortcomings inherent with conventional active vaccination by a novel passive immune-based strategy. One intramuscular injection of the CHIKV-dMAb produced antibodies in vivo more rapidly than active vaccination with a CHIKV-DNA vaccine. This dMAb neutralized diverse CHIKV clinical isolates and protected mice from viral challenge. Combinations of both afford rapid as well as long-lived protection.

[00366] The results presented herein demonstrate that a DNA based dMAb strategy induces rapid protection against an emerging viral infection, which can be combined with DNA vaccination providing a uniquely both short term and long-term protection against this emerging infectious disease. These studies have implications for pathogen treatment and control strategies.

METHODS

Construction and Expression of CHIKV Specific dMABs

[00367] Gene sequence information for an established anti–Env-specific CHIKV neutralizing human mAb were obtained from the National Center for Biotechnology Information database (Warter et al., 2011, J Immunol 186:3258-64). Human embryonic kidney 293T cells and Vero cells, used for expression confirmation studies, were maintained as described previously (Mallilankaraman et al., 2011, PLoS Negl Trop Dis 5:e928). The variable heavy (VH) and variable light (VL) chain segments for the CHIKV Env dMAb preparation were generated by using synthetic oligonucleotides with several modifications and were constructed as either a full-length immunoglobulin G (IgG; designated "CVM1-IgG") or Fab fragment (designated "CVM1-Fab") (Muthumani et al., 2013, Hum Vaccin Immunother 9:2253-62). For cloning of CVM1-IgG, a single open reading frame was assembled containing the heavy and light chain genes, separated by a furin cleavage site coupled with a P2A self-processing peptide sequence. This transgene was cloned into the pVax1 expression vector (Muthumani et al., 2013, Hum Vaccin Immunother 9:2253-62_. The CVM1-Fab VH and VL chains were cloned into separate pVax1 vectors. For tissue culture transfection, 100 μg of pVax1 DNA, CVM1-IgG, or CVM1-Fab (100 μg of each VH and VL construct) was used. The CHIKV Env–based DNA vaccine used in the study was developed and characterized as previously described (Muthumani et al., 2008, Vaccine 26:5128-34; Mallilankaraman et al., 2011, PLoS Negl Trop Dis 5:e928).

CHIKV-dMAb IgG quantification and binding assays

[00368] ELISA assays were performed with sera, collected and measured in duplicate, from mice administered CMV1-IgG or pVax1 to quantify expression kinetics and target antigen binding. These measurements and analyses were performed as previously described (Muthumani et al., 2015, Sci transl Med 7:301ra132).

Western blot and immunofluorescence analysis of dMAb generated IgG

[00369] For Western blot analysis of IgG expression CHIKV (viral isolate PC08) infected cells were lysed two days post infection and evaluated by previously published methods (Mallilankaraman et al., 2011, PLoS Negl Trop Dis 5:e928; Muthumani et al., 2015, Sci transl

Med 7:301ra132). For immunofluorescence analysis, chamber slides (Nalgene Nunc, Penfield, New York) were seeded with Vero cells (1×10^4) and infected for 2 hours with the viral isolate CHIKV PC08 at a multiplicity of infection of 1. Immunofluorescence analysis was performed as previously described (Muthumani et al., 2015, Sci transl Med 7:301ra132), with slides being visually evaluated by confocal microscopy (LSM710; Carl Zeiss). The resulting images were semiquantitatively analyzed using Zen software (Carl Zeiss).

dMAb DNA plasmid administration and *in vivo* analysis

[00370] CVM1-Fab and CVM1-IgG expression kinetics and functionality were evaluated in B6.Cg-Foxn1nu/J mice (Jackson Laboratory) following intramuscular injection of 100 μg control pVax1, CVM1-IgG, or 100 μg of each plasmid chain of CVM1-Fab. For studies that include the DNA vaccine, 25 μg of the CHIKV Env plasmid were injected 3 times at 2-week intervals. All injections were followed immediately by delivery of CHIKV dMAb DNA plasmid via electroporation (Flingai et al., 2015, Sci Rep 5:12616; Muthumani et al., 2015, Sci transl Med 7:301ra132; Broderick et al., 2014, Methods Mol iol 1143:123-30).

CHIKV challenge study

[00371] BALB/c mice received a single (100 μg) electroporation-enhanced intramuscular injection of CVM1-IgG, CMV-Fab (VH and VL), or control pVax1 plasmids. The CHIKV Env DNA vaccine was delivered as described above. Two or 35 days after DNA delivery, mice were challenged with 107 plaque-forming units (25 μL) of the viral isolate CHIKV Del-03 (JN578247) (Muruganandam et al., 2011, Can J Microbiol 57:1073-7) either subcutaneously (in the dorsal side of each hind foot) or intranasally (Mallilankaraman et al., 2011, PLoS Negl Trop Dis 5:e928). Mouse foot swelling (height by breadth) was measured daily up to 14 days after infection. In addition, the animals were monitored daily (for up to 20 days after infection) for survival and signs of infection (ie, changes in body weight and lethargy). Animals losing >30% of their body mass were euthanized, and serum samples were collected for cytokine quantification and other immune analysis. Blood samples were collected from the tail on days 7–14 after infection, and viremia levels were measured by a plaque assay.

Neutralizing antibody analysis

[00372] Anti-CHIKV neutralizing antibody titers from mice administered CVM1-IgG were determined by previously described methods (Wang et al., 2008, Vaccine 26:5030-9; Mallilankaraman et al., 2011, PLoS Negl Trop Dis 5:e928), using Vero cells infected with the following CHIKV isolates: LR2006-OPY1 (Indian Ocean Outbreak), IND-63WB1 and SL-CH1 (Asian-clade), Ross (ECSA-clade), and PC08 and DRDE-06 (ECSA-clade). Neutralization titers were calculated as the reciprocal of the highest dilution mediating 100% reduction of the cytopathic effects in the Vero cell monolayer. Data were generated and statistical analyses performed using the GraphPad Prism 5 software package (GraphPad Software). Nonlinear regression fitting with sigmoidal dose response was used to determine the level of antibody mediating 50% inhibition of infection (IC50). CHIKV Env pseudotype production and fluorescence-activated cell-sorting (FACS) analysis were performed as described previously (Muthumani et al., 2013, PLoS One 8:e84234).

Cytokine Quantitative Analysis

[00373] Sera were collected from CVM1-Fab, CVM1-IgG, and CHIKV-Env injected mice as well as CHIKV challenged mice (one week post challenge). TNF-α, IL-1β and IL-6 sera cytokine levels were measured using ELISA kits according to the manufacturer's instructions (R&D Systems).

Statistical analysis

[00374] A student t-test or a nonparametric Spearman's correlation test, were performed using GraphPad Prism software (Prism Inc.). Correlations between the variables in the control and experimental groups were statistically evaluated using the Spearman rank correlation test, with p values < 0.05 for all tests considered to be statistically significant.

RESULTS

Anti-CHIKV dMAbs design and confirmation of expression

[00375] Viral entry into host cells by CHIKV is mediated by Env, against which the majority of neutralizing antibodies are generated (Mallilankaraman et al., 2011, PLoS Negl Trop Dis 5:e928; Sun et al., 2013, eLife 2:e00435). Thus, a DNA plasmid (dMAb) expressing the light and

heavy immunoglobulin chains of a neutralizing anti-CHIKV mAb recognizing both E1 and E2 Env proteins was designed (Warter et al., 2011, J Immunol 186:3258-64; Pal et al., 2013, PLoS Pathog 9:e1003312). The complementary DNAs for the coding sequences of the VL and VH immunoglobulin chains for full-length anti-CHIKV dMAb were optimized for increased expression and cloned into a pVax1 vector, using previously described methods (Flingai et al., 2015, Sci Rep 5:12616; Muthumani et al., 2013, Hum Vaccin Immunother 9:2253-62). For the constructs expressing anti–CHIKV-Fab, the VH and VL genes were cloned separately. The optimized synthetic plasmids constructed from the anti-Env–specific CHIKV-neutralizing mAb were designated CVM1-IgG or CVM1-Fab, for the IgG and Fab antibodies, respectively. Human 293T cells were transfected with either the CVM1-IgG plasmid or the CVM1-Fab (VL, VH, or combined) plasmids to validate expression in vitro. As indicated in Figure 1A and 1B, anti-CHIKV antibody levels were measured by ELISA with recombinant CHIKV Env used as the binding antigen. These data indicate that the CVM1-Fab and CVM1-IgG expressed antibodies in the muscle that appeared to be properly assembled and biologically functional in vitro.

***In vivo* expression and quantification of CVM1-IgG and CVM1-Fab**

[00376] Following confirmation of in vitro expression, the ability of CVM1-Fab or CVM1-IgG to produce anti-CHIKV antibodies in vivo was measured. B6.Cg-Foxn1^{nu}/J mice aged 5–6 weeks were administered 100 μg of CVM1-IgG (CVM1-IgG is 1 plasmid), 100 μg each of CVM1 VH and VL (CVM1-Fab consists of 2 plasmids), or control vector by a single intramuscular electroporation-mediated injection. Sera were collected at indicated time points, and target antigen binding was measured by IgG quantification, using ELISA. Although mAbs generated from CVM1-Fab appeared more rapidly (ie, within 3 days after injection) than those from CVM1-IgG, both constructs generated similar mAb levels by day 15 (mean sera levels [±SD], 1587.23 ± 73.23 ng/mL of CVM1-Fab and 1341.29 ± 82.07 ng/mL of CVM1-IgG; Figure 1C). Mice were administered either CVM1-IgG or CVM1-Fab, and sera antibody levels were evaluated through a binding ELISA. Sera collected 15 days after injection from both CVM1-IgG and CVM1-Fab bound to CHIKV Env protein but not to an unrelated control antigen, human immunodeficiency virus type 1 Env (Figure 1D). These data indicate that in vivo produced anti-CHIKV antibodies from CVM1-IgG or CVM1-Fab constructs have similar biological characteristics to conventionally produced antigen specific antibodies.

***In vivo* specificity and broadly neutralizing activity in sera from CVM1-IgG injected mice**

[00377] The anti-CHIKV dMAb generated mAbs were tested for binding specificity and anti-CHIKV neutralizing activity. Sera from mice injected with CVM1-IgG were tested against fixed CHIKV PC08–infected Vero cells by immunofluorescence assays. The results indicated binding of the sera antibodies to the CHIKV-infected cells (Figure 2*A*). Confirmation of binding of sera from CVM1-IgG–injected mice to target proteins was tested by Western blot analysis. The detection of CHIKV E2 protein (50 kDa) expression in total cell lysate from the CHIKV-infected cells indicates specificity of CVM1-IgG expression (Figure 2*B*). The specificity of in vivo–produced CVM1-IgG antibody was further demonstrated through FACS analysis against cells infected with green fluorescent protein–encoded CHIKV (Figure 2*C*). Moreover, CVM1-Fab binding, demonstrated by immunohistochemical analysis and FACS analysis, was similar to that of the generated full-length CVM1-IgG (data not shown). Together, these findings indicate a strong specificity of the antibody generated from the CVM1-IgG plasmid.

[00378] Furthermore, the anti-CHIKV neutralizing activity in sera from mice that received CVM1-IgG was measured against that in 6 divergent CHIKV strains: LR2006-OPY1 (Indian Ocean Outbreak), IND-63WB1 (Asian-clade), Ross (ECSA-clade), PC08 (ECSA-clade), SL-CH1 (Asian-clade) and DRDE-06 (ECSA-clade) (Sziegler et al., 2007, Am J Trop Med Hyg 79:133-6). IC_{50} values were determined for each viral isolate. Sera from CVM1-IgG–injected mice effectively neutralized all 6 CHIKV isolates, demonstrating that a single injection can produce significant neutralizing levels of human anti-CHIKV IgG in mice (Figure 2*D*). Similar results were observed using sera from CVM1-Fab–injected mice (data not shown). These data indicate that antibodies produced in vivo by CVM1-IgG constructs have relevant biological activity (ie, binding and neutralizing activity against CHIKV)

CVM1-IgG injection protects mice from lethal CHIKV challenge

[00379] Previous studies demonstrated that early immunity against viruses is a key factor for controlling infections (Barouch et al., 2014, Nat Rev Microbiol 12:765-71; Hudson et al., 2003, Nat Med 9:129-34; Smith et al., 2015, Chikungunya Virus 18:86-95). To determine whether antibodies generated from CVM1-IgG or CVM1-Fab provide protection against early exposure

to CHIKV, groups of 10 mice received a single administration of pVax1, CVM1-IgG, or CVM1-Fab on day 0. Each group subsequently was challenged subcutaneously with virus on day 2 to mimic natural CHIKV infection (Figure 3*A*). Animal survival and weight changes were subsequently recorded for 20 days. All mice injected with pVax1 control plasmid died within a week of viral challenge. Conversely, 100% survival was observed in mice administered either CVM1-IgG or CVM1-Fab, compared with 0% survival among mice that received pVax1 plasmid ($P = .0033$), demonstrating that CVM1-IgG and CVM1-Fab plasmids confer protective immunity within 2 days after delivery.

[00380] The longevity of immune protection was next evaluated. A second group of mice (n = 10) was challenged with CHIKV 30 days after a single injection with CVM1-IgG, CVM1-Fab, or pVax1 on day 0 (Figure 3*B*). Mice were monitored for survival over the next 20 days. Mice injected with CVM1-Fab or CVM1-IgG demonstrated 70% and 90% survival, respectively, compared with no survival among pVax1-injected mice ($P = .0120$), indicating that CVM1-IgG provides a more durable degree of immune protection (Figure 3*B*).

[00381] To assess the ability of the CVM1-IgG plasmid to protect against infection at a mucosal surface, the protective efficacy of CVM1-IgG against subcutaneous versus intranasal viral challenge, previously demonstrated to produce visible CHIKV pathogenesis such as limb muscle weakness, footpad swelling, lethargy, and high mortality within 6–10 days of infection, was evaluated (Mallilankaraman et al., 2011, PLoS Negl Trop Dis 5:e928; Couderc et al., 2008, PLoS Pathog 4:e29). For simplicity, studies focused on the CVM1-IgG construct. Groups of 20 mice received a single administration of pVax1 or CVM1-IgG, with half (ie, 10) being challenged with CHIKV via a subcutaneous or intranasal route 2 days after injection. CVM1-IgG protected mice from both subcutaneous viral challenge ($P = .0024$; Figure 3*C*) and intranasal viral challenge ($P = .0073$; Figure 3*D*), compared with pVax1-injected mice, demonstrating that it can protect against systemic and mucosal infection.

[00382] An efficacy study comparing the protective efficacy of CVM1-IgG administration vs a CHIKV Env–expressing DNA vaccine (CHIKV Env) was next performed. A novel consensus-based DNA vaccine was developed by our laboratory and was capable of providing protection against CHIKV challenge in mice. The DNA vaccine also induced both measurable cellular immune responses, as well as potent neutralizing antibody responses in rhesus macaques [11, 12]. Groups of mice were administered a single injection of CVM1-IgG, CHIKV Env, or the

pVax1, followed by viral challenge on 2 days after injection. Mice that received a single immunization of CHIKV Env or pVax1 died within 6 days of viral challenge, whereas a single immunization of CVM1-IgG provided 100% protection (Figure 4A). CVM1-IgG clearly conferred protective immunity more rapidly than the CHIKV Env DNA vaccine (P = .0026).

Comparison between *in vivo* protective immunity conferred by CHIKV-IgG administration and CHIKV-Env DNA vaccination

[00383] Next, a long-term CHIKV challenge protection study was performed on day 35 following vaccination with the CHIKV Env DNA vaccine or administration of CVM1-IgG on day 0. The multibooster delivery of the CHIKV Env DNA vaccine conferred 100% protection (Figure 4*B*), while 80% survival was observed in mice administered CVM1-IgG (*P* = .0007). The kinetics of the induced antibody responses was measurable within 2 days of a single injection of CVM1-IgG, with peak levels by day 15 (approximately 1400 ng/mL) and detectable mAb levels maintained for at least 45 days after injection (Figure 6A). Although there is continued expression, these levels are decreased, compared with peak levels, supporting the partial protection noted in the experiment (Figure 4*B*).

Co-delivery of CVM1-IgG and the CHIKV-Env DNA vaccine produces systemic humoral immunity, cell-mediated immunity, and protection *in vivo*

[00384] One potential issue of combining antibody delivery with vaccination approaches is that the antibodies can neutralize many traditional vaccines (Mallilankaraman et al., 2011, PLoS Negl Trop Dis 5:e928; Flingai et al., 2015, Sci Rep 5:12616; Muthumani et al., 2015, Sci transl Med 7:301ra132; Laddy et al., 2008, PLoS One 3:e2517) and thus are incompatible platforms. The effect of co-administration of CVM1-IgG and CHIKV Env on mouse survival in the context of CHIKV challenge was also evaluated. In this experiment, 20 mice were administered at day 0 a single dose of CVM1-IgG and 3 doses of CHIKV Env DNA as described above. Subsequently, half of the animals were challenged with CHIKV at day 2 and the other half at day 35. Survival in these groups was followed as a function of time. Not unexpectedly, both of the challenge groups had 100% long-term survival (Figure 4*C*). Specifically, results of the day 2 CHIKV challenge experiment indicated the utility of the CVM1-IgG reagent in mediating protection from infection, with the survival percentage decreasing to approximately 30% by 4 days after

challenge in control (pVax1) animals. Figure 4*D* indicates levels of anti-CHIKV IgG, by time, generated in mice that received CVM1-IgG and CHIKV Env DNA vaccine; anti-CHIKV human IgG represents antibody produced by the CVM1-IgG plasmid and anti-CHIKV mouse IgG represents antibody induced by the CHIKV Env vaccine. Both human IgG and mouse IgG were detected and exhibited different expression kinetics. By 3 days after initial CHIKV Env DNA vaccination, mouse anti-Env antibody levels were essentially near 0 (mouse anti-CHIKV IgG). Conversely, 3 days after a single CVM1-IgG injection, human anti-Env antibody levels were significant (human anti-CHIKV IgG). These data underscore the importance of CVM1-IgG in mediating rapid protection from infection and death after CHIKV challenge.

[00385] Furthermore, T-cell responses induced in animals injected with CVM1-IgG, CHIKV Env, or CVM1-IgG plus CHIKV Env was evaluated by a quantitative enzyme-linked immunospot assay, which measures IFN-γ levels (Figure 6B). CHIKV Env elicited strong T-cell responses irrespective of codelivery with CVM1-IgG, showing the lack of interference of these approaches. Conversely, animals administered only CVM1-IgG did not develop T-cell responses, as would be expected. These findings demonstrate that both CVM1-IgG and CHIKV Env DNA vaccine can be administered simultaneously without reciprocal interference, providing immediate and long-lived protection via systemic humoral and cellular immunity.

CVM1-IgG administration reduces CHIKV viral loads and pro-inflammatory cytokine levels

[00386] Previous studies identified molecular correlates of CHIKV-associated disease severity, including viral load and proinflammatory cytokine levels (Ng et al., 2009, PLoS One 4:e4261; Chaaitanya et al., 2011, Viral Immunol 24:265-71). Thus, the ability of CVM1 IgG to suppress these disease-associated markers at early and late time points after viral challenge was assessed. Mice immunized with CVM1 IgG, CVM1 Fab, CHIKV Env, or CVM1 IgG plus CHIKV Env DNA vaccine generated mAb and significantly reduced viral loads (Figure 5*A*). In addition to viral load reduction, these mice did not exhibit footpad swelling, compared with control (pVax1) immunized mice, and consistently gained body weight during the 20-day experimental period (Figure 5*B* and 5C). Also the CVM1-IgG–generated mAb and the CHIKV Env DNA vaccine exhibited significantly reduced levels of CHIKV-mediated proinflammatory cytokines (ie, TNF-α, IL-6, and IL-β), compared with pVax1, 10 days after viral challenge (Figure 7). These

findings suggest that a single injection with CVM1-IgG suppresses CHIKV-associated pathology to an extent comparable to that induced by protective vaccination (Mallilankaraman et al., 2011, PLoS Negl Trop Dis 5:e928).

Electroporation-mediated delivery of optimized DNA plasmids for the in vivo rapid production of biologically functional mAbs.

[00387] The results demonstrate that mice injected with a single dose of CVM1 IgG were fully protected from viral challenge 2 days after administration, whereas no mice survived infection following a single immunization with CHIKV Env DNA vaccine, owing presumably to an insufficient time to mount protective immunity. However, complete protection was observed with CHIKV Env after a immunization regimen followed by challenge at later time points. A similar level of protection occurred in mice administered a single dose of CVM1-IgG, although protection waned to 80% over time. Notably, the codelivery of CVM1-IgG and CHIKV Env produced rapid and persistent humoral and cellular immunity, demonstrating that a combination approach provides for synergistic, beneficial effects. Importantly, codelivery of CVM1-IgG and CHIKV Env were not antagonistic in terms of the development of short- or long-term protective immune responses.

Example 2 - Rapid and long-term immunity elicited by DNA encoded antibody prophylaxis and DNA vaccination against Zika virus

[00388] Vaccination is known to exhibit a lag phase before generation of immunity; thus, there is a gap of time during infection before an immune response is in effect. The following provides specific novel approaches that utilize the benefit of vaccines and the native immune response along with a rapid generation of effective immunity using the DNA synthetic antibodies or dMabs.

[00389] An antibody-based prophylaxis/therapy entailing the electroporation mediated delivery of synthetic plasmids, encoding biologically active anti-Zika virus envelope mAb (designated dMAb), is designed and evaluated for anti-viral efficacy as well as for the ability to overcome shortcomings inherent with conventional active vaccination by a novel passive immune-based strategy. One intramuscular injection of the ZIKV-dMAb produces antibodies in vivo more rapidly than active vaccination with an ZIKV-DNA vaccine. This dMAb neutralized diverse

ZIKV clinical isolates and protected mice from viral challenge. Combinations of both afford rapid as well as long-lived protection.

[00390] A DNA based dMAb strategy induces rapid protection against an emerging viral infection, which can be combined with DNA vaccination providing a uniquely both short term and long-term protection against this emerging infectious disease. These studies have implications for pathogen treatment and control strategies.

dMAb IgG quantification and binding assays

[00391] ELISA assays are performed with sera from subjects administered an ZIKV-dMAb to quantify expression kinetics and target antigen binding.

Analysis of dMAb generated IgG

[00392] IgG expression of ZIKV infected cells are analyzed by western blot. For immunofluorescence analysis ZIKV infected cells are visually evaluated by confocal microscopy and quantitatively or semi-quantitatively analyzed.

dMAb DNA plasmid administration and *in vivo* analysis

[00393] Expression kinetics and functionality were evaluated in subjects following injection of control or ZIKV-dMAb. For studies that include the DNA vaccine, the ZIKV-DNA vaccine plasmid is administered.

Challenge study

[00394] Subjects receive electroporation-enhanced injection of ZIKV-dMAb or control plasmids. The ZIKV-DNA vaccine was delivered as described above. After DNA delivery, subjects are challenged with ZIKV. The animals are monitored for survival and signs of infection. Serum samples are collected for cytokine quantification and other immune analysis. Blood samples are collected from after infection and viremia levels are measured.

Neutralizing Antibody Analysis

[00395] Anti-ZIKV neutralizing antibody titers from subjects administered ZIKV-dMAb are determined. Neutralization titers may be calculated as the reciprocal of the highest dilution mediating 100% reduction of the cytopathic effects in the cells.

Cytokine Quantitative Analysis

[00396] Sera is collected from ZIKV-dMAb, and ZIKV-DNA vaccine injected subjects as well as ZIKV challenged subjects. TNF-α, IL-1β and IL-6 sera cytokine levels are measured.

Anti-ZIKV dMAbs design and confirmation of expression

[00397] The optimized synthetic plasmids constructed from the anti-ZIKV-neutralizing mAb were designed for the IgG and Fab antibodies. Cells are transfected with either the ZIKV-IgG plasmid or the ZIKV-Fab (VL, VH, or combined) plasmids to validate expression in vitro. The ZIKV-Fab and ZIKV-IgG expressed antibodies in the muscle that appeared to be properly assembled and biologically functional in vitro.

***In vivo* expression and quantification of anti-ZIKV dMAb**

[00398] Following confirmation of in vitro expression, the ability of ZIKV-Fab or ZIKV-IgG to produce anti-ZIKV antibodies in vivo is measured. Both constructs generate mAbs. Subjects are administered either ZIKV-IgG or ZIKV-Fab, and sera antibody levels are evaluated through a binding ELISA. Sera collected after injection from both ZIKV-IgG and ZIKV-Fab bind to ZIKV protein but not to an unrelated control antigen. These data indicate that in vivo produced anti-ZIKV antibodies from ZIKV-IgG or ZIKV-Fab constructs have similar biological characteristics to conventionally produced antigen specific antibodies.

***In vivo* specificity and broadly neutralizing activity in sera from anti-ZIKV dMAb injected subjects**

[00399] The anti-ZIKV dMAb generated mAbs are tested for binding specificity and anti-ZIKV neutralizing activity. Sera antibodies bind to ZIKV-infected cells. There is a strong specificity of the antibody generated from the anti-ZIKV dMAb plasmid.

[00400] Furthermore, the anti-ZIKV neutralizing activity in sera from subjects that received anti-ZIKV dMAb is measured against that in ZIKV strains. Sera from anti-ZIKV dMAb –

injected subects effectively neutralize ZIKV isolates, demonstrating that a single injection can produce significant neutralizing levels of human anti-ZIKV IgG. Thus, antibodies produced in vivo by anti-ZIKV dMAb constructs have relevant biological activity (ie, binding and neutralizing activity against ZIKV).

Anti-ZIKV dMAb injection protects mice from lethal ZIKV challenge

[00401] To determine whether antibodies generated from anti-ZIKV dMAb provide protection against early exposure to ZIKV, groups of 10 subjects receive of a control or anti-ZIKV dMAb on day 0. Each group subsequently is challenged subcutaneously with virus to mimic natural ZIKV infection. Subject survival and weight changes are subsequently recorded. Anti-ZIKV dMAb plasmids confer protective immunity.

[00402] The longevity of immune protection is next evaluated. A second group of subjects are challenged with ZIKV after injection with anti-ZIKV dMAb, or control plasmid on day 0. Subjects are monitored for survival. Anti-ZIKV dMAb provides a more durable degree of immune protection.

[00403] Anti-ZIKV dMAb protects subjects from both subcutaneous viral challenge and intranasal viral challenge compared with control-injected subjects, demonstrating that anti-ZIKV dMAbs can protect against systemic and mucosal infection.

[00404] An efficacy study comparing the protective efficacy of anti-ZIKV dMAb administration vs a ZIKV-DNA vaccine (ZIKV-DNA) is next performed. A novel consensus-based DNA vaccine was developed by our laboratory and is capable of providing protection against ZIKV challenge. The DNA vaccine also induced both measurable cellular immune responses, as well as potent neutralizing antibody responses. Groups of subjects are administered a single injection of anti-ZIKV dMAb, ZIKV-DNA, or the pVax1, followed by viral challenge. Anti-ZIKV dMAb confers protective immunity more rapidly than the ZIKV-DNA vaccine.

Comparison between *in vivo* protective immunity conferred by anti-ZIKV dMAb administration and ZIKV-DNA vaccination

[00405] Next, a long-term ZIKV challenge protection study was performed following vaccination with the ZIKV-DNA vaccine or administration of anti-ZIKV dMAb on day 0. ZIKV-DNA confers longer protective immunity than anti-ZIKV dMAb.

Co-delivery of anti-ZIKV dMAb and the ZIKV-DNA vaccine produces systemic humoral immunity, cell-mediated immunity, and protection *in vivo*

[00406] One potential issue of combining antibody delivery with vaccination approaches is that the antibodies can neutralize many traditional vaccines and thus are incompatible platforms. The effect of co-administration of anti-ZIKV dMAb and ZIKV-DNA on subject survival in the context of ZIKV challenge was is evaluated. Subjects are administered at day 0 anti-ZIKV dMAb and ZIKV-DNA. Subsequently, some animals are challenged with ZIKV at day 2 and the others at day 35. Survival in these groups is followed as a function of time. Anti-ZIKV dMAb mediates protection from infection, with the survival percentage decreasing to approximately 30% by 4 days after challenge in control (pVax1) animals. Both IgG finduced by anti-ZIKV dMAb and ZIKV-DNA vaccine are detected. Anti-ZIKV dMAb mediates rapid protection from infection and death after ZIKV challenge.

[00407] Furthermore, T-cell responses induced in subjects injected with Anti-ZIKV dMAb, ZIKV-DNA, or anti-ZIKV dMAb plus ZIKV-DNA are evaluated. ZIKV-DNA elicits strong T-cell responses irrespective of co-delivery with anti-ZIKV dMAb, showing the lack of interference of these approaches. Conversely, animals administered only anti-ZIKV dMAb do not develop T-cell responses. Both anti-ZIKV dMAb and ZIKV-DNA vaccine can be administered simultaneously without reciprocal interference, providing immediate and long-lived protection via systemic humoral and cellular immunity (Figure 8).

Electroporation-mediated delivery of optimized DNA plasmids for the in vivo rapid production of biologically functional mAbs

[00408] Subjects administered anti-ZIKV dMAbs are fully protected from viral challenge shortly after administration, whereas subjects do not survive infection following a single immunization with ZIKV-DNA vaccine, owing presumably to an insufficient time to mount protective immunity. However, ZIKV-DNA provides complete protection after an immunization regimen followed by challenge at later time points. A similar level of protection occurs in subjects administered a single dose of anti-ZIKV dMAbs, although protection wanes over time. Notably, the co-delivery of anti-ZIKV dMAbs and ZIKV-DNA produces rapid and persistent humoral and cellular immunity, suggesting that a combination approach can have additive or

synergistic effects. Importantly, co-delivery of anti-ZIKV dMAbs and ZIKV-DNA are not antagonistic in terms of the development of short- or long-term protective immune responses.

Example 3 - Rapid and long-term immunity elicited by DNA encoded antibody prophylaxis and DNA vaccination against Ebola virus

[00409] Vaccination is known to exhibit a lag phase before generation of immunity; thus, there is a gap of time during infection before an immune response is in effect. The following provides specific novel approaches that utilize the benefit of vaccines and the native immune response along with a rapid generation of effective immunity using the DNA synthetic antibodies or dMabs.

[00410] An antibody-based prophylaxis/therapy entailing the electroporation mediated delivery of synthetic plasmids, encoding biologically active anti-Ebola virus envelope mAb (designated dMAb), is designed and evaluated for anti-viral efficacy as well as for the ability to overcome shortcomings inherent with conventional active vaccination by a novel passive immune-based strategy. One intramuscular injection of the EBOV-dMAb produces antibodies in vivo more rapidly than active vaccination with an EBOV-DNA vaccine. This dMAb neutralized diverse EBOV clinical isolates and protected mice from viral challenge. Combinations of both afford rapid as well as long-lived protection.

[00411] A DNA based dMAb strategy induces rapid protection against an emerging viral infection, which can be combined with DNA vaccination providing a uniquely both short term and long-term protection against this emerging infectious disease. These studies have implications for pathogen treatment and control strategies.

dMAb IgG quantification and binding assays

[00412] ELISA assays are performed with sera from subjects administered an EBOV-dMAb to quantify expression kinetics and target antigen binding.

Analysis of dMAb generated IgG

[00413] IgG expression of EBOV infected cells are analyzed by western blot. For immunofluorescence analysis EBOV infected cells are visually evaluated by confocal microscopy and quantitatively or semi-quantitatively analyzed.

dMAb DNA plasmid administration and *in vivo* analysis

[00414] Expression kinetics and functionality were evaluated in subjects following injection of control or EBOV-dMAb. For studies that include the DNA vaccine, the EBOV-DNA vaccine plasmid is administered.

Challenge study

[00415] Subjects receive electroporation-enhanced injection of EBOV-dMAb or control plasmids. The EBOV-DNA vaccine was delivered as described above. After DNA delivery, subjects are challenged with EBOV. The animals are monitored for survival and signs of infection. Serum samples are collected for cytokine quantification and other immune analysis. Blood samples are collected from after infection and viremia levels are measured.

Neutralizing Antibody Analysis

[00416] Anti-EBOV neutralizing antibody titers from subjects administered EBOV-dMAb are determined. Neutralization titers may be calculated as the reciprocal of the highest dilution mediating 100% reduction of the cytopathic effects in the cells.

Cytokine Quantitative Analysis

[00417] Sera is collected from EBOV-dMAb, and EBOV-DNA vaccine injected subjects as well as EBOV challenged subjects. TNF-α, IL-1β and IL-6 sera cytokine levels are measured.

Anti-EBOV dMAbs design and confirmation of expression

[00418] The optimized synthetic plasmids constructed from the anti-EBOV-neutralizing mAb were designed for the IgG and Fab antibodies. Cells are transfected with either the EBOV-IgG plasmid or the EBOV-Fab (VL, VH, or combined) plasmids to validate expression in vitro. The EBOV-Fab and EBOV-IgG expressed antibodies in the muscle that appeared to be properly assembled and biologically functional in vitro.

***In vivo* expression and quantification of anti-EBOV dMAb**

[00419] Following confirmation of in vitro expression, the ability of EBOV-Fab or EBOV-IgG to produce anti-EBOV antibodies in vivo is measured. Both constructs generate mAbs. Subjects are administered either EBOV-IgG or EBOV-Fab, and sera antibody levels are evaluated through a binding ELISA. Sera collected after injection from both EBOV-IgG and EBOV-Fab bind to EBOV protein but not to an unrelated control antigen. These data indicate that in vivo produced anti-EBOV antibodies from EBOV-IgG or EBOV-Fab constructs have similar biological characteristics to conventionally produced antigen specific antibodies.

***In vivo* specificity and broadly neutralizing activity in sera from anti-EBOV dMAb injected subjects**

[00420] The anti-EBOV dMAb generated mAbs are tested for binding specificity and anti-EBOV neutralizing activity. Sera antibodies bind to EBOV-infected cells. There is a strong specificity of the antibody generated from the anti-EBOV dMAb plasmid.

[00421] Furthermore, the anti-EBOV neutralizing activity in sera from subjects that received anti-EBOV dMAb is measured against that in EBOV strains. Sera from anti-EBOV dMAb – injected subects effectively neutralize EBOV isolates, demonstrating that a single injection can produce significant neutralizing levels of human anti-EBOV IgG. Thus, antibodies produced in vivo by anti-EBOV dMAb constructs have relevant biological activity (ie, binding and neutralizing activity against EBOV).

Anti-EBOV dMAb injection protects mice from lethal EBOV challenge

[00422] To determine whether antibodies generated from anti-EBOV dMAb provide protection against early exposure to EBOV, groups of 10 subjects receive of a control or anti-EBOV dMAb on day 0. Each group subsequently is challenged subcutaneously with virus to mimic natural EBOV infection. Subject survival and weight changes are subsequently recorded. Anti-EBOV dMAb plasmids confer protective immunity.

[00423] The longevity of immune protection is next evaluated. A second group of subjects are challenged with EBOV after injection with anti-EBOV dMAb, or control plasmid on day 0.

Subjects are monitored for survival. Anti-EBOV dMAb provides a more durable degree of immune protection.

[00424] Anti-EBOV dMAb protects subjects from both subcutaneous viral challenge and intranasal viral challenge compared with control-injected subjects, demonstrating that anti-EBOV dMAbs can protect against systemic and mucosal infection.

[00425] An efficacy study comparing the protective efficacy of anti-EBOV dMAb administration vs a EBOV-DNA vaccine (EBOV-DNA) is next performed. A novel consensus-based DNA vaccine was developed by our laboratory and is capable of providing protection against EBOV challenge. The DNA vaccine also induced both measurable cellular immune responses, as well as potent neutralizing antibody responses. Groups of subjects are administered a single injection of anti-EBOV dMAb, EBOV-DNA, or the pVax1, followed by viral challenge. Anti-EBOV dMAb confers protective immunity more rapidly than the EBOV-DNA vaccine.

Comparison between *in vivo* protective immunity conferred by anti-EBOV dMAb administration and EBOV-DNA vaccination

[00426] Next, a long-term EBOV challenge protection study was performed following vaccination with the EBOV-DNA vaccine or administration of anti-EBOV dMAb on day 0. EBOV-DNA confers longer protective immunity than anti-EBOV dMAb.

Co-delivery of anti-EBOV dMAb and the EBOV-DNA vaccine produces systemic humoral immunity, cell-mediated immunity, and protection *in vivo*

[00427] One potential issue of combining antibody delivery with vaccination approaches is that the antibodies can neutralize many traditional vaccines and thus are incompatible platforms. The effect of co-administration of anti-EBOV dMAb and EBOV-DNA on subject survival in the context of EBOV challenge was is evaluated. Subjects are administered at day 0 anti-EBOV dMAb and EBOV-DNA. Subsequently, some animals are challenged with EBOV at day 2 and the others at day 35. Survival in these groups is followed as a function of time. Anti-EBOV dMAb mediates protection from infection, with the survival percentage decreasing to approximately 30% by 4 days after challenge in control (pVax1) animals. Both IgG finduced by anti-EBOV dMAb and EBOV-DNA vaccine are detected. Anti-EBOV dMAb mediates rapid protection from infection and death after EBOV challenge.

[00428] Furthermore, T-cell responses induced in subjects injected with Anti-EBOV dMAb, EBOV-DNA, or anti-EBOV dMAb plus EBOV-DNA are evaluated. EBOV-DNA elicits strong T-cell responses irrespective of co-delivery with anti-EBOV dMAb, showing the lack of interference of these approaches. Conversely, animals administered only anti-EBOV dMAb do not develop T-cell responses. Both anti-EBOV dMAb and EBOV-DNA vaccine can be administered simultaneously without reciprocal interference, providing immediate and long-lived protection via systemic humoral and cellular immunity.

Electroporation-mediated delivery of optimized DNA plasmids for the in vivo rapid production of biologically functional mAbs

[00429] Subjects administered anti-EBOV dMAbs are fully protected from viral challenge shortly after administration, whereas subjects do not survive infection following a single immunization with EBOV-DNA vaccine, owing presumably to an insufficient time to mount protective immunity. However, EBOV-DNA provides complete protection after an immunization regimen followed by challenge at later time points. A similar level of protection occurs in subjects administered a single dose of anti-EBOV dMAbs, although protection wanes over time. Notably, the co-delivery of anti-EBOV dMAbs and EBOV-DNA produces rapid and persistent humoral and cellular immunity, suggesting that a combination approach can have additive or synergistic effects. Importantly, co-delivery of anti-EBOV dMAbs and EBOV-DNA are not antagonistic in terms of the development of short- or long-term protective immune responses.

Example 4 - Rapid and long-term immunity elicited by DNA encoded antibody prophylaxis and DNA vaccination against Marburg virus

[00430] Vaccination is known to exhibit a lag phase before generation of immunity; thus, there is a gap of time during infection before an immune response is in effect. The following provides specific novel approaches that utilize the benefit of vaccines and the native immune response along with a rapid generation of effective immunity using the DNA synthetic antibodies or dMabs.

[00431] An antibody-based prophylaxis/therapy entailing the electroporation mediated delivery of synthetic plasmids, encoding biologically active anti-Marburg virus (MARV) mAb (designated dMAb), is designed and evaluated for anti-viral efficacy as well as for the ability to overcome shortcomings inherent with conventional active vaccination by a novel passive immune-based strategy. One intramuscular injection of the MARV-dMAb produces antibodies in vivo more rapidly than active vaccination with an MARV-DNA vaccine. This dMAb neutralized diverse MARV clinical isolates and protected mice from viral challenge. Combinations of both afford rapid as well as long-lived protection.

[00432] A DNA based dMAb strategy induces rapid protection against an emerging viral infection, which can be combined with DNA vaccination providing a uniquely both short term and long-term protection against this emerging infectious disease. These studies have implications for pathogen treatment and control strategies.

dMAb IgG quantification and binding assays

[00433] ELISA assays are performed with sera from subjects administered an MARV-dMAb to quantify expression kinetics and target antigen binding.

Analysis of dMAb generated IgG

[00434] IgG expression of MARV infected cells are analyzed by western blot. For immunofluorescence analysis MARV infected cells are visually evaluated by confocal microscopy and quantitatively or semi-quantitatively analyzed.

dMAb DNA plasmid administration and *in vivo* analysis

[00435] Expression kinetics and functionality were evaluated in subjects following injection of control or MARV-dMAb. For studies that include the DNA vaccine, the MARV-DNA vaccine plasmid is administered.

Challenge study

[00436] Subjects receive electroporation-enhanced injection of MARV-dMAb or control plasmids. The MARV-DNA vaccine was delivered as described above. After DNA delivery, subjects are challenged with MARV. The animals are monitored for survival and signs of

infection. Serum samples are collected for cytokine quantification and other immune analysis. Blood samples are collected from after infection and viremia levels are measured.

Neutralizing Antibody Analysis

[00437] Anti-MARV neutralizing antibody titers from subjects administered MARV-dMAb are determined. Neutralization titers may be calculated as the reciprocal of the highest dilution mediating 100% reduction of the cytopathic effects in the cells.

Cytokine Quantitative Analysis

[00438] Sera is collected from MARV-dMAb, and MARV-DNA vaccine injected subjects as well as MARV challenged subjects. TNF-α, IL-1β and IL-6 sera cytokine levels are measured.

Anti-MARV dMAbs design and confirmation of expression

[00439] The optimized synthetic plasmids constructed from the anti-MARV-neutralizing mAb were designed for the IgG and Fab antibodies. Cells are transfected with either the MARV-IgG plasmid or the MARV-Fab (VL, VH, or combined) plasmids to validate expression in vitro. The MARV-Fab and MARV-IgG expressed antibodies in the muscle that appeared to be properly assembled and biologically functional in vitro.

***In vivo* expression and quantification of anti-MARV dMAb**

[00440] Following confirmation of in vitro expression, the ability of MARV-Fab or MARV-IgG to produce anti-MARV antibodies in vivo is measured. Both constructs generate mAbs. Subjects are administered either MARV-IgG or MARV-Fab, and sera antibody levels are evaluated through a binding ELISA. Sera collected after injection from both MARV-IgG and MARV-Fab bind to MARV protein but not to an unrelated control antigen. These data indicate that in vivo produced anti-MARV antibodies from MARV-IgG or MARV-Fab constructs have similar biological characteristics to conventionally produced antigen specific antibodies.

***In vivo* specificity and broadly neutralizing activity in sera from anti-MARV dMAb injected subjects**

[00441] The anti-MARV dMAb generated mAbs are tested for binding specificity and anti-MARV neutralizing activity. Sera antibodies bind to MARV-infected cells. There is a strong specificity of the antibody generated from the anti-MARV dMAb plasmid.

[00442] Furthermore, the anti-MARV neutralizing activity in sera from subjects that received anti-MARV dMAb is measured against that in MARV strains. Sera from anti-MARV dMAb – injected subects effectively neutralize MARV isolates, demonstrating that a single injection can produce significant neutralizing levels of human anti-MARV IgG. Thus, antibodies produced in vivo by anti-MARV dMAb constructs have relevant biological activity (ie, binding and neutralizing activity against MARV).

Anti-MARV dMAb injection protects mice from lethal MARV challenge

[00443] To determine whether antibodies generated from anti-MARV dMAb provide protection against early exposure to MARV, groups of 10 subjects receive of a control or anti-MARV dMAb on day 0. Each group subsequently is challenged subcutaneously with virus to mimic natural MARV infection. Subject survival and weight changes are subsequently recorded. anti-MARV dMAb plasmids confer protective immunity.

[00444] The longevity of immune protection is next evaluated. A second group of subjects was challenged with MARV after injection with anti-MARV dMAb, or control plasmid on day 0. Subjects are monitored for survival. Anti-MARV dMAb provides a more durable degree of immune protection .

[00445] Anti-MARV dMAb protects subjects from both subcutaneous viral challenge and intranasal viral challenge compared with control-injected subjects, demonstrating that anti-MARV dMAbs can protect against systemic and mucosal infection.

[00446] An efficacy study comparing the protective efficacy of anti-MARV dMAb administration vs a MARV-DNA vaccine (MARV-DNA) is next performed. A novel consensus-based DNA vaccine was developed by our laboratory and is capable of providing protection against MARV challenge. The DNA vaccine also induced both measurable cellular immune responses, as well as potent neutralizing antibody responses. Groups of subjects are administered a single injection of anti-MARV dMAb, MARV-DNA, or the pVax1, followed by viral challenge. Anti-MARV dMAb confers protective immunity more rapidly than the MARV-DNA vaccine.

Comparison between *in vivo* protective immunity conferred by anti-MARV dMAb administration and MARV-DNA vaccination

[00447] Next, a long-term MARV challenge protection study was performed following vaccination with the MARV-DNA vaccine or administration of anti-MARV dMAb on day 0. MARV-DNA confers longer protective immunity than anti-MARV dMAb.

Co-delivery of anti-MARV dMAb and the MARV-DNA vaccine produces systemic humoral immunity, cell-mediated immunity, and protection *in vivo*

[00448] One potential issue of combining antibody delivery with vaccination approaches is that the antibodies can neutralize many traditional vaccines and thus are incompatible platforms. The effect of co-administration of anti-MARV dMAb and MARV-DNA on subject survival in the context of MARV challenge was is evaluated. Subjects are administered at day 0 anti-MARV dMAb and MARV-DNA. Subsequently, some animals are challenged with MARV at day 2 and the others at day 35. Survival in these groups is followed as a function of time. Anti-MARV dMAb mediates protection from infection, with the survival percentage decreasing to approximately 30% by 4 days after challenge in control (pVax1) animals. Both IgG finduced by anti-MARV dMAb and MARV-DNA vaccine are detected. Anti-MARV dMAb mediates rapid protection from infection and death after MARV challenge.

[00449] Furthermore, T-cell responses induced in subjects injected with Anti-MARV dMAb, MARV-DNA, or anti-MARV dMAb plus MARV-DNA are evaluated. MARV-DNA elicits strong T-cell responses irrespective of co-delivery with anti-MARV dMAb, showing the lack of interference of these approaches. Conversely, animals administered only anti-MARV dMAb do not develop T-cell responses. Both anti-MARV dMAb and MARV-DNA vaccine can be administered simultaneously without reciprocal interference, providing immediate and long-lived protection via systemic humoral and cellular immunity.

Electroporation-mediated delivery of optimized DNA plasmids for the in vivo rapid production of biologically functional mAbs

[00450] Subjects administered anti-MARV dMAbs are fully protected from viral challenge shortly after administration, whereas subjects do not survive infection following a single

immunization with MARV-DNA vaccine, owing presumably to an insufficient time to mount protective immunity. However, MARV-DNA provides complete protection after an immunization regimen followed by challenge at later time points. A similar level of protection occurs in subjects administered a single dose of anti-MARV dMAbs, although protection wanes over time. Notably, the co-delivery of anti-MARV dMAbs and MARV-DNA produces rapid and persistent humoral and cellular immunity, suggesting that a combination approach can have additive or synergistic effects. Importantly, co-delivery of anti-MARV dMAbs and MARV-DNA are not antagonistic in terms of the development of short- or long-term protective immune responses.

Example 5 - Rapid and long-term immunity elicited by DNA encoded antibody prophylaxis and DNA vaccination against Influenza

[00451] Vaccination is known to exhibit a lag phase before generation of immunity; thus, there is a gap of time during infection before an immune response is in effect. The following provides specific novel approaches that utilize the benefit of vaccines and the native immune response along with a rapid generation of effective immunity using the DNA synthetic antibodies or dMabs.

[00452] An antibody-based prophylaxis/therapy entailing the electroporation mediated delivery of synthetic plasmids, encoding biologically active anti-Influenza virus (Flu) mAb (designated dMAb), is designed and evaluated for anti-viral efficacy as well as for the ability to overcome shortcomings inherent with conventional active vaccination by a novel passive immune-based strategy. One intramuscular injection of the Flu-dMAb produces antibodies in vivo more rapidly than active vaccination with an Flu-DNA vaccine. This dMAb neutralized diverse Flu clinical isolates and protected mice from viral challenge. Combinations of both afford rapid as well as long-lived protection.

[00453] A DNA based dMAb strategy induces rapid protection against an emerging viral infection, which can be combined with DNA vaccination providing a uniquely both short term and long-term protection against this emerging infectious disease. These studies have implications for pathogen treatment and control strategies.

dMAb IgG quantification and binding assays

[00454] ELISA assays are performed with sera from subjects administered an Flu-dMAb to quantify expression kinetics and target antigen binding.

Analysis of dMAb generated IgG

[00455] IgG expression of Flu infected cells are analyzed by western blot. For immunofluorescence analysis Flu infected cells are visually evaluated by confocal microscopy and quantitatively or semi-quantitatively analyzed.

dMAb DNA plasmid administration and *in vivo* analysis

[00456] Expression kinetics and functionality were evaluated in subjects following injection of control or Flu-dMAb. For studies that include the DNA vaccine, the Flu-DNA vaccine plasmid is administered.

Challenge study

[00457] Subjects receive electroporation-enhanced injection of Flu-dMAb or control plasmids. The Flu-DNA vaccine was delivered as described above. After DNA delivery, subjects are challenged with Flu. The animals are monitored for survival and signs of infection. Serum samples are collected for cytokine quantification and other immune analysis. Blood samples are collected from after infection and viremia levels are measured.

Neutralizing Antibody Analysis

[00458] Anti-Flu neutralizing antibody titers from subjects administered Flu-dMAb are determined. Neutralization titers may be calculated as the reciprocal of the highest dilution mediating 100% reduction of the cytopathic effects in the cells.

Cytokine Quantitative Analysis

[00459] Sera is collected from Flu-dMAb, and Flu-DNA vaccine injected subjects as well as Flu challenged subjects. TNF-α, IL-1β and IL-6 sera cytokine levels are measured.

Anti-Flu dMAbs design and confirmation of expression

[00460] The optimized synthetic plasmids constructed from the anti-Flu-neutralizing mAb were designed for the IgG and Fab antibodies. Cells are transfected with either the Flu-IgG plasmid or the Flu-Fab (VL, VH, or combined) plasmids to validate expression in vitro. The Flu-Fab and Flu-IgG expressed antibodies in the muscle that appeared to be properly assembled and biologically functional in vitro.

***In vivo* expression and quantification of anti-Flu dMAb**

[00461] Following confirmation of in vitro expression, the ability of Flu-Fab or Flu-IgG to produce anti-Flu antibodies in vivo is measured. Both constructs generate mAbs. Subjects are administered either Flu-IgG or Flu-Fab, and sera antibody levels are evaluated through a binding ELISA. Sera collected after injection from both Flu-IgG and Flu-Fab bind to Flu protein but not to an unrelated control antigen. These data indicate that in vivo produced anti-Flu antibodies from Flu-IgG or Flu-Fab constructs have similar biological characteristics to conventionally produced antigen specific antibodies.

***In vivo* specificity and broadly neutralizing activity in sera from anti-Flu dMAb injected subjects**

[00462] The anti-Flu dMAb generated mAbs are tested for binding specificity and anti-Flu neutralizing activity. Sera antibodies bind to Flu-infected cells. There is a strong specificity of the antibody generated from the anti-Flu dMAb plasmid.

[00463] Furthermore, the anti-Flu neutralizing activity in sera from subjects that received anti-Flu dMAb is measured against that in Flu strains. Sera from anti-Flu dMAb –injected subects effectively neutralize Flu isolates, demonstrating that a single injection can produce significant neutralizing levels of human anti-Flu IgG. Thus, antibodies produced in vivo by anti-Flu dMAb constructs have relevant biological activity (ie, binding and neutralizing activity against Flu).

Anti-Flu dMAb injection protects mice from lethal Flu challenge

[00464] To determine whether antibodies generated from anti-Flu dMAb provide protection against early exposure to Flu, groups of 10 subjects receive of a control or anti-Flu dMAb on day 0. Each group subsequently is challenged subcutaneously with virus to mimic natural Flu

infection. Subject survival and weight changes are subsequently recorded. anti-Flu dMAb plasmids confer protective immunity.

[00465] The longevity of immune protection is next evaluated. A second group of subjects was challenged with Flu after injection with anti-Flu dMAb, or control plasmid on day 0. Subjects are monitored for survival. Anti-Flu dMAb provides a more durable degree of immune protection .

[00466] Anti-Flu dMAb protects subjects from both subcutaneous viral challenge and intranasal viral challenge compared with control-injected subjects, demonstrating that anti-Flu dMAbs can protect against systemic and mucosal infection.

[00467] An efficacy study comparing the protective efficacy of anti-Flu dMAb administration vs a Flu-DNA vaccine (Flu-DNA) is next performed. A novel consensus-based DNA vaccine was developed by our laboratory and is capable of providing protection against Flu challenge. The DNA vaccine also induced both measurable cellular immune responses, as well as potent neutralizing antibody responses. Groups of subjects are administered a single injection of anti-Flu dMAb, Flu-DNA, or the pVax1, followed by viral challenge. Anti-Flu dMAb confers protective immunity more rapidly than the Flu-DNA vaccine.

Comparison between *in vivo* protective immunity conferred by anti-Flu dMAb administration and Flu-DNA vaccination

[00468] Next, a long-term Flu challenge protection study was performed following vaccination with the Flu-DNA vaccine or administration of anti-Flu dMAb on day 0. Flu-DNA confers longer protective immunity than anti-Flu dMAb.

Co-delivery of anti-Flu dMAb and the Flu-DNA vaccine produces systemic humoral immunity, cell-mediated immunity, and protection *in vivo*

[00469] One potential issue of combining antibody delivery with vaccination approaches is that the antibodies can neutralize many traditional vaccines and thus are incompatible platforms. The effect of co-administration of anti-Flu dMAb and Flu-DNA on subject survival in the context of Flu challenge was is evaluated. Subjects are administered at day 0 anti-Flu dMAb and Flu-DNA. Subsequently, some animals are challenged with Flu at day 2 and the others at day 35. Survival in these groups is followed as a function of time. Anti-Flu dMAb mediates protection from

infection, with the survival percentage decreasing to approximately 30% by 4 days after challenge in control (pVax1) animals. Both IgG finduced by anti-Flu dMAb and Flu-DNA vaccine are detected. Anti-Flu dMAb mediates rapid protection from infection and death after Flu challenge.

[00470] Furthermore, T-cell responses induced in subjects injected with Anti-Flu dMAb, Flu-DNA, or anti-Flu dMAb plus Flu-DNA are evaluated. Flu-DNA elicits strong T-cell responses irrespective of co-delivery with anti-Flu dMAb, showing the lack of interference of these approaches. Conversely, animals administered only anti-Flu dMAb do not develop T-cell responses. Both anti-Flu dMAb and Flu-DNA vaccine can be administered simultaneously without reciprocal interference, providing immediate and long-lived protection via systemic humoral and cellular immunity.

Electroporation-mediated delivery of optimized DNA plasmids for the in vivo rapid production of biologically functional mAbs

[00471] Subjects administered anti-Flu dMAbs are fully protected from viral challenge shortly after administration, whereas subjects do not survive infection following a single immunization with Flu-DNA vaccine, owing presumably to an insufficient time to mount protective immunity. However, Flu-DNA provides complete protection after an immunization regimen followed by challenge at later time points. A similar level of protection occurs in subjects administered a single dose of anti-Flu dMAbs, although protection wanes over time. Notably, the co-delivery of anti-Flu dMAbs and Flu-DNA produces rapid and persistent humoral and cellular immunity, suggesting that a combination approach can have additive or synergistic effects. Importantly, co-delivery of anti-Flu dMAbs and Flu-DNA are not antagonistic in terms of the development of short- or long-term protective immune responses.

Example 5 - Functional anti-Zika "DNA monoclonal antibodies" (DMAb)

[00472] The studies presented herein demonstrate the generation of functional anti-Zika "DNA monoclonal antibodies" (DMAb) via intramuscular electroporation of plasmid DNA. Codon-optimized variable region DNA sequences from anti-Zika monoclonal antibodies were synthesized onto a human IgG1 constant domain. Plasmid DNA encoding antibody was

delivered to C3H mice mice. This study supports DMAb as an alternative to existing biologic therapies.

[00473] The ZIKV-Env (ZIKV-E) protein is a 505 amino acid protein having a fusion loop (Figure 9). The antibodies aginst the ZIKV-E protein are expressed in vivo through DNA monoclonal antibodies (dMABs) which express a heavy and light chain (Figure 10). ZIKV-Env specific monoclonal antibodies, 1C2A6, 1D4G7, 2B7D7, 3F12E9, 4D6E8, 5E6D9, 6F9D1, 9D10F4, 8A9F9, and 9F7E1, each bind ZIKV-Env in vitro (Figure 11 and Figure 12). The monoclonal antibodies show varying degress of sequence homology among both the V_H and V_L chains (Figures 13-15). The large VH CDR3 of 1D4G7 is clearly visible, as are several other fold differences in other CDR and in framework regions. Despite the sequence divergence of 3F12E9, it is still closer in overall sequence and conformation to 1C2A6, 8D10F4 and 8A9F9 than to 1D4G7. (Figure 15). 1D4G7 lacks a cleft between the VH and VL domains due to its large CDR3 loop. Sequence similarities translate to structural similarities, so overall CDR conformations and molecular shapes are conserved according to previously demonstrated clustering. (Figure 16). 1C2A6 has a free CYS residue distal to the CDRs exposed on the surface Another potentially relevant difference occurs in VH FR2 region. This residue is not directly involved in CDR conformation but does influence local residue packing. Two changes occur within the IMGT-defined CDR regions . The VL changes (F, F, S) directly impact the VL-VH interface. (Figure 17). A free CYS leaves a highly modifiable chemical group exposed on the molecule surface. (Figure 18). Developability index is highest for 1D4G7, very likely due to the long CDR3 loop which contains multiple nonpolar residues. Based on past experience, though, this alone does not appear to be an issue (Figure 19). Based on the high degrees of similarity, 1C2A6, 8D10F4 and 8A9F9 are likely to bind the same epitope in the same basic mode. Small differences between the three sequences include an exposed free CYS residue on 1C2A6 and a reduced number of predicted pi interactions at the VH-VL interface of 8D10F4. 3F12E9 has similarity to 1C2A6, 8D10F4 and 8A9F9 in the CDR regions, but also several important differences. mAb 1D4G7 is likely to bind in a different mode or to a completely different epitope than the other mAbs mentioned above.

Example 6 - In vivo protection against ZIKV infection and pathogenesis through passive antibody transfer and active immunization with a prMEnv DNA vaccine

[00474] In this study, novel, synthetic, DNA vaccine targeting the pre-membrane+envelope proteins (prMEnv) of ZIKV generated and evaluated for in vivo efficacy. Following initial in vitro development and evaluation studies of the plasmid construct, mice and non-human primates were immunized with this prMEnv DNA-based immunogen through electroporation-mediated enhanced DNA delivery. Vaccinated animals were found to generate antigen-specific cellular and humoral immunity and neutralization activity. In mice lacking receptors for interferon (IFN)-α/β (designated IFNAR$^{-/-}$) immunization with this DNA vaccine induced, following in vivo viral challenge, 100% protection against infection-associated weight loss or death in addition to preventing viral pathology in brain tissue. In addition, passive transfer of non-human primate anti-ZIKV immune serum protected IFNAR$^{-/-}$ mice against subsequent viral challenge. This initial study of this ZIKV vaccine in a pathogenic mouse model supports the importance of immune responses targeting prME in ZIKV infection and suggests that additional research on this vaccine approach may have relevance for ZIKV control in humans.

Cells, virus and animals

[00475] Human embryonic kidney 293T (American Type Culture Collection (ATCC) #CRL-N268, Manassas, VA, USA) and Vero CCL-81 (ATCC #CCL-81) cells were maintained in DMEM (Dulbecco's modified Eagle's medium; Gibco- Q3 Invitrogen) supplemented with 10% fetal bovine serum (FBS) and 1% penicillin and streptomycin and passaged upon confluence. Both ZIKV virus strains MR766 (a kind gift from Dr Susan Weiss) and PR209 (Bioqual, MD) were amplified in Vero cells and stocks were titred by standard plaque assay on Vero cells. Five- to six-week-old female C57BL/6 (The Jackson Laboratory) and IFNAR$^{-/-}$ (MMRRC repository-The Jackson Laboratory) mice were housed and treated/vaccinated in a temperature-controlled, light-cycled facility in accordance with the National Institutes of Health, Wistar and the Public Health Agency of Canada IACUC (Institutional Animal Care and Use Committee) guidelines.

[00476] The RMs were housed and treated/vaccinated at Bioqual, MD, USA. This study was carried out in strict accordance with the recommendations described in the Guide for the Care and Use of Laboratory Animals of the NIH, the Office of Animal Welfare, and the U.S.

Department of Agriculture. All animal immunization work was approved by the Bioqual Animal Care and Use Committee (IACUC). Bioqual is accredited by the American Association for Accreditation of Laboratory Animal Care. All the procedures were carried out under ketamine anesthesia by trained personnel under the supervision of veterinary staff, and all the efforts were made to protect the welfare of the animals and to minimize animal suffering in accordance with the 'Weatherall report for the use of non-human primates' recommendations. The animals were housed in adjoining individual primate cages allowing social interactions, under controlled conditions of humidity, temperature and light (12 h light/12 h dark cycles). Food and water were available ad libitum. The animals were monitored twice daily and fed commercial monkey chow, treats and fruits twice daily by trained personnel.

Construction of ZIKV-prME DNA vaccine

[00477] The ZIKV-prME plasmid DNA constructs encodes full-length precursor of membrane (prM) plus envelope (E) and Capsid proteins were synthesized. A consensus strategy was used and the consensus sequences were determined by the alignment of current ZIKV prME protein sequences. The vaccine insert was genetically optimized (i.e., codon and RNA optimization) for enhanced expression in humans and an IgE leader sequence was added to facilitate expression. The construct was synthesized commercially (Genscript, NJ, USA), and then subcloned into a modified pVax1 expression vector under the control of the cytomegalovirus immediate-early promoter as described before (Muthumani et al., 2016, Sci Transl Med 7:301ra132). The final construct is named ZIKV-prME vaccine and the control plasmid backbone is pVax1. In addition, a number of other matched DNA constructs encoding the prM and E genes from MR766 (DQ859059.1) and a 2016 Brazilin (AMA12084.1) outbreak strain were also designed, for further evaluation. Large-scale amplifications of DNA constructs were carried out by Inovio Pharmaceuticals Inc. (Plymouth Meeting, PA, USA) and purified plasmid DNA was formulated in water for immunizations. The size of the DNA inserts was confirmed via agarose gel electrophoresis. Phylogenetic analysis was performed by multiple alignment with ClustalW using MEGA version 5 software (Muthumani et al., 2016, Sci Transl Med 7:301ra132).

[00478] DNA immunizations and electroporation-mediated delivery enhancement

[00479] Female C57BL/6 mice (6–8 weeks old) and IFNAR$^{-/-}$ mice (5–6 weeks old) were immunized with 25 μg of DNA in a total volume of 20 or 30 μl of water delivered into the tibialis anterior muscle with in vivo electroporation delivery. In vivo electroporation was delivered with the CELLECTRA adaptive constant current electroporation device (Inovio Pharmaceuticals) at the same site immediately following DNA injection. A three-pronged CELLECTRA minimally invasive device was inserted ~ 2 mm into the muscle. Square-wave pulses were delivered through a triangular three-electrode array consisting of 26-gauge solid stainless steel electrodes and two constant current pulses of 0.1 Amps were delivered for 52 μs/pulse separated by a 1 s delay. Further protocols for the use of electroporation have been previously described in detail (Flingai et al., 2015, Sci Rep 5:12616). The mice were immunized three times at 2-week intervals and killed 1 week after the final immunization. The blood was collected after each immunization for the analysis of cellular and humoral immune responses (Muthumani et al., 2016, Sci Transl Med 7:301ra132). Rhesus macaque immunogenicity studies: five rhesus macaques were immunized intradermally at two sites two times at 5-week intervals with 2 mg ZIKV-prME vaccine. Electroporation was delivered immediately using the same device described for mouse immunizations.

Western blot analysis

[00480] For in vitro expression studies, transfections were performed using the GeneJammer reagent, following the manufacturer's protocols (Agilent). Briefly, the cells were grown to 50% confluence in a 35 mm dish and transfected with 1 μg of ZIKV-prME vaccine. The cells were collected 2 days after transfection, washed twice with PBS and lysed with cell lysis buffer (Cell Signaling Technology). Western Blot was used to verify the expression of the ZIKV-prME protein from the harvested cell lysate and the immune specificity of the mouse and RM serum through the use of either anti- Flavivirus or immune sera from the ZIKV-prME vaccinated mice, as described previously (Muthumani et al., 2016, Sci Transl Med 7:301ra132). In brief, 3–12% Bis-Tris NuPAGE gels (Life Technologies) were loaded with 5 μg or 1 μg of ZIKV envelope recombinant protein (rZIKV-E); transfected cell lysates or supernatant and the Odyssey protein Molecular Weight Marker (Product # 928-40000). The gels were run at 200 V for 50 min in MOPS buffer. The proteins were transferred onto nitrocellulose membranes using the iBlot 2 Gel Transfer Device (Life Technologies). The membranes were blocked in PBS Odyssey blocking

buffer (LI-COR Biosciences) for 1 h at room temperature. To detect vaccine expression, the anti-Flavivirus group antigen (MAB10216-Clone D1-4G2-4-15) antibody was diluted 1:500 and the immune serum from mice and RM was diluted 1:50 in Odyssey blocking buffer with 0.2% Tween 20 (Bio-Rad) and incubated with the membranes overnight at 4 °C. The membranes were washed with PBST and then incubated with the appropriate secondary antibody (goat anti-mouse IRDye680CW; LI-COR Biosciences) for mouse serum and flavivirus antibody; and goat anti-human IRDye800CW (LI-COR Biosciences) for RM sera at 1:15,000 dilution for mouse sera for 1 h at room temperature. After washing, the membranes were imaged on the Odyssey infrared imager (LI-COR Biosciences).

Immunofluorescence assays

[00481] For the immunofluorescence assay, the cells were grown on coverslips and transfected with 5 μg of ZIKV-prME vaccine. Two days after transfection, the cells were fixed with 4% paraformaldehyde for 15 min. Nonspecific binding was then blocked with normal goat serum diluted in PBS at room temperature for 1 h. The slides were then washed in PBS for 5 min and subsequently incubated with sera from immunized mice or RM at a 1:100 dilutions overnight at 4 °C. The slides were washed as described above and incubated with appropriate secondary antibody (goat anti-mouse IgGAF488; for mouse serum and goat anti-human IgG-AF488 for RM serum; Sigma) at 1:200 dilutions at room temperature for 1 h. After washing, Flouroshield mounting media with DAPI (Abcam) was added to stain the nuclei of all cells. After which, coverslips were mounted and the slides were observed under a microscope (EVOS Cell Imaging Systems; Life Technologies) (Muthumani et al., 2016, Sci Transl Med 7:301ra132). In addition, Vero, SK-N-SH or U87-MB cells were grown on four-chamber tissue culture treated glass slides and infected at MOI of 0.01 with ZIKV-MR766 or PR209 that were preincubated with/without RM immune sera (1:200), and stained at 4 days post ZIKV infection using pan flavirus antibody as described (Rossi et al., 2016, J Rop Med Hyg 94:1362-9).

Histopathology analysis

[00482] For histopathology, formalin-fixed, paraffin-embedded brain tissue was sectioned into 5 μm thick sagittal sections, placed on Superfrost microscope slides (Fisher Scientific) and backed at 37 °C overnight. The sections were deparaffinised using two changes of xylene and

rehydrated by immersing in 100%, 90% and then 70% ethanol. The sections were stained for nuclear structures using Harris haematoxylin (Surgipath) for 2 min followed by differentiation in 1% acid alcohol (Surgipath) and treatment with Scott's tap water for 2 min. Subsequently, the sections were counterstained for cytoplasmic structures using eosin (Surgipath) for 2 min. The slides were dehydrated with 70%, 90% and 100% ethanol, cleared in xylene and mounted using Permount (Fisher Scientific).

Splenocyte and PBMC isolation

[00483] Single-cell suspensions of splenocytes were prepared from all the mice. Briefly, the spleens from mice were collected individually in 5 ml of RPMI 1640 supplemented with 10% FBS (R10), then processed with a Stomacher 80 paddle blender (A.J. Seward and Co. Ltd.) for 30 s on high speed. The processed spleen samples were filtered through 45 mm nylon filters and then centrifuged at 1,500g for 10 min at 4 °C. The cell pellets were resuspended in 5 ml of ACK (ammonium–chloride–potassium) lysis buffer (Life Technologies) for 5 min at room temperature, and PBS was then added to stop the reaction. The samples were again centrifuged at 1,500g for 10 min at 4 °C. The cell pellets were resuspended in R10 and then passed through a 45 mm nylon filter before use in ELISpot assay and flow cytometric analysis (Muthumani et al., 2016, Sci Transl Med 7:301ra132). For RM, blood (20 ml at each time point) was collected in EDTA tubes and the PBMCs were isolated using a standard Ficoll-hypaque procedure with Accuspin tubes (Sigma-Aldrich, St. Louis, MO, USA). Five millitres of blood was also collected into sera tubes at each time point for sera isolation.

Flow cytometry and intracellular cytokine staining assay

[00484] The splenocytes were added to a 96-well plate (2×10^6/well) and were stimulated with ZIKV-prME pooled peptides for 5 h at 37 °C/5% CO2 in the presence of Protein Transport Inhibitor Cocktail (brefeldin A and monensin; eBioscience). The cell stimulation cocktail (plus protein transport inhibitors; PMA (phorbol 12-myristate 13-acetate), ionomycin, brefeldin A and monensin; eBioscience) was used as a positive control and R10 media as the negative control. All the cells were then stained for surface and intracellular proteins as described by the manufacturer's instructions (BD Biosciences, San Diego, CA, USA). Briefly, the cells were washed in FACS buffer (PBS containing 0.1% sodium azide and 1% FBS) before surface

staining with flourochrome-conjugated antibodies. The cells were washed with FACS buffer, fixed and permeabilised using the BD Cytofix/Ctyoperm TM (BD Biosciences) according to the manufacturer's protocol followed by intracellular staining. The following antibodies were used for surface staining: LIVE/DEAD Fixable Violet Dead Cell stain kit (Invitrogen), CD19 (V450; clone 1D3; BD Biosciences) CD4 (FITC; clone RM4-5; eBioscience), CD8 (APC-Cy7; clone 53-6.7; BD Biosciences); CD44 (BV711; clone IM7; BioLegend). For intracellular staining, the following antibodies were used: IFN-γ (APC; clone XMG1.2; BioLegend), TNF-α (PE; clone MP6-XT22; eBioscience), CD3 (PerCP/Cy5.5; clone 145-2C11; BioLegend); IL-2 (PeCy7; clone JES6-SH4; eBioscience). All the data were collected using a LSRII flow cytometer (BD Biosciences) and analyzed using FlowJo software (Tree Star, Ashland, OR, USA).

ELISpot assay

[00485] Briefly, 96-well ELISpot plates (Millipore) were coated with anti-mouse IFN- γ capture Ab (R&D Systems) and incubated overnight at 4 °C. The following day, the plates were washed with PBS and blocked for 2 h with PBST+1% BSA. Two hundred thousand splenocytes from immunized mice were added to each well and incubated overnight at 37 °C in 5% CO_2 in the presence of media alone (negative control), media with PMA/ionomycin (positive control) or media with peptide pools (1 μg/ml) consisting of 15-mers overlapping by nine amino acids and spanning the length of the ZIKV prME protein (Genscript). After 24 h, the cells were washed and then incubated overnight at 4 °C with biotinylated anti-mouse IFN-γ Ab (R&D Systems). Streptavidin–alkaline phosphatase (R&D Systems) was added to each well after washing and then incubated for 2 h at room temperature. The plate was washed, and then 5-bromo-4-chloro-3′-indolylphosphate p-toluidine salt and nitro blue tetrazolium chloride (chromogen colour reagent; R&D Systems) was added. Last, the plates were rinsed with distilled water, dried at room temperature and SFU were quantified by an automated ELISpot reader (CTL Limited), and the raw values were normalised to SFU per million splenocytes. For RM samples, the ELISPOT^{PRO} for monkey IFN-γ kit (MABTECH) was used as described by the manufacturer; two hundred thousand PBMCs were stimulated with peptide pools; and the plates were washed and spots were developed and counted as described before (Muthumani et al., 2016, Sci Transl Med 7:301ra132).

Humoral immune response: antibody-binding ELISA

[00486] An ELISA was used to determine the titers of mouse and RM sera as previously described (Muthumani et al., 2016, Sci Transl Med 7:301ra132). Briefly, 1 μg of purified rZIKV-E protein was used to coat 96-well microtiter plates (Nalgene Nunc International, Naperville, IL, USA) at 4 °C overnight. After blocking with 10% FBS in PBS for at least an hour, the plates were washed four times with 0.05% PBST (Tween20 in PBS). Serum samples from immunized mice and RMs were serially diluted in 1% FBS, added to the plates, then incubated for 1 h at room temperature. The plates were again washed four times in 0.05% PBST, then incubated with HRP-conjugated anti-mouse IgG (Sigma) at a 1:35,000 dilution for mouse sera for 1 h at room temperature. For RM sera, anti-monkey IgG HRP (Southern Biotech) was used at a 1:5,000 dilutions for 1 h at room temperature. The bound enzyme was detected by adding SIGMAFAST OPD (o-phenylenediamine dihydrochloride) substrate solution according to the manufacturer's instructions (Sigma-Aldrich). The reaction was stopped after 15 min with the addition of 1 N H_2SO_4. The optical density at 450 nm was read on a Synergy plate reader. All the mouse and RM serum samples were assayed in duplicate. End point titers were determined using the method described previously (Frey et al., 1998, J Immunol Methods 21:35-41).

Neutralization ($PRNT_{50}$) assay

[00487] The PRNT involving MR766 and Vero cells was described previously (Sun et al., 2006, J Infect Dis 193:1658-65). Briefly, heat-inactivated mouse or RM sera were serially diluted in serum-free DMEM (1:10 to 1: 1280) and incubated with an equal volume of ZIKV MR766 (100 PFU) at 37 °C for 2 h. The mixtures were added to the confluent layers of Vero cells and left at 37 °C for adsorption for 2 h. A 2 × DMEM media:soft-agar (1:1) overlay was added over cells and the plate was incubated for 5 days at 37 °C. The agar overlay was removed and the cells were fixed with 4% paraformaldehyde, washed with 1 × PBS, stained with crystal violet solution, washed with 1 × PBS and the plates were left to dry. The plaques in assays done in 24-well plates were scanned with an automated Immunospot reader (CTL Limited), and the plaques in sample wells and in negative control (DMEM only) and positive control (100 PFU MR766 ZIKV virus only) wells were counted using the automated software provided with the ELISpot reader. The percentage plaque reduction was calculated as follows: % reduction = 100 × {1 − (average number of plaques for each dilution/average number of plaques in positive control

wells)}. GraphPad Prism software was used to perform nonlinear regression analysis of % plaque reduction versus a log transformation of each individual serum dilution to facilitate linear interpolation of actual 50% PRNT titers at peak post vaccination response. The medians and interquartile ranges at 50% neutralization were calculated for each neutralization target overall and by vaccine treatment group; the geometric mean titers were also calculated. The titers represent the reciprocal of the highest dilution resulting in a 50% reduction in the number of plaques.

ZIKV challenge studies in IFNAR$^{-/-}$ mice

[00488] For the ZIKA challenge studies, IFNAR$^{-/-}$ mice (n = 10/group) were immunized once or twice with the ZIKA-prME vaccine or pVax1. The mice were with either 1 × 10^6 PFU or 2 × 10^6 PFU ZIKV-PR209 virus on day 15 (single immunization group) or day 21 one week after the second immunization (two immunization groups). Also, additional groups of IFNAR$^{-/-}$mice (n = 10/group) were immunized once and challenged with 2×10^6 PFU ZIKV-PR209 virus on day 15. Post challenge, the animals were weighed and body temperature was measured daily by a subcutaneously located temperature chip. In addition, they were observed for clinical signs of disease twice daily (decreased mobility; hunched posture; hind-limb knuckle walking (partial paralysis), paralysis of one hind limb or both hind limbs) and the blood was drawn for viral load determination. The criteria for killing on welfare grounds consisted of 20% weight loss or paralysis in one or both hind limbs.

Real-time RT-PCR assay for measurement of ZIKV load

[00489] The brains from treated mice were immersed in RNAlater (Ambion) 4 °C for 1 week, then stored at − 80 °C. The brain tissue was then weighed and homogenized in 600 µl RLT buffer in a 2 ml cryovial using a TissueLyser (Qiagen) with a stainless steel bead for 6 min at 30 cycles/s. Viral RNA was also isolated from blood with the RNeasy Plus mini kit (Qiagen). A ZIKV specific real-time RT-PCR assay was utilized for the detection of viral RNA from subject animals. RNA was reverse transcribed and amplified using the primers ZIKV 835 and ZIKV 911c and probe ZIKV 860FAM with the TaqMan Fast Virus 1-Step Master Mix (Applied Biosystems). A standard curve was generated in parallel for each plate and used for the quantification of viral genome copy numbers. The StepOnePlus Real-Time PCR System (ABI)

software version 2.3 was used to calculate the cycle threshold (Ct) values, and a Ct value ⩽38 for at least one of the replicates was considered positive, as previously described (Lanciotti et al., 2008, Emerg Infect Dis 14:1232-9). Pre-bleeds were negative in this assay.

Statistical analysis

[00490] Differences in fold increases in antibody titers were compared using Mann– Whitney analysis. Statistical analysis was performed using Graphpad, Prism 4 (Graphpad software, Inc. San Diego, CA, USA). For all the analyses, $P<0.05$ was considered to be significant. Log_{10} transformations were applied to end point binding ELISA titers and whole-virus $PRNT_{50}$ titers.

Construction of the ZIKV-prME consensus DNA vaccine

[00491] A consensus sequence of ZIKV prM (precursor membrane) and Env (envelope) genes (ZIKV-prME) was generated using prM and Env sequences from various ZIKV isolated between the years of 1952 and 2015, which caused infection in humans. The ZIKV-prME consensus sequence was cloned into the pVax1 vector after additional modifications and optimizations were made to improve its in vivo expression including the addition of a highly efficient immunoglobulin E (IgE) leader peptide sequence (Figure 20A). Optimal alignment of ZIKV-envelope sequences was performed using homology models and visualization on Discovery Studio 4.5. Reference models included PDB 5JHM and PDB 5IZ7. Aligned residues corresponding to specific regions on the prME antigen were labelled in the models for visualization purposes (Figure 20B). The optimized consensus vaccine selections are in general conservative or semi-conservative relative to multiple ZIKV strains analyzed in this study. Structural studies of EDE-specific neutralizing antibodies have revealed that these recognition determinants can be found at a serotype-invariant site at the envelope–dimer interface, which includes the exposed main chain of the fusion loop and two conserved glycan chains (N67- and N153-linked glycans) (Rouvinski et al., 2015, Nature 520:109-13). These two glycosylation sites are not highly conserved in other flaviviruses. Moreover, ZIKV does not possess the N67-linked glycosylation site, and the N154-linked glycosylation site (equivalent to the N153-linked glycosylation site in dengue) is absent in some of the isolated ZIKV strains. As part of the consensus design, therefore the construct was designed leaving out this glycosylation site. Lack of glycosylation at this site has been correlated with improved binding of EDE1 type broadly

neutralizing antibodies (bnAbs) to ZIKV-envelope protein (Rouvinski et al., 2015, Nature 520:109-13).

[00492] Subsequent to construction, expression of the ZIKV-prME protein from the plasmid was confirmed by western blot analysis and an indirect immunofluorescence assay. The protein extracts prepared from the cells transiently transfected with ZIKV-prME were analyzed for expression by western blot using panflavivirus antibody (Figure 20C) and sera collected from ZIKV-prME immunized mice (Figure 20D). ZIKV-prME expression was further detected by IFA by the staining of 293T cells transfected with ZIKV-prME plasmid at 48 h post transfection with anti-ZIKV-prME specific antibodies (Figure 20E).

[00493] ZIKV-prMEnv DNA vaccine induces antigen-specific T cells in C57BL/6 mice

[00494] The ability of the ZIKV-prMEnv plasmid vaccine to induce cellular immune responses was evaluated. Groups of four female C57BL/6 mice were immunized with either the control plasmid backbone (pVax1) or the ZIKV-prME plasmid vaccine three times at 2 week intervals through intramuscular (i.m.) injection followed by electroporation at the site of delivery (Figure 21A). The animals were killed 1 week after their third injection and bulk splenocytes harvested from each animal were evaluated in ELISpot assays for their ability to secrete interferon-γ (IFN-γ) after ex vivo exposure to peptide pools encompassing ZIKV-prME is included. The assay results show that splenocytes from ZIKV-prME immunized mice produced a cellular immune response after stimulation with multiple ZIKV-E peptide pools (Figure 21B). The region(s) of ZIKVEnv, which elicited the strongest cellular response(s) were evaluated by ELISpot assay in a matrix format using 22 peptide pools consisting of 15-mers (overlapping by 11 amino acids) spanning the entire ZIKV-prME protein. Several pools demonstrated elevated T cell responses, with peptide pool 15 exhibiting the highest number of spot-forming units (SFU) (Figure 21C). This matrix mapping analysis revealed a dominant prME epitope, 'IRCIGVSNRDFVEGM (SEQ ID NO:17)' (aa167-181). This peptide was confirmed to contain a H2-Db restricted epitope through analysis utilising the Immune Epitope Database Analysis Resource tool, which supports that in this haplotype the antigen is effectively processed.

[00495] Further evaluation of the cellular immunogenicity of the ZIKV-prMEnv vaccine entailed the determination of the polyfunctional properties of $CD8^+$ T cells collected 1 week after the final immunization. The results show that the ZIKV-prMEnv vaccination increased the

proportion of bifunctional vaccine-specific T cells expressing TNF-α (tumour necrosis factor-α) and IFN-γ. Importantly, ZIKV-prMEnv vaccination exhibited a strong ability to expand T cell functionality (Figure 21D).

[00496] In addition, comparative immune studies were performed with optimized plasmids encoding the prMEnv sequence of either a recently identified Brazilian ZIKV strain or of the original MR766 ZIKV strain. Induction of cellular immune responses in mice immunized with either plasmid was measured 1 week after the third vaccination through IFN-γ ELISpot analysis after stimulating splenocytes with the ZIKV-prMEnv peptide pools. The results illustrate that the T-cell responses induced by the consensus ZIKVprME DNA vaccine construct were consistently higher than those generated by either of these two non-consensus plasmid vaccines (Figures 27A and 27B). Detailed mapping analysis of the cellular responses induced by either the Brazilian or MR766 prME vaccines revealed that both vaccines induced significant cellular response against the dominant Env-specific CTL epitope as identified in Figure 21B and Figure 21C for the consensus ZIKV-prMEnv plasmid (data not shown). The consensus immunogen consistently induced more robust responses in these T-cell assays at the same dose and was evaluated further in additional assays.

Generation of a ZIKV recombinant envelope protein

[00497] At the onset of these studies, there were no available commercial reagents to evaluate specific anti-ZIKV immune responses. Therefore, by necessity, recombinant ZIKV-envelope protein (rZIKV-E) was generated to support the assays performed in this study. To generate this reagent, a consensus ZIKV-Envelope sequence based on the ZIKV-prME vaccine consensus antigen was cloned into a pET30a Escherichia coli expression vector (Figure 28A). The rZIKV-E antigen was produced in E. coli cultures, purified using nickel column chromatography and analyzed using SDS-PAGE, which showed overexpressed proteins of the predicted size in lysate from rZIKV-E transfected bacteria that could be detected by western analysis using an anti-His tag antibody (Figure 28B). The sera from mice immunized with the ZIKV-prME vaccine bound to rZIKV-Env that was used as a capture antigen in an ELISA (enzyme-linked immunosorbent assay; Figure 28C). A commercial antibody (designated panflavivirus) that reacts to the envelope protein of multiple flaviviruses, also bound to rZIKV-E. Western analysis demonstrated that immune sera from ZIKV-prMEnv immunized mice specifically recognized rZIKV-E (Figure

28D). These data indicate that the generated rZIKV-E reacted specifically with immune sera from ZIKV-prMEnv vaccinated mice, thus this recombinant protein was used for further immunogenicity studies.

Induction of functional humoral responses in C57BL/6 mice by the ZIKV-prME DNA vaccine

[00498] The ability of the consensus ZIKV-prMEnv vaccine to induce humoral immune responses in mice was evaluated. Groups of four C57BL/6 mice were immunized intramuscularly (i.m.) through electroporation-mediated delivery three times at 2-week intervals with 25 μg of either the empty control pVax1 or the consensus ZIKV-prMEnv vaccine plasmids. The sera were obtained from each immunized mouse and were tested by ELISA for ZIKV-specific IgG responses using immobilized rZIKV-E as the capture antigen. A significant increase in anti-ZIKV-specific IgG was observed on day 21 with a further boost in the sera IgG levels noted on day 35 (Figure 22A). Day 60 sera from vaccinated animals show that elevated ZIKV-specific antibody responses were maintained long term following the final boost. Most importantly, the sera from vaccinated mice contained very high levels of rZIKV-E-specific antibodies as indicated by the end point titers (Figure 22B). Additional assessment of the specificity of the vaccine-induced antibodies was performed by screening pooled sera from ZIKVprMEnv plasmid inoculated mice for its ability to detect rZIKV-E (envelope) by western analysis (Figure 22C) and to stain ZIKV (MR766 strain)-infected cells by an immunofluorescence assay (Figure 22D). The results from both these analyses confirmed specificity of the vaccine-induced humoral responses.

[00499] Furthermore, ZIKV-specific binding antibody responses were also assessed in mice immunized with plasmids encoding the prMEnv sequences from a Brazilian strain and the MR766 strain described above. Day 35 (1 week after third immunization) sera from pVax1- and both non-consensus vaccine-immunized mice were analyzed by ELISA for binding to rZIKV-E. This analysis indicates that both MR766 and Brazil vaccine plasmids induced significant antibody binding, and that immunization with the consensus ZIKV-prME DNA vaccine generates an effective humoral response against rZIKV-E (Figure 27C and Figure 27D).

[00500] A plaque reduction neutralization test (PRNT) assay was performed on pooled day 35 sera from mice immunized (3 ×) with either the control pVax1 plasmid, the consensus ZIKV-

prMEnv plasmid vaccine or a consensus ZIKV-C (capsid) plasmid vaccine. The PRNT assay used was a method adapted from a previously described technique for analyzing dengue virus, West Nile virus and other flaviviruses (Davis et al., 2001, J Virol 75:4040-7). As shown in Figure 22E, ZIKV-prME vaccination yielded significant neutralization response with anti- ZIKV reciprocal $PRNT_{50}$ dilution titers (inverse of the serum dilution at which 50% of the control ZIKV infection was inhibited) of 456 ± 5, whereas mice vaccinated with the ZIKV-Cap DNA vaccine demonstrated titers (33 ± 6) that were only minimally over pVax1 control plasmid vaccinated animals (titre = 15 ± 2).

Immune responses and protection against ZIKV in mice lacking the type I interferon receptor ($IFNAR^{-/-}$) following immunization with the ZIKV-prME DNA vaccine

[00501] Mechanisms of ZIKV-induced disease and immunity are poorly defined, and the protective versus the hypothetical pathogenic nature of the immune response to ZIKV infection is as yet unclear (Rossi et al., 2016, J Rop Med Hyg 94:1362-9). Most strains of mice are resistant to ZIKV infection, however, mice lacking IFN-α/β receptor ($IFNAR^{-/-}$) were found to be susceptible to infection and disease with most succumbing within 6–7 days post challenge (Lazear et al., 2016, Cell Host Microbe 19:720-30). The ability of the consensus ZIKV-prME plasmid vaccine to induce cellular and humoral immune responses in this mouse strain was investigated. Five to six week old female $IFNAR^{-/-}$ mice (n = 4) were immunized i.m., with electroporation-mediated delivery, three times at 2-week intervals with either the control pVax1 plasmid or ZIKV prME vaccine plasmid vaccine. The serum was collected from immunized mice at days 0, 14, 21, and 35, and splenocytes were harvested from mice 1 week following the final immunization (day 35). The splenocytes from vaccine-immunized mice produced a clear cellular immune response as indicated by levels of SFU per 10^6 cells in an ELISpot assay (Figure 29A). The results from ELISA analysis, using rZIKV-E as a capture antigen, show detectable anti-ZIKV serum IgG by day 14 (titers of ~ 1:1,000) and these levels were boosted with subsequent vaccinations with binding antibody titers reaching at least 1:100,000 (Figures 29B and 29C). By comparison, the $PRNT_{50}$ titer for the day 35 postimmunization samples was 1:60. The results indicate that $IFNAR^{-/-}$ mice immunized with the consensus ZIKV-prMEnv vaccine are capable of generating anti- ZIKV cellular and humoral immune responses supporting further study in this model of putative vaccine effects in a pathogenic challenge.

ZIKV-specific functional cellular and humoral responses elicited by the ZIKV-prMEnv DNA vaccine in non-human primates

[00502] NHPs were immunized by intradermal immunization using intradermal electroporation, based on recent studies showing potent immune responses in a lower voltage intradermal format (Hutnick et al., 2012, Hum gene Ther 23:943-50; Broderick et al., Mol Ther Nucleic Acids 1:e11). Rhesus macaques (RM; n = 5/group) were administered 2.0 mg of vaccine plasmid intradermally with electroporation, with each animal vaccinated twice 4 weeks apart. The sera and peripheral blood mononuclear cells (PBMCs) were collected at day 0 (pre-immunization) and week 6 (2 weeks post second immunization). ELISpot analysis of pre-immunization and week 6 PBMCs ex vivo stimulated with the ZIKV-prMEnv peptide pools showed that ZIKV-prMEnv immunization induced robust anti-ZIKV T cell responses in RM (Figure 23A).

[00503] Specific anti-ZIKV antibody responses in sera from vaccinated RM were assessed by ELISA. At week 6, rZIKV-Env-specific binding antibodies were detectable in animals vaccinated with ZIKV-prMEnv (Figure 23B). End point titers were determined for each animal at week 2 (after 1 immunization) and week 6 (after 2 immunizations; Figure 23C). The ELISA results were confirmed by western blot analysis using RM sera from the individual vaccinated animals (Figure 23D). The neutralization activity of the antibodies generated in RM at week 6 was evaluated by a $PRNT_{50}$ assay. All the vaccinated monkeys had significant neutralization activity with anti-ZIKV reciprocal $PRNT_{50}$ dilution titers ranging from 161 to 1380 (average 501 ± 224 standard error of the mean; Figure 23E). PRNT titers did not directly correlate with ELISA titer (data not shown).

[00504] The ability of the NHP vaccine immune sera to block ZIKV infection of Vero cells, neuroblastoma (SK-N-SH) or neural progenitor (U-87MG) cells in vitro was examined by IFA. ZIKV Q2 strains (MR766 or PR209) were pre-incubated in sera or dilution of NHP-immune sera and added to monolayers of each cell type. Four days post infection, ZIKV-positive cells were identified by IFA using pan flavirus antibody (Figures 30A–30C) and quantified the ZIKV-positive cells (Figures 30B–30D). The sera from ZIKA-prME vaccinated RM inhibited the ZIKV infection in each cell type.

Protection against ZIKV infection and disease in IFNAR$^{-/-}$ mice following ZIKV-prME immunization

[00505] In exploratory studies, 5–6-week-old IFNAR$^{(-/-)}$ mice (n = 10) were challenged with 1 $\times 10^6$ plaque-forming units (PFU) of the ZIKV-PR209 isolate, administered by either subcutaneous (s.c.); intraperitoneal (i.p.); intracranial; or intravenous (i.v.) routes. After the challenge, all the animals were monitored for clinical signs of infection, which included routine measurement of body weight as well as inspection for other signs of a moribund condition such as hind limb weakness and paralysis. No change in the general appearance of the mice was observed during the first 4 days after inoculation. However, after the fourth day, the mice in each of the groups demonstrated reduced overall activity, decreased mobility and a hunched posture often accompanied by hind-limb weakness, decreased water intake and obvious weight loss. The animals succumbed to the infection between day 6 and day 8 regardless of the route of viral challenge (Figure 31A–35E). On the basis of these data, the subsequent studies to evaluate ZIKV-prME-mediated protection in this model used the s.c. route for challenge.

[00506] The protective efficacy of the ZIKV-prMEnv vaccine was next evaluated in this IFNAR $^{-/-}$ mice model. Two groups of mice (n = 10) were immunized (25 μg of vaccine) by the i.m. route, through electroporation-mediated delivery with the ZIKV-prME vaccine. Also, two groups of 10 mice were immunized by the i.m. route through electroporation-mediated delivery with the control pVax1 vector. The immunizations were performed two times, two weeks apart, and all the animals were challenged on day 21 (1 week post second immunization). One set of control and vaccinated mice received 1 $\times$ 10^6 PFU of ZIKV-PR209 by the s.c. route and the other set of each group were challenged with a total of 2 $\times$ 10^6 PFU ZIKV-PR209 by the s.c. route. At 3 weeks post challenge, 100% of all ZIKV-prME vaccinated animals survived, whereas only 30% of the single- or 10% of double-dose challenged controls survived (Figures 24A and 24B). In all the challenges, the vaccinated animals were without signs of disease including no evidence of weight loss (Figures 24C and 24D). The infection of control mice with ZIKV-PR209 virus produced a marked decrease in body weight along with decreased mobility, hunched posture, hindlimb knuckle walking and/or paralysis of one or both hind limbs (Figures 24E and 24F).

[00507] The potential ability of a single immunization with the ZIKVprME DNA vaccine to protect IFNAR$^{-/-}$ mice from ZIKV challenge was evaluated. Groups of 10 mice were immunized i.m. with electroporation once with either control plasmid or ZIKV-prME vaccine and

challenged 2 weeks later with a double total dose of 2×10^6 PFU ZIKV-PR209 administration. Three weeks post challenge, 100% of the ZIKV-prME vaccinated animals survived, whereas only 10% of the control animals survived (Figure 25A). To determine gross histopathological changes, brain tissue was sectioned into 5 μm-thick sagittal sections, stained for nuclear structures and counterstained for cytoplasmic structures using eosin (Figure 25B). The mice were killed at day 7 or 8 post challenge for the analysis of histology and viral load. The ZIKV infection caused severe brain pathology in the mice. The unvaccinated control (pVax1) mice brain sections showed nuclear fragments within neutrophils (Figure 25B); perivascular cuffing of vessel within the cortex, lymphocyte infiltration and degenerating cells of the cerebral cortex (Figure 25B) and degenerating neurons within the hippocampus (Figure 25B). In contrast, however, the ZIKV prME vaccinated animals presented with normal histopathology in brain tissues (Figure 25B) supporting that protective antibodies induced by immunization with the synthetic ZIKA-prME vaccine could limit viral-induced disease in the brain. This observation demonstrates the potential for vaccination to protect the brain in this model. Consistent with the amelioration of body weight loss and mobility impairment in vaccinated mice following ZIKV challenge, a significantly lower viral load was noted in the blood (Figure 25C) and brain (Figure 25D) of the ZIKV-prME vaccinated animals compared with viral challenged pVax1 vaccinated animals in the high (2×10^6 PFU) dose challenge groups. Taken together, these data illustrate that ZIKV-prME DNA vaccine-mediated immune responses can protect mice against ZIKV challenge.

Passive transfer of anti-ZIKV immune sera protects mice against ZIKV infection

[00508] Next, whether transfer of immune sera from ZIKV-prMEnv vaccinated RM would prevent ZIKV-mediated pathogenesis in $IFNAR^{-/-}$ mice was tested. To this end, 150 μg equivalent IgG ($PRNT_{50}\approx1/160$) from week 6 RM were adoptively transferred into $IFNAR^{-/-}$ mice 1 day after the ZIKV viral challenge. Two groups of control mice were included, one group receiving pre-immune sera from RM and the other group receiving phosphate-buffered saline (PBS). The mice that received PBS or control sera lost 15 to 25% of their original body weight during the course of infection, and all died 6–8 days post infection. When vaccine immune sera from RMs were transferred to infection-susceptible mice, the animals lost weight on day 3 and 4, but subsequently regained it beginning on day 5 and 80% ultimately survived infectious

challenge (Figure 26A) demonstrating the ability of the NHP sera transfer to confer protection against clinical manifestations of ZIKV infection following viral challenge (Figure 26B). In repeated experiments performed to evaluate the efficacy of immune serum transfer in protection against challenge with ZIKV, the survival among ZIKV-prME immune sera recipients ranged from 80 to 100%. These studies show that anti-ZIKV vaccine immune sera had the ability to confer significant protection against ZIKV infection in the absence of an acquired adaptive anti-ZIKV immune response.

Vaccination with the ZIKV-prME consensus construct

[00509] Serious concerns have been raised by the recent spread of ZIKV and its associated pathogenesis in humans. Currently, there are no licensed vaccines or therapeutics for this emerging infectious agent. Very recently, a collection of experimental ZIKV vaccines have been shown to lower viral load post challenge in nonpathogenic animal infection models (Larocca et al., 2016, Nature 536:474-8; Abbink et al., 2016, Science 353:1192-32) These data are encouraging. In this regard, it is important to examine additional novel vaccine approaches targeting ZIKA in additional models. Here a synthetic DNA vaccine, designed to express a novel consensus ZIKV-prM and E antigen, was evaluated for immunogenicity following electroporation-enhanced immunization in mice and non-human primates. It was observed that ZIKV-prME DNA vaccination was immunogenic and generated antigen-specific T cells and binding and neutralizing antibodies in both mice and NHPs. Uniquely, the NHPs were immunized with ZIKV-prME through electroporation by the intradermal route, which uses lower voltage and a smaller transfection area than i.m. electroporation, as has been recently described (Trimble et al., 2016, Lancet 386:2078-88) Further study of such approaches may provide advantages in clinical settings.

[00510] The ZIKV-prME consensus construct includes a designed change of the potential NXS/T motif, which removes a putative glycosylation site. Deletion of glycosylation at this site has been correlated with improved binding of EDE1 type bnAbs (broadly neutralizing antibodies) against ZIKV-E protein (Muthumani et al., 2016, Sci Transl Med 7:301ra132). The antibody responses induced by the consensus ZIKV-prME appear as robust or in some cases superior in magnitude to those elicited by similarly developed ZIKV-prME-MR766 and ZIKV-prME-Brazil vaccines. These constructs were sequence matched with the original ZIKV-MR766

isolate or a recently circulating ZIKV strain from Brazil, respectively. While supportive, further study will provide more insight into the effects of such incorporated designed changes on induced immune responses.

[00511] As there are few pathogenic challenge models for ZIKV, the putative protective nature of the immune responses of the ZIKV-prME vaccine in C57BL/6 and IFNAR$^{-/-}$ mice was compared. Both the strains of mice responded with a robust humoral immune response when immunized with ZIKV-prME. The T-cell responses were also induced, but appear to be more robust in wild-type C57BL/6 compared with those induced in the IFNAR$^{-/-}$ animals, supporting a partial defect in innate to adaptive immunity transition as expected owing to the knock-out phenotype in the mouse. However, based on the induction of antigen specific immunity, the model was useful for evaluation of the impact of the vaccine on both infection and pathogenesis. A single vaccination with ZIKV-prME in IFNAR$^{-/-}$ mice was protective against disease and death in this model, including protection of neuro-pathogenesis. Flavivirus-neutralizing antibodies directed against the Env antigen are thought to have a key role in protection against disease, an idea supported directly by passive antibody transfer experiments in animal models and indirectly by epidemiological data from prospective studies in geographical areas that are prone to mosquito-borne viral infections (Weaver et al., 2016, Antiviral Res 130:69-80; Roa et al., 2016, Lancet 387:843; Samarasekera et al., 2016, Lancet 387:521-4). Although immunization of IFNAR$^{-/-}$ mice with the ZIKV-prME DNA vaccine as well as serum transfer from immunized NHPs were protective in this murine model, the IFNAR$^{-/-}$ vaccinated as opposed to serum-transferred mice exhibited improved control of weight loss as an indication of control of pathogenesis. Although additional studies are needed, this result potentially suggests a role for the T-cell response in this aspect of protection in this model. In addition, it was observed that control IFNAR$^{-/-}$ mice who recovered from challenge remain viral positive by PCR for at least several weeks, suggesting an additional benefit of vaccination. This study supports the potential of vaccination and, in this case this synthetic DNA vaccination, to impact prevention of disease in a susceptible host.

[00512] It is understood that the foregoing detailed description and accompanying examples are merely illustrative and are not to be taken as limitations upon the scope of the invention, which is defined solely by the appended claims and their equivalents.

[00513] Various changes and modifications to the disclosed embodiments will be apparent to those skilled in the art. Such changes and modifications, including without limitation those relating to the chemical structures, substituents, derivatives, intermediates, syntheses, compositions, formulations, or methods of use of the invention, may be made without departing from the spirit and scope thereof.

2017238168 15 May 2024

CLAIMS

1. A composition for generating a persistent or systemic immune response comprising:

a) a first nucleic acid sequence encoding a Chikungunya virus antigen having an amino acid sequence that is at least 98% identical to an amino acid sequence set forth in any of SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 87, and SEQ ID NO: 88; and

b) a second nucleic acid sequence encoding one or more antibodies having an amino acid sequence that is at least 98% identical to the amino acid sequence set forth in SEQ ID NO: 59 and SEQ ID NO: 61 or antigen binding fragments thereof, wherein the one or more antibodies or antigen binding fragments thereof are specific for the antigen.

2. The composition of claim 1, wherein the antibody comprises a heavy chain polypeptide, or antigen binding fragment thereof, and a light chain polypeptide, or antigen binding fragment thereof.

3. The composition of claim 2, wherein the heavy chain polypeptide, or antigen binding fragment thereof, is encoded by a third nucleic acid sequence and the light chain polypeptide, or antigen binding fragment thereof, is encoded by a fourth nucleic acid sequence.

4. The composition of claim 3, wherein the second nucleic acid sequence comprises the third nucleic acid sequence and the fourth nucleic acid sequence.

5. The composition of claim 4, wherein the second nucleic acid sequence further comprises a promoter for expressing the third nucleic acid sequence and the fourth nucleic acid sequence as a single transcript.

2017238168 15 May 2024

6. The composition of claim 5, wherein the promoter is a cytomegalovirus (CMV) promoter.

7. The composition of claim 5, wherein the second nucleic acid sequence further comprises a fifth nucleic acid sequence encoding a protease cleavage site, wherein the fifth nucleic acid sequence is located between the third nucleic acid sequence and fourth nucleic acid sequence.

8. The composition of claim 7, wherein a protease recognizes and cleaves the protease cleavage site.

9. The composition of any one of claims 2-8, wherein the heavy chain polypeptide comprises a variable heavy region and a constant heavy region 1.

10. The composition of any one of claims 2-9, wherein the heavy chain polypeptide comprises a variable heavy region, a constant heavy region 1, a hinge region, a constant heavy region 2 and a constant heavy region 3.

11. The composition of any one of claims 2-10, wherein the light chain polypeptide comprises a variable light region and a constant light region.

12. The composition of any one of claims 1-11, wherein the second nucleic acid sequence further comprises a Kozak sequence.

13. The composition of any one of claims 1-12, wherein the fourth nucleic acid sequence further comprises an immunoglobulin (Ig) signal peptide.

14. The composition of claim 13, wherein the Ig signal peptide comprises an IgE or IgG signal peptide.

2017238168 15 May 2024

15. The composition of any one of claims 1-14, wherein the first nucleic acid sequence encodes an antigen having an amino acid sequence set forth in any of SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 87, and SEQ ID NO: 88.

16. The composition of any one of claims 1-14, wherein the first nucleic acid sequence comprises a nucleic acid sequence having at least about 97% identity over an entire length of the nucleic acid sequence set forth in any of SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 95, and SEQ ID NO: 96.

17. The composition of any one of claims 1-16, wherein the second nucleic acid sequence comprises a nucleic acid sequence encoding the amino acid sequence set forth in SEQ ID NOs: 59 and SEQ ID NO: 61.

18. The composition of any one of claims 1-16, wherein the second nucleic acid sequence comprises a nucleic acid sequence having at least about 97% identity over an entire length of the nucleic acid sequence set forth in SEQ ID NO: 58 and SEQ ID NO: 60.

19. A method of inducing an immune response comprising administering the composition of any one of claims 1-18 to an individual in an amount effective to induce an immune response in said individual.

20. Use of the composition of any one of claims 1-18 in the manufacture of a medicament for inducing an immune response in an individual.

21. The method of claim 19 or the use of claim 20, wherein the immune response is persistent.

22. The method of claim 19 or 21 or the use of claim 20 or 21, wherein the immune response is systemic.

2017238168 15 May 2024

23. A method of treating an individual who has been diagnosed with a disease or disorder comprising administering a therapeutically effective amount of the composition of any one of claims 1-18 to an individual.

24. Use of the composition of any one of claims 1-18 in the manufacture of a medicament for treating an individual who has been diagnosed with a disease or disorder.

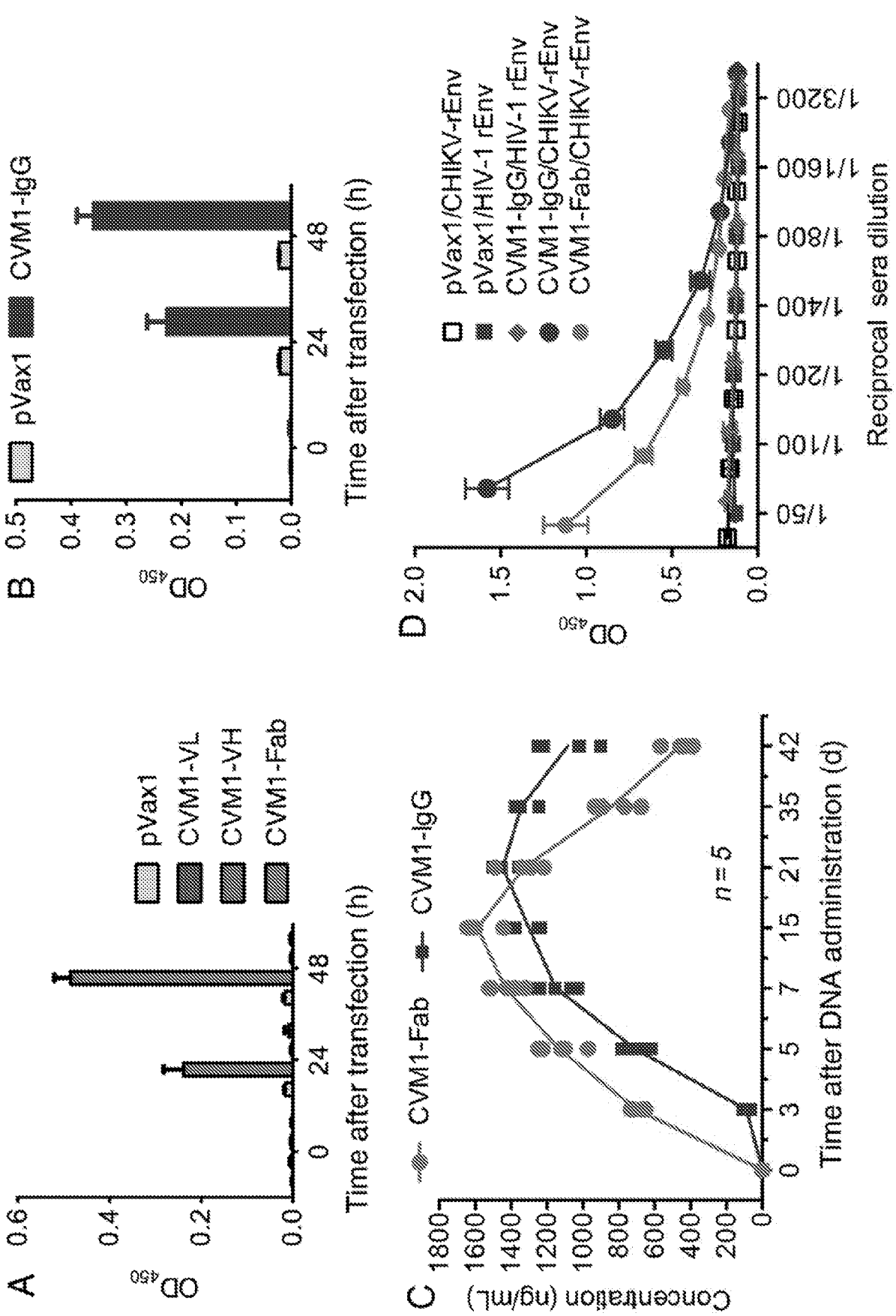


Figure 1A – Figure 1D

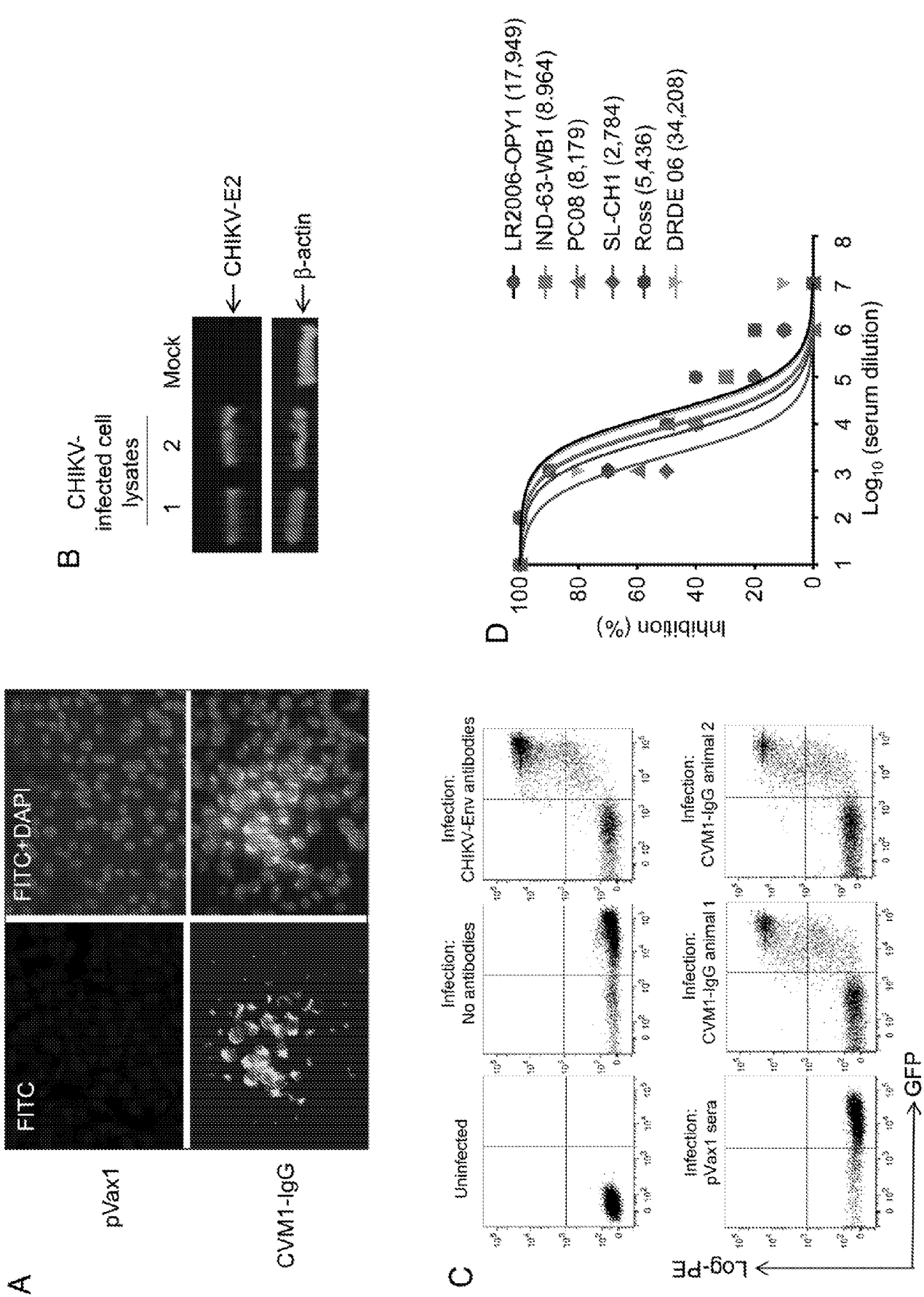


Figure 2A – Figure 2D

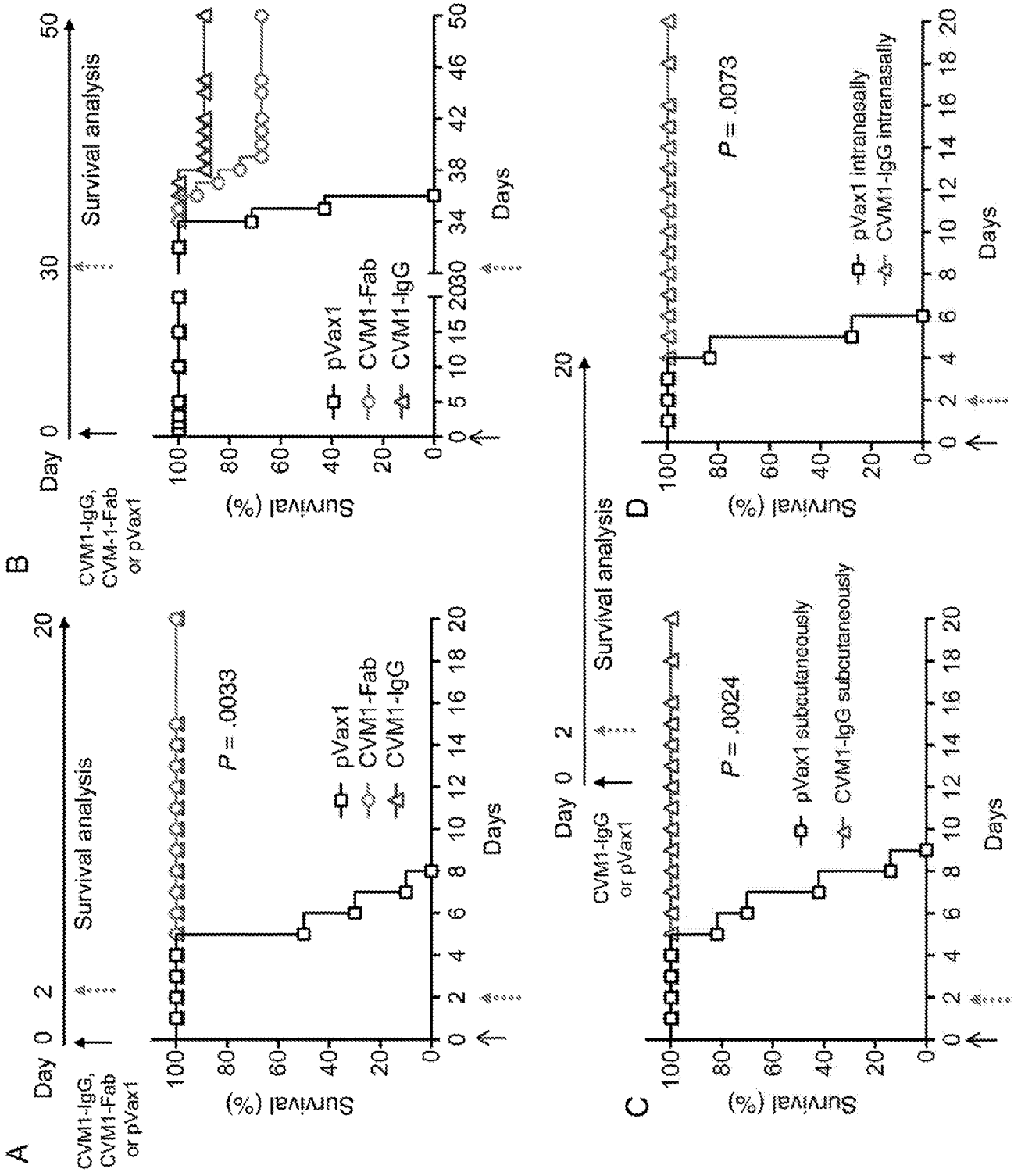


Figure 3A – Figure 3D

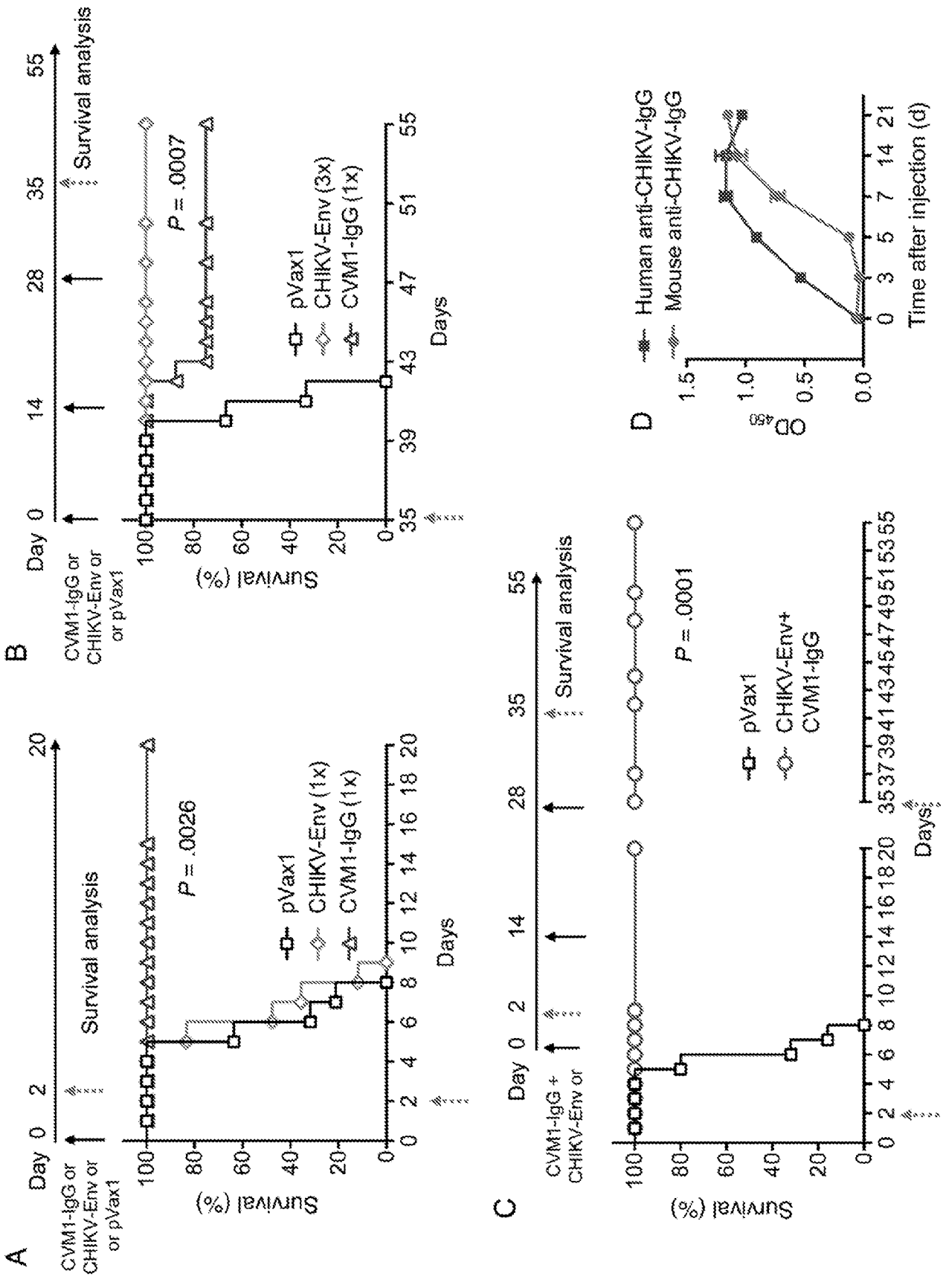


Figure 4A – Figure 4D

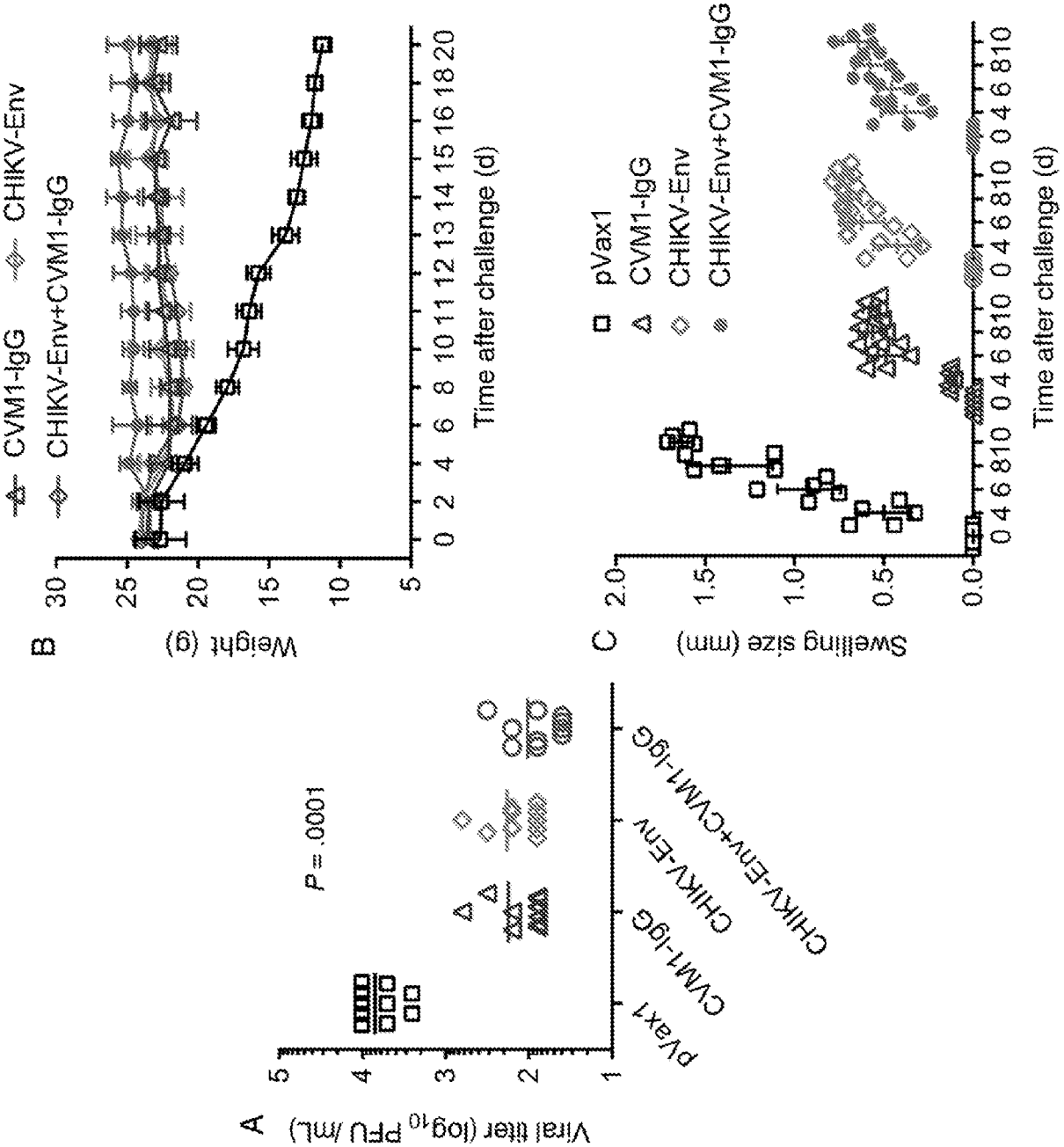


Figure 5A – Figure 5C

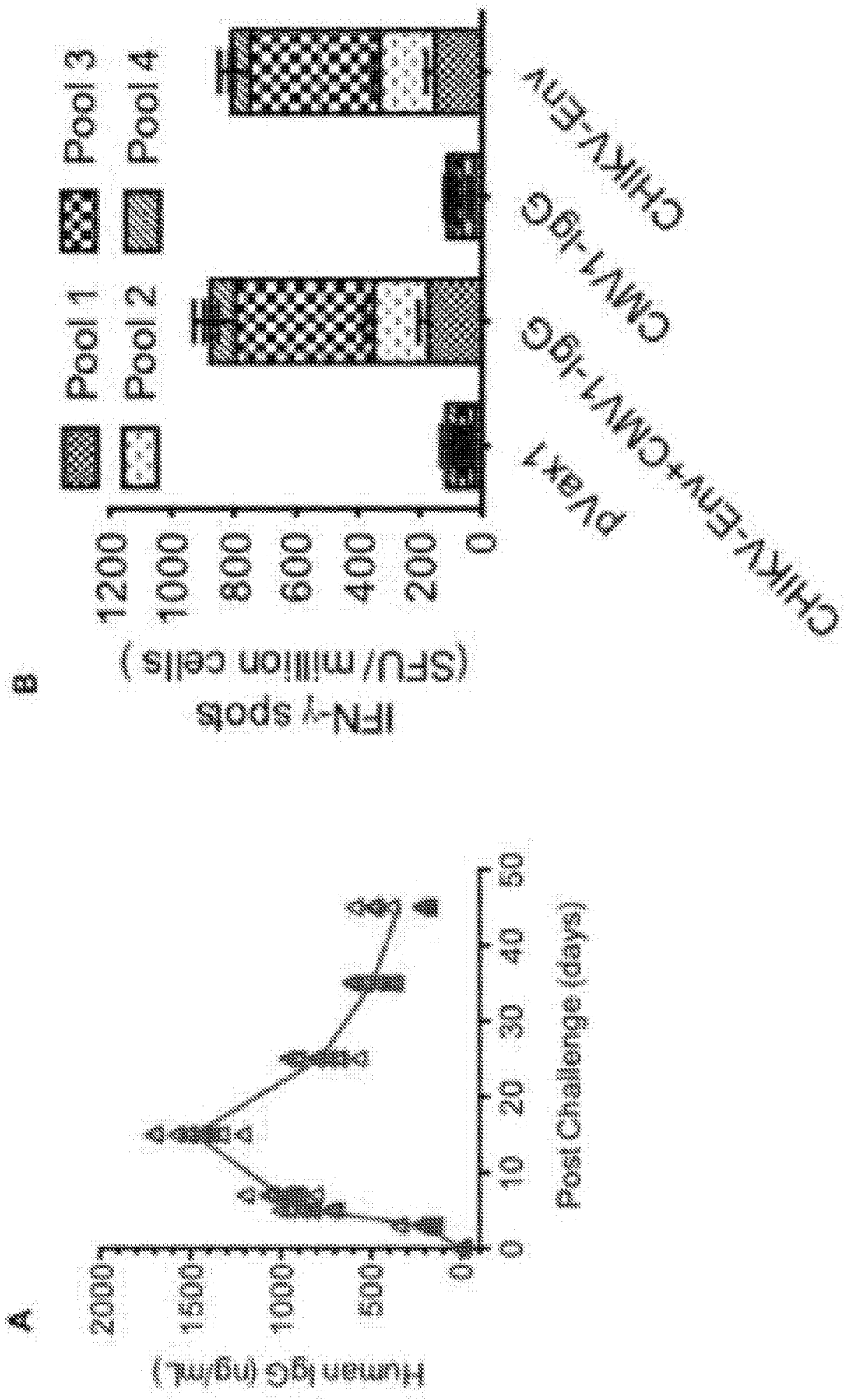


Figure 6A – Figure 6B

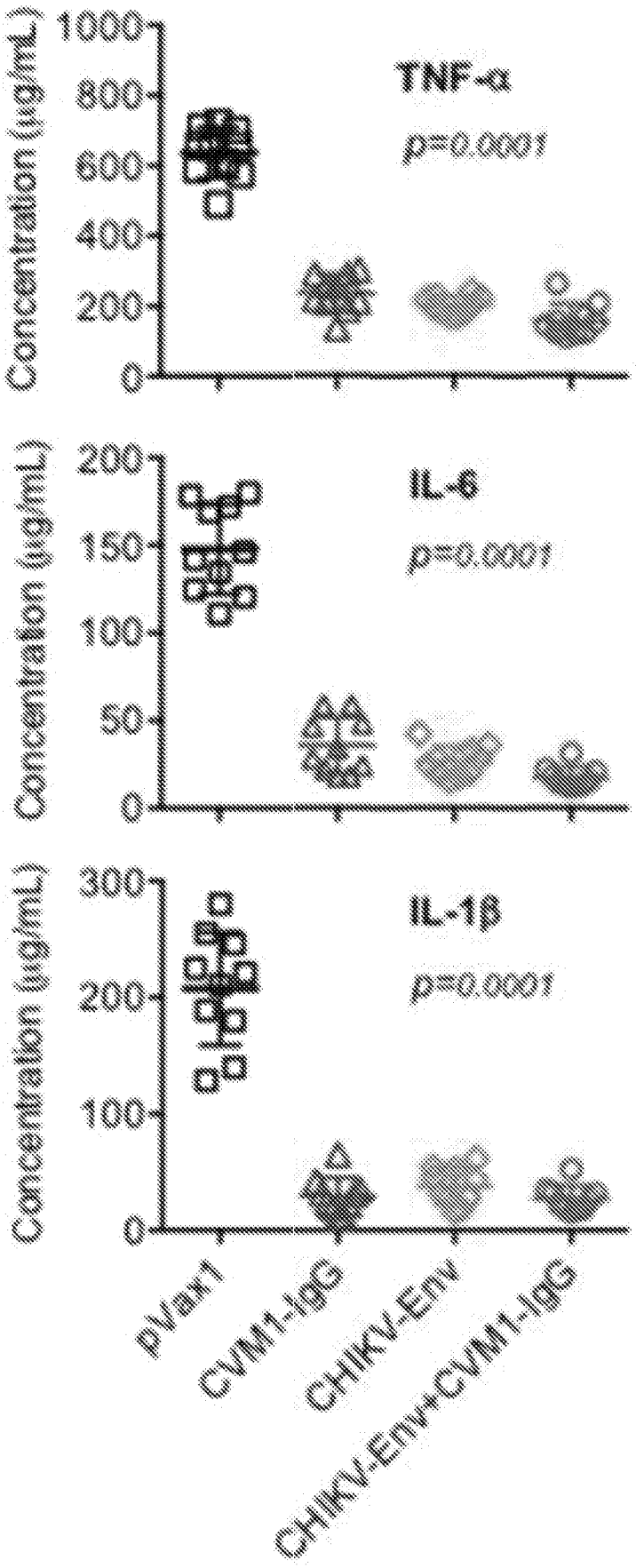

Concentration (µg/mL)
1000
800
600
400
200
0
TNF-α
p=0.0001
Concentration (µg/mL)
200
150
100
50
0
IL-6
p=0.0001
Concentration (µg/mL)
300
200
100
0
IL-1β
p=0.0001
pVax1
CVM1-IgG
CHIKV-Env
CHIKV-Env+CVM1-IgG

Figure 7

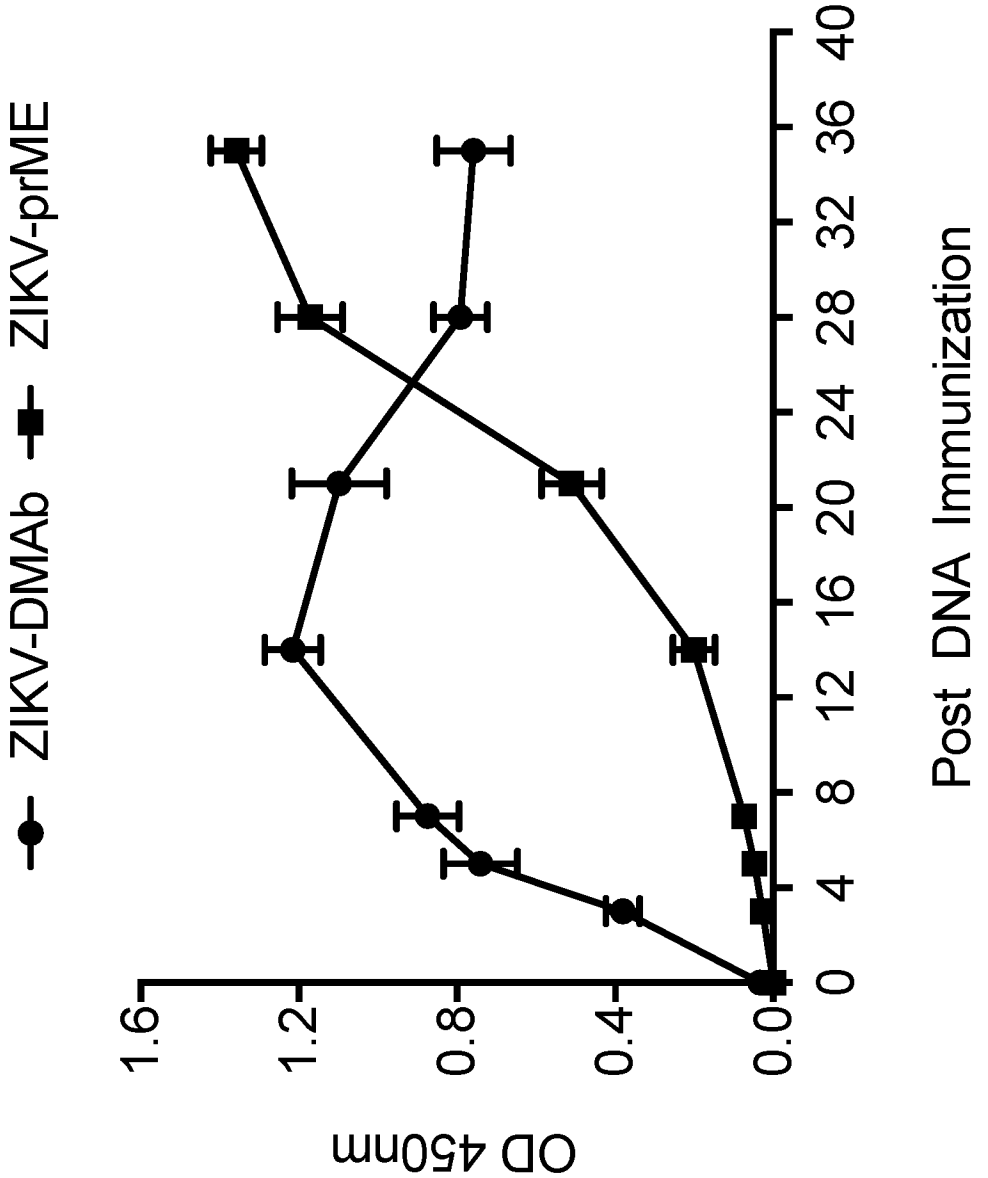

ZIKV-DMAb
ZIKV-prME
OD 450nm
0.0
0.4
0.8
1.2
1.6
0
4
8
12
16
20
24
28
32
36
40
Post DNA Immunization
(Days)

Figure 8

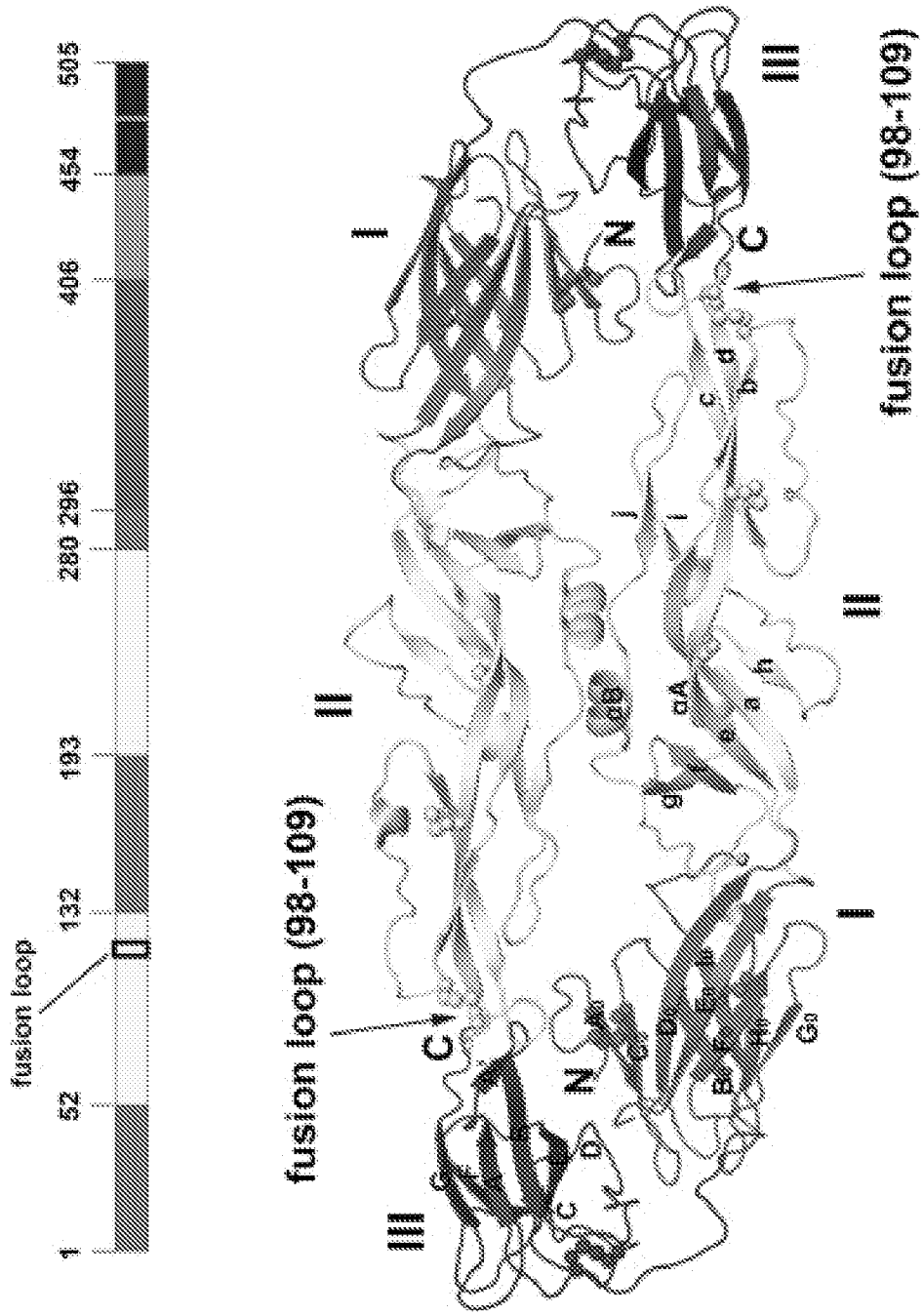

fusion loop
1
52
132
193
280 296
406
454
505
fusion loop (98-109)
fusion loop (98-109)
I
II
III
N
C

Figure 9

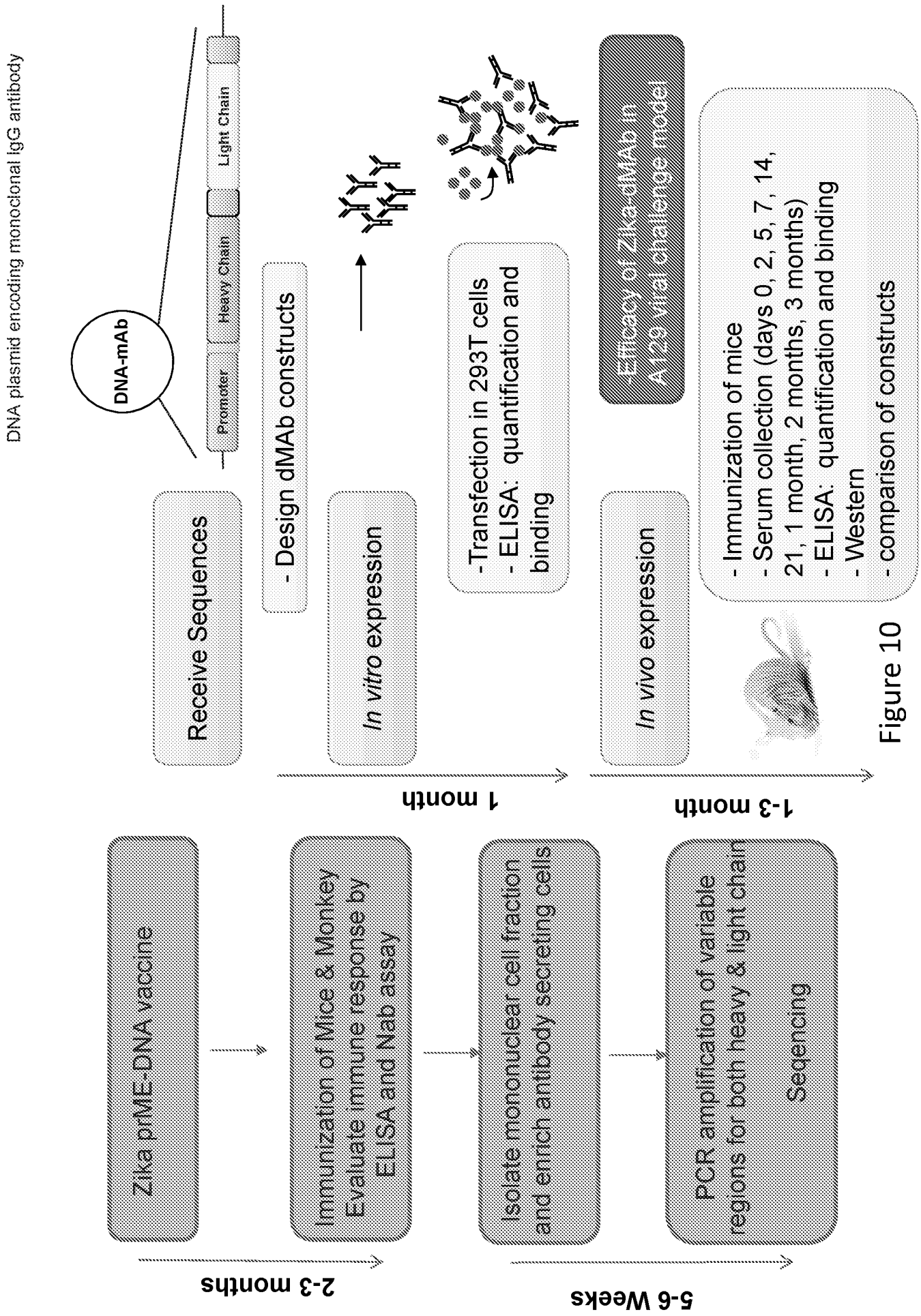

DNA plasmid encoding monoclonal IgG antibody
DNA-mAb
Promoter
Heavy Chain
Light Chain
Receive Sequences
- Design dMAb constructs
In vitro expression
- Transfection in 293T cells
- ELISA: quantification and binding
In vivo expression
Efficacy of Zika dMAb in A129 viral challenge model
- Immunization of mice
- Serum collection (days 0, 2, 5, 7, 14, 21, 1 month, 2 months, 3 months)
- ELISA: quantification and binding
- Western
- comparison of constructs
1 month
1-3 month
Zika prME-DNA vaccine
Immunization of Mice & Monkey
Evaluate immune response by ELISA and Nab assay
Isolate mononuclear cell fraction and enrich antibody secreting cells
PCR amplification of variable regions for both heavy & light chain
Seqencing
2-3 months
5-6 Weeks

Figure 10

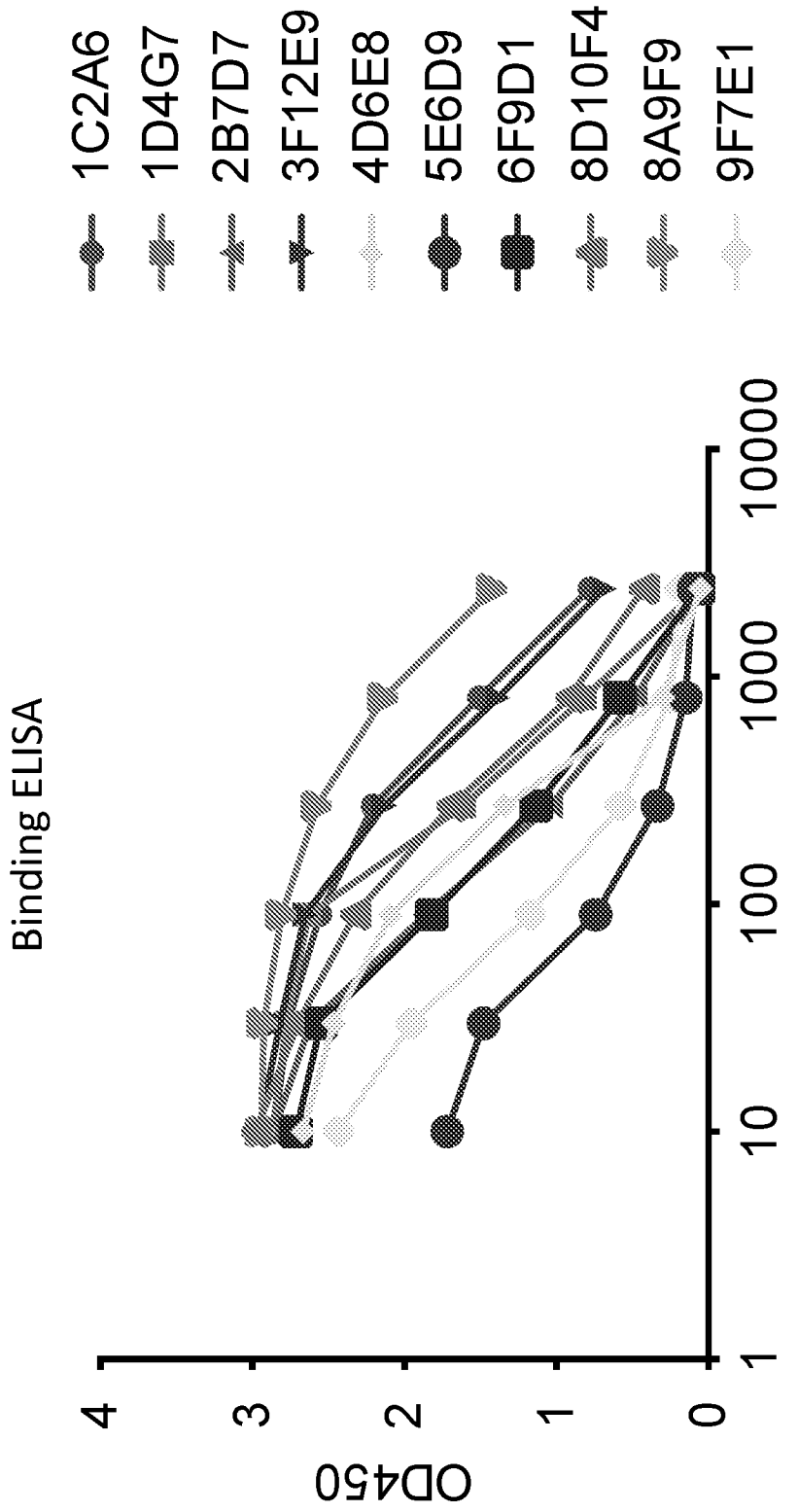

Binding ELISA
OD450
4
3
2
1
0
1
10
100
1000
10000
Dilutions
1C2A6
1D4G7
2B7D7
3F12E9
4D6E8
5E6D9
6F9D1
8D10F4
8A9F9
9F7E1

Figure 11

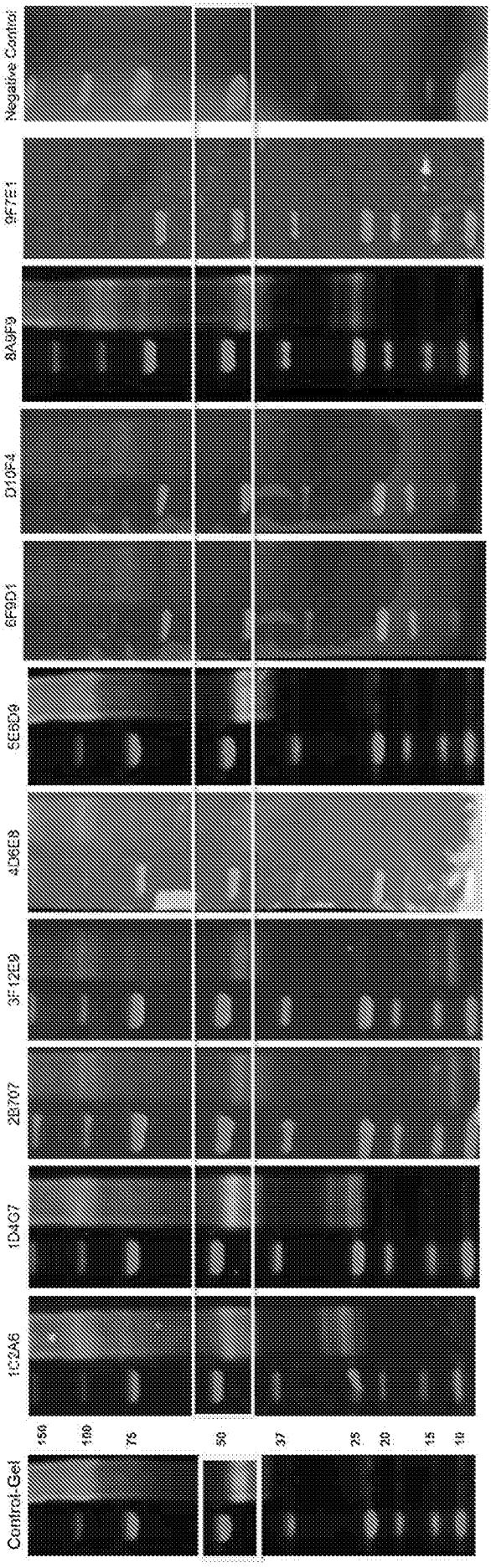

Control Gel
1C2A6
1D4G7
2B7D7
3F12E9
4D6E8
5E8D9
6F9D1
D10F4
8A3F9
9F7E1
Negative Control
150
100
75
50
37
25
20
15
10

Figure 12

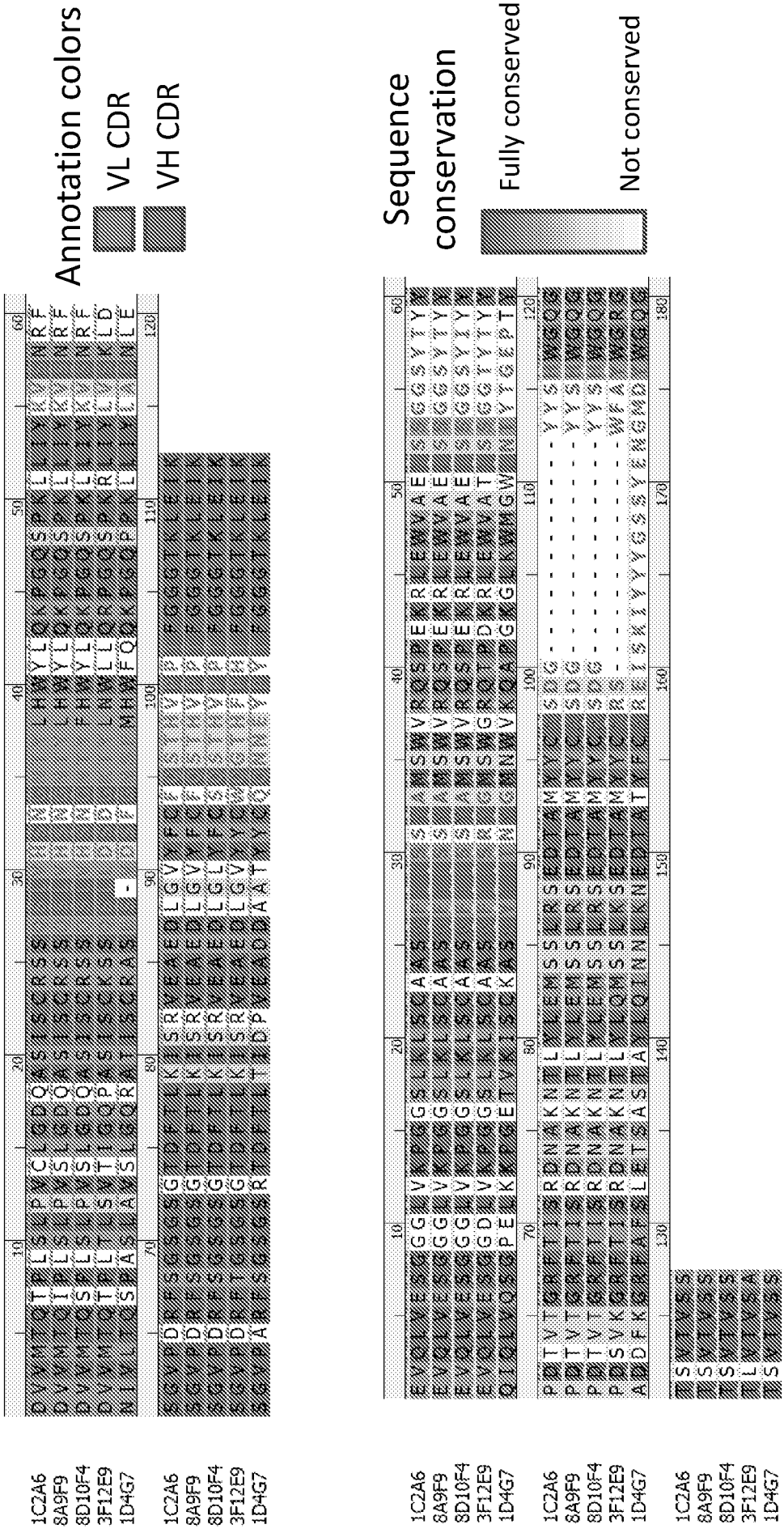

Annotation colors
VL CDR
VH CDR
Sequence conservation
Fully conserved
Not conserved
1C2A6
8A9F9
8D10F4
3F12E9
1D4G7

Figure 13

VH identity

	8A9F9_H	1D4G7_H	8D10F4_H	3F12E9_H	1C2A6_H
8A9F9_H	100	43.3	99.1	80.9	100
1D4G7_H	43.3	100	43.3	44.9	43.3
8D10F4_H	99.1	43.3	100	80	99.1
3F12E9_H	80.9	44.9	80	100	80.9
1C2A6_H	100	43.3	99.1	80.9	100

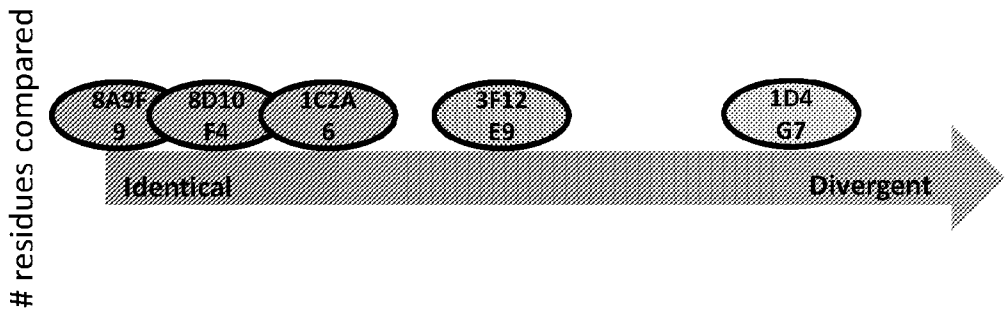
VL identity'

	8A9F9_L	1D4G7_L	8D10F4_L	3F12E9_L	1C2A6_L
8A9F9_L	100	64.3	96.4	76.8	98.2
1D4G7_L	64.3	100	65.2	58.9	63.4
8D10F4_L	96.4	65.2	100	75	95.5
3F12E9_L	76.8	58.9	75	100	77.7
1C2A6_L	98.2	63.4	95.5	77.7	100

Model RMSD

RMSD	8D10F4	1C2A6	8A9F9	3F12E9	1D4G7
8D10F4		227	227	226	219
1C2A6	0.302		227	226	219
8A9F9	0.385	0.347		226	219
3F12E9	0.723	0.752	0.722		219
1D4G7	1.364	1.388	1.351	1.434	

RMSD (Å)



- The VH and VL chains in 1C2A6, 8D10F4 and 8A9F9 are identical or nearly identical.
- 1C2A6, 8D10F4 and 8A9F9 are likely to bind the same epitope in the same manner. There may be affinity differences, as with any antibody changes.
- 1D4G7 and 3F12E9 represent more divergent Fv's than 1C2A6, 8D10F4 and 8A9F9.
- 3F12E9 is more similar to the set of three mAbs cited above than it is to 1D4G7. It may bind similarly.
- Backbone variation according to RMSD measurement shows the same pattern as sequence identity.

Figure 14

- All Fv models are superimposed in ribbon format to emphasize overall fold.
- The large VH CDR3 of 1D4G7 is clearly visible, as are several other fold differences in other CDR and in framework regions.
- Despite the sequence divergence of 3F12E9, it is still closer in overall sequence and conformation to 1C2A6, 8D10F4 and 8A9F9 than to 1D4G7.

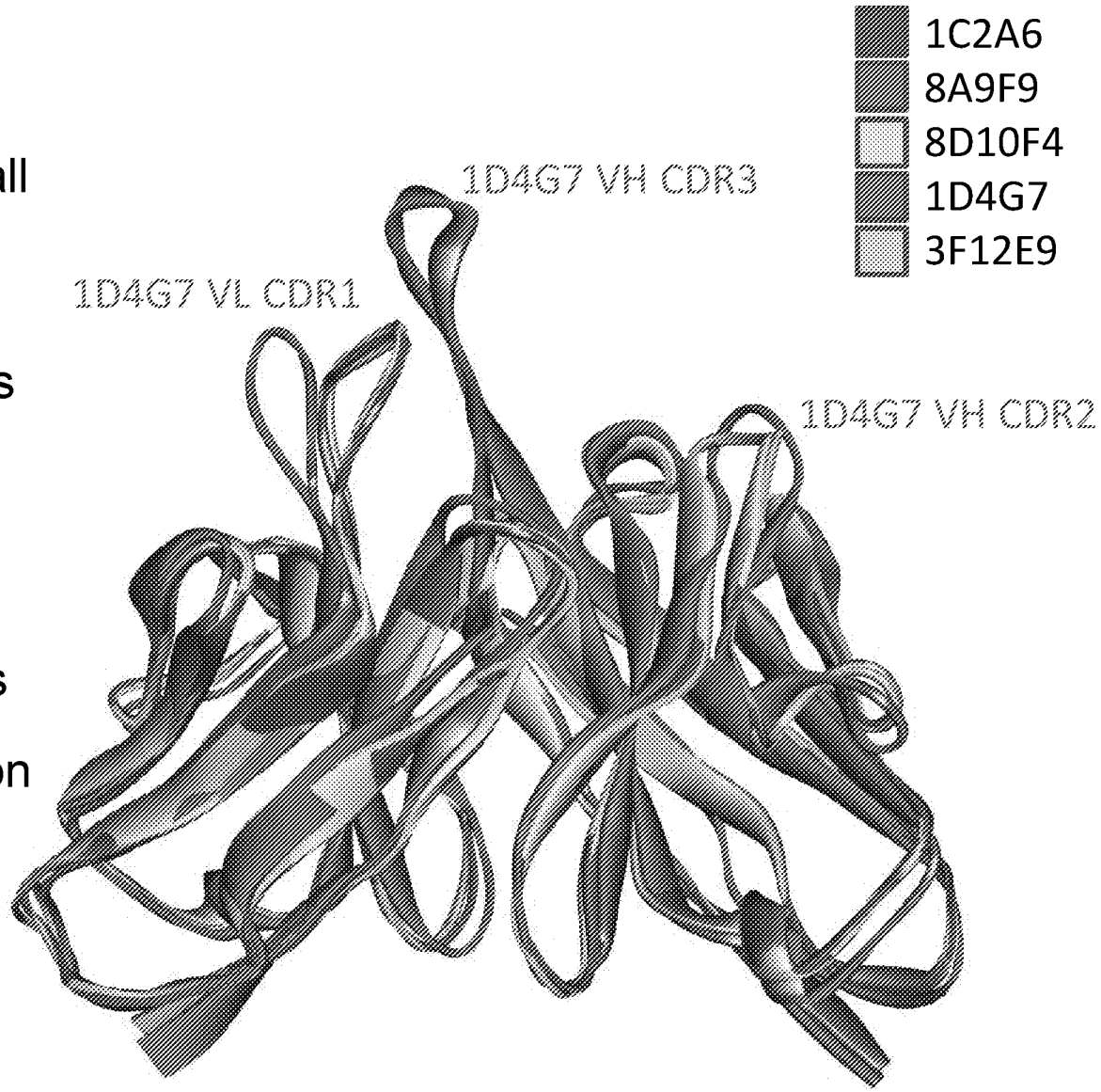
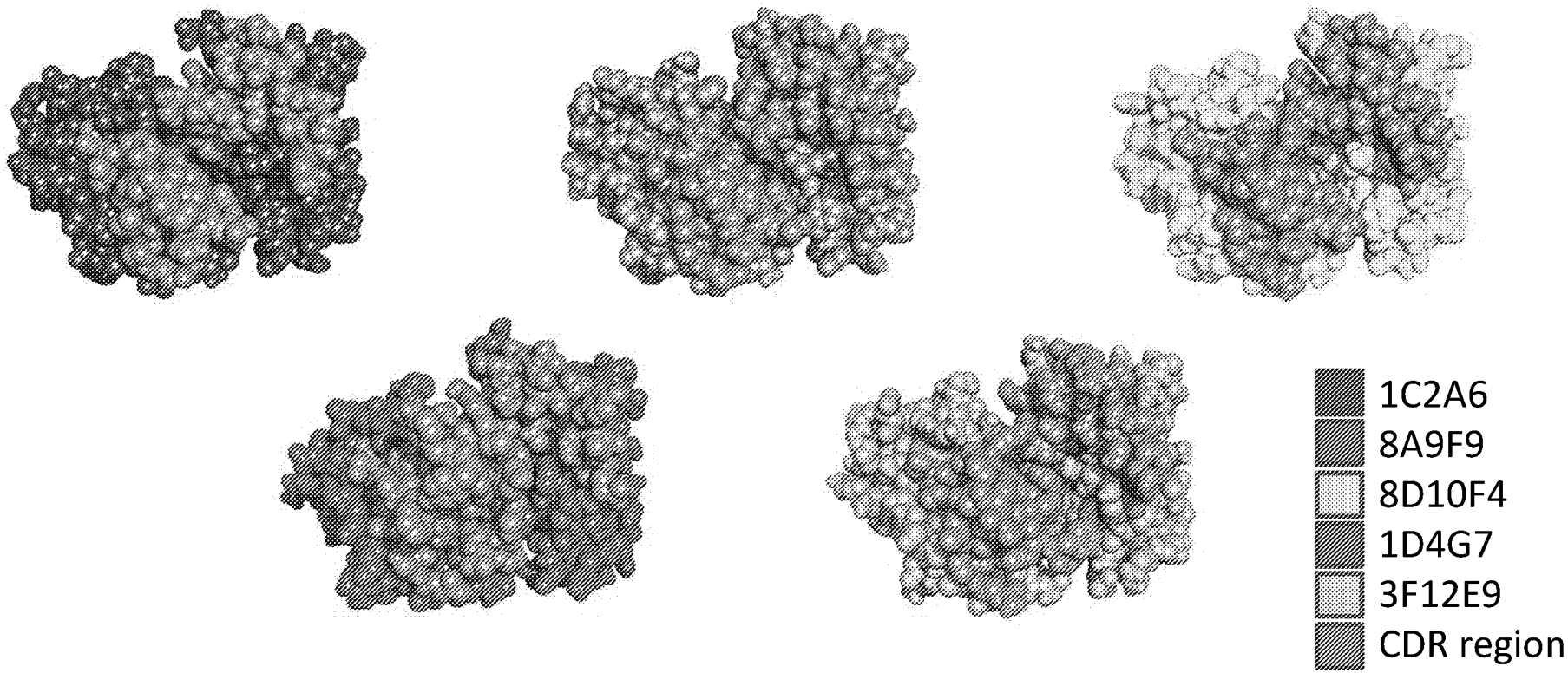


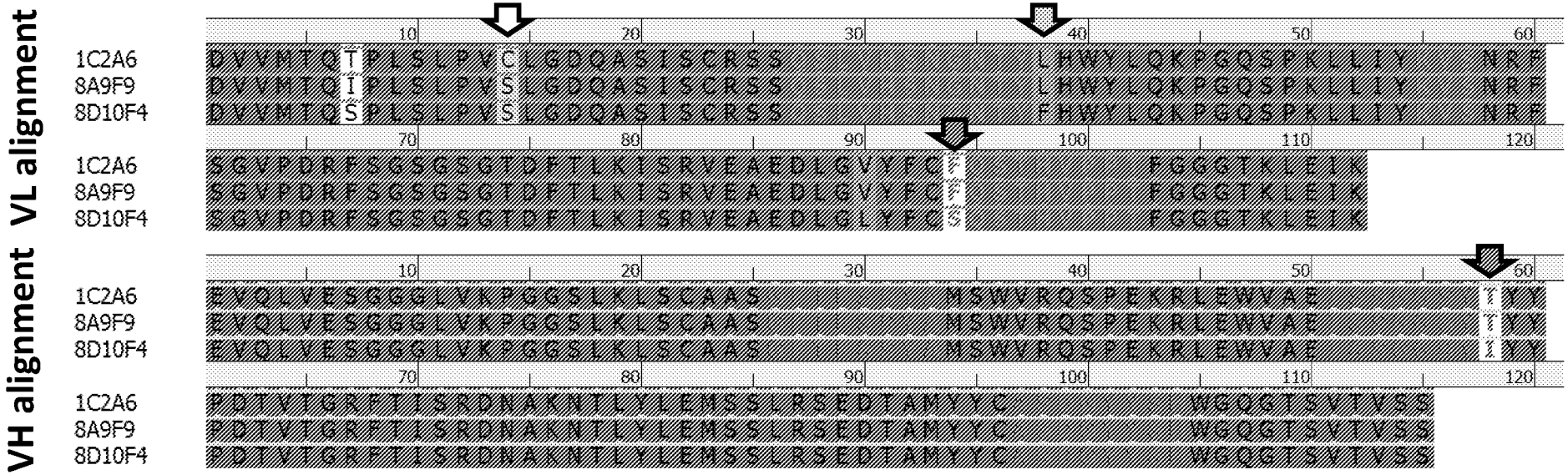
Figure 15



- 1D4G7 lacks a cleft between the VH and VL domains due to its large CDR3 loop.

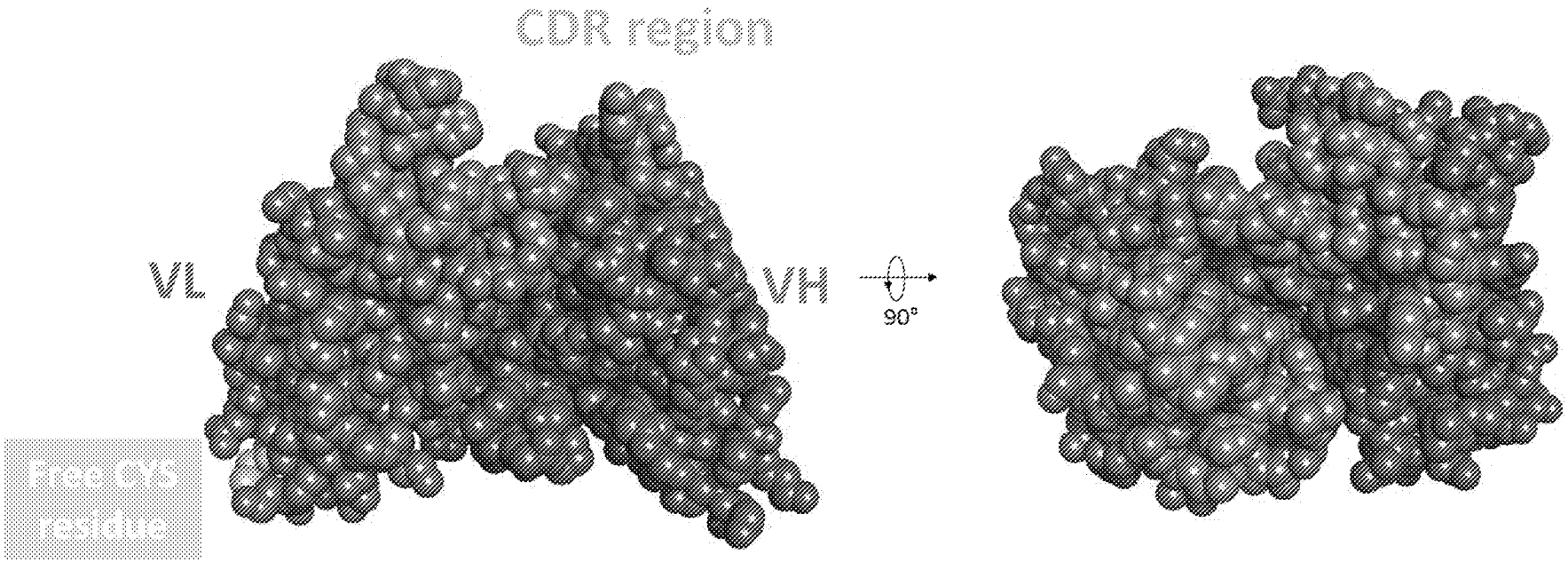
- Sequence similarities translate to structural similarities, so overall CDR conformations and molecular shapes are conserved according to previously demonstrated clustering.

Figure 16



- 1C2A6 has a free CYS residue distal to the CDRs exposed on the surface (yellow arrow).
- Another potentially relevant difference occurs in VH FR2 region (orange arrow). This residue is not directly involved in CDR conformation but does influence local residue packing.
- Two changes occur within the IMGT-defined CDR regions (red arrows). The VL changes (F, F, S) directly impact the VL-VH interface.

Figure 17



- A free CYS leaves a highly modifiable chemical group exposed on the molecule surface.

- As this mAb is nearly identical to two others (the CYS being unique to 1C2A6), if the other two mAbs show similar neutralizing activity it may be better to go with a mAb that does not have a free CYS.

Figure 18

Protein	Developability Index (Fv)	Molecular Charge	Total Pi Interactions	Total Hydrogen Bonds	Ligand Contact Surface Area	Ligand Polar Contact Surface Area	Ligand Nonpolar Contact Surface Area	Receptor Contact Surface Area	Receptor Polar Contact Surface Area	Receptor Nonpolar Contact Surface Area
8D10F4	57.447	2.52	6	4	211.61	85.863	125.75	205	82.854	122.15
1C2A6	57.237	2.73	9	2	186.67	73.108	113.56	182.2	69.19	113.01
8A9F9	60.132	2.94	9	2	186.67	73.108	113.56	182.2	69.19	113.01
3F12E9	60.661	6.71	10	5	224.98	72.912	152.06	223.97	72.732	151.23
1D4G7	70.578	0.84	10	6	323.22	116.31	206.91	331.6	172.51	159.09

- Developability index is highest for 1D4G7, very likely due to the long CDR3 loop which contains multiple nonpolar residues. Based on past experience, though, this alone does not appear to be an issue.

- F→S variation in the interface/CDR region of 8D10F4 is responsible for the reduced number of predicted pi interactions compared to 1C2A6 and 8A9F9.

- Additional features such as potential post-translational modifications can be assessed. These may be less relevant but can be run.

Figure 19

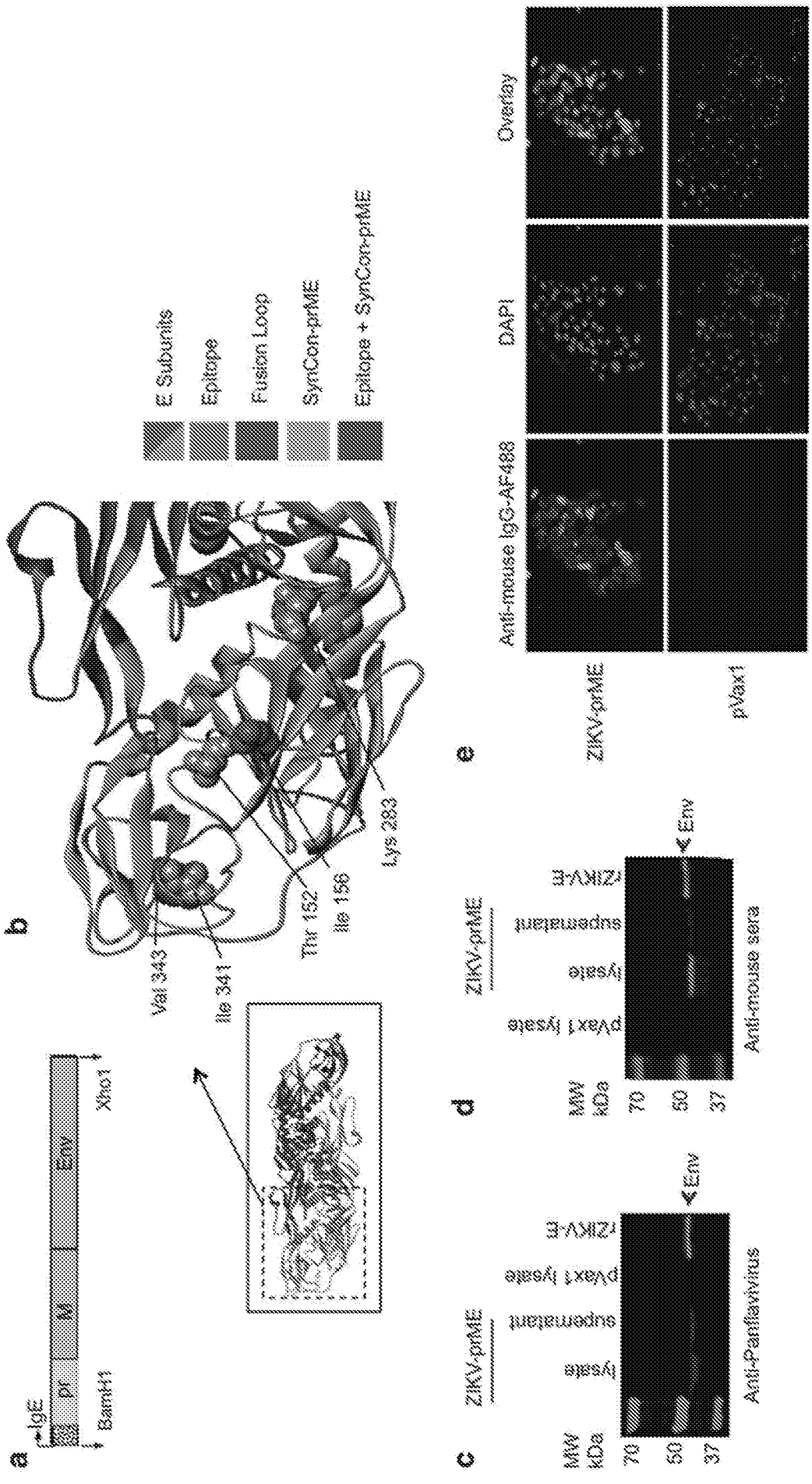


Figure 20A – Figure 20E

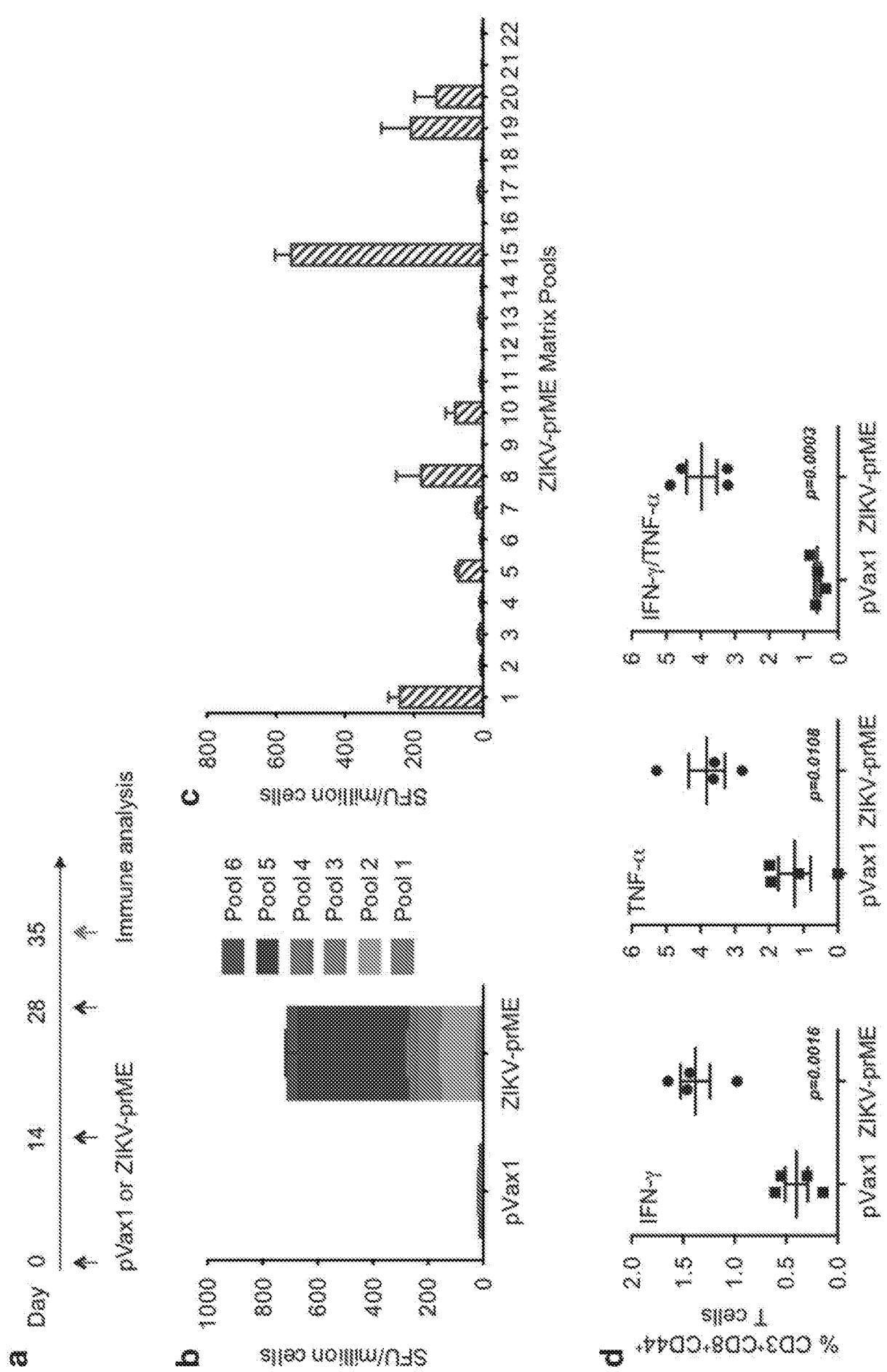


Figure 21A – Figure 21D

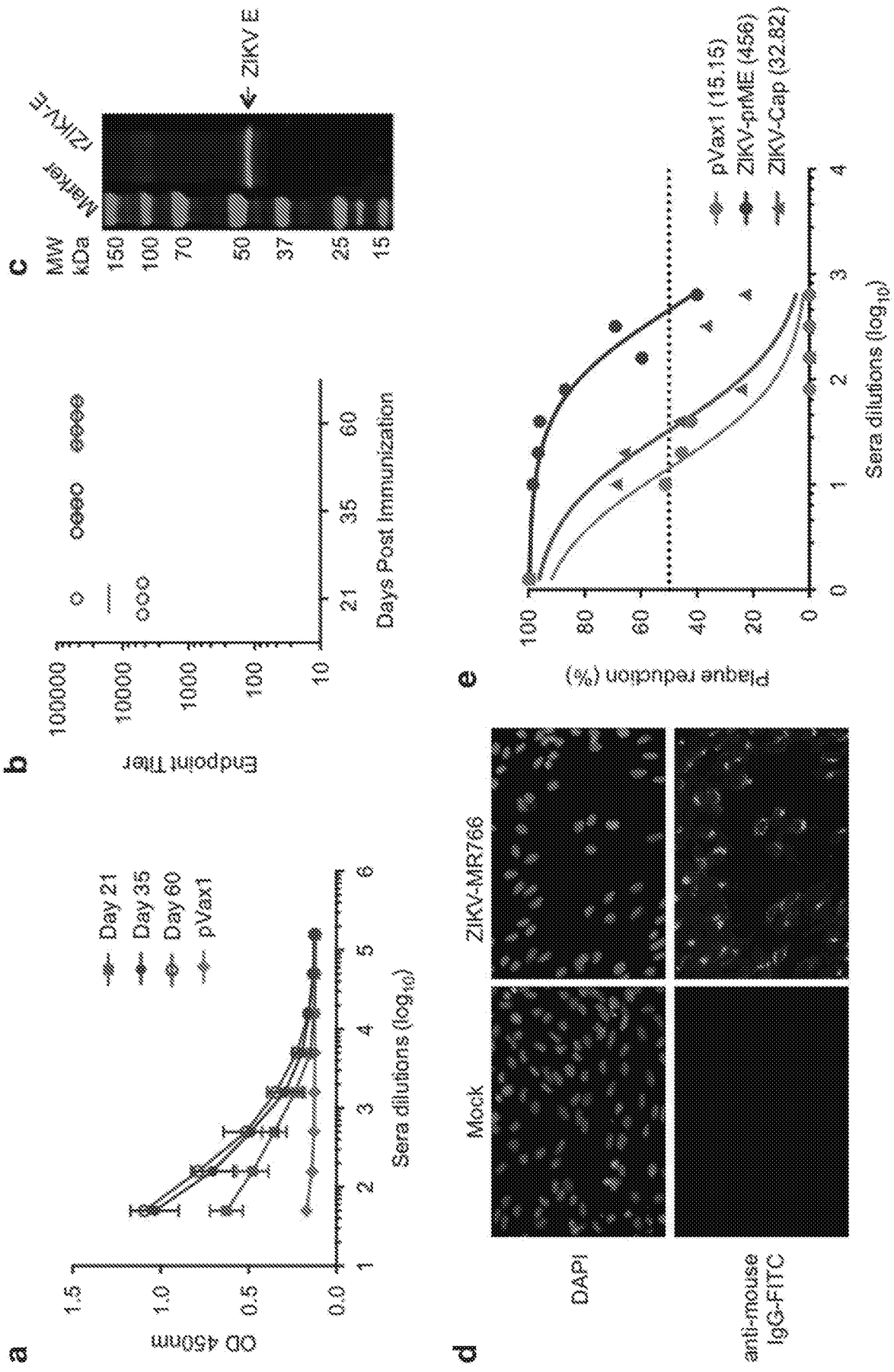


Figure 22A – Figure 22E

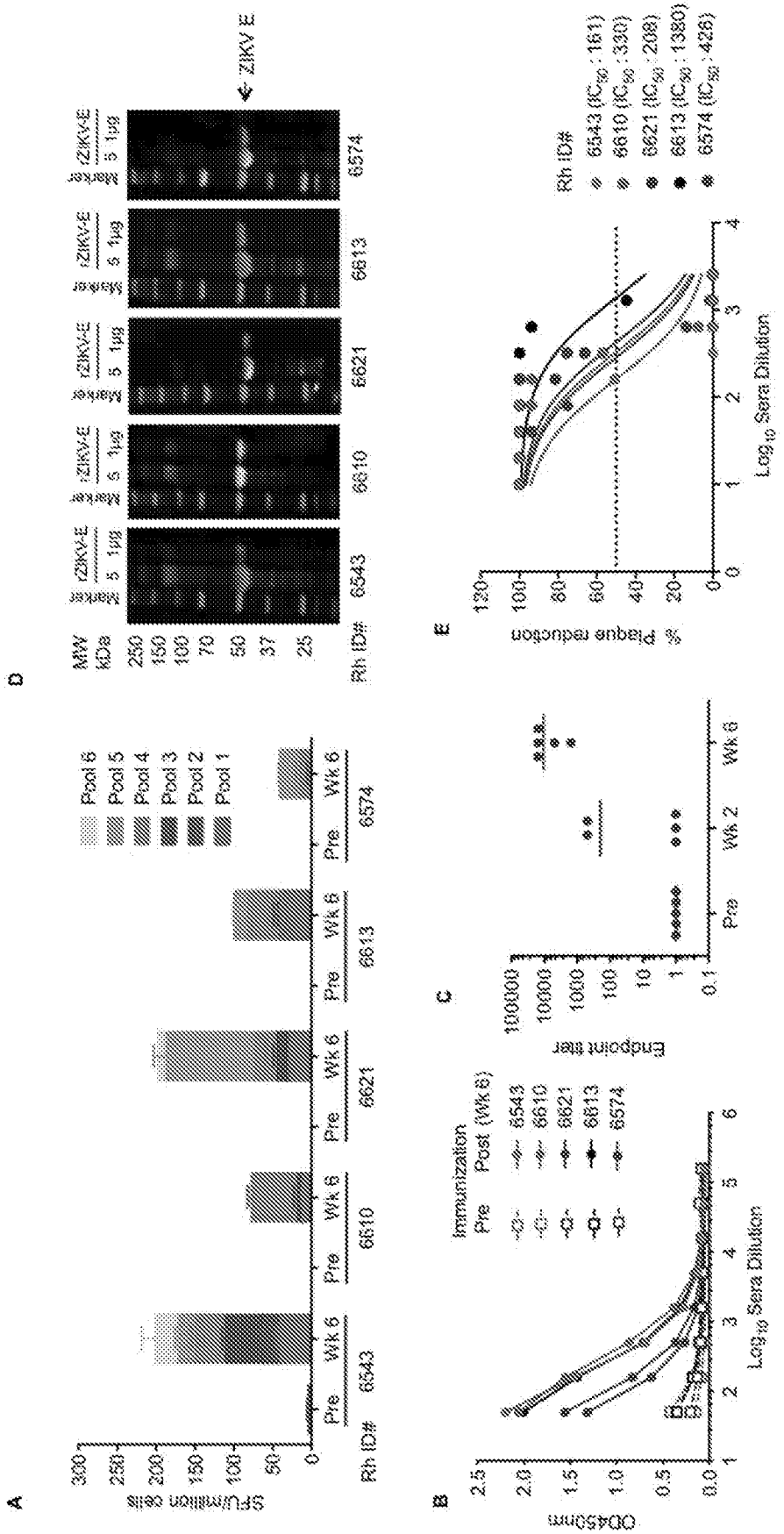


Figure 23A – Figure 23E

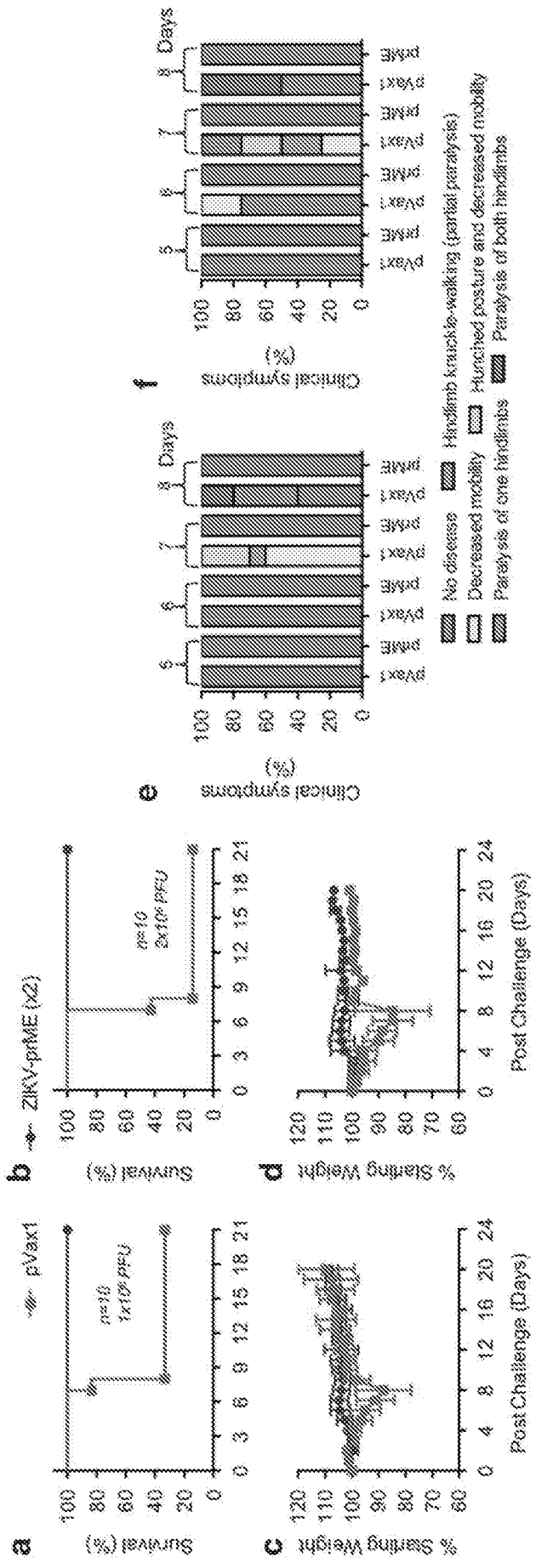


Figure 24A – Figure 24F

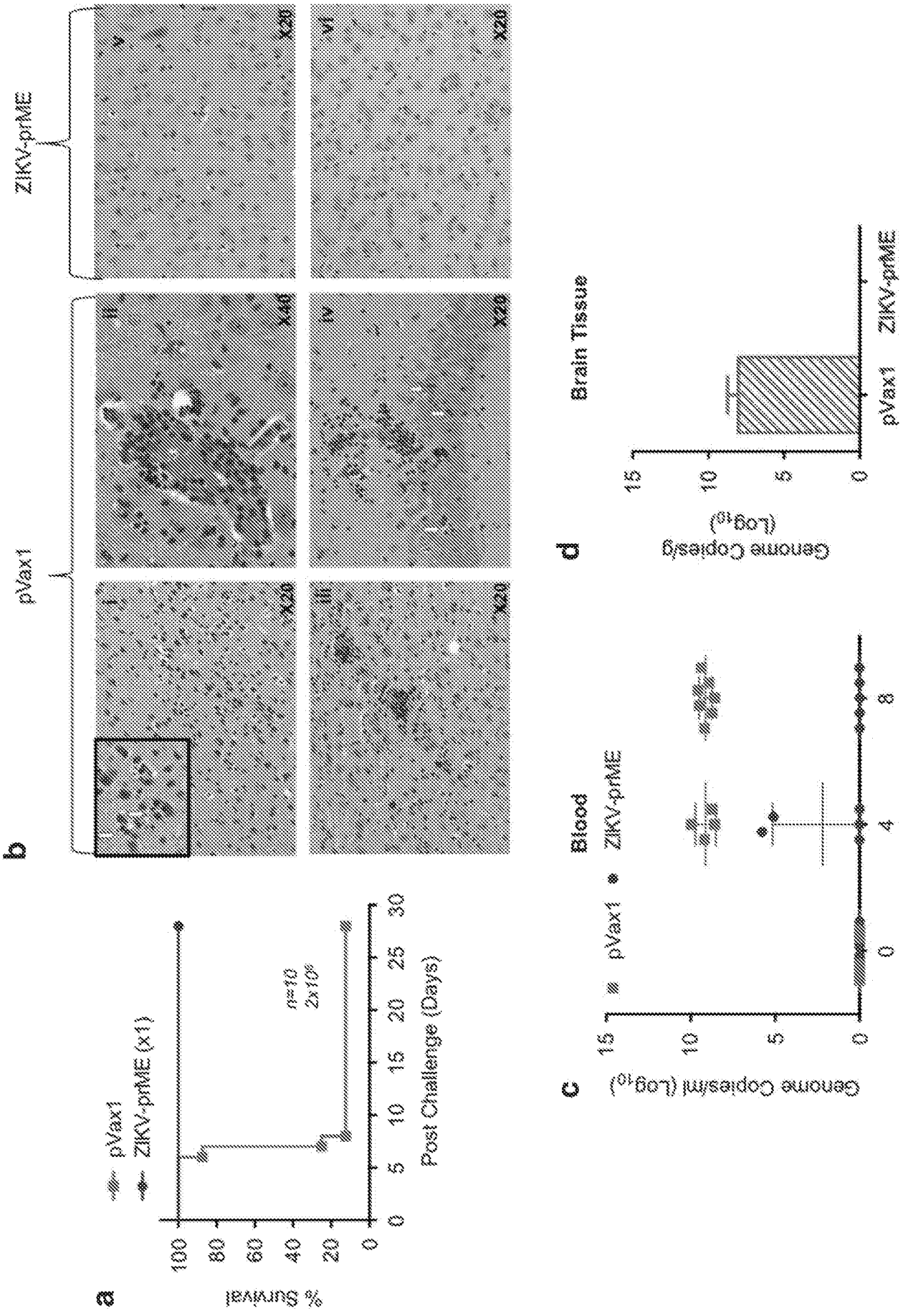


Figure 25A – Figure 25D

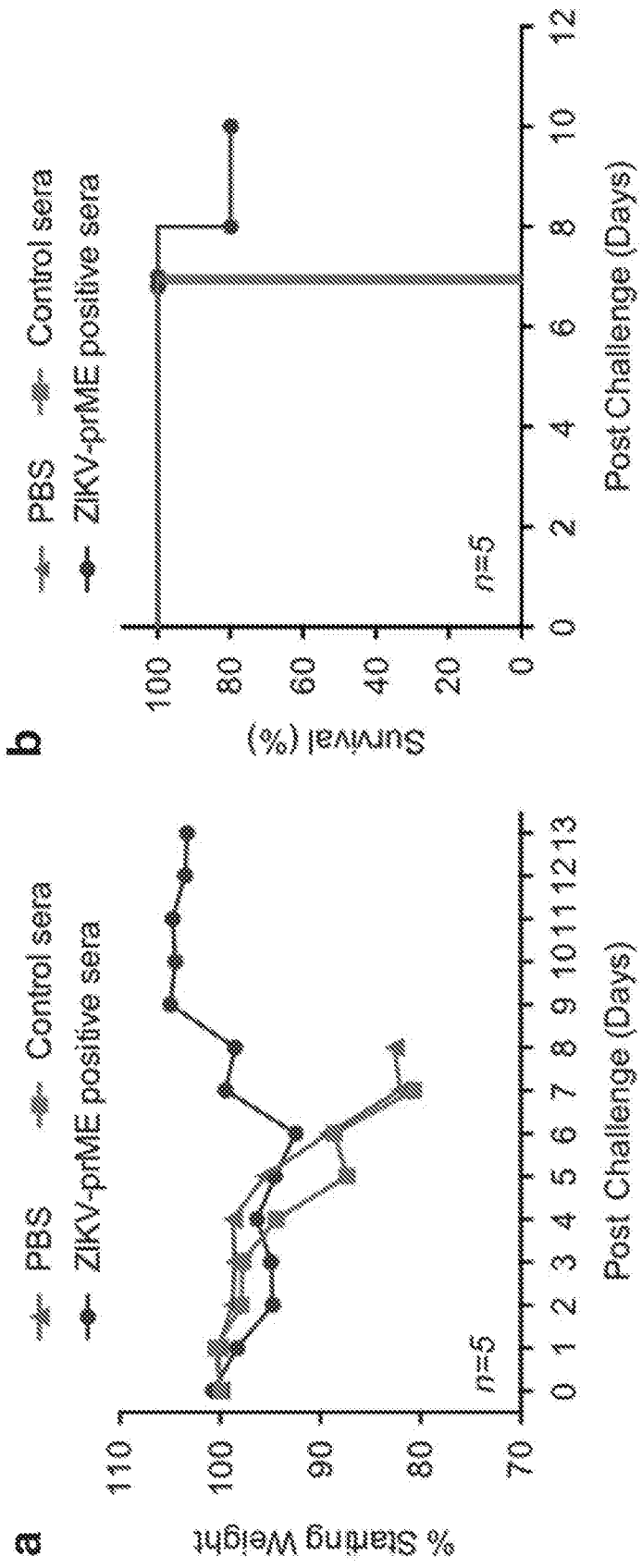


Figure 26A – Figure 26B

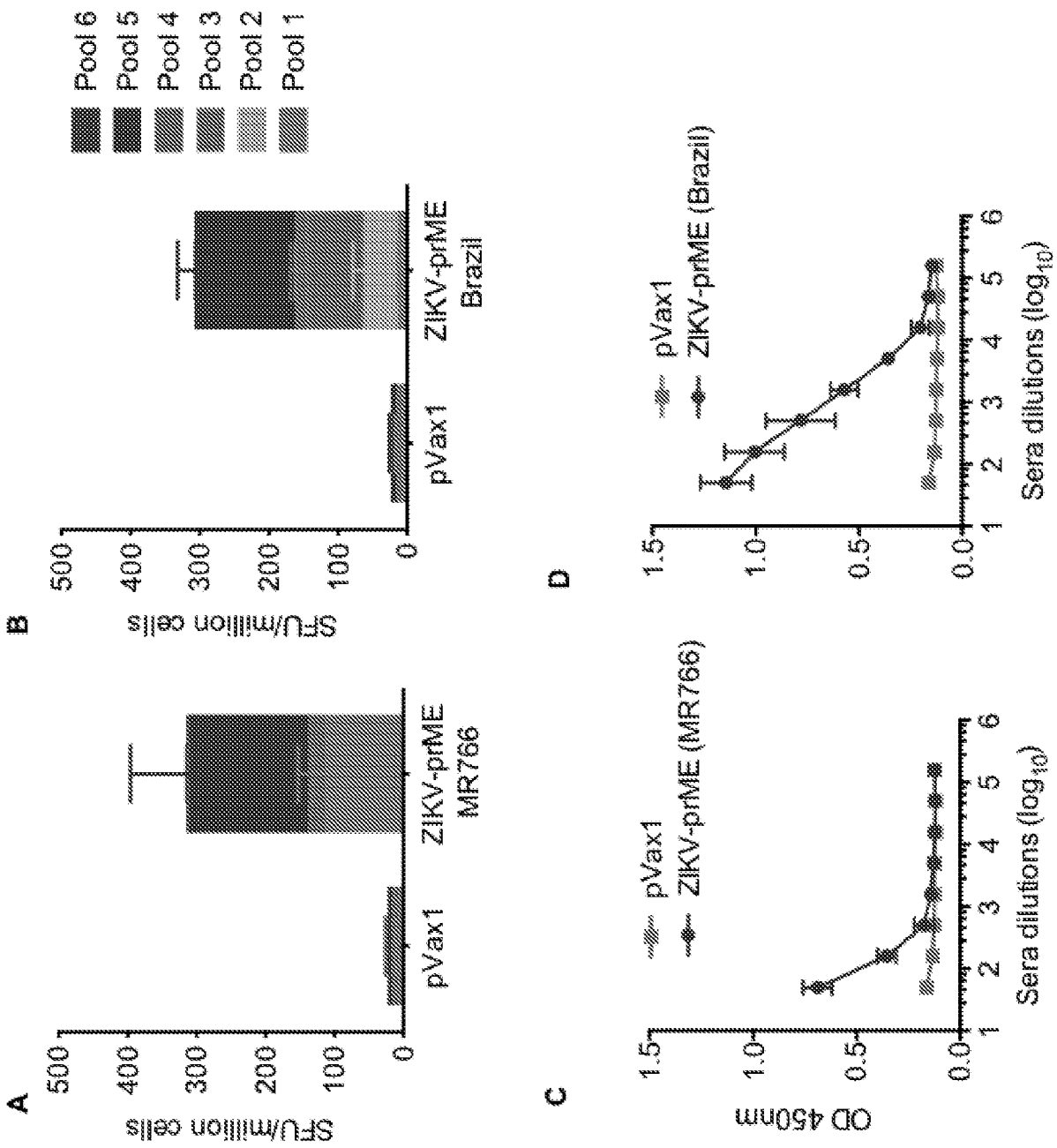


Figure 27A – Figure 27D

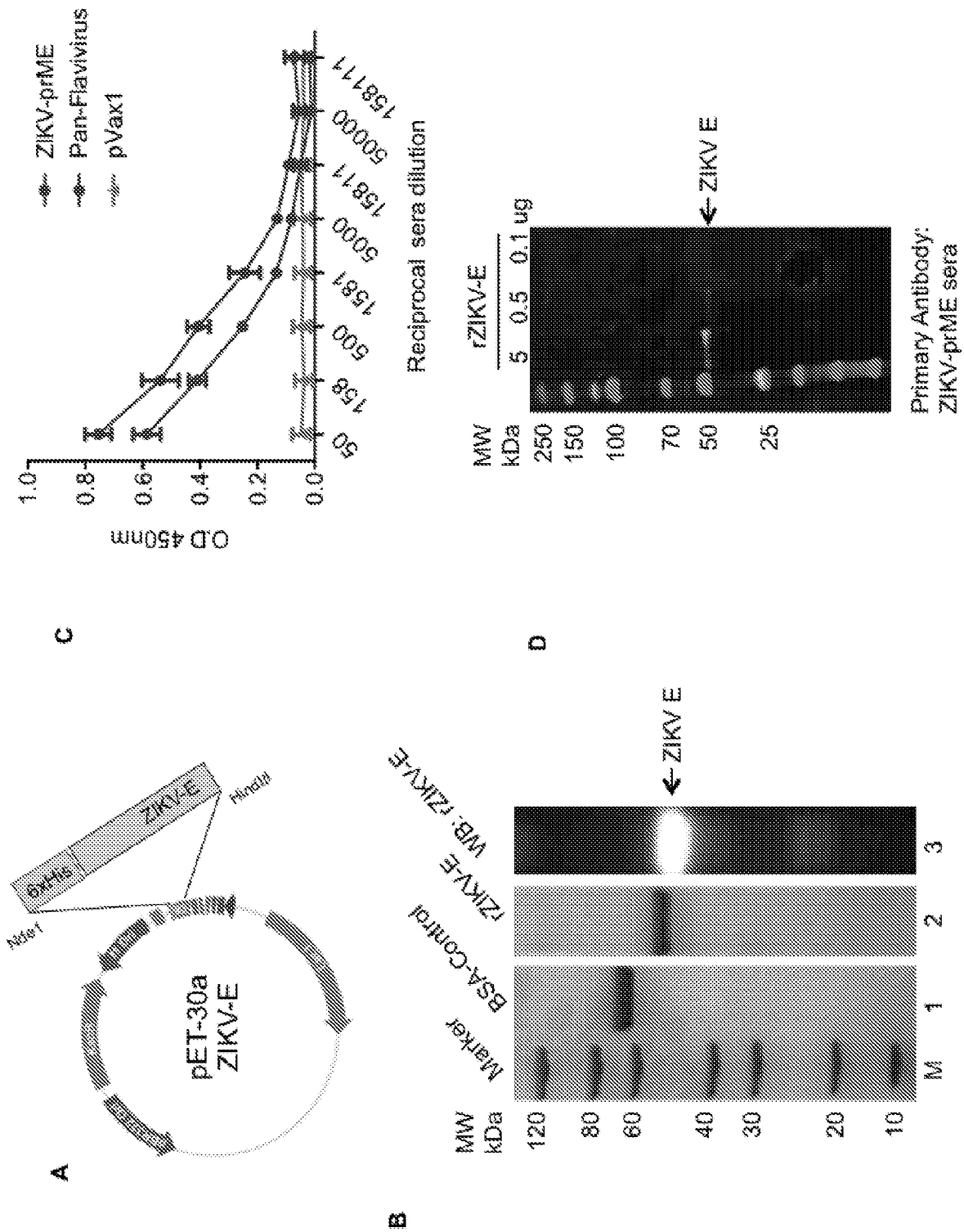


Figure 28A – Figure 28D

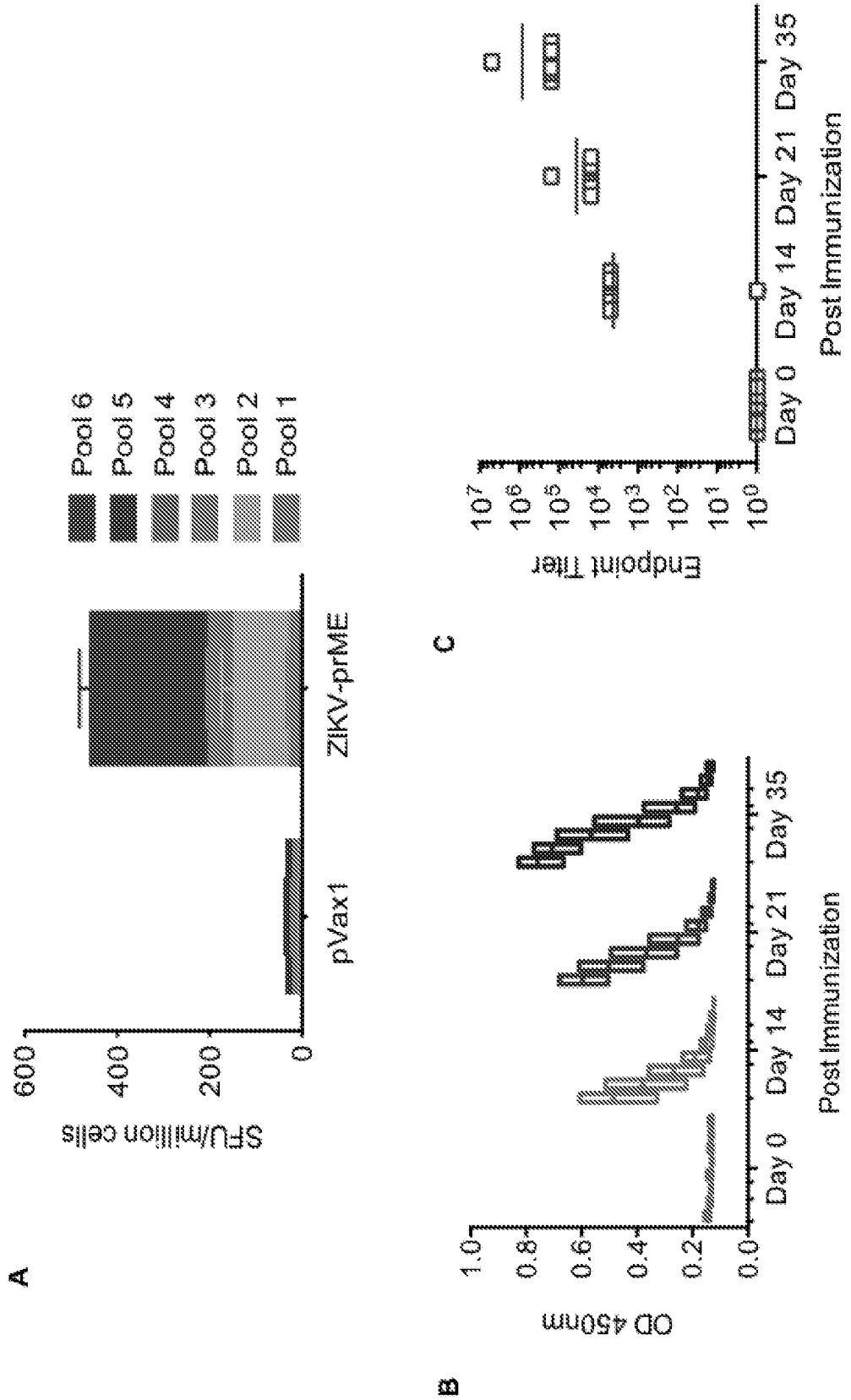


Figure 29A – Figure 29C

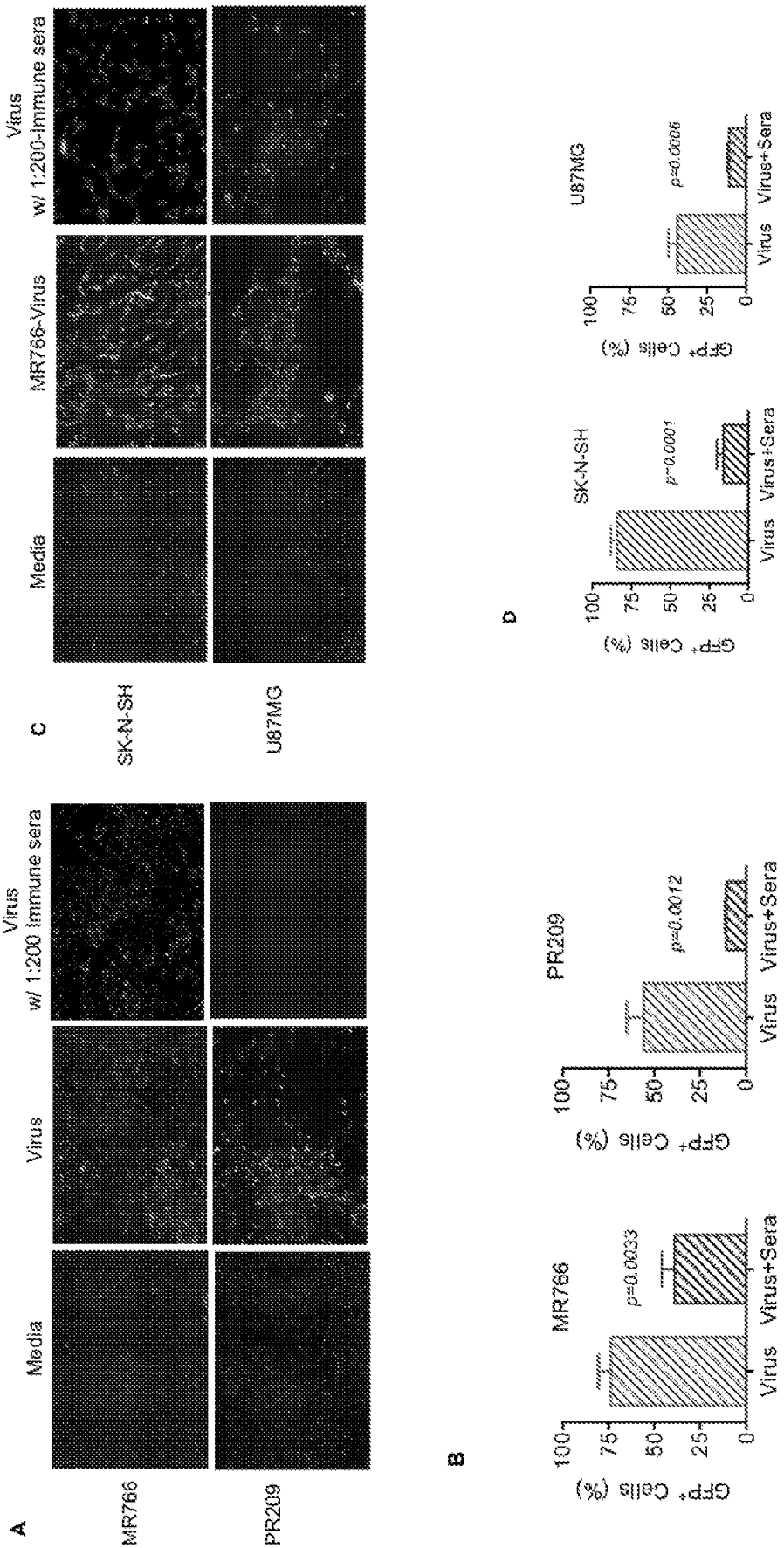


Figure 30A – Figure 30D

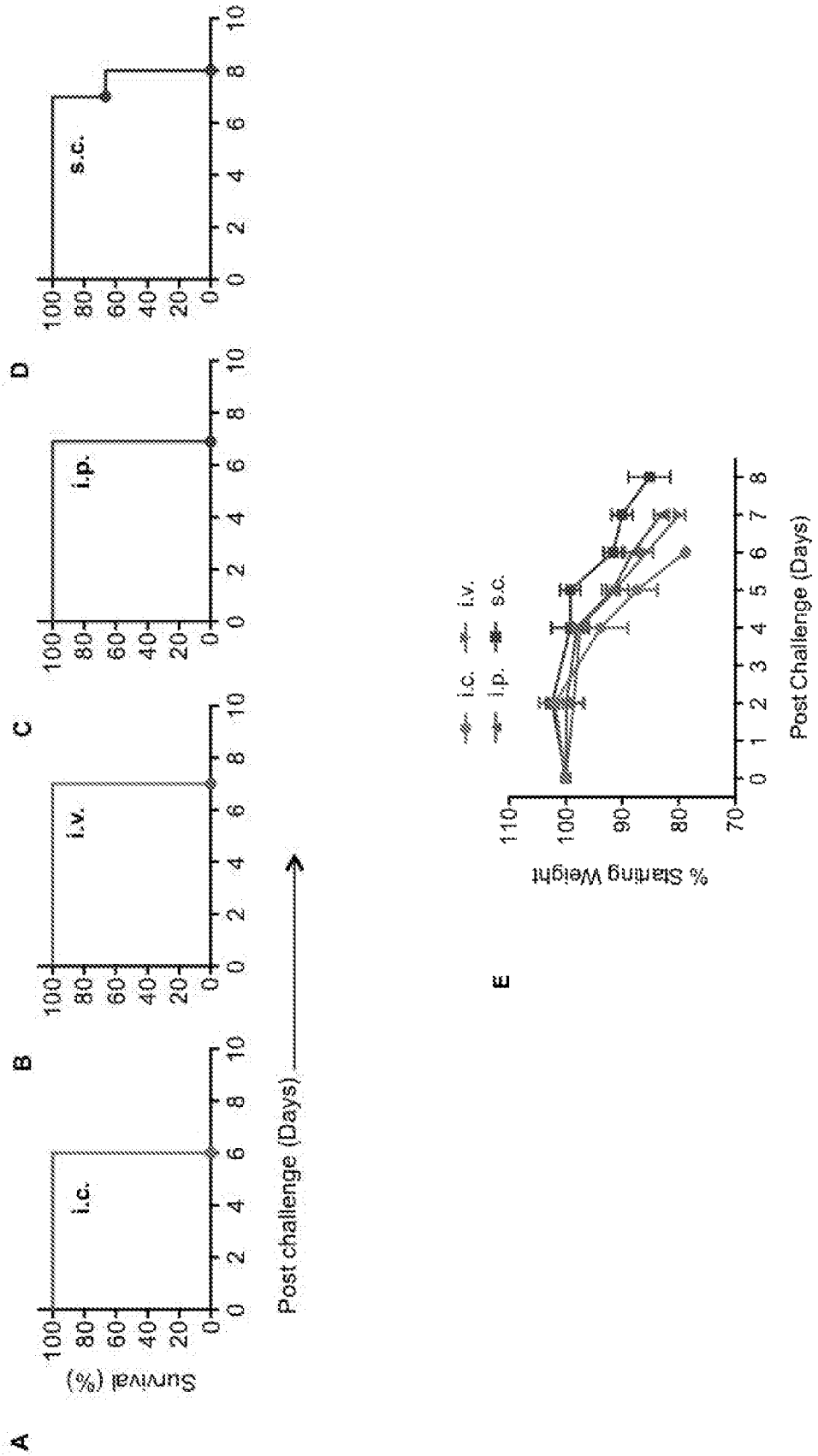


Figure 31A – Figure 31E

SEQUENCE LISTING

<110> WEINER, David
MUTHUMANI, Karupiah
Flingai, Seleeke
SARDESAI, Niranjan
Elliott, Sarah
Yan, Jian
Patel, Ami

<120> DNA ANTIBODY CONSTRUCTS AND METHOD OF USING SAME

<130> 206108-0033-30-WO.606194

<150> US 62/311,316
<151> 2016-03-21

<150> US 62/396,750
<151> 2016-09-19

<150> US 62/417,093
<151> 2016-11-03

<150> US 62/417,093
<151> 2016-11-03

<150> US 62/332,381
<151> 2016-05-04

<150> US 62/376,162
<151> 2016-08-17

<150> US 62/429,454
<151> 2016-12-02

<150> US 62/429,473
<151> 2016-12-02

<160> 171

<170> PatentIn version 3.5

<210> 1
<211> 738
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of HIV-1 Env-4E10 Ig

<400> 1

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Arg
20 25 30

Pro Gly Ser Ser Val Thr Val Ser Cys Lys Ala Ser Gly Gly Ser Phe
35 40 45

```
Ser Thr Tyr Ala Leu Ser Trp Val Arg Gln Ala Pro Gly Arg Gly Leu
    50                  55                  60

Glu Trp Met Gly Gly Val Ile Pro Leu Leu Thr Ile Thr Asn Tyr Ala
65                  70                  75                  80

Pro Arg Phe Gln Gly Arg Ile Thr Ile Thr Ala Asp Arg Ser Thr Ser
                85                  90                  95

Thr Ala Tyr Leu Glu Leu Asn Ser Leu Arg Pro Glu Asp Thr Ala Val
            100                 105                 110

Tyr Tyr Cys Ala Arg Glu Gly Thr Thr Gly Trp Gly Trp Leu Gly Lys
        115                 120                 125

Pro Ile Gly Ala Phe Ala His Trp Gly Gln Gly Thr Leu Val Thr Val
    130                 135                 140

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
145                 150                 155                 160

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
                165                 170                 175

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
            180                 185                 190

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
        195                 200                 205

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
    210                 215                 220

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
225                 230                 235                 240

Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro
                245                 250                 255

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
            260                 265                 270

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
        275                 280                 285

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
    290                 295                 300
```

```
Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
305                 310                 315                 320

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
                325                 330                 335

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
            340                 345                 350

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
        355                 360                 365

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
    370                 375                 380

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
385                 390                 395                 400

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
                405                 410                 415

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
            420                 425                 430

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
        435                 440                 445

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
    450                 455                 460

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys
465                 470                 475                 480

Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala
                485                 490                 495

Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr Gln Val
            500                 505                 510

Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Glu Ile Val
        515                 520                 525

Leu Thr Gln Ser Pro Gly Thr Gln Ser Leu Ser Pro Gly Glu Arg Ala
    530                 535                 540

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Asn Asn Lys Leu Ala
```

545 550 555 560

Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly
565 570 575

Ala Ser Ser Arg Pro Ser Gly Val Ala Asp Arg Phe Ser Gly Ser Gly
580 585 590

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp
595 600 605

Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Gln Ser Leu Ser Thr Phe
610 615 620

Gly Gln Gly Thr Lys Val Glu Lys Arg Thr Val Ala Ala Pro Ser Val
625 630 635 640

Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser
645 650 655

Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln
660 665 670

Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val
675 680 685

Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu
690 695 700

Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu
705 710 715 720

Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg
725 730 735

Gly Glu

<210> 2
<211> 768
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of HIV-1 Env-PG9 Ig

<400> 2

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

```
Thr His Ala Glu Phe Gly Leu Ser Trp Val Phe Leu Val Ala Phe Leu
            20                  25                  30

Arg Gly Val Gln Cys Gln Arg Leu Val Glu Ser Gly Gly Gly Val Val
        35                  40                  45

Gln Pro Gly Ser Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp
    50                  55                  60

Phe Ser Arg Gln Gly Met His Trp Val Arg Gln Ala Pro Gly Gln Gly
65                  70                  75                  80

Leu Glu Trp Val Ala Phe Ile Lys Tyr Asp Gly Ser Glu Lys Tyr His
                85                  90                  95

Ala Asp Ser Val Trp Gly Arg Leu Ser Ile Ser Arg Asp Asn Ser Lys
            100                 105                 110

Asp Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala
        115                 120                 125

Thr Tyr Phe Cys Val Arg Glu Ala Gly Gly Pro Asp Tyr Arg Asn Gly
    130                 135                 140

Tyr Asn Tyr Tyr Asp Phe Tyr Asp Gly Tyr Tyr Asn Tyr His Tyr Met
145                 150                 155                 160

Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
                165                 170                 175

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
            180                 185                 190

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
        195                 200                 205

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
    210                 215                 220

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
225                 230                 235                 240

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
                245                 250                 255

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
```

```
            260                 265                 270

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
        275                 280                 285

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
    290                 295                 300

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
305                 310                 315                 320

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
                325                 330                 335

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
            340                 345                 350

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
        355                 360                 365

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
    370                 375                 380

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
385                 390                 395                 400

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
                405                 410                 415

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
            420                 425                 430

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
        435                 440                 445

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
    450                 455                 460

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
465                 470                 475                 480

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
                485                 490                 495

Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser
            500                 505                 510
```

```
Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu
        515                 520                 525

Asn Pro Gly Pro Met Ala Trp Thr Pro Leu Phe Leu Phe Leu Leu Thr
    530                 535                 540

Cys Cys Pro Gly Gly Ser Asn Ser Gln Ser Ala Leu Thr Gln Pro Ala
545                 550                 555                 560

Ser Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser Cys Asn Gly
                565                 570                 575

Thr Ser Asn Asp Val Gly Gly Tyr Glu Ser Val Ser Trp Tyr Gln Gln
            580                 585                 590

His Pro Gly Lys Ala Pro Lys Val Val Ile Tyr Asp Val Ser Lys Arg
        595                 600                 605

Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr
    610                 615                 620

Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Gly Asp Tyr
625                 630                 635                 640

Tyr Cys Lys Ser Leu Thr Ser Thr Arg Arg Arg Val Phe Gly Thr Gly
                645                 650                 655

Thr Lys Leu Thr Val Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr
            660                 665                 670

Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu
        675                 680                 685

Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp
    690                 695                 700

Lys Ala Asp Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro
705                 710                 715                 720

Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu
                725                 730                 735

Thr Pro Glu Gln Trp Lys Ser His Lys Ser Tyr Ser Cys Gln Val Thr
            740                 745                 750

His Glu Gly Ser Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
        755                 760                 765
```

<210> 3
<211> 792
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding the Heavy Chain (VH-CH1) of HIV-1 Env Fab

<400> 3
aagcttgccg ccaccatgga gactgataca ctgctgctgt gggtgctgct gctgtgggtg 60

ccagggtcaa ccggagatgg ggctcaggtc cagctggtcc agagcggcgg acagatgaag 120

aaacccggcg agagcatgag gatctcctgc agagcatctg gatacgagtt catcgactgt 180

accctgaact ggattaggct ggctcctgga aagagaccag agtggatggg gtggctgaaa 240

ccacgagggg gagcagtgaa ttacgcccgg cccctgcagg gacgagtgac catgaccagg 300

gacgtgtaca gcgataccgc cttcctggag ctgcggtccc tgacagtgga cgatactgct 360

gtctacttct gcacacgcgg aaagaactgt gactataatt gggattttga acactggggc 420

cggggaacac ccgtgatcgt cagctccccc agtactaagg gaccttcagt gtttccactg 480

gccccctcta gtaaatccac ctctggaggg acagccgctc tgggatgcct ggtgaaagat 540

tatttccccg aacctgtgac cgtcagttgg aactcagggg ctctgacttc tggcgtgcac 600

acctttcctg cagtcctgca gtcaagcggg ctgtacagtc tgtcctctgt ggtcactgtg 660

cctagttcaa gcctgggcac tcagacctat atttgtaacg tgaatcataa gccatccaat 720

acaaaagtgg acaaaaaagc cgaacccaaa tcctgttacc cttatgatgt gcccgactac 780

gcctgactcg ag 792

<210> 4
<211> 756
<212> DNA
<213> Artificial Sequence

<220>
<223> Light Chain (VL-CL) of HIV-1 Env Fab

<400> 4
aagcttgccg ccaccatgga aaccgataca ctgctgctgt gggtgctgct gctgtgggtg 60

ccaggaagta ccggggatgg ggctcaggtc cagattgtgc tgactcagtc ccctgggacc 120

ctgtctctga gtccaggcga gacagctatc atttcatgcc gaactagcca gtacggcagc 180

ctggcttggt atcagcagcg accaggacag gcaccacgac tggtcatcta ctcaggcagc 240

acaagggccg ctggcatccc cgacaggttc tccggcagca ggtgggggcc tgattacaac 300

ctgactatct ctaatctgga gagtggggac tttggcgtgt actattgcca gcagtatgag 360

ttcttcggcc agggaactaa ggtgcaggtg gacatcaaaa gaaccgtggc agccccatcc 420

gtcttcattt ttccccttc tgatgagcag ctgaagtcag gcaccgccag cgtggtctgt 480

ctgctgaaca atttctaccc ccgggaagcc aaggtgcagt ggaaagtgga caacgctctg 540

cagagtggaa attcacagga gagcgtgacc gaacaggact ccaaggattc tacatatagt 600

ctgagcagca ccctgaccct gagtaaagca gattacgaga agcacaaagt gtatgcctgt 660

gaagtcacac atcagggcct gaggagcccc gtgactaaaa gtttcaaccg aggagagtgc 720

taccttatg atgtgcccga ctacgcctaa ctcgag 756

<210> 5
<211> 731
<212> PRT
<213> Artificial Sequence

<220>
<223> VRC01 IgG

<400> 5

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1 5 10 15

His Ser Gln Val Gln Leu Val Gln Ser Gly Gly Gln Met Lys Lys Pro
20 25 30

Gly Glu Ser Met Arg Ile Ser Cys Arg Ala Ser Gly Tyr Glu Phe Ile
35 40 45

Asp Cys Thr Leu Asn Trp Ile Arg Leu Ala Pro Gly Lys Arg Pro Glu
50 55 60

Trp Met Gly Trp Leu Lys Pro Arg Gly Gly Ala Val Asn Tyr Ala Arg
65 70 75 80

Pro Leu Gln Gly Arg Val Thr Met Thr Arg Asp Val Tyr Ser Asp Thr
85 90 95

Ala Phe Leu Glu Leu Arg Ser Leu Thr Val Asp Asp Thr Ala Val Tyr
100 105 110

Phe Cys Thr Arg Gly Lys Asn Cys Asp Tyr Asn Trp Asp Phe Glu His
115 120 125

Trp Gly Arg Gly Thr Pro Val Ile Val Ser Ser Pro 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 Lys Ala Glu Pro Lys
225                 230                 235                 240

Ser Cys Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
    370                 375                 380

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
385                 390                 395                 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415
```

```
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg
465                 470                 475                 480

Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp
                485                 490                 495

Val Glu Glu Asn Pro Gly Pro Met Asp Trp Thr Trp Ile Leu Phe Leu
            500                 505                 510

Val Ala Ala Ala Thr Arg Val His Ser Glu Ile Val Leu Thr Gln Ser
        515                 520                 525

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Thr Ala Ile Ile Ser Cys
    530                 535                 540

Arg Thr Ser Gln Tyr Gly Ser Leu Ala Trp Tyr Gln Gln Arg Pro Gly
545                 550                 555                 560

Gln Ala Pro Arg Leu Val Ile Tyr Ser Gly Ser Thr Arg Ala Ala Gly
                565                 570                 575

Ile Pro Asp Arg Phe Ser Gly Ser Arg Trp Gly Pro Asp Tyr Asn Leu
            580                 585                 590

Thr Ile Ser Asn Leu Glu Ser Gly Asp Phe Gly Val Tyr Tyr Cys Gln
        595                 600                 605

Gln Tyr Glu Phe Phe Gly Gln Gly Thr Lys Val Gln Val Asp Ile Lys
    610                 615                 620

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
625                 630                 635                 640

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
                645                 650                 655

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
            660                 665                 670
```

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
675 680 685

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
690 695 700

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Arg Ser
705 710 715 720

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
725 730

<210> 6
<211> 819
<212> DNA
<213> Artificial Sequence

<220>
<223> Optimized Nucleic Acid Sequence Encoding IgG Heavy Chain

<400> 6
ggatccgcca ccatggaaac cgacactctg ctgctgtggg tgctgctgct gtgggtgccc 60

ggctcaacag gcgacggcgc tcaggtccag ctggtccagt ctggagctgt gatcaagacc 120

cctggcagct ccgtcaaaat ttcttgcaga gcaagtggct acaacttccg ggactatagc 180

atccactggg tgcggctgat tcctgataag ggatttgagt ggatcggctg gatcaagcca 240

ctgtggggcg ctgtgtccta cgcaaggcag ctgcaggggc gcgtctccat gacacgacag 300

ctgtctcagg acccagacga tcccgattgg ggggtggcct acatggagtt cagtggactg 360

actcccgcag acaccgccga tatttttgc gtgcggagag gctcctgcga ctactgtggg 420

gatttcccat ggcagtattg gtgtcaggga actgtggtcg tggtctctag tgcatcaacc 480

aagggcccca gcgtgtttcc tctggcccca tcaagcaaaa gtacatcagg aggaactgca 540

gctctgggat gtctggtgaa ggattacttc cccgagcctg tgaccgtcag ctggaactcc 600

ggagcactga cctccggagt gcacacattt cccgctgtcc tgcagtcctc tgggctgtac 660

tctctgagtt cagtggtcac agtgcctagc tcctctctgg gcacccagac atatatctgc 720

aacgtcaatc ataagccaag taatactaaa gtggacaaga aagtcgaacc caaatcatgt 780

taccctatg acgtgcctga ttatgcttga taactcgag 819

<210> 7
<211> 753
<212> DNA
<213> Artificial Sequence

<220>
<223> Optimized Nucleic Acid Sequence Encoding IgG Light Chain

<400> 7
ggatccgcca ccatggagac tgatacactg ctgctgtggg tgctgctgct gtgggtgcct 60

ggctcaaccg gcgacggggc tcaggtccag attgtgctga cccagagccc tggcatcctg 120

tcactgagcc caggagagac cgcaacactg ttctgcaagg cctcccaggg cgggaacgct 180

atgacatggt accagaaacg gagaggacag gtgccccgac tgctgatcta tgacacttca 240

aggcgagcaa gcggagtgcc tgatcgattt gtcggcagcg gctctgggac agacttcttt 300

ctgactatta ataagctgga cagagaggat ttcgctgtgt actattgcca gcagtttgaa 360

ttctttggac tgggcagcga gctggaagtg cacaggaccg tcgccgctcc aagtgtgttc 420

atttttcccc ctagcgatga gcagctgaaa tccgggacag cctctgtggt ctgtctgctg 480

aacaatttct acccccgcga agcaaaggtg cagtggaaag tcgacaacgc cctgcagagt 540

ggcaattcac aggagagcgt gaccgaacag gactccaagg attctacata tagtctgagc 600

tccactctga ccctgtctaa agctgattac gagaagcaca aagtgtatgc atgcgaagtc 660

actcatcagg gcctgtctag tcctgtgacc aagagcttta accgagggga gtgttaccca 720

tatgacgtcc ccgattacgc ctgataactc gag 753

<210> 8
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> IgE1 Signal Peptide of VRC-1 IgG

<400> 8

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1 5 10 15

His Ser

<210> 9
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Variable Heavy Region of VRC01 IgG

<400> 9

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

Ser Met Arg Ile Ser Cys Arg Ala Ser Gly Tyr Glu Phe Ile Asp Cys
20 25 30

```
Thr Leu Asn Trp Ile Arg Leu Ala Pro Gly Lys Arg Pro Glu Trp Met
        35                  40                  45

Gly Trp Leu Lys Pro Arg Gly Gly Ala Val Asn Tyr Ala Arg Pro Leu
    50                  55                  60

Gln Gly Arg Val Thr Met Thr Arg Asp Val Tyr Ser Asp Thr Ala Phe
65                  70                  75                  80

Leu Glu Leu Arg Ser Leu Thr Val Asp Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95

Thr Arg Gly Lys Asn Cys Asp Tyr Asn Trp Asp Phe Glu His Trp Gly
            100                 105                 110

Arg Gly Thr Pro Val Ile Val Ser Ser Pro Ser Thr Lys Gly
        115                 120                 125
```

<210> 10
<211> 98
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Heavy region 1 (CH1) of VRC01 IgG

<400> 10

```
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
1               5                   10                  15

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
            20                  25                  30

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
        35                  40                  45

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

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
65                  70                  75                  80

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Ala Glu Pro Lys
                85                  90                  95

Ser Cys
```

<210> 11
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge Region of VRC01 IgG

<400> 11

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
1 5 10 15

<210> 12
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Heavy Region 2 (CH2) of VRC01 IgG

<400> 12

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1 5 10 15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
20 25 30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65 70 75 80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
85 90 95

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
100 105 110

<210> 13
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Heavy Region 3 (CH3) of VRC01 IgG

<400> 13

```
Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp
1               5                   10                  15

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
            20                  25                  30

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
        35                  40                  45

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
    50                  55                  60

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
65                  70                  75                  80

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
                85                  90                  95

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
            100                 105
```

<210> 14
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Furin Cleavage Site of VRC01 IgG

<400> 14

```
Arg Gly Arg Lys Arg Arg Ser
1               5
```

<210> 15
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> GSG Linker and P2A Peptide of VRC01 IgG

<400> 15

```
Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
1               5                   10                  15

Glu Glu Asn Pro Gly Pro
            20
```

<210> 16
<211> 104
<212> PRT

<213> Artificial Sequence

<220>
<223> Variable Light Region (VL) of VRC01 IgG

<400> 16

```
Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1               5                  10                  15

Glu Thr Ala Ile Ile Ser Cys Arg Thr Ser Gln Tyr Gly Ser Leu Ala
            20                  25                  30

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

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

Trp Gly Pro Asp Tyr Asn Leu Thr Ile Ser Asn Leu Glu Ser Gly Asp
65                  70                  75                  80

Phe Gly Val Tyr Tyr Cys Gln Gln Tyr Glu Phe Phe Gly Gln Gly Thr
                85                  90                  95

Lys Val Gln Val Asp Ile Lys Arg
            100
```

<210> 17
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Light Region (CL, kappa) of VRC01 IgG

<400> 17

```
Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
1               5                  10                  15

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

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
        35                  40                  45

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
    50                  55                  60

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
65                  70                  75                  80
```

```
His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Arg Ser Pro
                85                  90                  95

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
            100                 105
```

<210> 18
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IgG Heavy Chain Signal Peptide of HIV-1 Env-PG9 Ig

<400> 18

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                   10                  15

Thr His Ala
```

<210> 19
<211> 154
<212> PRT
<213> Artificial Sequence

<220>
<223> Variable Heavy Region of HIV-1 Env-PG9 Ig

<400> 19

```
Glu Phe Gly Leu Ser Trp Val Phe Leu Val Ala Phe Leu Arg Gly Val
1               5                   10                  15

Gln Cys Gln Arg Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly
            20                  25                  30

Ser Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Arg
        35                  40                  45

Gln Gly Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp
    50                  55                  60

Val Ala Phe Ile Lys Tyr Asp Gly Ser Glu Lys Tyr His Ala Asp Ser
65                  70                  75                  80

Val Trp Gly Arg Leu Ser Ile Ser Arg Asp Asn Ser Lys Asp Thr Leu
                85                  90                  95

Tyr Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Thr Tyr Phe
```

100 105 110

Cys Val Arg Glu Ala Gly Gly Pro Asp Tyr Arg Asn Gly Tyr Asn Tyr
115 120 125

Tyr Asp Phe Tyr Asp Gly Tyr Tyr Asn Tyr His Tyr Met Asp Val Trp
130 135 140

Gly Lys Gly Thr Thr Val Thr Val Ser Ser
145 150

<210> 20
<211> 98
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Heavy region 1 (CH1) of HIV-1 Env-PG9 Ig

<400> 20

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

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

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val

<210> 21
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge Region of HIV-1 Env-PG9 Ig

<400> 21

```
Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
1               5                   10                  15
```

<210> 22
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Heavy Region 2 (CH2) of HIV-1 Env-PG9 Ig

<400> 22

```
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1               5                   10                  15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            20                  25                  30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
        35                  40                  45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50                  55                  60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65                  70                  75                  80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
            100                 105                 110
```

<210> 23
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Heavy Region 3 (CH3) of HIV-1 Env-PG9 Ig

<400> 23

```
Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp
1               5                   10                  15

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
            20                  25                  30

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
        35                  40                  45
```

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
50 55 60

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
65 70 75 80

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
85 90 95

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
100 105

<210> 24
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Furin Cleavage Site of HIV-1 Env-PG9 Ig

<400> 24

Arg Gly Arg Lys Arg Arg Ser
1 5

<210> 25
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> GSG Linker and P2A Peptide of HIV-1 Env-PG9 Ig

<400> 25

Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
1 5 10 15

Glu Glu Asn Pro Gly Pro
20

<210> 26
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Human Lamba Light Chain Signal Peptide of HIV-1 Env-PG9 Ig

<400> 26

Met Ala Trp Thr Pro Leu Phe Leu Phe Leu Leu Thr Cys Cys Pro Gly
1 5 10 15

Gly Ser Asn Ser
20

<210> 27
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<223> Variable Light Region (VL) of HIV-1 Env-PG9 Ig

<400> 27

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 Asn Gly Thr Ser Asn Asp Val Gly Gly Tyr
20 25 30

Glu Ser Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Val
35 40 45

Val Ile Tyr Asp Val Ser Lys 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 Gly Asp Tyr Tyr Cys Lys Ser Leu Thr Ser Thr
85 90 95

Arg Arg Arg Val Phe Gly Thr Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 28
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Light Region (CL, lamba) of HIV-1 Env-PG9 Ig

<400> 28

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

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
20 25 30

Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
35 40 45

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
50 55 60

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
65 70 75 80

Ser His Lys Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
85 90 95

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
100 105

<210> 29
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IgG Heavy Chain Signal Peptide of HIV-1 Env-4E10 Ig

<400> 29

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala

<210> 30
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<223> Variable Heavy Region of HIV-1 Env-4E10 Ig

<400> 30

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

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

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

Gly Gly Val Ile Pro Leu Leu Thr Ile Thr Asn Tyr Ala Pro Arg Phe
50 55 60

Gln Gly Arg Ile Thr Ile Thr Ala Asp Arg Ser Thr Ser Thr Ala Tyr
65 70 75 80

Leu Glu Leu Asn Ser Leu Arg Pro Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Gly Thr Thr Gly Trp Gly Trp Leu Gly Lys Pro Ile Gly
100 105 110

Ala Phe Ala His Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 31
<211> 98
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Heavy region 1 (CH1) of HIV-1 Env-4E10 Ig

<400> 31

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

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

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val

<210> 32
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge Region of HIV-1 Env-4E10 Ig

<400> 32

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro

1 5 10 15

<210> 33
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Heavy Region 2 (CH2) of HIV-1 Env-4E10 Ig

<400> 33

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1 5 10 15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
20 25 30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65 70 75 80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
85 90 95

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
100 105 110

<210> 34
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Heavy Region 3 (CH3) of HIV-1 Env-4E10 Ig

<400> 34

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp
1 5 10 15

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
20 25 30

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
35 40 45

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
50 55 60

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
65 70 75 80

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
85 90 95

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
100 105

<210> 35
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Furin Cleavage Site of HIV-1 Env-4E10 Ig

<400> 35

Arg Gly Arg Lys Arg Arg Ser
1 5

<210> 36
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> GSG Linker and P2A Peptide of HIV-1 Env-4E10 Ig

<400> 36

Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
1 5 10 15

Glu Glu Asn Pro Gly Pro
20

<210> 37
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Human Kappa Light Chain Signal Peptide of HIV-1 Env-4E10 Ig

<400> 37

Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser
1 5 10 15

Gly Ala Tyr Gly

20

<210> 38
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> Variable Light Region (VL) of HIV-1 Env-4E10 Ig

<400> 38

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

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Asn Asn
20 25 30

Lys 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 Pro Ser Gly Val Ala 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 Gln Ser Leu
85 90 95

Ser Thr Phe Gly Gln Gly Thr Lys Val Glu
100 105

<210> 39
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Constant Light Region (CL, kappa) of HIV-1 Env-4E10 Ig

<400> 39

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
1 5 10 15

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
20 25 30

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
35 40 45

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
50 55 60

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
65 70 75 80

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
85 90 95

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu
100 105

<210> 40
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding the VH-CH1 of anti-Her-2 Fab

<400> 40
ggatccgcca ccatggactg gacatggatt ctgtttctgg tcgccgccgc tacaagagtg 60

cattccgaag tgcagctggt cgagagtgga gggggactgg tgcagcccgg cggatctctg 120

cgactgagtt gcgccgcttc aggcttcacc tttacagact acaccatgga ttgggtgaga 180

caggcacctg gcaagggact ggagtgggtg gctgatgtca acccaaatag tgggggctca 240

atctacaacc agaggttcaa gggcaggttc accctgagcg tggacaggtc caaaaacact 300

ctgtatctgc agatgaattc tctgcgggct gaagataccg cagtctacta ttgcgcccgc 360

aatctgggcc caagcttcta ctttgactat tgggggcagg gcacactggt gactgtcagc 420

tccgcttcta caaagggacc aagcgtgttc ccactggcac cctctagtaa atccacctct 480

ggagggacag cagccctggg ctgtctggtg aaagactatt tccccgagcc tgtgactgtc 540

agctggaact ccggagcact gactagcgga gtgcacacct ttccagccgt cctgcagtca 600

agcggcctgt actccctgtc ctctgtggtc acagtgccta gttcaagcct gggaactcag 660

acctatattt gtaatgtgaa ccataaacca agcaatacaa aggtggacaa gaaggtggaa 720

ccaaaatcct gctgataact cgag 744

<210> 41
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of the VH-CH1 of anti-Her-2 Fab

<400> 41

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val

```
1               5                   10                  15

His Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
            20                  25                  30

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr
        35                  40                  45

Asp Tyr Thr Met Asp Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
    50                  55                  60

Trp Val Ala Asp Val Asn Pro Asn Ser Gly Gly Ser Ile Tyr Asn Gln
65                  70                  75                  80

Arg Phe Lys Gly Arg Phe Thr Leu Ser Val Asp Arg Ser Lys Asn Thr
                85                  90                  95

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
            100                 105                 110

Tyr Cys Ala Arg Asn Leu Gly Pro Ser Phe Tyr Phe Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
    130                 135                 140

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
145                 150                 155                 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
                165                 170                 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
            180                 185                 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
        195                 200                 205

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
    210                 215                 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
225                 230                 235                 240
```

<210> 42
<211> 720
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding the VL-CL of anti-Her-2 Fab

<400> 42
ggatccgcca ccatggattg gacttggatt ctgttcctgg tcgccgccgc tacccgcgtg 60

cattccgata ttcagatgac tcagagcccc tcctcactgt cagccagcgt gggcgaccga 120

gtcaccatca catgcaaagc ttctcaggat gtgagtattg gggtcgcatg gtaccagcag 180

aagccaggca aagcacccaa gctgctgatc tattccgcct cttacaggta tacaggagtg 240

cccagcagat tcagtggctc aggaagcggg actgacttta ctctgaccat cagctccctg 300

cagcctgagg atttcgctac ctactattgc cagcagtact atatctaccc atatacctttt 360

ggccagggaa caaaagtgga gatcaagcgg accgtggccg ctccctccgt cttcatttttt 420

ccccccttctg acgaacagct gaagagcgga acagcaagcg tggtctgtct gctgaacaat 480

ttctaccctc gcgaggccaa agtgcagtgg aaggtcgata acgctctgca gtccgggaat 540

tctcaggaga gtgtgactga acaggactca aaagatagca cctattccct gtctagtaca 600

ctgactctga gcaaggcaga ctacgaaaag cacaaagtgt atgcctgtga ggtcacccac 660

caggggctgt caagtcccgt caccaagtcc ttcaatagag gcgaatgctg ataactcgag 720

<210> 43
<211> 232
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of the VL-CL of anti-Her-2 Fab

<400> 43

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1 5 10 15

His Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
20 25 30

Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Ser
35 40 45

Ile Gly Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu
50 55 60

Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Ser Arg Phe
65 70 75 80

Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
85 90 95

```
Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Tyr Ile Tyr
            100                 105                 110

Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val
        115                 120                 125

Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys
    130                 135                 140

Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
145                 150                 155                 160

Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
                165                 170                 175

Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
            180                 185                 190

Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
        195                 200                 205

Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
    210                 215                 220

Lys Ser Phe Asn Arg Gly Glu Cys
225                 230
```

<210> 44
<211> 2241
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding anti-DENV Human IgG

<400> 44

```
ggatccgcca ccatggactg gacttggagg attctgtttc tggtcgccgc cgctactggg       60

actcacgctc aggcacatct ggtcgaatct ggaggaggag tggtccagcc tggccgatcc      120

ctgcgactgt cttgcgcagc tagcgccttc aacttcagca caaacgcaat gcactgggtg      180

cgacaggcac caggcaaggg actggagtgg gtcgctgtga tctcatacga cggaagccat      240

aagtactatg cagattctgt gaaaggccgg ttcaccattt ccagggacaa ttctaagaac      300

accctgtatc tgcagatgaa tagcctgcgc gcagccgata ccgcagtgta ctattgcgca      360

actgtcggcg tgctgacctg gccagtgaac gccgaatact ttcaccattg gggacagggc      420

agtctggtct cagtgagctc cgcaagtact aagggaccat cagtgttccc actggcaccc      480

tctagtaaat ctactagtgg cgggaccgct gcactgggat gtctggtgaa ggactatttc      540
```

cccgagcctg tcaccgtgag ctggaattcc ggagccctga caagcggcgt ccacactttt 600
cccgctgtgc tgcagtcaag cggactgtac tccctgtcct ctgtggtcac tgtgcctagt 660
tcaagcctgg gcactcagac ctatatctgc aatgtgaacc acaagccctc taacaccaaa 720
gtcgacaaga aagtggaacc taagagctgt gataaaacac atacttgccc accttgtcca 780
gcaccagagc tgctgggagg accaagcgtg ttcctgtttc cacccaagcc taaagacaca 840
ctgatgatta gccggacacc tgaagtcact tgcgtggtcg tggacgtgtc ccacgaggac 900
cccgaagtca agtttaattg gtacgtggat ggcgtcgagg tgcataacgc caagaccaaa 960
ccccgggagg aacagtacaa tagcacatat agagtcgtgt ccgtcctgac tgtgctgcat 1020
caggattggc tgaatgggaa ggagtataag tgcaaagtgt ctaacaaggc tctgcctgca 1080
ccaatcgaga aaaccattag caaggctaaa ggccagccta gggaaccaca ggtgtacaca 1140
ctgcctccaa gtcgcgacga gctgaccaag aatcaggtct ccctgacatg tctggtgaaa 1200
ggcttctatc catcagatat cgccgtggag tgggaaagca acgggcagcc cgaaaacaat 1260
tacaagacca cacccctgt gctggactct gatggcagtt tctttctgta ttctaagctg 1320
accgtggaca aaagtagatg gcagcagggg aatgtctttt catgtagcgt gatgcacgag 1380
gccctgcaca accattacac acagaagtcc ctgtctctga gtcccggaaa gaggggccgc 1440
aaacggagat cagggagcgg agctactaat ttcagcctgc tgaaacaggc aggggatgtg 1500
gaggaaaacc ccggacctat ggcttggacc ccactgttcc tgtttctgct gacatgctgt 1560
cccgggggca gcaattctca gagtgtcctg acacagccac catcagtgag cggagcacca 1620
ggacagaggg tgaccatctc ctgcacaggc agcagcagca acattggcgc cgggtacgac 1680
gtgcattggt atcagcagct gcccggcacc gctcctaagc tgctgatctg tggcaacaat 1740
aaccgcccat ctggggtgcc cgatcgattc tccggctcta aaagtgggac ttcagccagc 1800
ctggctatta ccggcctgca ggccgaggac gaagctgatt actattgcca gagctacgac 1860
tcaagcctga ccggagtcgt gttcggagga ggaaccaagc tgacagtcct gggacagcct 1920
aaagccgctc caagcgtgac actgtttcct ccatcctctg aggaactgca ggcaaacaag 1980
gccaccctgg tgtgcctgat ttccgacttc taccccgggg cagtcactgt ggcttggaag 2040
gcagatagtt cacctgtcaa agccggagtg gagactacca caccatcaaa gcagagcaat 2100
aacaaatacg cagccagctc ctatctgtcc ctgaccctg agcagtggaa gtctcacaaa 2160
tcctattctt gccaggtcac tcacgaagga agcactgtgg agaaaactgt cgcaccaacc 2220
gaatgtagtt gataactcga g 2241

<210> 45
<211> 739
<212> PRT

<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of anti-DENV Human IgG

<400> 45

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                  10                  15

Thr His Ala Gln Ala His Leu Val Glu Ser Gly Gly Gly Val Val Gln
            20                  25                  30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Ala Phe Asn Phe
        35                  40                  45

Ser Thr Asn Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    50                  55                  60

Glu Trp Val Ala Val Ile Ser Tyr Asp Gly Ser His Lys Tyr Tyr Ala
65                  70                  75                  80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
                85                  90                  95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Ala Asp Thr Ala Val
            100                 105                 110

Tyr Tyr Cys Ala Thr Val Gly Val Leu Thr Trp Pro Val Asn Ala Glu
        115                 120                 125

Tyr Phe His His Trp Gly Gln Gly Ser Leu Val Ser Val Ser Ser Ala
    130                 135                 140

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
145                 150                 155                 160

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
                165                 170                 175

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
            180                 185                 190

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
        195                 200                 205

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
    210                 215                 220
```

```
Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
225                 230                 235                 240

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
                245                 250                 255

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
            260                 265                 270

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
        275                 280                 285

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
    290                 295                 300

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
305                 310                 315                 320

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                325                 330                 335

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            340                 345                 350

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        355                 360                 365

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
    370                 375                 380

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
385                 390                 395                 400

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                405                 410                 415

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            420                 425                 430

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
        435                 440                 445

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
    450                 455                 460

Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser
465                 470                 475                 480
```

```
Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
                485                 490                 495

Glu Glu Asn Pro Gly Pro Met Ala Trp Thr Pro Leu Phe Leu Phe Leu
            500                 505                 510

Leu Thr Cys Cys Pro Gly Gly Ser Asn Ser Gln Ser Val Leu Thr Gln
        515                 520                 525

Pro Pro Ser Val Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys
    530                 535                 540

Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His Trp Tyr
545                 550                 555                 560

Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Cys Gly Asn Asn
                565                 570                 575

Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly
            580                 585                 590

Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala
        595                 600                 605

Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser Leu Thr Gly Val Val Phe
    610                 615                 620

Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro Lys Ala Ala Pro
625                 630                 635                 640

Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys
                645                 650                 655

Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr
            660                 665                 670

Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly Val Glu Thr
        675                 680                 685

Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr
    690                 695                 700

Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Lys Ser Tyr Ser Cys
705                 710                 715                 720

Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val Ala Pro Thr
                725                 730                 735
```

Glu Cys Ser

<210> 46
<211> 265
<212> PRT
<213> Artificial Sequence

<220>
<223> IgG Heavy Chain

<400> 46

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1 5 10 15

Gly Ser Thr Gly Asp Gly Ala Gln Val Gln Leu Val Gln Ser Gly Ala
20 25 30

Val Ile Lys Thr Pro Gly Ser Ser Val Lys Ile Ser Cys Arg Ala Ser
35 40 45

Gly Tyr Asn Phe Arg Asp Tyr Ser Ile His Trp Val Arg Leu Ile Pro
50 55 60

Asp Lys Gly Phe Glu Trp Ile Gly Trp Ile Lys Pro Leu Trp Gly Ala
65 70 75 80

Val Ser Tyr Ala Arg Gln Leu Gln Gly Arg Val Ser Met Thr Arg Gln
85 90 95

Leu Ser Gln Asp Pro Asp Asp Pro Asp Trp Gly Val Ala Tyr Met Glu
100 105 110

Phe Ser Gly Leu Thr Pro Ala Asp Thr Ala Glu Tyr Phe Cys Val Arg
115 120 125

Arg Gly Ser Cys Asp Tyr Cys Gly Asp Phe Pro Trp Gln Tyr Trp Cys
130 135 140

Gln Gly Thr Val Val Val Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
145 150 155 160

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
165 170 175

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
180 185 190

```
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
        195                 200                 205

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
    210                 215                 220

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
225                 230                 235                 240

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
                245                 250                 255

Tyr Pro Tyr Asp Val Pro Asp Tyr Ala
            260                 265
```

<210> 47
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<223> IgG Light Chain

<400> 47

```
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1               5                   10                  15

Gly Ser Thr Gly Asp Gly Ala Gln Val Gln Ile Val Leu Thr Gln Ser
            20                  25                  30

Pro Gly Ile Leu Ser Leu Ser Pro Gly Glu Thr Ala Thr Leu Phe Cys
        35                  40                  45

Lys Ala Ser Gln Gly Gly Asn Ala Met Thr Trp Tyr Gln Lys Arg Arg
    50                  55                  60

Gly Gln Val Pro Arg Leu Leu Ile Tyr Asp Thr Ser Arg Arg Ala Ser
65                  70                  75                  80

Gly Val Pro Asp Arg Phe Val Gly Ser Gly Ser Gly Thr Asp Phe Phe
                85                  90                  95

Leu Thr Ile Asn Lys Leu Asp Arg Glu Asp Phe Ala Val Tyr Tyr Cys
            100                 105                 110

Gln Gln Phe Glu Phe Phe Gly Leu Gly Ser Glu Leu Glu Val His Arg
        115                 120                 125
```

```
Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
    130                 135                 140

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
145                 150                 155                 160

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
                165                 170                 175

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
            180                 185                 190

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
        195                 200                 205

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
    210                 215                 220

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Tyr Pro Tyr Asp Val Pro
225                 230                 235                 240

Asp Tyr Ala
```

<210> 48
<211> 256
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of the Heavy Chain (VH-CH1) of HIV-1 Env Fab

<400> 48

```
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1               5                   10                  15

Gly Ser Thr Gly Asp Gly Ala Gln Val Gln Leu Val Gln Ser Gly Gly
            20                  25                  30

Gln Met Lys Lys Pro Gly Glu Ser Met Arg Ile Ser Cys Arg Ala Ser
        35                  40                  45

Gly Tyr Glu Phe Ile Asp Cys Thr Leu Asn Trp Ile Arg Leu Ala Pro
    50                  55                  60

Gly Lys Arg Pro Glu Trp Met Gly Trp Leu Lys Pro Arg Gly Gly Ala
65                  70                  75                  80

Val Asn Tyr Ala Arg Pro Leu Gln Gly Arg Val Thr Met Thr Arg Asp
```

85 90 95

Val Tyr Ser Asp Thr Ala Phe Leu Glu Leu Arg Ser Leu Thr Val Asp
100 105 110

Asp Thr Ala Val Tyr Phe Cys Thr Arg Gly Lys Asn Cys Asp Tyr Asn
115 120 125

Trp Asp Phe Glu His Trp Gly Arg Gly Thr Pro Val Ile Val Ser Ser
130 135 140

Pro Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
145 150 155 160

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
165 170 175

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
180 185 190

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
195 200 205

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
210 215 220

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
225 230 235 240

Lys Ala Glu Pro Lys Ser Cys Tyr Pro Tyr Asp Val Pro Asp Tyr Ala
245 250 255

<210> 49
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of the Light Chain (VL-CL) of HIV-1 Env Fab

<400> 49

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1 5 10 15

Gly Ser Thr Gly Asp Gly Ala Gln Val Gln Ile Val Leu Thr Gln Ser
20 25 30

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Thr Ala Ile Ile Ser Cys
35 40 45

```
Arg Thr Ser Gln Tyr Gly Ser Leu Ala Trp Tyr Gln Gln Arg Pro Gly
    50                  55                  60

Gln Ala Pro Arg Leu Val Ile Tyr Ser Gly Ser Thr Arg Ala Ala Gly
65                  70                  75                  80

Ile Pro Asp Arg Phe Ser Gly Ser Arg Trp Gly Pro Asp Tyr Asn Leu
                85                  90                  95

Thr Ile Ser Asn Leu Glu Ser Gly Asp Phe Gly Val Tyr Tyr Cys Gln
            100                 105                 110

Gln Tyr Glu Phe Phe Gly Gln Gly Thr Lys Val Gln Val Asp Ile Lys
        115                 120                 125

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
    130                 135                 140

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
145                 150                 155                 160

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
                165                 170                 175

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
            180                 185                 190

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
        195                 200                 205

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Arg Ser
    210                 215                 220

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Tyr Pro Tyr Asp Val
225                 230                 235                 240

Pro Asp Tyr Ala
```

<210> 50
<211> 1536
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding HIV-1 PG9 Fab

<400> 50

ggatccgcca ccatggcaag acccctgtgc accctgctgc tgctgatggc aaccctggcc 60

ggagccctgg cacagagcgc cctgacccag cccgcaagcg tctccggctc accaggccag 120

agcatcacta ttagttgcaa cgggactagc aacgacgtgg gaggctatga gagtgtcagc 180

tggtaccagc agcatcccgg aaaagcacca aaagtggtca tctacgatgt cagtaaaagg 240

ccaagtgggg tctcaaatag gttctcaggg agtaaatctg ggaatacagc atctctgacc 300

atctccggac tgggcgcaga agatgaaggc gactactatt gcaaaagcct gacctcaacc 360

agacggcgag tctttgggac aggcaccaag ctgacagtcc tgacagtcgc tgcccctcc 420

gtcttcattt ttccaccttc agatgagcag ctgaaatctg gcactgcatc tgtggtctgc 480

ctgctgaaca acttctatcc acgagaggcc aaggtgcagt ggaaagtgga taacgcactg 540

cagtccggca atagtcagga aagcgtgact gagcaggatt ccaaggacag tacctatagc 600

ctgtccagta cactgaccct gtccaaggct gactacgaaa aacataaggt gtatgcatgt 660

gaagtgactc accagggact gaggtcacca gtcactaagt cttttaacag gggagagtgc 720

ggcgggggag gatctggagg cggcggctct ggaggggggag gctcaggggg cggaggaagc 780

ggcggaggag ggtccggagg aggaggcagt cagagactgg tcgaaagcgg gggaggagtg 840

gtgcagcctg ggtcctcact gagactgtca tgcgctgcca gtggctttga tttttcacga 900

cagggaatgc attgggtcag gcaggcaccc ggacagggcc tggaatgggt cgccttcatt 960

aagtacgacg gaagcgagaa gtaccatgcc gactcagtgt ggggaaggct gagcatctca 1020

agggacaact caaaggacac cctgtacctg cagatgaata gcctgagagt ggaagatacc 1080

gctacttatt tctgcgtgcg agaggccgga gggccagatt accggaacgg gtacaattac 1140

tatgatttct acgacggcta ctacaattac cattatatgg atgtctgggg caaaggaact 1200

acagtcaccg tgagctccgc aagtactaag ggaccttccg tgtttcctct ggctcccagt 1260

tccaaaagta catccggagg aacagccgct ctgggatgtc tggtcaagga ctattttccc 1320

gagcccgtga ctgtctcctg gaacagcggg gctctgacaa gcggggtgca cacctttcct 1380

gccgtgctgc agtccagtgg gctgtacagt ctgtctagtg tcgtcactgt gccaagctca 1440

agtctgggga cccagacata catttgtaat gtgaaccata aaccctcaaa caccaaagtg 1500

gacaagaaag tggaacctaa aagctgataa ctcgag 1536

<210> 51
<211> 504
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of HIV-1 PG9 Fab

<400> 51

```
Met Ala Arg Pro Leu Cys Thr Leu Leu Leu Leu Met Ala Thr Leu Ala
1               5                  10                  15

Gly Ala Leu Ala Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly
            20                  25                  30

Ser Pro Gly Gln Ser Ile Thr Ile Ser Cys Asn Gly Thr Ser Asn Asp
        35                  40                  45

Val Gly Gly Tyr Glu Ser Val Ser Trp Tyr Gln Gln His Pro Gly Lys
    50                  55                  60

Ala Pro Lys Val Val Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly Val
65                  70                  75                  80

Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr
                85                  90                  95

Ile Ser Gly Leu Gly Ala Glu Asp Glu Gly Asp Tyr Tyr Cys Lys Ser
            100                 105                 110

Leu Thr Ser Thr Arg Arg Arg Val Phe Gly Thr Gly Thr Lys Leu Thr
        115                 120                 125

Val Leu 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

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 Arg
    210                 215                 220

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly
225                 230                 235                 240

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                245                 250                 255
```

```
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Arg Leu Val Glu Ser
            260                 265                 270

Gly Gly Gly Val Val Gln Pro Gly Ser Ser Leu Arg Leu Ser Cys Ala
        275                 280                 285

Ala Ser Gly Phe Asp Phe Ser Arg Gln Gly Met His Trp Val Arg Gln
    290                 295                 300

Ala Pro Gly Gln Gly Leu Glu Trp Val Ala Phe Ile Lys Tyr Asp Gly
305                 310                 315                 320

Ser Glu Lys Tyr His Ala Asp Ser Val Trp Gly Arg Leu Ser Ile Ser
                325                 330                 335

Arg Asp Asn Ser Lys Asp Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg
            340                 345                 350

Val Glu Asp Thr Ala Thr Tyr Phe Cys Val Arg Glu Ala Gly Gly Pro
        355                 360                 365

Asp Tyr Arg Asn Gly Tyr Asn Tyr Tyr Asp Phe Tyr Asp Gly Tyr Tyr
    370                 375                 380

Asn Tyr His Tyr Met Asp Val Trp Gly Lys Gly Thr Thr Val Thr Val
385                 390                 395                 400

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
                405                 410                 415

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
            420                 425                 430

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
        435                 440                 445

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
    450                 455                 460

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
465                 470                 475                 480

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
                485                 490                 495

Asp Lys Lys Val Glu Pro Lys Ser
            500
```

<210> 52
<211> 1503
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding HIV-1 4E10 Fab

<400> 52
ggatccgcca ccatggcaag acctctgtgc actctgctgc tgctgatggc tactctggcc 60

ggggctctgg ctgagattgt cctgacccag tcccctggca ctcagtcact gtcccccggc 120

gagcgcgcaa ctctgtcctg cagagcaagc cagtccgtcg ggaacaacaa gctggcatgg 180

taccagcagc gcccaggaca ggcacccagg ctgctgatct acggagcaag ctcccggcct 240

agcggagtcg ctgatagatt ctccggaagc ggctccggga ccgatttcac tctgaccatc 300

tccaggctgg aacctgagga ttttgccgtg tattactgtc agcagtacgg gcagagcctg 360

tcaactttcg gccagggaac taaagtcgaa aagagaaccg tggccgcacc aagcgtcttt 420

atttttcccc ctagcgatga acagctgaaa tccgggactg cttccgtggt ctgcctgctg 480

aataacttct atccaagaga ggcaaaggtg cagtggaaag tggacaacgc cctgcagagc 540

ggaaactcac aggaatctgt gacagagcag gactccaagg atagcacata cagtctgtcc 600

tcaactctga ccctgtccaa agctgactat gagaagcata aagtctacgc atgtgaggtg 660

acccaccagg gactgaggtc ccccgtcact aagtccttca atagaggcga gtgcgggggc 720

gggggcagtg gcggaggggg aagtgggggc ggagggagtg gcggcggcgg gagtggcggc 780

ggcggctcag ggggcggcgg ctcccaggtc cagctggtcc agagcggagc cgaggtcaag 840

agaccaggct cttcagtcac cgtgagctgc aaagccagcg gaggctcctt tagcacttac 900

gccctgtcat gggtgcggca ggccccaggc cgaggcctgg agtggatggg cggcgtgatc 960

cccctgctga ccattactaa ctatgccccc agatttggag gccggatcac catcacagct 1020

gacagatcca catccacagc ttacctggag ctgaacagtc tgaggcccga ggacactgca 1080

gtctactact gtgcacgaga aggcaccact ggatgggggt ggctggggaa gcccatcggg 1140

gcttttgcac attggggcgg agggacactg gtgactgtga gctctgccag cactaaaggg 1200

cccagtgtct tccctctggc cccaagttcc aagagtacat caggggcac cgccgcactg 1260

gggtgtctgg tgaaggatta cttcccagag cccgtgacag tcagttggaa cagcggcgct 1320

ctgaccagtg gggtgcacac tttcccagcc gtgctgcaga gttcagggct gtactccctg 1380

tcctcagtgg tgactgtgcc ctcaagcagt ctggggactc agacttacat ttgtaatgtg 1440

aaccataaac cctcaaatac taaagtggac aaaaaagtgg aaccaaagag ctgataactc 1500

gag 1503

<210> 53
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of HIV-1 4E10 Fab

<400> 53

```
Met Ala Arg Pro Leu Cys Thr Leu Leu Leu Leu Met Ala Thr Leu Ala
1               5                  10                  15

Gly Ala Leu Ala Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Gln Ser
            20                  25                  30

Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
        35                  40                  45

Val Gly Asn Asn Lys Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala
    50                  55                  60

Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Pro Ser Gly Val Ala
65                  70                  75                  80

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
                85                  90                  95

Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr
            100                 105                 110

Gly Gln Ser Leu Ser Thr Phe Gly Gln Gly Thr Lys Val Glu Lys Arg
        115                 120                 125

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
    130                 135                 140

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
145                 150                 155                 160

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
                165                 170                 175

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
            180                 185                 190

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
        195                 200                 205
```

```
His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Arg Ser Pro
    210                 215                 220

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly
225                 230                 235                 240

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
                245                 250                 255

Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly
            260                 265                 270

Ala Glu Val Lys Arg Pro Gly Ser Ser Val Thr Val Ser Cys Lys Ala
        275                 280                 285

Ser Gly Gly Ser Phe Ser Thr Tyr Ala Leu Ser Trp Val Arg Gln Ala
    290                 295                 300

Pro Gly Arg Gly Leu Glu Trp Met Gly Gly Val Ile Pro Leu Leu Thr
305                 310                 315                 320

Ile Thr Asn Tyr Ala Pro Arg Phe Gly Gly Arg Ile Thr Ile Thr Ala
                325                 330                 335

Asp Arg Ser Thr Ser Thr Ala Tyr Leu Glu Leu Asn Ser Leu Arg Pro
            340                 345                 350

Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Glu Gly Thr Thr Gly Trp
        355                 360                 365

Gly Trp Leu Gly Lys Pro Ile Gly Ala Phe Ala His Trp Gly Gly Gly
    370                 375                 380

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
385                 390                 395                 400

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
                405                 410                 415

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
            420                 425                 430

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
        435                 440                 445

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
    450                 455                 460
```

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
465 470 475 480

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
485 490

<210> 54
<211> 1446
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding the HIV-1 VRC01 IgG1 Heavy Chain (VH/CH1/Hinge/CH2/CH3)

<400> 54
ggatccgcca ccatggattg gacatggatt ctgttcctgg tcgccgccgc aactagagtg 60

cattcacagg tgcagctggt gcagtcaggc gggcagatga agaaacccgg cgagagtatg 120

cgaatctcat gccgggctag cgggtacgaa ttcatcgact gtaccctgaa ctggattaga 180

ctggcacctg ggaagaggcc agagtggatg ggatggctga aacctagagg cggggcagtg 240

aattacgcca gaccactgca gggcagggtc actatgaccc gcgacgtgta ttctgatacc 300

gcattcctgg agctgcgaag tctgacagtc gacgatactg ccgtgtactt ctgcacacgg 360

ggcaagaact gtgactataa ttgggatttt gaacactggg gcagggggac acctgtcatt 420

gtgagctccc caagtactaa gggaccctca gtgtttcccc tggccccttc tagtaaaagt 480

acctcaggag gcacagccgc tctgggatgc ctggtgaagg attacttccc tgagccagtc 540

accgtgagtt ggaactcagg cgccctgaca agcggggtcc atacttttcc agctgtgctg 600

cagtcaagcg ggctgtactc cctgtcctct gtggtcacag tgcccagttc aagcctggga 660

acacagactt atatctgtaa cgtcaatcac aagcctagca atactaaagt ggacaagaaa 720

gccgagccta agagctgcga accaaagtcc tgtgataaaa cccatacatg ccctccctgt 780

ccagctcctg aactgctggg cggcccatcc gtgttcctgt ttccacccaa gcccaaagac 840

accctgatga ttagcaggac tcctgaggtc acctgcgtgg tcgtggacgt gtcccacgag 900

gaccccgaag tcaagtttaa ctggtacgtg gatggcgtcg aagtgcataa tgccaagaca 960

aaaccccggg aggaacagta caactctacc tatagagtcg tgagtgtcct gacagtgctg 1020

caccaggact ggctgaacgg gaaggagtat aagtgcaaag tgtctaataa ggccctgcca 1080

gctcccatcg agaaaacaat ttccaaggca aaaggccagc caagggaacc ccaggtgtac 1140

actctgcctc catcccgcga cgagctgact aagaaccagg tctctctgac ctgtctggtg 1200

aaaggattct atccaagcga tatcgccgtg gagtgggaat ccaatggcca gcccgagaac 1260

aattacaaga ccacaccccc tgtgctggac agcgatggct ccttctttct gtattcaaag 1320

ctgaccgtgg ataaaagccg ctggcagcag gggaacgtct ttagctgctc cgtgatgcac 1380

gaagctctgc acaatcatta cacccagaag tctctgagtc tgtcacctgg caagtgataa 1440

ctcgag 1446

<210> 55
<211> 474
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of the HIV-1 VRC01 IgG1 Heavy Chain (VH/CH1/CH2/CH3)

<400> 55

```
Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1               5                  10                  15

His Ser Gln Val Gln Leu Val Gln Ser Gly Gly Gln Met Lys Lys Pro
            20                  25                  30

Gly Glu Ser Met Arg Ile Ser Cys Arg Ala Ser Gly Tyr Glu Phe Ile
        35                  40                  45

Asp Cys Thr Leu Asn Trp Ile Arg Leu Ala Pro Gly Lys Arg Pro Glu
    50                  55                  60

Trp Met Gly Trp Leu Lys Pro Arg Gly Gly Ala Val Asn Tyr Ala Arg
65                  70                  75                  80

Pro Leu Gln Gly Arg Val Thr Met Thr Arg Asp Val Tyr Ser Asp Thr
                85                  90                  95

Ala Phe Leu Glu Leu Arg Ser Leu Thr Val Asp Asp Thr Ala Val Tyr
            100                 105                 110

Phe Cys Thr Arg Gly Lys Asn Cys Asp Tyr Asn Trp Asp Phe Glu His
        115                 120                 125

Trp Gly Arg Gly Thr Pro Val Ile Val Ser Ser Pro 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 Lys Ala Glu Pro Lys
225                 230                 235                 240

Ser Cys Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
                245                 250                 255

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
    290                 295                 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
                325                 330                 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
        355                 360                 365

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
    370                 375                 380

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
385                 390                 395                 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430
```

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
435 440 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
450 455 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
465 470

<210> 56
<211> 708
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding the HIV-1 VRC01 IgG Light Chain (VL/CL)

<400> 56
ggatccgcca ccatggattg gacttggatt ctgttcctgg tggcagccgc taccagagtc 60

cattccgaaa ttgtgctgac ccagtctccc ggaacactgt ctctgagtcc tggcgagaca 120

gccatcattt cctgtaggac ttctcagtac gggagtctgg catggtatca gcagcgacca 180

ggacaggctc ctcgactggt catctactca ggaagcactc gggcagccgg cattcccgac 240

cgattctccg ggtctcggtg gggacctgat tacaacctga ccatctcaaa tctggaaagc 300

ggagactttg gcgtgtacta ttgccagcag tatgagttct ttgggcaggg aaccaaggtc 360

caggtggaca tcaaacgcac agtcgctgca ccaagcgtgt tcatctttcc accctcagat 420

gaacagctga agtccggcac cgcctctgtg gtgtgcctgc tgaacaattt ctaccccgg 480

gaggcaaagg tccagtggaa agtggacaac gccctgcagt ctggcaatag tcaggagtca 540

gtgactgaac aggacagcaa ggattccacc tattctctgt cctctactct gaccctgagc 600

aaagctgatt acgagaagca caaagtgtat gcatgtgagg tcacccacca gggactgcgg 660

tcacccgtca ccaagagctt caatcgcgga gagtgttgat aactcgag 708

<210> 57
<211> 228
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of the HIV-1 VRC01 IgG Light Chain (VL/CL)

<400> 57

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1 5 10 15

His Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser
20 25 30

```
Pro Gly Glu Thr Ala Ile Ile Ser Cys Arg Thr Ser Gln Tyr Gly Ser
        35                  40                  45

Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Val Ile
    50                  55                  60

Tyr Ser Gly Ser Thr Arg Ala Ala Gly Ile Pro Asp Arg Phe Ser Gly
65                  70                  75                  80

Ser Arg Trp Gly Pro Asp Tyr Asn Leu Thr Ile Ser Asn Leu Glu Ser
                85                  90                  95

Gly Asp Phe Gly Val Tyr Tyr Cys Gln Gln Tyr Glu Phe Phe Gly Gln
            100                 105                 110

Gly Thr Lys Val Gln Val Asp Ile Lys Arg Thr Val Ala Ala Pro Ser
        115                 120                 125

Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala
    130                 135                 140

Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
145                 150                 155                 160

Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser
                165                 170                 175

Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr
            180                 185                 190

Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys
        195                 200                 205

Glu Val Thr His Gln Gly Leu Arg Ser Pro Val Thr Lys Ser Phe Asn
    210                 215                 220

Arg Gly Glu Cys
225
```

<210> 58
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding the Heavy Chain (VH-CH1) of the CHIKV-Env-Fab

<400> 58
ggatccgcca ccatggattg gacatggagg attctgtttc tggtcgccgc cgctactgga 60

actcacgctc aggtgcagct ggtgcagtca gggtccgaac tgaagaaacc aggggcatct 120

gtgaaggtca gttgcaaagc ctcaggctac accctgacac ggtatgccat gacttgggtg 180

cgccaggctc ctggacaggg actggagtgg atgggctgga tcaacactta caccggaaat 240

ccaacttatg tgcaggggtt caccggccga ttcgtgtttt ctctggacac ttccgtctct 300

accgcctttc tgcacattac aagtctgaag gcagaggaca ctgccgtgta cttctgcgct 360

agggaaggcg gagcaagagg ctttgattat tggggccagg gaaccctggt gacagtcagc 420

tccgccagca caaagggacc ctccgtgttc ccactggctc cctctagtaa aagtacatca 480

gggggcactg ccgctctggg atgtctggtc aaagattact tccccgaacc tgtgaccgtc 540

agctggaact ccggagctct gaccagcggg gtgcatacat ttcccgcagt cctgcagtca 600

agcggactgt actccctgtc ctctgtggtc acagtgccta gttcaagcct ggggacacag 660

acttatatct gtaatgtgaa ccataagcca agcaacacca aagtggacaa aaaagtggaa 720

cctaagagct gctgataact cgag 744

<210> 59
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of the Heavy Chain (VH-CH1) of the CHIKV-Env-Fab

<400> 59

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Gln Val Gln Leu Val Gln Ser Gly Ser Glu Leu Lys Lys
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Leu
35 40 45

Thr Arg Tyr Ala Met Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60

Glu Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Asn Pro Thr Tyr Val
65 70 75 80

Gln Gly Phe Thr Gly Arg Phe Val Phe Ser Leu Asp Thr Ser Val Ser
85 90 95

```
Thr Ala Phe Leu His Ile Thr Ser Leu Lys Ala Glu Asp Thr Ala Val
            100                 105                 110

Tyr Phe Cys Ala Arg Glu Gly Gly Ala Arg Gly Phe Asp Tyr Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
    130                 135                 140

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
145                 150                 155                 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
                165                 170                 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
            180                 185                 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
        195                 200                 205

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
    210                 215                 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
225                 230                 235                 240
```

<210> 60
<211> 738
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding the Light Chain (VL-CL) of the CHIKV-Env-Fab

<400> 60

```
ggatccgcca ccatggcatg gaccccactg ttcctgttcc tgctgacttg ttgtcctggc       60

gggagcaatt cacagagcgt cctgacccag ccccttctg tgtccggagc accaggacag       120

cgagtcacaa tctcttgcac tggaagctcc tctaacattg gggccagcca cgacgtgcat      180

tggtaccagc agctgccagg gaccgctccc acactgctga tctatgtgaa ctctaatagg      240

cctagtggcg tcccagatag attttcaggg agcaagtccg gcacctctgc tagtctggca      300

attacaggac tgcaggctga ggacgaagca gattactatt gccagagtta cgactcaaac      360

ctgtcaggca gcgcagtgtt cggaggagga actaagctga ccgtcctggg acagcccaaa      420

gccgctcctt ctgtgaccct gtttcccccc agttcagagg aactgcaggc caacaaggct      480

actctggtgt gtctgatctc cgacttctac cctggagcag tgaccgtcgc atggaaggcc      540
```

gatagctccc cagtgaaagc tggggtcgag accacaactc ccagcaagca gtccaacaac 600

aagtacgcag cctctagtta tctgtcactg acacctgaac agtggaagag ccacaaatcc 660

tattcttgcc aagtgactca tgagggcagt accgtggaaa agacagtcgc cccaactgag 720

tgttcctgat aactcgag 738

<210> 61
<211> 238
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino Acid Sequence of the Light Chain (VL-CL) of the CHIKV-Env-Fab

<400> 61

Met Ala Trp Thr Pro Leu Phe Leu Phe Leu Leu Thr Cys Cys Pro Gly
1 5 10 15

Gly Ser Asn Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly
20 25 30

Ala Pro Gly Gln Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn
35 40 45

Ile Gly Ala Ser His Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr
50 55 60

Ala Pro Thr Leu Leu Ile Tyr Val Asn Ser Asn Arg Pro Ser Gly Val
65 70 75 80

Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala
85 90 95

Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser
100 105 110

Tyr Asp Ser Asn Leu Ser Gly Ser Ala Val Phe Gly Gly Gly Thr Lys
115 120 125

Leu Thr Val Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe
130 135 140

Pro Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys
145 150 155 160

Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala
165 170 175

```
Asp Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys
            180                 185                 190

Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro
        195                 200                 205

Glu Gln Trp Lys Ser His Lys Ser Tyr Ser Cys Gln Val Thr His Glu
    210                 215                 220

Gly Ser Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
225                 230                 235
```

<210> 62
<211> 2238
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding HIV-1 Env-4E10 Ig

<400> 62

```
ggatccgcca ccatggattg gacatggagg attctgtttc tggtcgccgc cgctacagga       60
actcacgccc aggtgcagct ggtgcagtca ggagccgaag tgaagcgacc aggcagctcc      120
gtcactgtgt cctgcaaagc atctggcgga tcattcagca cctacgccct gagctgggtg      180
agacaggctc ctggacgagg actggaatgg atgggaggcg tcatcccact gctgacaatt      240
actaactacg ccccccgatt tcagggcagg atcaccatta cagcagaccg ctccacttct      300
accgcctatc tggagctgaa tagcctgaga ccagaagata ccgcagtgta ctattgcgcc      360
cgggagggaa ccacaggatg gggatggctg ggaaagccca tcggggcttt cgcacactgg      420
ggccagggaa ccctggtcac agtgtctagt gccagcacaa agggcccctc cgtgtttccc      480
ctggctcctt caagcaaaag tacttcagga gggaccgccg ctctgggatg tctggtgaag      540
gactacttcc ctgagccagt caccgtgtcc tggaactctg gcgctctgac ctccggagtg      600
catacatttc ccgcagtcct gcagtcctct gggctgtact ctctgagttc agtggtcact      660
gtgcctagct cctctctggg cacacagact tatatctgca acgtgaatca caagccctcc      720
aataccaaag tcgacaagaa agtggaacct aagtcttgtg ataaaaccca tacatgccca      780
ccttgtccag cacctgagct gctgggcgga ccttccgtgt tcctgtttcc acccaagcca      840
aaagacacac tgatgattag ccggacacct gaagtgactt gtgtggtcgt ggacgtcagc      900
cacgaggacc ccgaagtgaa gttcaactgg tacgtggatg gcgtcgaggt gcataatgcc      960
aagaccaaac ccagggagga acagtacaac tctacttata gggtcgtgag tgtcctgacc     1020
gtgctgcacc aggactggct gaacgggaag gagtataagt gcaaagtgtc caataaggcc     1080
```

ctgccagctc ccatcgagaa aacaatttct aaggctaaag gccagccacg cgaaccccag 1140

gtgtacactc tgcctcccag cagggacgag ctgaccaaga accaggtgag tctgacatgt 1200

ctggtcaaag gcttctatcc aagcgatatc gccgtggagt gggaatccaa tggacagccc 1260

gaaaacaatt acaagactac ccccccctgtg ctggacagtg atggatcatt ctttctgtat 1320

tccaagctga ccgtggacaa atctcgctgg cagcagggga acgtctttag ctgctccgtg 1380

atgcacgagg ccctgcacaa tcattacaca cagaagtctc tgagtctgtc accaggcaag 1440

cggggacgca aaaggagaag cgggtccggc gctactaact tcagcctgct gaaacaggca 1500

ggggatgtgg aggaaaatcc tggcccaatg gtcctgcaga cccaggtgtt tatctcactg 1560

ctgctgtgga ttagcggggc ttatggcgaa atcgtgctga ctcagagccc cggaacccag 1620

tctctgagtc ctggggagcg cgctacactg agctgtcgag catcacagag cgtggggaac 1680

aataagctgg catggtacca gcagaggcct ggccaggctc caagactgct gatctatggc 1740

gcaagttcac ggcctagcgg agtggcagac cgcttctccg gatctgggag tggcaccgat 1800

tttactctga ccattagcag gctggagcca gaagacttcg ctgtgtacta ttgccagcag 1860

tacggccagt cactgagcac atttggacag gggactaagg tcgaaaaaag aaccgtggca 1920

gccccaagtg tcttcatttt tccaccctca gacgagcagc tgaagagtgg aacagcctca 1980

gtcgtgtgtc tgctgaacaa tttctacccc agggaggcca aggtccagtg gaaagtggat 2040

aacgctctgc agagcggcaa ttcccaggag tctgtgacag aacaggacag taaggattca 2100

acttatagcc tgagctccac actgactctg tccaaagcag attacgagaa gcacaaagtg 2160

tatgcctgcg aagtcaccca tcagggactg tctagtcctg tgacaaagtc ttttaacaga 2220

ggggagtgat aactcgag 2238

<210> 63
<211> 2328
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding HIV-1 Env-PG9 Ig

<400> 63
ggatccgcca ccatggactg gacttggagg attctgtttc tggtcgccgc cgcaactgga 60

actcacgctg aatttggact gtcatgggtc tttctggtgg cctttctgcg aggggtccag 120

tgccagaggc tggtggagtc cggaggagga gtggtccagc caggcagctc cctgcgactg 180

agttgtgccg cttcagggtt cgacttttct agacagggca tgcactgggt gcggcaggca 240

ccaggacagg gactggagtg ggtggctttc atcaagtacg acggaagtga aaaatatcat 300

gccgattcag tgtgggggcg gctgtcaatt agccgcgaca actccaagga taccctgtac 360

ctgcagatga attctctgag ggtcgaggac acagctactt atttctgcgt gagggaagca 420

ggcggacctg attacagaaa cgggtataat tactatgact tttacgatgg ctactataac 480
taccactata tggacgtgtg gggcaaggga accacagtca cagtgtctag tgcatcaact 540
aaaggcccaa gcgtgtttcc cctggcccct tcaagcaagt ccacttctgg aggaaccgca 600
gcactgggat gtctggtgaa ggattacttc cctgagccag tcaccgtgag ttggaactca 660
ggcgccctga ctagcggagt ccataccttt cctgctgtgc tgcagtcctc tgggctgtac 720
agcctgagtt cagtggtcac agtgccaagc tcctctctgg gcacccagac atatatctgc 780
aacgtgaatc acaagcctag caatactaag gtcgacaaaa gagtggaacc aaagagctgt 840
gataaaactc atacctgccc accttgtcca gcacctgagc tgctgggagg gccttccgtg 900
ttcctgtttc cacccaagcc aaaagacacc ctgatgatta gccggacacc agaagtcact 960
tgcgtggtcg tggacgtgag ccacgaggac cccgaagtca agtttaactg gtacgtggat 1020
ggcgtcgagg tgcataatgc taagacaaaa ccacgggagg aacagtacaa ctccacatat 1080
cgcgtcgtgt ctgtcctgac tgtgctgcac caggactggc tgaacggcaa ggagtataag 1140
tgcaaagtgt ccaataaggc actgccagcc cccatcgaga aaaccatttc taaggccaaa 1200
ggccagccac gagaacccca ggtgtacaca ctgcctccaa gtagggacga gctgactaag 1260
aaccaggtct ctctgacctg tctggtgaaa ggcttctatc cctctgatat cgctgtggag 1320
tgggaaagta atggacagcc tgaaaacaat tacaagacta ccccccctgt gctggacagc 1380
gatggcagct tcttcctgta tagcaagctg accgtggaca aatccagatg gcagcagggg 1440
aacgtcttta gttgctcagt gatgcacgag gcactgcaca atcattacac ccagaaaagc 1500
ctgtccctgt ctcctggcaa gaggggaaga aaaaggagaa gtgggtcagg cgcaacaaac 1560
ttcagcctgc tgaagcaggc cggagatgtg gaggaaaatc ctgggccaat ggcttggacc 1620
cccctgttcc tgtttctgct gacatgctgt cctggcggaa gcaactccca gtctgcactg 1680
acacagccag caagtgtgtc agggagccca ggacagagca tcaccatttc ctgtaacggc 1740
acaagcaatg acgtcggggg ctacgagtcc gtgtcttggt atcagcagca tcctggaaag 1800
gccccaaaag tcgtgatcta cgatgtcagc aaacgccccc ctggggtgag taaccgattc 1860
agtggatcaa agagcgggaa taccgcttct ctgacaatta gtggcctgca ggcagaggac 1920
gaaggagatt actattgcaa atcactgaca agcactcggc gccgagtctt cggaaccggg 1980
acaaagctga ctgtgctggg ccagcccaaa gctgcaccta gcgtgaccct gtttccaccc 2040
agttcagagg aactgcaggc taataaggca acactggtgt gtctgatctc cgacttctac 2100
cctggcgctg tcactgtggc ctggaaggct gatagctccc cagtcaaagc aggagtggaa 2160
acaactaccc cctccaagca gtctaacaac aagtacgccg cttctagtta tctgtcactg 2220
actcccgagc agtggaagag ccacaaatcc tattcttgcc aggtgaccca tgagggctcc 2280

actgtcgaaa agaccgtggc ccctacagag tgttcttgat aactcgag 2328

<210> 64
<211> 2217
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence Encoding VRC01 IgG

<400> 64
ggatccgcca ccatggattg gacatggatt ctgttcctgg tcgccgccgc aactagagtg 60

cattcacagg tgcagctggt gcagtcaggc gggcagatga agaaacccgg cgagagtatg 120

cgaatctcat gccgggctag cgggtacgaa ttcatcgact gtaccctgaa ctggattaga 180

ctggcacctg ggaagaggcc agagtggatg ggatggctga aacctagagg cggggcagtg 240

aattacgcca gaccactgca gggcagggtc actatgaccc gcgacgtgta ttctgatacc 300

gcattcctgg agctgcgaag tctgacagtc gacgatactg ccgtgtactt ctgcacacgg 360

ggcaagaact gtgactataa ttgggatttt gaacactggg gcaaggggac acctgtcatt 420

gtgagctccc caagtactaa gggaccctca gtgtttcccc tggccccttc tagtaaaagt 480

acctcaggag gcacagccgc tctgggatgc ctggtgaagg attacttccc tgagccagtc 540

accgtgagtt ggaactcagg cgccctgaca agcggggtcc atacttttcc agctgtgctg 600

cagtcaagcg ggctgtactc cctgtcctct gtggtcacag tgcccagttc aagcctggga 660

acacagactt atatctgtaa cgtcaatcac aagcctagca atactaaagt ggacaagaaa 720

gccgagccta agagctgcga accaaagtcc tgtgataaaa cccatacatg ccctccctgt 780

ccagctcctg aactgctggg cggcccatcc gtgttcctgt ttccacccaa gcccaaagac 840

accctgatga ttagcaggac tcctgaggtc acctgcgtgg tcgtggacgt gtcccacgag 900

gaccccgaag tcaagtttaa ctggtacgtg gatggcgtcg aagtgcataa tgccaagaca 960

aaaccccggg aggaacagta caactctacc tatagagtcg tgagtgtcct gacagtgctg 1020

caccaggact ggctgaacgg gaaggagtat aagtgcaaag tgtctaataa ggccctgcca 1080

gctcccatcg agaaaacaat ttccaaggca aaaggccagc caagggaacc ccaggtgtac 1140

actctgcctc catcccgcga cgagctgact aagaaccagg tctctctgac ctgtctggtg 1200

aaaggattct atccaagcga tatcgccgtg gagtgggaat ccaatggcca gcccgagaac 1260

aattacaaga ccacaccccc tgtgctggac agcgatggct ccttctttct gtattcaaag 1320

ctgaccgtgg ataaaagccg ctggcagcag gggaacgtct ttagctgctc cgtgatgcac 1380

gaagctctgc acaatcatta cacccagaag tctctgagtc tgtcacctgg caagagggga 1440

cgaaaacgga gaagcggcag cggagctaca aacttcagcc tgctgaaaca ggcaggcgac 1500

gtggaggaaa atcctgggcc aatggattgg acttggattc tgttcctggt ggcagccgct 1560

accagagtcc attccgaaat tgtgctgacc cagtctcccg gaacactgtc tctgagtcct 1620

ggcgagacag ccatcatttc ctgtaggact tctcagtacg ggagtctggc atggtatcag 1680

cagcgaccag gacaggctcc tcgactggtc atctactcag gaagcactcg ggcagccggc 1740

attcccgacc gattctccgg gtctcggtgg ggacctgatt acaacctgac catctcaaat 1800

ctggaaagcg gagactttgg cgtgtactat tgccagcagt atgagttctt tgggcaggga 1860

accaaggtcc aggtggacat caaacgcaca gtcgctgcac caagcgtgtt catctttcca 1920

ccctcagatg aacagctgaa gtccggcacc gcctctgtgg tgtgcctgct gaacaatttc 1980

taccccccggg aggcaaaggt ccagtggaaa gtggacaacg ccctgcagtc tggcaatagt 2040

caggagtcag tgactgaaca ggacagcaag gattccacct attctctgtc ctctactctg 2100

accctgagca aagctgatta cgagaagcac aaagtgtatg catgtgaggt cacccaccag 2160

ggactgcggt cacccgtcac caagagcttc aatcgcggag agtgttgata actcgag 2217

<210> 65
<211> 2223
<212> DNA
<213> Artificial Sequence

<220>
<223> CHIKV snapi nucleic acid sequence

<400> 65
ggatccgcca ccatggactg gacttggatt ctgtttctgg tcgccgccgc tacccgagtg 60

cattcacagg tgcagctgca gcagcctggg gccgctctgg tgaagccagg agctagcgca 120

atgatgtcct gcaaagcctc tggctacact ttcacctcct attggatcac ctgggtgaag 180

cagcgacctg gacagggact ggagtggatc ggcgacatct acccaggcac cgggagaaca 240

atctacaagg aaaaattcaa gacaaaagcc acactgactg tggacaccag ctcctctaca 300

gcttttatgc agctgaacag cctgacttcc gaggatagcg ccgtgtacta ttgcgcaaga 360

ggatacggct ctccttacta tgccctggac tattgggggc agggaactag cgtcaccgtg 420

agttcagcat ctaccaaggg accaagcgtg ttcccactgg cacctagctc caaatccact 480

tctggcggga ccgccgctct gggatgtctg gtgaaggatt acttccctga gccagtcaca 540

gtgagttgga actcaggggc tctgaccagc ggagtccaca catttcctgc agtgctgcag 600

tctagtggac tgtactccct gtcaagcgtg gtcactgtcc catcctctag tctgggcacc 660

cagacatata tctgcaacgt gaatcacaag ccatccaata ccaaagtcga taagaaagtg 720

gagcccaagt cttgtgacaa aactcatacc tgccctccct gtccagcacc tgaactgctg 780

ggaggcccaa gcgtgttcct gtttccaccc aagcctaaag acaccctgat gattagcagg 840

acaccagagg tcacttgcgt ggtcgtggac gtgagccacg aagaccccga ggtcaagttc 900

aactggtacg tggatggcgt cgaagtgcat aatgccaaga caaaaccccg ggaggaacag 960

tacaactcaa cctatcgggt cgtgagcgtc ctgacagtgc tgcaccagga ctggctgaac 1020

ggaaaggagt acaagtgcaa agtgtctaat aaggccctgc cagctcccat cgaaaaaacc 1080

attagcaagg ctaaaggcca gccaagagag ccccaggtgt acacactgcc tccatcaagg 1140

gacgaactga caaagaacca ggtcagcctg acttgtctgg tgaaaggctt ctatcccagc 1200

gatatcgcag tggaatggga gtccaatggg cagcctgaga acaattacaa gaccacaccc 1260

cctgtgctgg acagcgatgg gtccttcttt ctgtattcca agctgacagt ggataaatct 1320

cggtggcagc agggaaacgt ctttagttgc tcagtgatgc acgaagccct gcacaatcat 1380

tacactcaga agagcctgtc cctgtctccc ggaaagaggg gccgcaaacg gagaagtggc 1440

tcaggggcaa ccaacttctc tctgctgaaa caggccggcg atgtggagga aaatcctggg 1500

ccaatggact ggacatggat tctgttcctg gtggcagccg ctacaagggt ccattccgac 1560

attgtgctga ctcagtctcc tgcaagtctg gccgtgtctc agggacagcg agcaaccatc 1620

agttgtaagg ctagccagtc cgtcgactac gatggggaca gttacgtgaa ctggtatcag 1680

cagaagcctg gacagtcccc aaaactgctg atctatgatg ctagtaatct ggagtcaggc 1740

attcccgcac gattctctgg aagtggctca gggacagact tcaccctgaa cattcaccct 1800

gtcgaggaag aggacgtggc tacctactat tgccaggaaa gcaatgagga cccccgcact 1860

ttcgggggag gcaccaagct ggagatcaaa cgaactgtcg cagcccccag cgtgttcatc 1920

tttccaccct cagacgaaca gctgaagagc ggaaccgcat ccgtggtgtg cctgctgaac 1980

aacttctacc cccgcgaggc caaggtccag tggaaagtgg ataacgctct gcagtcaggc 2040

aatagccagg aatccgtgac tgagcaggat tctaaggaca gtacctattc actgtcaagc 2100

acactgactc tgagcaaagc agactacgaa aagcataaag tgtatgcctg cgaagtcacc 2160

caccaggggc tgaggtctcc agtcactaag tctttcaaca gaggggaatg ctgataactc 2220

gag 2223

<210> 66
<211> 2241
<212> DNA
<213> Artificial Sequence

<220>
<223> DVSF-1 WT nucleic acid sequence

<400> 66
ggatccgcca ccatggactg gacttggagg attctgtttc tggtcgccgc cgctactggg 60

actcacgctc aggcacatct ggtcgaatct ggaggaggag tggtccagcc tggccgatcc 120

ctgcgactgt cttgcgcagc tagcgccttc aacttcagca caaacgcaat gcactgggtg 180

cgacaggcac caggcaaggg actggagtgg gtcgctgtga tctcatacga cggaagccat 240

aagtactatg cagattctgt gaaaggccgg ttcaccattt ccagggacaa ttctaagaac 300

accctgtatc tgcagatgaa tagcctgcgc gcagccgata ccgcagtgta ctattgcgca 360

actgtcggcg tgctgacctg gccagtgaac gccgaatact ttcaccattg gggacagggc 420

agtctggtct cagtgagctc cgcaagtact aagggaccat cagtgttccc actggcaccc 480

tctagtaaat ctactagtgg cgggaccgct gcactgggat gtctggtgaa ggactatttc 540

cccgagcctg tcaccgtgag ctggaattcc ggagccctga caagcggcgt ccacacttttt 600

cccgctgtgc tgcagtcaag cggactgtac tccctgtcct ctgtggtcac tgtgcctagt 660

tcaagcctgg gcactcagac ctatatctgc aatgtgaacc acaagccctc taacaccaaa 720

gtcgacaaga aagtggaacc taagagctgt gataaaacac atacttgccc accttgtcca 780

gcaccagagc tgctgggagg accaagcgtg ttcctgtttc cacccaagcc taaagacaca 840

ctgatgatta gccggacacc tgaagtcact tgcgtggtcg tggacgtgtc ccacgaggac 900

cccgaagtca agtttaattg gtacgtggat ggcgtcgagg tgcataacgc caagaccaaa 960

ccccgggagg aacagtacaa tagcacatat agagtcgtgt ccgtcctgac tgtgctgcat 1020

caggattggc tgaatgggaa ggagtataag tgcaaagtgt ctaacaaggc tctgcctgca 1080

ccaatcgaga aaaccattag caaggctaaa ggccagccta gggaaccaca ggtgtacaca 1140

ctgcctccaa gtcgcgacga gctgaccaag aatcaggtct ccctgacatg tctggtgaaa 1200

ggcttctatc catcagatat cgccgtggag tgggaaagca acgggcagcc cgaaaacaat 1260

tacaagacca cacccctgt gctggactct gatggcagtt tctttctgta ttctaagctg 1320

accgtggaca aaagtagatg gcagcagggg aatgtctttt catgtagcgt gatgcacgag 1380

gccctgcaca accattacac acagaagtcc ctgtctctga gtcccggaaa gaggggccgc 1440

aaacggagat cagggagcgg agctactaat ttcagcctgc tgaaacaggc aggggatgtg 1500

gaggaaaacc ccggacctat ggcttggacc ccactgttcc tgtttctgct gacatgctgt 1560

cccgggggca gcaattctca gagtgtcctg acacagccac catcagtgag cggagcacca 1620

ggacagaggg tgaccatctc ctgcacaggc agcagcagca acattggcgc cgggtacgac 1680

gtgcattggt atcagcagct gcccggcacc gctcctaagc tgctgatctg tggcaacaat 1740

aaccgcccat ctggggtgcc cgatcgattc tccggctcta aaagtgggac ttcagccagc 1800

ctggctatta ccggcctgca ggccgaggac gaagctgatt actattgcca gagctacgac 1860

tcaagcctga ccggagtcgt gttcggagga ggaaccaagc tgacagtcct gggacagcct 1920

aaagccgctc caagcgtgac actgtttcct ccatcctctg aggaactgca ggcaaacaag 1980

gccaccctgg tgtgcctgat ttccgacttc taccccgggg cagtcactgt ggcttggaag 2040

gcagatagtt cacctgtcaa agccggagtg gagactacca caccatcaaa gcagagcaat 2100

aacaaatacg cagccagctc ctatctgtcc ctgacccctg agcagtggaa gtctcacaaa 2160

tcctattctt gccaggtcac tcacgaagga agcactgtgg agaaaactgt cgcaccaacc 2220

gaatgtagtt gataactcga g 2241

<210> 67
<211> 739
<212> PRT
<213> Artificial Sequence

<220>
<223> DVSF-1 WT amino acid sequence

<400> 67

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Gln Ala His Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Ala Phe Asn Phe
35 40 45

Ser Thr Asn Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Val Ile Ser Tyr Asp Gly Ser His Lys Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Ala Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Thr Val Gly Val Leu Thr Trp Pro Val Asn Ala Glu
115 120 125

Tyr Phe His His Trp Gly Gln Gly Ser Leu Val Ser Val Ser Ser Ala
130 135 140

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
145 150 155 160

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
165 170 175

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
180 185 190

```
Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
        195                 200                 205

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
    210                 215                 220

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
225                 230                 235                 240

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
                245                 250                 255

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
            260                 265                 270

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
        275                 280                 285

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
    290                 295                 300

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
305                 310                 315                 320

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                325                 330                 335

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            340                 345                 350

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        355                 360                 365

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
    370                 375                 380

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
385                 390                 395                 400

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                405                 410                 415

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            420                 425                 430

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
```

```
        435                 440                 445

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
    450                 455                 460

Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser
465                 470                 475                 480

Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
                485                 490                 495

Glu Glu Asn Pro Gly Pro Met Ala Trp Thr Pro Leu Phe Leu Phe Leu
            500                 505                 510

Leu Thr Cys Cys Pro Gly Gly Ser Asn Ser Gln Ser Val Leu Thr Gln
        515                 520                 525

Pro Pro Ser Val Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys
    530                 535                 540

Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His Trp Tyr
545                 550                 555                 560

Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Cys Gly Asn Asn
                565                 570                 575

Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly
            580                 585                 590

Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala
        595                 600                 605

Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser Leu Thr Gly Val Val Phe
    610                 615                 620

Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro Lys Ala Ala Pro
625                 630                 635                 640

Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys
                645                 650                 655

Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr
            660                 665                 670

Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly Val Glu Thr
        675                 680                 685
```

Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr
690 695 700

Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Lys Ser Tyr Ser Cys
705 710 715 720

Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val Ala Pro Thr
725 730 735

Glu Cys Ser

<210> 68
<211> 2241
<212> DNA
<213> Artificial Sequence

<220>
<223> DVSF-1 LALA nucleic acid sequence

<400> 68
ggatccgcca ccatggactg gacttggagg attctgtttc tggtcgccgc cgctactggg 60

actcacgctc aggcacatct ggtcgaatct ggaggaggag tggtccagcc tggccgatcc 120

ctgcgactgt cttgcgcagc tagcgccttc aacttcagca caaacgcaat gcactgggtg 180

cgacaggcac caggcaaggg actggagtgg gtcgctgtga tctcatacga cggaagccat 240

aagtactatg cagattctgt gaaaggccgg ttcaccattt ccagggacaa ttctaagaac 300

accctgtatc tgcagatgaa tagcctgcgc gcagccgata ccgcagtgta ctattgcgca 360

actgtcggcg tgctgacctg gccagtgaac gccgaatact ttcaccattg gggacagggc 420

agtctggtct cagtgagctc cgcaagtact aagggaccat cagtgttccc actggcaccc 480

tctagtaaat ctactagtgg cgggaccgct gcactgggat gtctggtgaa ggactatttc 540

cccgagcctg tcaccgtgag ctggaattcc ggagccctga caagcggcgt ccacactttt 600

cccgctgtgc tgcagtcaag cggactgtac tccctgtcct ctgtggtcac tgtgcctagt 660

tcaagcctgg gcactcagac ctatatctgc aatgtgaacc acaagccctc taacaccaaa 720

gtcgacaaga aagtggaacc taagagctgt gataaaacac atacttgccc accttgtcca 780

gcaccagagg cagctggagg accaagcgtg ttcctgtttc cacccaagcc taaagacaca 840

ctgatgatta gccggacacc tgaagtcact tgcgtggtcg tggacgtgtc ccacgaggac 900

cccgaagtca agtttaattg gtacgtggat ggcgtcgagg tgcataacgc caagaccaaa 960

ccccgggagg aacagtacaa tagcacatat agagtcgtgt ccgtcctgac tgtgctgcat 1020

caggattggc tgaatgggaa ggagtataag tgcaaagtgt ctaacaaggc tctgcctgca 1080

ccaatcgaga aaaccattag caaggctaaa ggccagccta gggaaccaca ggtgtacaca 1140

ctgcctccaa gtcgcgacga gctgaccaag aatcaggtct ccctgacatg tctggtgaaa 1200

ggcttctatc catcagatat cgccgtggag tgggaaagca acgggcagcc cgaaaacaat 1260

tacaagacca cacccccctgt gctggactct gatggcagtt tctttctgta ttctaagctg 1320

accgtggaca aaagtagatg gcagcagggg aatgtctttt catgtagcgt gatgcacgag 1380

gccctgcaca accattacac acagaagtcc ctgtctctga gtcccggaaa gaggggccgc 1440

aaacggagat cagggagcgg agctactaat ttcagcctgc tgaaacaggc aggggatgtg 1500

gaggaaaacc ccggacctat ggcttggacc ccactgttcc tgtttctgct gacatgctgt 1560

cccgggggca gcaattctca gagtgtcctg acacagccac catcagtgag cggagcacca 1620

ggacagaggg tgaccatctc ctgcacaggc agcagcagca acattggcgc cgggtacgac 1680

gtgcattggt atcagcagct gcccggcacc gctcctaagc tgctgatctg tggcaacaat 1740

aaccgcccat ctggggtgcc cgatcgattc tccggctcta aaagtgggac ttcagccagc 1800

ctggctatta ccggcctgca ggccgaggac gaagctgatt actattgcca gagctacgac 1860

tcaagcctga ccggagtcgt gttcggagga ggaaccaagc tgacagtcct gggacagcct 1920

aaagccgctc caagcgtgac actgtttcct ccatcctctg aggaactgca ggcaaacaag 1980

gccaccctgg tgtgcctgat ttccgacttc taccccgggg cagtcactgt ggcttggaag 2040

gcagatagtt cacctgtcaa agccggagtg gagactacca caccatcaaa gcagagcaat 2100

aacaaatacg cagccagctc ctatctgtcc ctgacccctg agcagtggaa gtctcacaaa 2160

tcctattctt gccaggtcac tcacgaagga agcactgtgg agaaaactgt cgcaccaacc 2220

gaatgtagtt gataactcga g 2241

<210> 69
<211> 739
<212> PRT
<213> Artificial Sequence

<220>
<223> DVSF-1 LALA amino acid sequence

<400> 69

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Gln Ala His Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Ala Phe Asn Phe
35 40 45

Ser Thr Asn Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

```
Glu Trp Val Ala Val Ile Ser Tyr Asp Gly Ser His Lys Tyr Tyr Ala
65                  70                  75                  80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
                85                  90                  95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Ala Asp Thr Ala Val
            100                 105                 110

Tyr Tyr Cys Ala Thr Val Gly Val Leu Thr Trp Pro Val Asn Ala Glu
        115                 120                 125

Tyr Phe His His Trp Gly Gln Gly Ser Leu Val Ser Val Ser Ser Ala
    130                 135                 140

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
145                 150                 155                 160

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
                165                 170                 175

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
            180                 185                 190

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
        195                 200                 205

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
    210                 215                 220

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
225                 230                 235                 240

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
                245                 250                 255

Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
            260                 265                 270

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
        275                 280                 285

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
    290                 295                 300

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
```

```
305                 310                 315                 320

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                325                 330                 335

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            340                 345                 350

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        355                 360                 365

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
    370                 375                 380

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
385                 390                 395                 400

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                405                 410                 415

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            420                 425                 430

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
        435                 440                 445

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
    450                 455                 460

Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser
465                 470                 475                 480

Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
                485                 490                 495

Glu Glu Asn Pro Gly Pro Met Ala Trp Thr Pro Leu Phe Leu Phe Leu
            500                 505                 510

Leu Thr Cys Cys Pro Gly Gly Ser Asn Ser Gln Ser Val Leu Thr Gln
        515                 520                 525

Pro Pro Ser Val Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys
    530                 535                 540

Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His Trp Tyr
545                 550                 555                 560
```

```
Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Cys Gly Asn Asn
                565                 570                 575

Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly
            580                 585                 590

Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala
        595                 600                 605

Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser Leu Thr Gly Val Val Phe
    610                 615                 620

Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro Lys Ala Ala Pro
625                 630                 635                 640

Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys
                645                 650                 655

Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr
            660                 665                 670

Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly Val Glu Thr
        675                 680                 685

Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr
    690                 695                 700

Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Lys Ser Tyr Ser Cys
705                 710                 715                 720

Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val Ala Pro Thr
                725                 730                 735

Glu Cys Ser
```

<210> 70
<211> 2241
<212> DNA
<213> Artificial Sequence

<220>
<223> DVSF-2 WT nucleic acid sequence

<400> 70

```
ggatccgcca ccatggactg gacatggaga atcctgttcc tggtcgccgc cgcaaccggg       60

acacacgccg aagtgcagct ggtggaatct ggaggggggat gggtgcagcc aggagggtcc      120

ctgcgactgt cttgcgccgc tagtggcttc acttttttcca gatacgacat gcactgggtc      180
```

aggcaggtga ccggaaaggg cctggaatgg gtgagcgcaa tcaccacagc cggagacaca 240

tactatcccg attctgtgaa gggccggttc accattagtc gggagaacgc caaaagctcc 300

ctgtatctgc agatgaacaa tctgagagct ggcgacaccg cactgtacta ttgcgctagg 360

ggccccccta cagattgctc tagtggacga tgtctgggag tcggagtggg actggaccca 420

tgggggcagg gaacactggt cactgtgtca agcgcctcca caaagggacc ctctgtgttc 480

cctctggctc catcctctaa aagtacttca ggaggaaccg cagcactggg atgtctggtg 540

aaggattact tcccagagcc cgtcaccgtg agctggaact ccggagctct gactagcggc 600

gtccatacct ttcctgcagt gctgcagagt tcaggcctgt acagcctgag ctccgtggtc 660

accgtgccat ctagttcact ggggacccag acatatatct gcaacgtgaa tcacaagcca 720

tctaatacaa aagtcgacaa gaaagtggaa cccaagagtt gtgataaaac tcatacctgc 780

ccaccatgtc ctgcaccaga gctgctggga ggaccatccg tgttcctgtt tcctccaaag 840

cccaaagaca cactgatgat tagcaggaca cccgaagtca cttgcgtggt cgtggacgtg 900

agccacgagg accccgaagt caagtttaac tggtacgtgg atggcgtcga ggtgcataat 960

gccaagacca aaccccggga ggaacagtac aacagtacct atagagtcgt gtcagtcctg 1020

acagtgctgc accaggactg gctgaacggg aaagagtata agtgcaaagt gtccaataag 1080

gcactgcccg cccctatcga gaaaaccatt tctaaggcca aaggacagcc ccgagaacct 1140

caggtgtaca cactgccccc tagccgcgac gagctgacaa agaaccaggt ctccctgact 1200

tgtctggtga aagggttcta tccttcagat atcgccgtgg agtgggaaag caatggacag 1260

ccagaaaaca attacaagac taccccaccc gtgctggact ctgatggcag tttctttctg 1320

tatagcaagc tgaccgtgga caaatcccgc tggcagcagg ggaacgtctt tagctgctcc 1380

gtgatgcatg aggccctgca caatcattac actcagaagt ctctgagtct gtcacctgga 1440

aagaggggac gaaaacgaag aagcggctcc ggagcaacca acttcagcct gctgaaacag 1500

gccggggatg tggaggaaaa tccaggaccc atggcatgga ctcctctgtt cctgtttctg 1560

ctgacctgct gtccaggcgg gagcaacagc tcctacgagg tgacccagcc tccatctgtc 1620

agtgtgtcac ccggccagac cgcttcaatc acatgtagcg gggacaagct gggaaagaaa 1680

tacacaagtt ggtatcagca gaaaccagga cagtcacccc tgctggtcat ctaccaggat 1740

actaagcgcc ctagcggcat tccagaacgg ttcagcggct ccaactctgg gaatacagct 1800

actctgacca tctccggcac ccaggccatg gacgaggctg attactattg ccaggcatgg 1860

gattctacaa ctcacgtcat tttcggaggc gggaccaagc tgacagtgct ggggcagccc 1920

aaagctgcac ctagcgtcac cctgtttccc ccttctagtg aggaactgca ggctaataag 1980

gcaacactgg tgtgtctgat ttccgacttc tacccaggag cagtcactgt ggcatggaag 2040

gctgattcaa gccccgtcaa agccggagtg gaaaccacaa ctccttcaaa gcagagcaac 2100

aacaagtacg ccgcttcctc ttatctgtcc ctgactcccg agcagtggaa gtctcacaaa 2160

agttattcat gccaggtgac ccatgagggc tccactgtcg aaaagaccgt ggcccctaca 2220

gagtgttctt gataactcga g 2241

<210> 71
<211> 739
<212> PRT
<213> Artificial Sequence

<220>
<223> DVSF-2 WT amino acid sequence

<400> 71

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Trp Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Arg Tyr Asp Met His Trp Val Arg Gln Val Thr Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Ala Ile Thr Thr Ala Gly Asp Thr Tyr Tyr Pro Asp
65 70 75 80

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Ser Ser
85 90 95

Leu Tyr Leu Gln Met Asn Asn Leu Arg Ala Gly Asp Thr Ala Leu Tyr
100 105 110

Tyr Cys Ala Arg Gly Pro Pro Thr Asp Cys Ser Ser Gly Arg Cys Leu
115 120 125

Gly Val Gly Val Gly Leu Asp Pro Trp Gly Gln Gly Thr Leu Val Thr
130 135 140

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
145 150 155 160

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
165 170 175

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala

```
                180                 185                 190

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
        195                 200                 205

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
    210                 215                 220

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
225                 230                 235                 240

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
                245                 250                 255

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
            260                 265                 270

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        275                 280                 285

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
    290                 295                 300

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
305                 310                 315                 320

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
                325                 330                 335

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            340                 345                 350

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        355                 360                 365

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
    370                 375                 380

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
385                 390                 395                 400

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                405                 410                 415

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
            420                 425                 430
```

```
Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
        435                 440                 445

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
    450                 455                 460

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg
465                 470                 475                 480

Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln
                485                 490                 495

Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Ala Trp Thr Pro Leu
            500                 505                 510

Phe Leu Phe Leu Leu Thr Cys Cys Pro Gly Gly Ser Asn Ser Ser Tyr
        515                 520                 525

Glu Val Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln Thr Ala
    530                 535                 540

Ser Ile Thr Cys Ser Gly Asp Lys Leu Gly Lys Lys Tyr Thr Ser Trp
545                 550                 555                 560

Tyr Gln Gln Lys Pro Gly Gln Ser Pro Leu Leu Val Ile Tyr Gln Asp
                565                 570                 575

Thr Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser
            580                 585                 590

Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met Asp Glu
        595                 600                 605

Ala Asp Tyr Tyr Cys Gln Ala Trp Asp Ser Thr Thr His Val Ile Phe
    610                 615                 620

Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro Lys Ala Ala Pro
625                 630                 635                 640

Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys
                645                 650                 655

Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr
            660                 665                 670

Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly Val Glu Thr
        675                 680                 685
```

Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr
690 695 700

Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Lys Ser Tyr Ser Cys
705 710 715 720

Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val Ala Pro Thr
725 730 735

Glu Cys Ser

<210> 72
<211> 2241
<212> DNA
<213> Artificial Sequence

<220>
<223> DVSF-2 LALA nucleic acid sequence

<400> 72
ggatccgcca ccatggactg gacatggaga atcctgttcc tggtcgccgc cgctactggg 60

actcacgccg aagtgcagct ggtcgagagt ggaggggggat gggtgcagcc cggcggcagc 120

ctgaggctgt cttgcgccgc tagtggcttc actttttcta gatacgacat gcactgggtc 180

cggcaggtga ccgggaaggg actggaatgg gtgagcgcca tcaccacagc aggggacaca 240

tactatcccg attctgtgaa gggcaggttc accattagta gggagaacgc aaaaagctcc 300

ctgtatctgc agatgaacaa tctgagagcc ggcgacaccg ctctgtacta ttgcgccagg 360

ggccctccca cagattgctc tagtggacgc tgtctgggag tcggagtggg actggaccca 420

tggggacagg ggacactggt caccgtgagc agcgcctcca ctaagggacc aagcgtgttc 480

cctctggcac catcctctaa aagtacttca gggggcaccg cagccctggg atgtctggtg 540

aaggattact tcccagagcc cgtcacagtg agctggaact ccggggccct gacttccgga 600

gtccacacct ttcctgctgt gctgcagagt tcaggcctgt actctctgag ctccgtggtc 660

acagtgccat ctagttcact gggaacccag acatatatct gcaacgtgaa tcacaagcca 720

agtaatacta aagtcgacaa gaaagtggaa cccaagtctt gtgataaaac tcatacctgc 780

ccaccctgtc ctgcaccaga ggctgcagga gggccatccg tgttcctgtt tcctccaaag 840

cccaaagaca ccctgatgat tagccggaca cccgaagtca cttgcgtggt cgtggacgtg 900

tcccacgagg accccgaagt caagtttaac tggtacgtgg atggcgtcga ggtgcataat 960

gccaagacaa aacccaggga ggaacagtac aacagtacct atagagtcgt gtcagtcctg 1020

acagtgctgc accaggactg gctgaacgga aaggagtata agtgcaaagt gtctaataag 1080

gctctgcccg cacctatcga gaaaaccatt agcaaggcca aagggcagcc ccgagaacct 1140

caggtgtaca cactgccccc ttcccgcgac gagctgacaa agaaccaggt ctctctgact 1200

tgtctggtga aaggattcta tccttcagat atcgccgtgg agtgggaaag caatgggcag 1260

ccagaaaaca attacaagac taccccaccc gtgctggact ctgatggcag tttctttctg 1320

tatagcaagc tgaccgtgga caaatcccgc tggcagcagg gaaacgtctt tagctgctcc 1380

gtgatgcatg aggccctgca caatcattac acccagaagt ctctgagtct gtcacctggg 1440

aagcgaggac gaaaaaggag aagcggctcc ggagctacaa acttctccct gctgaaacag 1500

gcaggagatg tggaggaaaa tccagggccc atggcctgga ctcctctgtt cctgtttctg 1560

ctgacctgct gtccaggcgg aagcaacagc tcctacgagg tgacccagcc tccaagcgtg 1620

agcgtgagcc caggccagac cgcttcaatc acatgtagcg gagacaagct ggggaagaaa 1680

tacactagtt ggtatcagca gaaaccaggg cagtcacccc tgctggtcat ctaccaggat 1740

accaagcgcc ctagcggcat tccagaacga ttcagcggct ccaactctgg aaatacagcc 1800

actctgacca tcagcggcac ccaggcaatg gacgaggccg attactattg ccaggcttgg 1860

gattccacaa ctcacgtcat tttcgggggc ggaaccaagc tgacagtgct gggacagccc 1920

aaagccgctc cttccgtcac cctgtttccc ccttctagtg aggaactgca ggccaataag 1980

gccaccctgg tgtgcctgat tagcgacttc taccccggag ctgtcactgt ggcatggaag 2040

gccgattcaa gccccgtcaa agcaggggtg gaaaccacaa ctccttcaaa gcagagcaac 2100

aacaagtacg cagcctcctc ttatctgtcc ctgacccctg agcagtggaa gtctcataaa 2160

agttattcat gtcaggtcac ccatgagggc agcacagtgg aaaaaaccgt ggcaccaaca 2220

gaatgtagct gataactcga g 2241

<210> 73
<211> 739
<212> PRT
<213> Artificial Sequence

<220>
<223> DVSF-2 LALA amino acid sequence

<400> 73

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Trp Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Arg Tyr Asp Met His Trp Val Arg Gln Val Thr Gly Lys Gly Leu

```
    50                  55                  60

Glu Trp Val Ser Ala Ile Thr Thr Ala Gly Asp Thr Tyr Tyr Pro Asp
65                  70                  75                  80

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Ser Ser
                85                  90                  95

Leu Tyr Leu Gln Met Asn Asn Leu Arg Ala Gly Asp Thr Ala Leu Tyr
            100                 105                 110

Tyr Cys Ala Arg Gly Pro Pro Thr Asp Cys Ser Ser Gly Arg Cys Leu
        115                 120                 125

Gly Val Gly Val Gly Leu Asp Pro Trp Gly Gln Gly Thr Leu Val Thr
    130                 135                 140

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
145                 150                 155                 160

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                165                 170                 175

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
            180                 185                 190

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
        195                 200                 205

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
    210                 215                 220

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
225                 230                 235                 240

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
                245                 250                 255

Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu
            260                 265                 270

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        275                 280                 285

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
    290                 295                 300
```

```
Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
305                 310                 315                 320

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
                325                 330                 335

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            340                 345                 350

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        355                 360                 365

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
    370                 375                 380

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
385                 390                 395                 400

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                405                 410                 415

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
            420                 425                 430

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
        435                 440                 445

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
    450                 455                 460

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg
465                 470                 475                 480

Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln
                485                 490                 495

Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Ala Trp Thr Pro Leu
            500                 505                 510

Phe Leu Phe Leu Leu Thr Cys Cys Pro Gly Gly Ser Asn Ser Ser Tyr
        515                 520                 525

Glu Val Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln Thr Ala
    530                 535                 540

Ser Ile Thr Cys Ser Gly Asp Lys Leu Gly Lys Lys Tyr Thr Ser Trp
545                 550                 555                 560
```

```
Tyr Gln Gln Lys Pro Gly Gln Ser Pro Leu Leu Val Ile Tyr Gln Asp
                565                 570                 575

Thr Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser
            580                 585                 590

Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met Asp Glu
        595                 600                 605

Ala Asp Tyr Tyr Cys Gln Ala Trp Asp Ser Thr Thr His Val Ile Phe
    610                 615                 620

Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro Lys Ala Ala Pro
625                 630                 635                 640

Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys
                645                 650                 655

Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr
            660                 665                 670

Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala Gly Val Glu Thr
        675                 680                 685

Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr
    690                 695                 700

Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Lys Ser Tyr Ser Cys
705                 710                 715                 720

Gln Val Thr His Glu Gly Ser Thr Val Glu Lys Thr Val Ala Pro Thr
                725                 730                 735

Glu Cys Ser
```

<210> 74
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> DVSF-3 WT nucleic acid sequence

<400> 74

```
ggatccgcca ccatggactg gacatggaga atcctgttcc tggtcgccgc cgcaaccggg       60

acacacgccg aagtgcagct ggtggaatca gggggagggc tggtgcagcc tggaagaagt      120

ctgaggctgt catgcgccgc tagcggcttc acctttgacg attacgccat gttctgggtg      180
```

aggcaggctc caggcaaggg actggaatgg atcagcggca tttcctggaa ctctgcaact 240
atcgggtatg ccgactccgt gaaaggacgg tttaccattt caagagacaa cgccaagaaa 300
agcctggatc tgcagatgaa ttccctgcgg cccgacgata ccgctctgta ctattgcgca 360
aagggaggac ctagaggcct gcagctgctg agctcctggg tggactactg gggacagggc 420
actctggtca ccgtgtctag tgcttccaca aagggacctt ctgtgttccc actggcaccc 480
tcaagcaaat caacaagcgg aggaactgca gcactgggat gtctggtgaa ggattatttc 540
cccgagcctg tcaccgtgag ttggaactca ggagcactga cttccggagt ccacaccttt 600
ccagcagtgc tgcagtcctc tggactgtac agcctgagtt cagtggtcac agtgcctagc 660
tcctctctgg gcacacagac ttatatctgc aacgtgaatc acaagcctag caatactaaa 720
gtcgacaaga aagtggaacc aaagtcctgt gataaaaccc atacatgccc accttgtcca 780
gcaccagagc tgctgggggg accaagcgtg ttcctgtttc cacccaagcc caaagacaca 840
ctgatgattt ctcggacccc tgaagtcaca tgtgtggtcg tggacgtgag ccacgaggac 900
cccgaagtca agttcaactg gtacgtggat ggcgtcgagg tgcataatgc taagaccaaa 960
ccccgagagg aacagtacaa cagcacttat cgggtcgtgt ccgtcctgac cgtgctgcac 1020
caggactggc tgaacgggaa ggagtataag tgcaaagtgt ccaataaggc cctgcctgct 1080
ccaatcgaga aaacaatttc taaggcaaaa ggacagcctc gcgaaccaca ggtgtacact 1140
ctgcctccat cccgagacga gctgaccaag aaccaggtct ctctgacatg tctggtgaaa 1200
ggcttctatc caagtgatat cgctgtggag tgggaaagca atgggcagcc cgaaaacaat 1260
tacaagacca cacccctgt gctggacagc gatggctcct tctttctgta ttctaagctg 1320
accgtggata aaagtagatg gcagcagggg aacgtctttt cctgctctgt gatgcatgag 1380
gccctgcaca atcattacac acagaagagt ctgtcactga gcccagggaa gcgaggacgg 1440
aaacggagat ccgggtctgg agcaaccaac ttctccctgc tgaaacaggc aggcgacgtg 1500
gaggaaaatc caggacctat ggtcctgcag acccaggtgt ttatctctct gctgctgtgg 1560
attagtggcg cctacgggga tatccagatg acacagtccc ccagttcact gagtgcctca 1620
gtcggcgaca gggtgactat cacctgtcgc gctagccagg atattaggcg ctacctgaac 1680
tggtatcagc agcgaccagg acgagtgcct cagctgctga tctacactac ctccaccctg 1740
cagtctggag tcccaagtag gttcagcggc tccgggtctg tgacagactt tacactgact 1800
attagctccc tgcagcccga agatttcggc acttactatt gccagcagag ttattcacca 1860
ccccacacat ttggacaggg cactaagctg gaaatcaaaa ctgtcgctgc accctcagtg 1920
ttcatttttc ctccatctga cgagcagctg aagtcaggca ccgccagcgt cgtgtgtctg 1980
ctgaacaatt tctaccctcg cgaggctaag gtccagtgga aagtggataa cgcactgcag 2040

tctgggaata gtcaggagtc agtgacagaa caggacagca aggattccac ttattctctg 2100

tctagtaccc tgacactgag caaagccgac tacgagaagc acaaagtcta tgcttgcgaa 2160

gtgacccatc aggggctgag aagtcccgtg acaaagagct tcaacagggg agagtgttga 2220

taactcgag 2229

<210> 75
<211> 735
<212> PRT
<213> Artificial Sequence

<220>
<223> DVSF-3 WT amino acid sequence

<400> 75

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Asp Asp Tyr Ala Met Phe Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Ile Ser Gly Ile Ser Trp Asn Ser Ala Thr Ile Gly Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys
85 90 95

Ser Leu Asp Leu Gln Met Asn Ser Leu Arg Pro Asp Asp Thr Ala Leu
100 105 110

Tyr Tyr Cys Ala Lys Gly Gly Pro Arg Gly Leu Gln Leu Leu Ser Ser
115 120 125

Trp Val Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
130 135 140

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
145 150 155 160

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
165 170 175

```
Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
            180                 185                 190

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
        195                 200                 205

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
    210                 215                 220

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
225                 230                 235                 240

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
                245                 250                 255

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
            260                 265                 270

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
        275                 280                 285

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
    290                 295                 300

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
305                 310                 315                 320

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                325                 330                 335

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            340                 345                 350

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        355                 360                 365

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
    370                 375                 380

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
385                 390                 395                 400

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                405                 410                 415

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            420                 425                 430
```

```
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
        435                 440                 445

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
    450                 455                 460

Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser
465                 470                 475                 480

Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
                485                 490                 495

Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr Gln Val Phe Ile Ser
            500                 505                 510

Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Asp Ile Gln Met Thr Gln
        515                 520                 525

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
    530                 535                 540

Cys Arg Ala Ser Gln Asp Ile Arg Arg Tyr Leu Asn Trp Tyr Gln Gln
545                 550                 555                 560

Arg Pro Gly Arg Val Pro Gln Leu Leu Ile Tyr Thr Thr Ser Thr Leu
                565                 570                 575

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Val Thr Asp
            580                 585                 590

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Gly Thr Tyr
        595                 600                 605

Tyr Cys Gln Gln Ser Tyr Ser Pro Pro His Thr Phe Gly Gln Gly Thr
    610                 615                 620

Lys Leu Glu Ile Lys Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
625                 630                 635                 640

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
                645                 650                 655

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
            660                 665                 670

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
        675                 680                 685
```

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
690 695 700

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
705 710 715 720

Gly Leu Arg Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
725 730 735

<210> 76
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> DVSF-3 LALA nucleic acid sequence

<400> 76
ggatccgcca ccatggactg gacttggaga atcctgtttc tggtcgccgc cgcaactgga 60

acccacgccg aggtgcagct ggtcgaatca gggggaggcc tggtgcagcc tgggagaagt 120

ctgcggctgt catgcgccgc tagcggcttc acctttgacg attacgcaat gttctgggtg 180

aggcaggcac caggcaaggg actggaatgg atcagcggca tttcctggaa ctctgctacc 240

atcggatatg cagacagcgt gaaagggagg tttacaattt ctagagacaa cgccaagaaa 300

agtctggatc tgcagatgaa ttcactgcgc cccgacgata ccgccctgta ctattgcgct 360

aagggcggac ccaggggcct gcagctgctg agctcctggg tggactactg ggggcagggc 420

actctggtca ccgtgtctag tgcctccaca aagggcccta gcgtgttccc actggctccc 480

tcaagcaaat caacaagcgg gggcactgca gccctgggat gtctggtgaa ggattatttc 540

cccgagcctg tcaccgtgag ttggaactca ggggctctga ctagcggcgt ccacaccttt 600

cccgcagtgc tgcagtcctc tggcctgtac agcctgagtt cagtggtcac tgtccctagc 660

tcctctctgg gaacacagac ttatatctgc aacgtgaatc acaagccttc caataccaaa 720

gtcgacaaga aagtggaacc aaagtcttgt gataaaaccc atacatgccc tccctgtcca 780

gcaccagagg ctgcaggagg gccaagcgtg ttcctgtttc cacccaagcc caaagacaca 840

ctgatgatta gccggacccc tgaagtcaca tgcgtggtcg tggacgtgag ccacgaggac 900

cccgaagtca agtttaactg gtacgtggat ggcgtcgagg tgcataatgc taagaccaaa 960

ccccgagagg aacagtacaa cagtacttat agggtcgtgt cagtcctgac cgtgctgcac 1020

caggactggc tgaacgggaa ggagtataag tgcaaagtgt ccaataaggc actgcctgcc 1080

ccaatcgaga aaactatttc taaggctaaa ggccagccta gagaaccaca ggtgtacacc 1140

ctgcctccaa gccgggacga gctgaccaag aaccaggtca gcctgacatg tctggtgaaa 1200

ggattctatc catccgatat cgcagtggag tgggaatcta atgggcagcc cgaaaacaat 1260

tacaagacca cacccctgt gctggacagc gatggcagct tcttcctgta tagcaagctg 1320

accgtggata aatcccgctg gcagcagggg aacgtctttt cctgctctgt gatgcatgag 1380

gccctgcaca atcattacac acagaagagt ctgtcactga gcccaggaaa gcgagggagg 1440

aaaaggagat ccggatctgg ggctactaac ttctccctgc tgaagcaggc aggcgacgtg 1500

gaggaaaatc ccggacctat ggtcctgcag acacaggtgt ttatcagcct gctgctgtgg 1560

atttccggcg cttacggaga tatccagatg actcagtccc ccagttcact gagtgcatca 1620

gtcggcgacc gggtgactat cacctgtcgc gcctctcagg atattcggcg ctacctgaat 1680

tggtatcagc agcgaccagg acgagtgcct cagctgctga tctacactac ctccacactg 1740

cagtctggcg tcccaagtag gttcagcggc tccggatctg tgactgactt tacactgact 1800

attagctccc tgcagcccga ggatttcggc acctactatt gccagcagag ttattcacca 1860

ccccacacat ttgggcaggg cactaagctg gaaatcaaaa ccgtcgccgc tcccagcgtg 1920

ttcatctttc ctccaagtga cgagcagctg aagtcaggaa cagccagcgt ggtgtgcctg 1980

ctgaacaatt tctaccctag agaagccaag gtccagtgga aagtggataa cgctctgcag 2040

tctgggaata gtcaggagtc agtgacagaa caggacagca aggattccac ttattctctg 2100

tctagtaccc tgacactgag caaagcagac tacgagaagc ataaagtgta tgcctgcgaa 2160

gtcacccacc aggggctgcg gtcaccagtc acaaaatcct ttaacagagg cgaatgctga 2220

taactcgag 2229

<210> 77
<211> 735
<212> PRT
<213> Artificial Sequence

<220>
<223> DSVF-3 LALA amino acid sequence

<400> 77

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Asp Asp Tyr Ala Met Phe Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

```
Glu Trp Ile Ser Gly Ile Ser Trp Asn Ser Ala Thr Ile Gly Tyr Ala
65                  70                  75                  80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys
                85                  90                  95

Ser Leu Asp Leu Gln Met Asn Ser Leu Arg Pro Asp Asp Thr Ala Leu
            100                 105                 110

Tyr Tyr Cys Ala Lys Gly Gly Pro Arg Gly Leu Gln Leu Leu Ser Ser
        115                 120                 125

Trp Val Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
    130                 135                 140

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
145                 150                 155                 160

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
                165                 170                 175

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
            180                 185                 190

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
        195                 200                 205

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
    210                 215                 220

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
225                 230                 235                 240

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
                245                 250                 255

Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
            260                 265                 270

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
        275                 280                 285

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
    290                 295                 300

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
305                 310                 315                 320
```

```
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                325                 330                 335

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            340                 345                 350

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        355                 360                 365

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
    370                 375                 380

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
385                 390                 395                 400

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                405                 410                 415

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            420                 425                 430

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
        435                 440                 445

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
    450                 455                 460

Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser
465                 470                 475                 480

Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
                485                 490                 495

Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr Gln Val Phe Ile Ser
            500                 505                 510

Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Asp Ile Gln Met Thr Gln
        515                 520                 525

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr
    530                 535                 540

Cys Arg Ala Ser Gln Asp Ile Arg Arg Tyr Leu Asn Trp Tyr Gln Gln
545                 550                 555                 560

Arg Pro Gly Arg Val Pro Gln Leu Leu Ile Tyr Thr Thr Ser Thr Leu
                565                 570                 575
```

```
Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Val Thr Asp
            580                 585                 590

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Gly Thr Tyr
        595                 600                 605

Tyr Cys Gln Gln Ser Tyr Ser Pro Pro His Thr Phe Gly Gln Gly Thr
    610                 615                 620

Lys Leu Glu Ile Lys Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
625                 630                 635                 640

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
                645                 650                 655

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
            660                 665                 670

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
        675                 680                 685

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
    690                 695                 700

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
705                 710                 715                 720

Gly Leu Arg Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
                725                 730                 735
```

<210> 78
<211> 2217
<212> DNA
<213> Artificial Sequence

<220>
<223> Anti-PSMA nucleic acid sequence

<400> 78

```
ggatccgcca ccatggattg gacatggagg attctgtttc tggtcgccgc cgccacagga       60

acccacgccg aagtgcagct ggtgcagtca ggagccgagg tgaagaaacc aggcgaaagt      120

ctgaaaatct catgcaaagg aagtgggtac tcattcacta gcaactggat tggatgggtg      180

cggcagatgc caggcaaggg actggagtgg atgggaatca tctaccccgg ggactccgat      240

acacgctata gtccttcatt tcagggccag gtgacaatct ctgccgacaa aagcatttcc      300

actgcttatc tgcagtggag ctccctgaag gcttccgata ccgcaatgta ctattgcgcc      360
```

aggcagacag gcttcctgtg gtctagtgac ctgtggggga gaggcaccct ggtcacagtg 420

tcaagcgcct ctaccaaagg accaagcgtg ttcccactgg ctccttcctc taagtctact 480

agtggcggaa ccgccgctct gggatgtctg gtgaaggatt acttccctga gccagtcaca 540

gtgtcctgga actctggcgc tctgaccagc ggagtccaca catttcccgc agtgctgcag 600

agttcaggcc tgtactccct gagctccgtg gtcacagtcc cttctagttc actgggaact 660

cagacctata tctgcaacgt gaatcacaaa ccttccaata ctaaggtcga caagaaagtg 720

gaaccaaaat cttgtgataa gacacatact tgccctccct gtccagcacc tgagctgctg 780

ggcggcccaa gcgtgttcct gtttccaccc aagcccaaag ataccctgat gattagcagg 840

acaccagaag tcacttgcgt ggtcgtggac gtgtcccacg aggaccccga agtcaagttc 900

aactggtacg tggacggcgt cgaggtgcat aatgctaaga ccaaaccaag agaggaacag 960

tacaactcaa cctatcgggt cgtgagcgtc ctgacagtgc tgcaccagga ctggctgaac 1020

ggaaaggagt ataagtgcaa agtgtctaac aaggccctgc cagctcccat cgagaagact 1080

attagcaagg ctaaagggca gccacgcgaa ccccaggtgt acaccctgcc tccatcacga 1140

gatgagctga caaaaaacca ggtctctctg acttgtctgg tgaagggatt ctatccctct 1200

gacatcgcag tggagtggga aagtaatggg cagcctgaaa acaattacaa gaccacaccc 1260

cctgtgctgg acagtgatgg atcattcttt ctgtatagta aactgaccgt ggataagtca 1320

agatggcagc aggggaacgt cttttcatgc agcgtgatgc atgaggccct gcacaatcat 1380

tacacccaga agtccctgtc tctgagtcct ggcaaacggg gacgcaagag gagatcagga 1440

agcggggcta caaacttctc cctgctgaag caggcagggg acgtggagga aaatcctggc 1500

ccaatggtcc tgcagaccca ggtgtttatc tccctgctgc tgtggatttc tggggcatac 1560

ggcgccatcc agctgacaca gtctcccagc tccctgtccg catctgtcgg cgaccgagtg 1620

accatcacat gtagggccag ccaggatatt tctagtgctc tggcatggta ccagcagaag 1680

cctgggaaag caccaaagct gctgatctat gatgcctcaa gcctggaatc cggagtgcct 1740

agccggttct ccggatacgg aagtgggaca gactttactc tgaccattaa cagcctgcag 1800

cctgaggatt tcgccactta ctattgccag cagttcaata gctatccact gacttttgga 1860

gggggcacca aagtggaaat caagcgaact gtcgcagccc ctagcgtgtt cattttcca 1920

ccctccgatg agcagctgaa gagcggcacc gcttccgtgg tgtgcctgct gaacaacttc 1980

tacccacgcg aggccaaagt ccagtggaag gtggacaacg ctctgcagtc tggaaatagt 2040

caggagtcag tgactgaaca ggacagcaaa gattccacct attctctgtc ctctacactg 2100

actctgagca aggcagacta cgagaagcat aaagtgtatg cctgcgaagt cacccaccag 2160

gggctgtcct caccagtcac taaatctttc aatcggggag aatgttgata actcgag 2217

<210> 79
<211> 731
<212> PRT
<213> Artificial Sequence

<220>
<223> Anti-PSMA amino acid sequence

<400> 79

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                  10                  15

Thr His Ala Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
            20                  25                  30

Pro Gly Glu Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe
        35                  40                  45

Thr Ser Asn Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu
    50                  55                  60

Glu Trp Met Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser
65                  70                  75                  80

Pro Ser Phe Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser
                85                  90                  95

Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met
            100                 105                 110

Tyr Tyr Cys Ala Arg Gln Thr Gly Phe Leu Trp Ser Ser Asp Leu Trp
        115                 120                 125

Gly Arg Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
    130                 135                 140

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
145                 150                 155                 160

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
                165                 170                 175

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
            180                 185                 190

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
        195                 200                 205

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
```

```
    210                 215                 220

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
225                 230                 235                 240

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
                245                 250                 255

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
            260                 265                 270

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
        275                 280                 285

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
    290                 295                 300

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
305                 310                 315                 320

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
                325                 330                 335

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
            340                 345                 350

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
        355                 360                 365

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
    370                 375                 380

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
385                 390                 395                 400

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
                405                 410                 415

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
            420                 425                 430

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
        435                 440                 445

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
    450                 455                 460
```

```
Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr
465                 470                 475                 480

Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly
                485                 490                 495

Pro Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile
            500                 505                 510

Ser Gly Ala Tyr Gly Ala Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu
        515                 520                 525

Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
    530                 535                 540

Asp Ile Ser Ser Ala Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
545                 550                 555                 560

Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro
                565                 570                 575

Ser Arg Phe Ser Gly Tyr Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
            580                 585                 590

Asn Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Phe
        595                 600                 605

Asn Ser Tyr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
    610                 615                 620

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
625                 630                 635                 640

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
                645                 650                 655

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
            660                 665                 670

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
        675                 680                 685

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
    690                 695                 700

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
705                 710                 715                 720
```

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
725 730

<210> 80
<211> 733
<212> PRT
<213> Artificial Sequence

<220>
<223> CHIKV-snapi amino acid sequence

<400> 80

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1 5 10 15

His Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Ala Leu Val Lys Pro
20 25 30

Gly Ala Ser Ala Met Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr
35 40 45

Ser Tyr Trp Ile Thr Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu
50 55 60

Trp Ile Gly Asp Ile Tyr Pro Gly Thr Gly Arg Thr Ile Tyr Lys Glu
65 70 75 80

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

Ala Phe Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr
100 105 110

Tyr Cys Ala Arg Gly Tyr Gly Ser Pro Tyr Tyr Ala Leu Asp Tyr Trp
115 120 125

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
130 135 140

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
145 150 155 160

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
165 170 175

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
180 185 190

```
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
        195                 200                 205

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
    210                 215                 220

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
225                 230                 235                 240

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
                245                 250                 255

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
            260                 265                 270

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
        275                 280                 285

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
    290                 295                 300

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
305                 310                 315                 320

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
                325                 330                 335

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
            340                 345                 350

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
        355                 360                 365

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
    370                 375                 380

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
385                 390                 395                 400

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
                405                 410                 415

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
            420                 425                 430

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
        435                 440                 445
```

```
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
    450                 455                 460

Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr
465                 470                 475                 480

Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly
                485                 490                 495

Pro Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg
            500                 505                 510

Val His Ser Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val
        515                 520                 525

Ser Gln Gly Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val
    530                 535                 540

Asp Tyr Asp Gly Asp Ser Tyr Val Asn Trp Tyr Gln Gln Lys Pro Gly
545                 550                 555                 560

Gln Ser Pro Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Glu Ser Gly
                565                 570                 575

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
            580                 585                 590

Asn Ile His Pro Val Glu Glu Glu Asp Val Ala Thr Tyr Tyr Cys Gln
        595                 600                 605

Glu Ser Asn Glu Asp Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu Glu
    610                 615                 620

Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser
625                 630                 635                 640

Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn
                645                 650                 655

Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala
            660                 665                 670

Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys
        675                 680                 685

Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp
    690                 695                 700
```

```
Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu
705                 710                 715                 720

Arg Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
                725                 730
```

<210> 81
<211> 457
<212> PRT
<213> Artificial Sequence

<220>
<223> CHIKV E1 consensus

<400> 81

```
Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1               5                   10                  15

His Ser Tyr Glu His Val Thr Val Ile Pro Asn Thr Val Gly Val Pro
            20                  25                  30

Tyr Lys Thr Leu Val Asn Arg Pro Gly Tyr Ser Pro Met Val Leu Glu
        35                  40                  45

Met Glu Leu Leu Ser Val Thr Leu Glu Pro Thr Leu Ser Leu Asp Tyr
    50                  55                  60

Ile Thr Cys Glu Tyr Lys Thr Val Ile Pro Ser Pro Tyr Val Lys Cys
65                  70                  75                  80

Cys Gly Thr Ala Glu Cys Lys Asp Lys Asn Leu Pro Asp Tyr Ser Cys
                85                  90                  95

Lys Val Phe Thr Gly Val Tyr Pro Phe Met Trp Gly Gly Ala Tyr Cys
            100                 105                 110

Phe Cys Asp Ala Glu Asn Thr Gln Leu Ser Glu Ala His Val Glu Lys
        115                 120                 125

Ser Glu Ser Cys Lys Thr Glu Phe Ala Ser Ala Tyr Arg Ala His Thr
    130                 135                 140

Ala Ser Ala Ser Ala Lys Leu Arg Val Leu Tyr Gln Gly Asn Asn Ile
145                 150                 155                 160

Thr Val Thr Ala Tyr Ala Asn Gly Asp His Ala Val Thr Val Lys Asp
                165                 170                 175
```

```
Ala Lys Phe Ile Val Gly Pro Met Ser Ser Ala Trp Thr Pro Phe Asp
            180                 185                 190

Asn Lys Ile Val Val Tyr Lys Gly Asp Val Tyr Asn Met Asp Tyr Pro
        195                 200                 205

Pro Phe Gly Ala Gly Arg Pro Gly Gln Phe Gly Asp Ile Gln Ser Arg
    210                 215                 220

Thr Pro Glu Ser Lys Asp Val Tyr Ala Asn Thr Gln Leu Val Leu Gln
225                 230                 235                 240

Arg Pro Ala Val Gly Thr Val His Val Pro Tyr Ser Gln Ala Pro Ser
                245                 250                 255

Gly Phe Lys Tyr Trp Leu Lys Glu Arg Gly Ala Ser Leu Gln His Thr
            260                 265                 270

Ala Pro Phe Gly Cys Gln Ile Ala Thr Asn Pro Val Arg Ala Val Asn
        275                 280                 285

Cys Ala Val Gly Asn Met Pro Ile Ser Ile Asp Ile Pro Glu Ala Ala
    290                 295                 300

Phe Thr Arg Val Val Asp Ala Pro Ser Leu Thr Asp Met Ser Cys Glu
305                 310                 315                 320

Val Pro Ala Cys Thr His Ser Ser Asp Phe Gly Gly Val Ala Ile Ile
                325                 330                 335

Lys Tyr Ala Ala Ser Lys Lys Gly Lys Cys Ala Val His Ser Met Thr
            340                 345                 350

Asn Ala Val Thr Ile Arg Glu Ala Glu Ile Glu Val Glu Gly Asn Ser
        355                 360                 365

Gln Leu Gln Ile Ser Phe Ser Thr Ala Leu Ala Ser Ala Glu Phe Arg
    370                 375                 380

Val Gln Val Cys Ser Thr Gln Val His Cys Ala Ala Glu Cys His Pro
385                 390                 395                 400

Pro Lys Asp His Ile Val Asn Tyr Pro Ala Ser His Thr Thr Leu Gly
                405                 410                 415

Val Gln Asp Ile Ser Ala Thr Ala Met Ser Trp Val Gln Lys Ile Thr
            420                 425                 430
```

```
Gly Gly Val Gly Leu Val Val Ala Val Ala Ala Leu Ile Leu Ile Val
        435                 440                 445

Val Leu Cys Val Ser Phe Ser Arg His
    450                 455
```

<210> 82
<211> 441
<212> PRT
<213> Artificial Sequence

<220>
<223> CHIKV E2 consensus

<400> 82

```
Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1               5                  10                  15

His Ser Ser Thr Lys Asp Asn Phe Asn Val Tyr Lys Ala Thr Arg Pro
            20                  25                  30

Tyr Leu Ala His Cys Pro Asp Cys Gly Glu Gly His Ser Cys His Ser
        35                  40                  45

Pro Val Ala Leu Glu Arg Ile Arg Asn Glu Ala Thr Asp Gly Thr Leu
    50                  55                  60

Lys Ile Gln Val Ser Leu Gln Ile Gly Ile Lys Thr Asp Asp Ser His
65                  70                  75                  80

Asp Trp Thr Lys Leu Arg Tyr Met Asp Asn His Met Pro Ala Asp Ala
                85                  90                  95

Glu Arg Ala Gly Leu Phe Val Arg Thr Ser Ala Pro Cys Thr Ile Thr
            100                 105                 110

Gly Thr Met Gly His Phe Ile Leu Ala Arg Cys Pro Lys Gly Glu Thr
        115                 120                 125

Leu Thr Val Gly Phe Thr Asp Ser Arg Lys Ile Ser His Ser Cys Thr
    130                 135                 140

His Pro Phe His His Asp Pro Pro Val Ile Gly Arg Glu Lys Phe His
145                 150                 155                 160

Ser Arg Pro Gln His Gly Lys Glu Leu Pro Cys Ser Thr Tyr Val Gln
                165                 170                 175
```

```
Ser Thr Ala Ala Thr Thr Glu Glu Ile Glu Val His Met Pro Pro Asp
            180                 185                 190

Thr Pro Asp Arg Thr Leu Met Ser Gln Gln Ser Gly Asn Val Lys Ile
        195                 200                 205

Thr Val Asn Gly Gln Thr Val Arg Tyr Lys Cys Asn Cys Gly Gly Ser
    210                 215                 220

Asn Glu Gly Leu Thr Thr Thr Asp Lys Val Ile Asn Asn Cys Lys Val
225                 230                 235                 240

Asp Gln Cys His Ala Ala Val Thr Asn His Lys Lys Trp Gln Tyr Asn
                245                 250                 255

Ser Pro Leu Val Pro Arg Asn Ala Glu Leu Gly Asp Arg Lys Gly Lys
            260                 265                 270

Ile His Ile Pro Phe Pro Leu Ala Asn Val Thr Cys Arg Val Pro Lys
        275                 280                 285

Ala Arg Asn Pro Thr Val Thr Tyr Gly Lys Asn Gln Val Ile Met Leu
    290                 295                 300

Leu Tyr Pro Asp His Pro Thr Leu Leu Ser Tyr Arg Asn Met Gly Glu
305                 310                 315                 320

Glu Pro Asn Tyr Gln Glu Glu Trp Val Met His Lys Lys Glu Val Val
                325                 330                 335

Leu Thr Val Pro Thr Glu Gly Leu Glu Val Thr Trp Gly Asn Asn Glu
            340                 345                 350

Pro Tyr Lys Tyr Trp Pro Gln Leu Ser Thr Asn Gly Thr Ala His Gly
        355                 360                 365

His Pro His Glu Ile Ile Leu Tyr Tyr Tyr Glu Leu Tyr Pro Thr Met
    370                 375                 380

Thr Val Val Val Val Ser Val Ala Thr Phe Ile Leu Leu Ser Met Val
385                 390                 395                 400

Gly Met Ala Ala Gly Met Cys Met Cys Ala Arg Arg Arg Cys Ile Thr
                405                 410                 415

Pro Tyr Glu Leu Thr Pro Gly Ala Thr Val Pro Phe Leu Leu Ser Leu
            420                 425                 430
```

```
Ile Cys Cys Ile Arg Thr Ala Lys Ala
        435                 440


<210>  83
<211>  279
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CHIKV capsid consensus

<400>  83

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1               5                  10                  15


His Ser Met Glu Phe Ile Pro Thr Gln Thr Phe Tyr Asn Arg Arg Tyr
            20                  25                  30


Gln Pro Arg Pro Trp Thr Pro Arg Pro Thr Ile Gln Val Ile Arg Pro
        35                  40                  45


Arg Pro Arg Pro Gln Arg Gln Ala Gly Gln Leu Ala Gln Leu Ile Ser
    50                  55                  60


Ala Val Asn Lys Leu Thr Met Arg Ala Val Pro Gln Gln Lys Pro Arg
65                  70                  75                  80


Arg Asn Arg Lys Asn Lys Lys Gln Lys Gln Lys Gln Gln Ala Pro Gln
                85                  90                  95


Asn Asn Thr Asn Gln Lys Lys Gln Pro Pro Lys Lys Lys Pro Ala Gln
            100                 105                 110


Lys Lys Lys Lys Pro Gly Arg Arg Glu Arg Met Cys Met Lys Ile Glu
        115                 120                 125


Asn Asp Cys Ile Phe Glu Val Lys His Glu Gly Lys Val Thr Gly Tyr
    130                 135                 140


Ala Cys Leu Val Gly Asp Lys Val Met Lys Pro Ala His Val Lys Gly
145                 150                 155                 160


Thr Ile Asp Asn Ala Asp Leu Ala Lys Leu Ala Phe Lys Arg Ser Ser
                165                 170                 175


Lys Tyr Asp Leu Glu Cys Ala Gln Ile Pro Val His Met Lys Ser Asp
            180                 185                 190
```

```
Ala Ser Lys Phe Thr His Glu Lys Pro Glu Gly Tyr Tyr Asn Trp His
        195                 200                 205

His Gly Ala Val Gln Tyr Ser Gly Gly Arg Phe Thr Ile Pro Thr Gly
    210                 215                 220

Ala Gly Lys Pro Gly Asp Ser Gly Arg Pro Ile Phe Asp Asn Lys Gly
225                 230                 235                 240

Arg Val Val Ala Ile Val Leu Gly Gly Ala Asn Glu Gly Ala Arg Thr
                245                 250                 255

Ala Leu Ser Val Val Thr Trp Asn Lys Asp Ile Val Thr Lys Ile Thr
            260                 265                 270

Pro Glu Gly Ala Glu Glu Trp
        275
```

<210> 84
<211> 439
<212> PRT
<213> Artificial Sequence

<220>
<223> CHIKV E1 consensus

<400> 84

```
Tyr Glu His Val Thr Val Ile Pro Asn Thr Val Gly Val Pro Tyr Lys
1               5                   10                  15

Thr Leu Val Asn Arg Pro Gly Tyr Ser Pro Met Val Leu Glu Met Glu
            20                  25                  30

Leu Leu Ser Val Thr Leu Glu Pro Thr Leu Ser Leu Asp Tyr Ile Thr
        35                  40                  45

Cys Glu Tyr Lys Thr Val Ile Pro Ser Pro Tyr Val Lys Cys Cys Gly
    50                  55                  60

Thr Ala Glu Cys Lys Asp Lys Asn Leu Pro Asp Tyr Ser Cys Lys Val
65                  70                  75                  80

Phe Thr Gly Val Tyr Pro Phe Met Trp Gly Gly Ala Tyr Cys Phe Cys
                85                  90                  95

Asp Ala Glu Asn Thr Gln Leu Ser Glu Ala His Val Glu Lys Ser Glu
            100                 105                 110
```

```
Ser Cys Lys Thr Glu Phe Ala Ser Ala Tyr Arg Ala His Thr Ala Ser
        115                 120                 125

Ala Ser Ala Lys Leu Arg Val Leu Tyr Gln Gly Asn Asn Ile Thr Val
    130                 135                 140

Thr Ala Tyr Ala Asn Gly Asp His Ala Val Thr Val Lys Asp Ala Lys
145                 150                 155                 160

Phe Ile Val Gly Pro Met Ser Ser Ala Trp Thr Pro Phe Asp Asn Lys
                165                 170                 175

Ile Val Val Tyr Lys Gly Asp Val Tyr Asn Met Asp Tyr Pro Pro Phe
            180                 185                 190

Gly Ala Gly Arg Pro Gly Gln Phe Gly Asp Ile Gln Ser Arg Thr Pro
        195                 200                 205

Glu Ser Lys Asp Val Tyr Ala Asn Thr Gln Leu Val Leu Gln Arg Pro
    210                 215                 220

Ala Val Gly Thr Val His Val Pro Tyr Ser Gln Ala Pro Ser Gly Phe
225                 230                 235                 240

Lys Tyr Trp Leu Lys Glu Arg Gly Ala Ser Leu Gln His Thr Ala Pro
                245                 250                 255

Phe Gly Cys Gln Ile Ala Thr Asn Pro Val Arg Ala Val Asn Cys Ala
            260                 265                 270

Val Gly Asn Met Pro Ile Ser Ile Asp Ile Pro Glu Ala Ala Phe Thr
        275                 280                 285

Arg Val Val Asp Ala Pro Ser Leu Thr Asp Met Ser Cys Glu Val Pro
    290                 295                 300

Ala Cys Thr His Ser Ser Asp Phe Gly Gly Val Ala Ile Ile Lys Tyr
305                 310                 315                 320

Ala Ala Ser Lys Lys Gly Lys Cys Ala Val His Ser Met Thr Asn Ala
                325                 330                 335

Val Thr Ile Arg Glu Ala Glu Ile Glu Val Glu Gly Asn Ser Gln Leu
            340                 345                 350

Gln Ile Ser Phe Ser Thr Ala Leu Ala Ser Ala Glu Phe Arg Val Gln
        355                 360                 365
```

```
Val Cys Ser Thr Gln Val His Cys Ala Ala Glu Cys His Pro Pro Lys
    370                 375                 380

Asp His Ile Val Asn Tyr Pro Ala Ser His Thr Thr Leu Gly Val Gln
385                 390                 395                 400

Asp Ile Ser Ala Thr Ala Met Ser Trp Val Gln Lys Ile Thr Gly Gly
                405                 410                 415

Val Gly Leu Val Val Ala Val Ala Ala Leu Ile Leu Ile Val Val Leu
            420                 425                 430

Cys Val Ser Phe Ser Arg His
        435
```

<210> 85
<211> 423
<212> PRT
<213> Artificial Sequence

<220>
<223> CHIKV E2 consensus

<400> 85

```
Ser Thr Lys Asp Asn Phe Asn Val Tyr Lys Ala Thr Arg Pro Tyr Leu
1               5                   10                  15

Ala His Cys Pro Asp Cys Gly Glu Gly His Ser Cys His Ser Pro Val
            20                  25                  30

Ala Leu Glu Arg Ile Arg Asn Glu Ala Thr Asp Gly Thr Leu Lys Ile
        35                  40                  45

Gln Val Ser Leu Gln Ile Gly Ile Lys Thr Asp Asp Ser His Asp Trp
    50                  55                  60

Thr Lys Leu Arg Tyr Met Asp Asn His Met Pro Ala Asp Ala Glu Arg
65                  70                  75                  80

Ala Gly Leu Phe Val Arg Thr Ser Ala Pro Cys Thr Ile Thr Gly Thr
                85                  90                  95

Met Gly His Phe Ile Leu Ala Arg Cys Pro Lys Gly Glu Thr Leu Thr
            100                 105                 110

Val Gly Phe Thr Asp Ser Arg Lys Ile Ser His Ser Cys Thr His Pro
        115                 120                 125
```

```
Phe His His Asp Pro Pro Val Ile Gly Arg Glu Lys Phe His Ser Arg
    130                 135                 140

Pro Gln His Gly Lys Glu Leu Pro Cys Ser Thr Tyr Val Gln Ser Thr
145                 150                 155                 160

Ala Ala Thr Thr Glu Glu Ile Glu Val His Met Pro Pro Asp Thr Pro
                165                 170                 175

Asp Arg Thr Leu Met Ser Gln Gln Ser Gly Asn Val Lys Ile Thr Val
            180                 185                 190

Asn Gly Gln Thr Val Arg Tyr Lys Cys Asn Cys Gly Gly Ser Asn Glu
        195                 200                 205

Gly Leu Thr Thr Thr Asp Lys Val Ile Asn Asn Cys Lys Val Asp Gln
    210                 215                 220

Cys His Ala Ala Val Thr Asn His Lys Lys Trp Gln Tyr Asn Ser Pro
225                 230                 235                 240

Leu Val Pro Arg Asn Ala Glu Leu Gly Asp Arg Lys Gly Lys Ile His
                245                 250                 255

Ile Pro Phe Pro Leu Ala Asn Val Thr Cys Arg Val Pro Lys Ala Arg
            260                 265                 270

Asn Pro Thr Val Thr Tyr Gly Lys Asn Gln Val Ile Met Leu Leu Tyr
        275                 280                 285

Pro Asp His Pro Thr Leu Leu Ser Tyr Arg Asn Met Gly Glu Glu Pro
    290                 295                 300

Asn Tyr Gln Glu Glu Trp Val Met His Lys Lys Glu Val Val Leu Thr
305                 310                 315                 320

Val Pro Thr Glu Gly Leu Glu Val Thr Trp Gly Asn Asn Glu Pro Tyr
                325                 330                 335

Lys Tyr Trp Pro Gln Leu Ser Thr Asn Gly Thr Ala His Gly His Pro
            340                 345                 350

His Glu Ile Ile Leu Tyr Tyr Tyr Glu Leu Tyr Pro Thr Met Thr Val
        355                 360                 365

Val Val Val Ser Val Ala Thr Phe Ile Leu Leu Ser Met Val Gly Met
    370                 375                 380
```

```
Ala Ala Gly Met Cys Met Cys Ala Arg Arg Arg Cys Ile Thr Pro Tyr
385                 390                 395                 400

Glu Leu Thr Pro Gly Ala Thr Val Pro Phe Leu Leu Ser Leu Ile Cys
                405                 410                 415

Cys Ile Arg Thr Ala Lys Ala
            420
```

<210> 86
<211> 261
<212> PRT
<213> Artificial Sequence

<220>
<223> CHIKV capsid consensus

<400> 86

```
Met Glu Phe Ile Pro Thr Gln Thr Phe Tyr Asn Arg Arg Tyr Gln Pro
1               5                   10                  15

Arg Pro Trp Thr Pro Arg Pro Thr Ile Gln Val Ile Arg Pro Arg Pro
            20                  25                  30

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

Asn Lys Leu Thr Met Arg Ala Val Pro Gln Gln Lys Pro Arg Arg Asn
    50                  55                  60

Arg Lys Asn Lys Lys Gln Lys Gln Lys Gln Gln Ala Pro Gln Asn Asn
65                  70                  75                  80

Thr Asn Gln Lys Lys Gln Pro Pro Lys Lys Lys Pro Ala Gln Lys Lys
                85                  90                  95

Lys Lys Pro Gly Arg Arg Glu Arg Met Cys Met Lys Ile Glu Asn Asp
            100                 105                 110

Cys Ile Phe Glu Val Lys His Glu Gly Lys Val Thr Gly Tyr Ala Cys
        115                 120                 125

Leu Val Gly Asp Lys Val Met Lys Pro Ala His Val Lys Gly Thr Ile
    130                 135                 140

Asp Asn Ala Asp Leu Ala Lys Leu Ala Phe Lys Arg Ser Ser Lys Tyr
145                 150                 155                 160
```

```
Asp Leu Glu Cys Ala Gln Ile Pro Val His Met Lys Ser Asp Ala Ser
                165                 170                 175

Lys Phe Thr His Glu Lys Pro Glu Gly Tyr Tyr Asn Trp His His Gly
            180                 185                 190

Ala Val Gln Tyr Ser Gly Gly Arg Phe Thr Ile Pro Thr Gly Ala Gly
        195                 200                 205

Lys Pro Gly Asp Ser Gly Arg Pro Ile Phe Asp Asn Lys Gly Arg Val
    210                 215                 220

Val Ala Ile Val Leu Gly Gly Ala Asn Glu Gly Ala Arg Thr Ala Leu
225                 230                 235                 240

Ser Val Val Thr Trp Asn Lys Asp Ile Val Thr Lys Ile Thr Pro Glu
                245                 250                 255

Gly Ala Glu Glu Trp
            260
```

<210> 87
<211> 998
<212> PRT
<213> Artificial Sequence

<220>
<223> CHIKV Env consensus

<400> 87

```
Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1               5                   10                  15

His Ser Ser Leu Ala Ile Pro Val Met Cys Leu Leu Ala Asn Thr Thr
            20                  25                  30

Phe Pro Cys Ser Gln Pro Pro Cys Thr Pro Cys Cys Tyr Glu Lys Glu
        35                  40                  45

Pro Glu Glu Thr Leu Arg Met Leu Glu Asp Asn Val Met Arg Pro Gly
    50                  55                  60

Tyr Tyr Gln Leu Leu Gln Ala Ser Leu Thr Cys Ser Pro His Arg Gln
65                  70                  75                  80

Arg Arg Arg Gly Arg Lys Arg Arg Ser Ala Thr Met Asp Trp Thr Trp
                85                  90                  95

Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val His Ser Ser Thr Lys
```

```
                100                 105                 110

Asp Asn Phe Asn Val Tyr Lys Ala Thr Arg Pro Tyr Leu Ala His Cys
        115                 120                 125

Pro Asp Cys Gly Glu Gly His Ser Cys His Ser Pro Val Ala Leu Glu
    130                 135                 140

Arg Ile Arg Asn Glu Ala Thr Asp Gly Thr Leu Lys Ile Gln Val Ser
145                 150                 155                 160

Leu Gln Ile Gly Ile Lys Thr Asp Asp Ser His Asp Trp Thr Lys Leu
                165                 170                 175

Arg Tyr Met Asp Asn His Met Pro Ala Asp Ala Glu Arg Ala Gly Leu
            180                 185                 190

Phe Val Arg Thr Ser Ala Pro Cys Thr Ile Thr Gly Thr Met Gly His
        195                 200                 205

Phe Ile Leu Ala Arg Cys Pro Lys Gly Glu Thr Leu Thr Val Gly Phe
    210                 215                 220

Thr Asp Ser Arg Lys Ile Ser His Ser Cys Thr His Pro Phe His His
225                 230                 235                 240

Asp Pro Pro Val Ile Gly Arg Glu Lys Phe His Ser Arg Pro Gln His
                245                 250                 255

Gly Lys Glu Leu Pro Cys Ser Thr Tyr Val Gln Ser Thr Ala Ala Thr
            260                 265                 270

Thr Glu Glu Ile Glu Val His Met Pro Pro Asp Thr Pro Asp Arg Thr
        275                 280                 285

Leu Met Ser Gln Gln Ser Gly Asn Val Lys Ile Thr Val Asn Gly Gln
    290                 295                 300

Thr Val Arg Tyr Lys Cys Asn Cys Gly Gly Ser Asn Glu Gly Leu Thr
305                 310                 315                 320

Thr Thr Asp Lys Val Ile Asn Asn Cys Lys Val Asp Gln Cys His Ala
                325                 330                 335

Ala Val Thr Asn His Lys Lys Trp Gln Tyr Asn Ser Pro Leu Val Pro
            340                 345                 350
```

```
Arg Asn Ala Glu Leu Gly Asp Arg Lys Gly Lys Ile His Ile Pro Phe
        355                 360                 365

Pro Leu Ala Asn Val Thr Cys Arg Val Pro Lys Ala Arg Asn Pro Thr
    370                 375                 380

Val Thr Tyr Gly Lys Asn Gln Val Ile Met Leu Leu Tyr Pro Asp His
385                 390                 395                 400

Pro Thr Leu Leu Ser Tyr Arg Asn Met Gly Glu Glu Pro Asn Tyr Gln
                405                 410                 415

Glu Glu Trp Val Met His Lys Lys Glu Val Val Leu Thr Val Pro Thr
            420                 425                 430

Glu Gly Leu Glu Val Thr Trp Gly Asn Asn Glu Pro Tyr Lys Tyr Trp
        435                 440                 445

Pro Gln Leu Ser Thr Asn Gly Thr Ala His Gly His Pro His Glu Ile
    450                 455                 460

Ile Leu Tyr Tyr Tyr Glu Leu Tyr Pro Thr Met Thr Val Val Val Val
465                 470                 475                 480

Ser Val Ala Thr Phe Ile Leu Leu Ser Met Val Gly Met Ala Ala Gly
                485                 490                 495

Met Cys Met Cys Ala Arg Arg Arg Cys Ile Thr Pro Tyr Glu Leu Thr
            500                 505                 510

Pro Gly Ala Thr Val Pro Phe Leu Leu Ser Leu Ile Cys Cys Ile Arg
        515                 520                 525

Thr Ala Lys Ala Arg Gly Arg Lys Arg Arg Ser Ala Thr Met Asp Trp
    530                 535                 540

Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val His Ser Tyr
545                 550                 555                 560

Glu His Val Thr Val Ile Pro Asn Thr Val Gly Val Pro Tyr Lys Thr
                565                 570                 575

Leu Val Asn Arg Pro Gly Tyr Ser Pro Met Val Leu Glu Met Glu Leu
            580                 585                 590

Leu Ser Val Thr Leu Glu Pro Thr Leu Ser Leu Asp Tyr Ile Thr Cys
        595                 600                 605
```

```
Glu Tyr Lys Thr Val Ile Pro Ser Pro Tyr Val Lys Cys Cys Gly Thr
    610                 615                 620

Ala Glu Cys Lys Asp Lys Asn Leu Pro Asp Tyr Ser Cys Lys Val Phe
625                 630                 635                 640

Thr Gly Val Tyr Pro Phe Met Trp Gly Gly Ala Tyr Cys Phe Cys Asp
                645                 650                 655

Ala Glu Asn Thr Gln Leu Ser Glu Ala His Val Glu Lys Ser Glu Ser
            660                 665                 670

Cys Lys Thr Glu Phe Ala Ser Ala Tyr Arg Ala His Thr Ala Ser Ala
        675                 680                 685

Ser Ala Lys Leu Arg Val Leu Tyr Gln Gly Asn Asn Ile Thr Val Thr
    690                 695                 700

Ala Tyr Ala Asn Gly Asp His Ala Val Thr Val Lys Asp Ala Lys Phe
705                 710                 715                 720

Ile Val Gly Pro Met Ser Ser Ala Trp Thr Pro Phe Asp Asn Lys Ile
                725                 730                 735

Val Val Tyr Lys Gly Asp Val Tyr Asn Met Asp Tyr Pro Pro Phe Gly
            740                 745                 750

Ala Gly Arg Pro Gly Gln Phe Gly Asp Ile Gln Ser Arg Thr Pro Glu
        755                 760                 765

Ser Lys Asp Val Tyr Ala Asn Thr Gln Leu Val Leu Gln Arg Pro Ala
    770                 775                 780

Val Gly Thr Val His Val Pro Tyr Ser Gln Ala Pro Ser Gly Phe Lys
785                 790                 795                 800

Tyr Trp Leu Lys Glu Arg Gly Ala Ser Leu Gln His Thr Ala Pro Phe
                805                 810                 815

Gly Cys Gln Ile Ala Thr Asn Pro Val Arg Ala Val Asn Cys Ala Val
            820                 825                 830

Gly Asn Met Pro Ile Ser Ile Asp Ile Pro Glu Ala Ala Phe Thr Arg
        835                 840                 845

Val Val Asp Ala Pro Ser Leu Thr Asp Met Ser Cys Glu Val Pro Ala
    850                 855                 860
```

```
Cys Thr His Ser Ser Asp Phe Gly Gly Val Ala Ile Ile Lys Tyr Ala
865                 870                 875                 880

Ala Ser Lys Lys Gly Lys Cys Ala Val His Ser Met Thr Asn Ala Val
                885                 890                 895

Thr Ile Arg Glu Ala Glu Ile Glu Val Glu Gly Asn Ser Gln Leu Gln
            900                 905                 910

Ile Ser Phe Ser Thr Ala Leu Ala Ser Ala Glu Phe Arg Val Gln Val
        915                 920                 925

Cys Ser Thr Gln Val His Cys Ala Ala Glu Cys His Pro Pro Lys Asp
    930                 935                 940

His Ile Val Asn Tyr Pro Ala Ser His Thr Thr Leu Gly Val Gln Asp
945                 950                 955                 960

Ile Ser Ala Thr Ala Met Ser Trp Val Gln Lys Ile Thr Gly Gly Val
                965                 970                 975

Gly Leu Val Val Ala Val Ala Ala Leu Ile Leu Ile Val Val Leu Cys
            980                 985                 990

Val Ser Phe Ser Arg His
        995


<210>  88
<211>  980
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CHIKV Env consensus

<400>  88

Ser Leu Ala Ile Pro Val Met Cys Leu Leu Ala Asn Thr Thr Phe Pro
1               5                   10                  15

Cys Ser Gln Pro Pro Cys Thr Pro Cys Cys Tyr Glu Lys Glu Pro Glu
            20                  25                  30

Glu Thr Leu Arg Met Leu Glu Asp Asn Val Met Arg Pro Gly Tyr Tyr
        35                  40                  45

Gln Leu Leu Gln Ala Ser Leu Thr Cys Ser Pro His Arg Gln Arg Arg
    50                  55                  60
```

```
Arg Gly Arg Lys Arg Arg Ser Ala Thr Met Asp Trp Thr Trp Ile Leu
65                  70                  75                  80

Phe Leu Val Ala Ala Ala Thr Arg Val His Ser Ser Thr Lys Asp Asn
                85                  90                  95

Phe Asn Val Tyr Lys Ala Thr Arg Pro Tyr Leu Ala His Cys Pro Asp
            100                 105                 110

Cys Gly Glu Gly His Ser Cys His Ser Pro Val Ala Leu Glu Arg Ile
        115                 120                 125

Arg Asn Glu Ala Thr Asp Gly Thr Leu Lys Ile Gln Val Ser Leu Gln
    130                 135                 140

Ile Gly Ile Lys Thr Asp Asp Ser His Asp Trp Thr Lys Leu Arg Tyr
145                 150                 155                 160

Met Asp Asn His Met Pro Ala Asp Ala Glu Arg Ala Gly Leu Phe Val
                165                 170                 175

Arg Thr Ser Ala Pro Cys Thr Ile Thr Gly Thr Met Gly His Phe Ile
            180                 185                 190

Leu Ala Arg Cys Pro Lys Gly Glu Thr Leu Thr Val Gly Phe Thr Asp
        195                 200                 205

Ser Arg Lys Ile Ser His Ser Cys Thr His Pro Phe His His Asp Pro
    210                 215                 220

Pro Val Ile Gly Arg Glu Lys Phe His Ser Arg Pro Gln His Gly Lys
225                 230                 235                 240

Glu Leu Pro Cys Ser Thr Tyr Val Gln Ser Thr Ala Ala Thr Thr Glu
                245                 250                 255

Glu Ile Glu Val His Met Pro Pro Asp Thr Pro Asp Arg Thr Leu Met
            260                 265                 270

Ser Gln Gln Ser Gly Asn Val Lys Ile Thr Val Asn Gly Gln Thr Val
        275                 280                 285

Arg Tyr Lys Cys Asn Cys Gly Gly Ser Asn Glu Gly Leu Thr Thr Thr
    290                 295                 300

Asp Lys Val Ile Asn Asn Cys Lys Val Asp Gln Cys His Ala Ala Val
305                 310                 315                 320
```

```
Thr Asn His Lys Lys Trp Gln Tyr Asn Ser Pro Leu Val Pro Arg Asn
                325                 330                 335

Ala Glu Leu Gly Asp Arg Lys Gly Lys Ile His Ile Pro Phe Pro Leu
            340                 345                 350

Ala Asn Val Thr Cys Arg Val Pro Lys Ala Arg Asn Pro Thr Val Thr
        355                 360                 365

Tyr Gly Lys Asn Gln Val Ile Met Leu Leu Tyr Pro Asp His Pro Thr
    370                 375                 380

Leu Leu Ser Tyr Arg Asn Met Gly Glu Glu Pro Asn Tyr Gln Glu Glu
385                 390                 395                 400

Trp Val Met His Lys Lys Glu Val Val Leu Thr Val Pro Thr Glu Gly
                405                 410                 415

Leu Glu Val Thr Trp Gly Asn Asn Glu Pro Tyr Lys Tyr Trp Pro Gln
            420                 425                 430

Leu Ser Thr Asn Gly Thr Ala His Gly His Pro His Glu Ile Ile Leu
        435                 440                 445

Tyr Tyr Tyr Glu Leu Tyr Pro Thr Met Thr Val Val Val Val Ser Val
    450                 455                 460

Ala Thr Phe Ile Leu Leu Ser Met Val Gly Met Ala Ala Gly Met Cys
465                 470                 475                 480

Met Cys Ala Arg Arg Arg Cys Ile Thr Pro Tyr Glu Leu Thr Pro Gly
                485                 490                 495

Ala Thr Val Pro Phe Leu Leu Ser Leu Ile Cys Cys Ile Arg Thr Ala
            500                 505                 510

Lys Ala Arg Gly Arg Lys Arg Arg Ser Ala Thr Met Asp Trp Thr Trp
        515                 520                 525

Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val His Ser Tyr Glu His
    530                 535                 540

Val Thr Val Ile Pro Asn Thr Val Gly Val Pro Tyr Lys Thr Leu Val
545                 550                 555                 560

Asn Arg Pro Gly Tyr Ser Pro Met Val Leu Glu Met Glu Leu Leu Ser
```

```
                565                 570                 575

Val Thr Leu Glu Pro Thr Leu Ser Leu Asp Tyr Ile Thr Cys Glu Tyr
            580                 585                 590

Lys Thr Val Ile Pro Ser Pro Tyr Val Lys Cys Cys Gly Thr Ala Glu
        595                 600                 605

Cys Lys Asp Lys Asn Leu Pro Asp Tyr Ser Cys Lys Val Phe Thr Gly
    610                 615                 620

Val Tyr Pro Phe Met Trp Gly Gly Ala Tyr Cys Phe Cys Asp Ala Glu
625                 630                 635                 640

Asn Thr Gln Leu Ser Glu Ala His Val Glu Lys Ser Glu Ser Cys Lys
                645                 650                 655

Thr Glu Phe Ala Ser Ala Tyr Arg Ala His Thr Ala Ser Ala Ser Ala
            660                 665                 670

Lys Leu Arg Val Leu Tyr Gln Gly Asn Asn Ile Thr Val Thr Ala Tyr
        675                 680                 685

Ala Asn Gly Asp His Ala Val Thr Val Lys Asp Ala Lys Phe Ile Val
    690                 695                 700

Gly Pro Met Ser Ser Ala Trp Thr Pro Phe Asp Asn Lys Ile Val Val
705                 710                 715                 720

Tyr Lys Gly Asp Val Tyr Asn Met Asp Tyr Pro Pro Phe Gly Ala Gly
                725                 730                 735

Arg Pro Gly Gln Phe Gly Asp Ile Gln Ser Arg Thr Pro Glu Ser Lys
            740                 745                 750

Asp Val Tyr Ala Asn Thr Gln Leu Val Leu Gln Arg Pro Ala Val Gly
        755                 760                 765

Thr Val His Val Pro Tyr Ser Gln Ala Pro Ser Gly Phe Lys Tyr Trp
    770                 775                 780

Leu Lys Glu Arg Gly Ala Ser Leu Gln His Thr Ala Pro Phe Gly Cys
785                 790                 795                 800

Gln Ile Ala Thr Asn Pro Val Arg Ala Val Asn Cys Ala Val Gly Asn
                805                 810                 815
```

```
Met Pro Ile Ser Ile Asp Ile Pro Glu Ala Ala Phe Thr Arg Val Val
            820                 825                 830

Asp Ala Pro Ser Leu Thr Asp Met Ser Cys Glu Val Pro Ala Cys Thr
        835                 840                 845

His Ser Ser Asp Phe Gly Gly Val Ala Ile Ile Lys Tyr Ala Ala Ser
    850                 855                 860

Lys Lys Gly Lys Cys Ala Val His Ser Met Thr Asn Ala Val Thr Ile
865                 870                 875                 880

Arg Glu Ala Glu Ile Glu Val Glu Gly Asn Ser Gln Leu Gln Ile Ser
                885                 890                 895

Phe Ser Thr Ala Leu Ala Ser Ala Glu Phe Arg Val Gln Val Cys Ser
            900                 905                 910

Thr Gln Val His Cys Ala Ala Glu Cys His Pro Pro Lys Asp His Ile
        915                 920                 925

Val Asn Tyr Pro Ala Ser His Thr Thr Leu Gly Val Gln Asp Ile Ser
    930                 935                 940

Ala Thr Ala Met Ser Trp Val Gln Lys Ile Thr Gly Gly Val Gly Leu
945                 950                 955                 960

Val Val Ala Val Ala Ala Leu Ile Leu Ile Val Val Leu Cys Val Ser
                965                 970                 975

Phe Ser Arg His
            980
```

<210> 89
<211> 1374
<212> DNA
<213> Artificial Sequence

<220>
<223> CHIKV E1 consensus

<400> 89

```
atggactgga cctggatcct gtttctggtc gctgctgcca cccgggtgca cagctacgag       60

cacgtgaccg tgatccccaa caccgtgggc gtgccctaca agaccctggt gaacaggccc      120

ggctacagcc ccatggtgct ggaaatggaa ctgctgtccg tgaccctgga acccaccctg      180

agcctggact acatcacctg cgagtacaag acagtgatcc ccagccccta cgtgaagtgc      240

tgcggcaccg ccgagtgcaa ggacaagaac ctgcccgact acagctgcaa ggtgttcacc      300
```

ggcgtgtacc ccttcatgtg gggcggagcc tactgcttct gcgacgccga gaacacccag 360

ctgtccgagg cccacgtgga gaagagcgag agctgcaaga ccgagttcgc cagcgcctac 420

cgggcccaca cagccagcgc cagcgccaag ctgcgggtgc tgtaccaggg caacaacatc 480

accgtgaccg cctacgccaa cggcgaccac gccgtgacag tgaaggacgc caagttcatc 540

gtgggcccca tgagcagcgc ctggaccccc ttcgacaaca agatcgtggt gtacaagggc 600

gacgtgtaca acatggacta ccccccccttc ggagccggca gacccggcca gttcggcgac 660

atccagagcc ggacccccga gagcaaggac gtgtacgcca atacccagct ggtgctgcag 720

agacccgccg tgggcaccgt gcacgtgcct tacagccagg cccccagcgg cttcaagtac 780

tggctgaaag agaggggcgc cagcctgcag cacaccgccc ccttcggctg ccagatcgcc 840

accaaccccg tgcgggccgt gaattgtgcc gtgggcaaca tgcccatcag catcgacatc 900

cccgaggccg ccttcaccag ggtggtggac gcccccagcc tgaccgacat gagctgcgag 960

gtgcccgcct gcacccacag cagcgacttc ggcggcgtgg ccatcatcaa gtacgccgcc 1020

agcaagaaag gcaagtgcgc cgtgcacagc atgaccaatg ccgtgaccat ccgggaggcc 1080

gagatcgagg tggagggcaa cagccagctg cagatcagct tcagcaccgc cctggccagc 1140

gccgagttcc gggtgcaggt ctgcagcacc caggtgcact gtgccgccga gtgtcacccc 1200

cccaaggacc acatcgtgaa ctaccccgcc agccacacca ccctgggcgt gcaggacatc 1260

agcgccaccg ccatgagctg ggtgcagaag atcacaggcg gcgtcggcct ggtggtggcc 1320

gtggccgccc tgatcctgat cgtggtgctg tgcgtgagct tcagccggca ctga 1374

<210> 90
<211> 1326
<212> DNA
<213> Artificial Sequence

<220>
<223> CHIKV E2 consensus

<400> 90
atggactgga cctggatcct gttcctggtc gctgctgcca caagagtgca cagcagcacc 60

aaggacaact tcaacgtgta caaggccacc cggccctacc tggcccactg ccccgattgc 120

ggcgagggcc acagctgcca cagccccgtg gccctggaac ggatccggaa cgaggccacc 180

gacggcaccc tgaagatcca ggtgtccctg cagatcggca tcaagaccga cgacagccac 240

gactggacca agctgcggta catggacaac cacatgcccg ccgacgccga gagagccggc 300

ctgttcgtcc ggaccagcgc cccctgcacc atcaccggca ccatgggcca cttcatcctg 360

gcccggtgcc ccaagggcga gacactgacc gtgggcttca ccgacagccg gaagatcagc 420

cactcctgca cccacccctt ccaccacgac ccccccgtga tcggccggga gaagttccac 480

agcaggcccc agcacggcaa agagctgccc tgcagcacct acgtgcagag caccgccgcc 540

acaaccgagg aaatcgaggt gcacatgccc cccgataccc ccgaccggac cctgatgagc 600

cagcagagcg gcaacgtgaa gatcaccgtg aacggccaga ccgtgcggta caagtgcaac 660

tgcggcggca gcaacgaggg cctgaccacc accgacaagg tgatcaacaa ctgcaaggtg 720

gaccagtgcc acgccgccgt gaccaaccac aagaagtggc agtacaacag ccccctggtg 780

ccccggaatg ccgagctggg cgaccggaag ggcaagatcc acatcccctt ccccctggcc 840

aacgtgacct gccgggtgcc caaggcccgg aaccccaccg tgacctacgg caagaaccag 900

gtgatcatgc tgctgtaccc cgaccacccc accctgctgt cctaccggaa catgggcgag 960

gaacccaact accaagagga gtgggtcatg cacaagaaag aagtggtgct gaccgtcccc 1020

accgagggcc tggaagtgac ctggggcaac aacgagccct acaagtactg gccccagctg 1080

tccaccaacg gcaccgccca cggccacccc cacgagatca tcctgtacta ctacgagctg 1140

taccctacca tgaccgtggt ggtggtgtcc gtggccacct ttatcctgct gtccatggtc 1200

ggcatggccg ctggcatgtg catgtgcgcc aggaggcgct gtatcacccc ctacgagctg 1260

acacctggcg ccaccgtgcc ctttctgctg tccctgatct gctgcatccg gaccgccaag 1320

gcctga 1326

<210> 91
<211> 840
<212> DNA
<213> Artificial Sequence

<220>
<223> CHIKV capsid consensus

<400> 91
atggactgga cctggatcct gttcctggtg gccgctgcca cccgggtgca cagcatggaa 60

ttcatcccca cccagacctt ctacaaccgg cgctaccagc ccagaccctg gacccccagg 120

cccaccatcc aggtgatccg gcccaggccc agaccccaga ggcaggccgg gcagctggca 180

cagctgatca gcgccgtgaa caagctgacc atgagagccg tgccccagca gaagcccagg 240

cggaaccgga agaacaagaa gcagaagcag aaacagcagg ccccccagaa caacaccaac 300

cagaagaagc agcccccccaa gaagaagcct gcccagaaga agaagaaacc cggcaggcgg 360

gagcggatgt gcatgaagat cgagaacgac tgcatcttcg aggtgaagca cgagggcaag 420

gtgaccggct acgcctgcct ggtcggcgac aaagtgatga agcccgccca cgtgaagggc 480

accatcgaca acgccgacct ggccaagctg gccttcaagc ggagcagcaa gtacgacctg 540

gaatgcgccc agatccccgt gcacatgaag agcgacgcca gcaagttcac ccacgagaag 600

cccgagggct actacaactg gcaccacgga gccgtgcagt acagcggcgg caggttcacc 660

atccccacag gcgccggaaa gcccggcgac agcggcaggc ccatcttcga caacaagggc 720

cgggtggtgg ccatcgtgct gggcggagcc aacgagggcg ccaggaccgc cctgagcgtg 780

gtgacctgga acaaggacat cgtgaccaag atcacccccg agggcgccga agagtggtga 840

<210> 92
<211> 1320
<212> DNA
<213> Artificial Sequence

<220>
<223> CHIKV E1 consensus

<400> 92
tacgagcacg tgaccgtgat ccccaacacc gtgggcgtgc cctacaagac cctggtgaac 60

aggcccggct acagccccat ggtgctggaa atggaactgc tgtccgtgac cctggaaccc 120

accctgagcc tggactacat cacctgcgag tacaagacag tgatccccag cccctacgtg 180

aagtgctgcg gcaccgccga gtgcaaggac aagaacctgc ccgactacag ctgcaaggtg 240

ttcaccggcg tgtaccccct catgtggggc ggagcctact gcttctgcga cgccgagaac 300

acccagctgt ccgaggccca cgtggagaag agcgagagct gcaagaccga gttcgccagc 360

gcctaccggg cccacacagc cagcgccagc gccaagctgc gggtgctgta ccagggcaac 420

aacatcaccg tgaccgccta cgccaacggc gaccacgccg tgacagtgaa ggacgccaag 480

ttcatcgtgg gccccatgag cagcgcctgg acccccttcg acaacaagat cgtggtgtac 540

aagggcgacg tgtacaacat ggactacccc cccttcggag ccggcagacc cggccagttc 600

ggcgacatcc agagccggac ccccgagagc aaggacgtgt acgccaatac ccagctggtg 660

ctgcagagac ccgccgtggg caccgtgcac gtgccttaca gccaggcccc cagcggcttc 720

aagtactggc tgaaagagag gggcgccagc ctgcagcaca ccgccccctt cggctgccag 780

atcgccacca accccgtgcg ggccgtgaat tgtgccgtgg gcaacatgcc catcagcatc 840

gacatccccg aggccgcctt caccagggtg gtggacgccc ccagcctgac cgacatgagc 900

tgcgaggtgc ccgcctgcac ccacagcagc gacttcggcg gcgtggccat catcaagtac 960

gccgccagca agaaaggcaa gtgcgccgtg cacagcatga ccaatgccgt gaccatccgg 1020

gaggccgaga tcgaggtgga gggcaacagc cagctgcaga tcagcttcag caccgccctg 1080

gccagcgccg agttccgggt gcaggtctgc agcacccagg tgcactgtgc cgccgagtgt 1140

cacccccccа aggaccacat cgtgaactac cccgccagcc acaccaccct gggcgtgcag 1200

gacatcagcg ccaccgccat gagctgggtg cagaagatca caggcggcgt cggcctggtg 1260

gtggccgtgg ccgccctgat cctgatcgtg gtgctgtgcg tgagcttcag ccggcactga 1320

<210> 93
<211> 1273
<212> DNA
<213> Artificial Sequence

<220>
<223> CHIKV E1 consensus

<400> 93
cagcaccaag gacaacttca acgtgtacaa ggccacccgg ccctacctgg cccactgccc 60

cgattgcggc gagggccaca gctgccacag ccccgtggcc ctggaacgga tccggaacga 120

ggccaccgac ggcaccctga agatccaggt gtccctgcag atcggcatca agaccgacga 180

cagccacgac tggaccaagc tgcggtacat ggacaaccac atgcccgccg acgccgagag 240

agccggcctg ttcgtccgga ccagcgcccc ctgcaccatc accggcacca tgggccactt 300

catcctggcc cggtgcccca agggcgagac actgaccgtg ggcttcaccg acagccggaa 360

gatcagccac tcctgcaccc acccccttcca ccacgacccc cccgtgatcg gccgggagaa 420

gttccacagc aggccccagc acggcaaaga gctgccctgc agcacctacg tgcagagcac 480

cgccgccaca accgaggaaa tcgaggtgca catgcccccc gataccccccg accggaccct 540

gatgagccag cagagcggca acgtgaagat caccgtgaac ggccagaccg tgcggtacaa 600

gtgcaactgc ggcggcagca acgagggcct gaccaccacc gacaaggtga tcaacaactg 660

caaggtggac cagtgccacg ccgccgtgac caaccacaag aagtggcagt acaacagccc 720

cctggtgccc cggaatgccg agctgggcga ccggaagggc aagatccaca tccccttccc 780

cctggccaac gtgacctgcc gggtgcccaa ggcccggaac cccaccgtga cctacggcaa 840

gaaccaggtg atcatgctgc tgtaccccga ccaccccacc ctgctgtcct accggaacat 900

gggcgaggaa cccaactacc aagaggagtg ggtcatgcac aagaaagaag tggtgctgac 960

cgtccccacc gagggcctgg aagtgacctg gggcaacaac gagccctaca agtactggcc 1020

ccagctgtcc accaacggca ccgcccacgg ccacccccac gagatcatcc tgtactacta 1080

cgagctgtac cctaccatga ccgtggtggt ggtgtccgtg gccaccttta tcctgctgtc 1140

catggtcggc atggccgctg gcatgtgcat gtgcgccagg aggcgctgta tcacccccta 1200

cgagctgaca cctggcgcca ccgtgccctt tctgctgtcc ctgatctgct gcatccggac 1260

cgccaaggcc tga 1273

<210> 94
<211> 786
<212> DNA
<213> Artificial Sequence

<220>
<223> CHIKV capsid consensus

<400> 94
atggaattca tccccaccca gaccttctac aaccggcgct accagcccag accctggacc 60

cccaggccca ccatccaggt gatccggccc aggcccagac cccagaggca ggccgggcag 120

ctggcacagc tgatcagcgc cgtgaacaag ctgaccatga gagccgtgcc ccagcagaag 180

cccaggcgga accggaagaa caagaagcag aagcagaaac agcaggcccc ccagaacaac 240

accaaccaga agaagcagcc ccccaagaag aagcctgccc agaagaagaa gaaacccggc 300

aggcgggagc ggatgtgcat gaagatcgag aacgactgca tcttcgaggt gaagcacgag 360

ggcaaggtga ccggctacgc ctgcctggtc ggcgacaaag tgatgaagcc cgcccacgtg 420

aagggcacca tcgacaacgc cgacctggcc aagctggcct tcaagcggag cagcaagtac 480

gacctggaat gcgcccagat ccccgtgcac atgaagagcg acgccagcaa gttcacccac 540

gagaagcccg agggctacta caactggcac cacggagccg tgcagtacag cggcggcagg 600

ttcaccatcc ccacaggcgc cggaaagccc ggcgacagcg gcaggcccat cttcgacaac 660

aagggccggg tggtggccat cgtgctgggc ggagccaacg agggcgccag gaccgccctg 720

agcgtggtga cctggaacaa ggacatcgtg accaagatca cccccgaggg cgccgaagag 780

tggtga 786

<210> 95
<211> 3008
<212> DNA
<213> Artificial Sequence

<220>
<223> CHIKV Env consensus

<400> 95
atggactgga cctggatcct gttcctggtg gctgctgcca cccgcgtgca cagcagcctg 60

gccatccccg tgatgtgcct gctggccaac accaccttcc cttgcagcca gccccctgc 120

acccccctgct gctacgagaa agagcccgag gaaaccctgc ggatgctgga agataacgtg 180

atgaggcccg gctactacca gctgctccag gccagcctga cctgctcccc ccaccggcag 240

cggcggcgcg ggcgcaaacg ccgctctgcc accatggact ggacctggat cctgttcctg 300

gtcgctgctg ccacaagagt gcacagcagc accaaggaca acttcaacgt gtacaaggcc 360

acccggccct acctggccca ctgccccgat tgcggcgagg gccacagctg ccacagcccc 420

gtggccctgg aacggatccg gaacgaggcc accgacggca ccctgaagat ccaggtgtcc 480

ctgcagatcg gcatcaagac cgacgacagc cacgactgga ccaagctgcg gtacatggac 540

aaccacatgc ccgccgacgc cgagagagcc ggcctgttcg tccggaccag cgccccctgc 600

accatcaccg gcaccatggg ccacttcatc ctggcccggt gccccaaggg cgagacactg 660

accgtgggct tcaccgacag ccggaagatc agccactcct gcacccaccc cttccaccac 720

gaccccccccg tgatcggccg ggagaagttc cacagcaggc cccagcacgg caaagagctg 780

ccctgcagca cctacgtgca gagcaccgcc gccacaaccg aggaaatcga ggtgcacatg 840

ccccccgata cccccgaccg gaccctgatg agccagcaga gcggcaacgt gaagatcacc 900

gtgaacggcc agaccgtgcg gtacaagtgc aactgcggcg gcagcaacga gggcctgacc 960
accaccgaca aggtgatcaa caactgcaag gtggaccagt gccacgccgc cgtgaccaac 1020
cacaagaagt ggcagtacaa cagccccctg gtgccccgga atgccgagct gggcgaccgg 1080
aagggcaaga tccacatccc cttccccctg gccaacgtga cctgccgggt gcccaaggcc 1140
cggaacccca ccgtgaccta cggcaagaac caggtgatca tgctgctgta ccccgaccac 1200
cccaccctgc tgtcctaccg gaacatgggc gaggaaccca actaccaaga ggagtgggtc 1260
atgcacaaga aagaagtggt gctgaccgtc cccaccgagg gcctggaagt gacctggggc 1320
aacaacgagc cctacaagta ctggccccag ctgtccacca acggcaccgc ccacggccac 1380
ccccacgaga tcatcctgta ctactacgag ctgtacccta ccatgaccgt ggtggtggtg 1440
tccgtggcca cctttatcct gctgtccatg gtcggcatgg ccgctggcat gtgcatgtgc 1500
gccaggaggc gctgtatcac cccctacgag ctgacacctg gcgccaccgt gccctttctg 1560
ctgtccctga tctgctgcat ccggaccgcc aaggcccgcg ggcgcaaacg ccgctctgcc 1620
accatggact ggacctggat cctgtttctg gtcgctgctg ccacccgggt gcacagctac 1680
gagcacgtga ccgtgatccc caacaccgtg ggcgtgccct acaagaccct ggtgaacagg 1740
cccggctaca gccccatggt gctggaaatg gaactgctgt ccgtgaccct ggaacccacc 1800
ctgagcctgg actacatcac ctgcgagtac aagacagtga tccccagccc ctacgtgaag 1860
tgctgcggca ccgccgagtg caaggacaag aacctgcccg actacagctg caaggtgttc 1920
accggcgtgt acccccttcat gtggggcgga gcctactgct tctgcgacgc cgagaacacc 1980
cagctgtccg aggcccacgt ggagaagagc gagagctgca agaccgagtt cgccagcgcc 2040
taccgggccc acacagccag cgccagcgcc aagctgcggg tgctgtacca gggcaacaac 2100
atcaccgtga ccgcctacgc caacggcgac cacgccgtga cagtgaagga cgccaagttc 2160
atcgtgggcc ccatgagcag cgcctggacc cccttcgaca acaagatcgt ggtgtacaag 2220
ggcgacgtgt acaacatgga ctacccccccc ttcggagccg gcagacccgg ccagttcggc 2280
gacatccaga gccggacccc cgagagcaag gacgtgtacg ccaataccca gctggtgctg 2340
cagagacccg ccgtgggcac cgtgcacgtg ccttacagcc aggcccccag cggcttcaag 2400
tactggctga aagagagggg cgccagcctg cagcacaccg ccccttcgg ctgccagatc 2460
gccaccaacc ccgtgcgggc cgtgaattgt gccgtgggca acatgcccat cagcatcgac 2520
atccccgagg ccgccttcac cagggtggtg gacgcccccа gcctgaccga catgagctgc 2580
gaggtgcccg cctgcaccca cagcagcgac ttcggcggcg tggccatcat caagtacgcc 2640
gccagcaaga aaggcaagtg cgccgtgcac agcatgacca atgccgtgac catccgggag 2700
gccgagatcg aggtggaggg caacagccag ctgcagatca gcttcagcac cgccctggcc 2760

agcgccgagt tccgggtgca ggtctgcagc acccaggtgc actgtgccgc cgagtgtcac 2820

ccccccaagg accacatcgt gaactacccc gccagccaca ccaccctggg cgtgcaggac 2880

atcagcgcca ccgccatgag ctgggtgcag aagatcacag gcggcgtcgg cctggtggtg 2940

gccgtggccg ccctgatcct gatcgtggtg ctgtgcgtga gcttcagccg gcactgatga 3000

gcggccgc 3008

<210> 96
<211> 2954
<212> DNA
<213> Artificial Sequence

<220>
<223> CHIKV Env consensus

<400> 96
agcctggcca tccccgtgat gtgcctgctg gccaacacca ccttcccttg cagccagccc 60

ccctgcaccc cctgctgcta cgagaaagag cccgaggaaa ccctgcggat gctggaagat 120

aacgtgatga ggcccggcta ctaccagctg ctccaggcca gcctgacctg ctcccccccac 180

cggcagcggc ggcgcgggcg caaacgccgc tctgccacca tggactggac ctggatcctg 240

ttcctggtcg ctgctgccac aagagtgcac agcagcacca aggacaactt caacgtgtac 300

aaggccaccc ggccctacct ggcccactgc cccgattgcg gcgagggcca cagctgccac 360

agccccgtgg ccctggaacg gatccggaac gaggccaccg acggcaccct gaagatccag 420

gtgtccctgc agatcggcat caagaccgac gacagccacg actggaccaa gctgcggtac 480

atggacaacc acatgcccgc cgacgccgag agagccggcc tgttcgtccg gaccagcgcc 540

ccctgcacca tcaccggcac catgggccac ttcatcctgg cccggtgccc caagggcgag 600

acactgaccg tgggcttcac cgacagccgg aagatcagcc actcctgcac ccacccccttc 660

caccacgacc cccccgtgat cggccgggag aagttccaca gcaggcccca gcacggcaaa 720

gagctgccct gcagcaccta cgtgcagagc accgccgcca caaccgagga aatcgaggtg 780

cacatgcccc ccgatacccc cgaccggacc ctgatgagcc agcagagcgg caacgtgaag 840

atcaccgtga acggccagac cgtgcggtac aagtgcaact gcggcggcag caacgagggc 900

ctgaccacca ccgacaaggt gatcaacaac tgcaaggtgg accagtgcca cgccgccgtg 960

accaaccaca agaagtggca gtacaacagc cccctggtgc cccggaatgc cgagctgggc 1020

gaccggaagg gcaagatcca catccccttc cccctggcca acgtgacctg ccgggtgccc 1080

aaggcccgga accccaccgt gacctacggc aagaaccagg tgatcatgct gctgtacccc 1140

gaccacccca ccctgctgtc ctaccggaac atgggcgagg aacccaacta ccaagaggag 1200

tgggtcatgc acaagaaaga agtggtgctg accgtcccca ccgagggcct ggaagtgacc 1260

tggggcaaca acgagcccta caagtactgg ccccagctgt ccaccaacgg caccgcccac 1320

ggccaccccc acgagatcat cctgtactac tacgagctgt accctaccat gaccgtggtg 1380
gtggtgtccg tggccacctt tatcctgctg tccatggtcg gcatggccgc tggcatgtgc 1440
atgtgcgcca ggaggcgctg tatcaccccc tacgagctga cacctggcgc caccgtgccc 1500
tttctgctgt ccctgatctg ctgcatccgg accgccaagg cccgcgggcg caaacgccgc 1560
tctgccacca tggactggac ctggatcctg tttctggtcg ctgctgccac ccgggtgcac 1620
agctacgagc acgtgaccgt gatccccaac accgtgggcg tgccctacaa gaccctggtg 1680
aacaggcccg gctacagccc catggtgctg gaaatggaac tgctgtccgt gaccctggaa 1740
cccaccctga gcctggacta catcacctgc gagtacaaga cagtgatccc cagcccctac 1800
gtgaagtgct gcggcaccgc cgagtgcaag gacaagaacc tgcccgacta cagctgcaag 1860
gtgttcaccg gcgtgtaccc cttcatgtgg ggcggagcct actgcttctg cgacgccgag 1920
aacacccagc tgtccgaggc ccacgtggag aagagcgaga gctgcaagac cgagttcgcc 1980
agcgcctacc gggcccacac agccagcgcc agcgccaagc tgcgggtgct gtaccagggc 2040
aacaacatca ccgtgaccgc ctacgccaac ggcgaccacg ccgtgacagt gaaggacgcc 2100
aagttcatcg tgggccccat gagcagcgcc tggacccccc tcgacaacaa gatcgtggtg 2160
tacaagggcg acgtgtacaa catggactac ccccccttcg gagccggcag acccggccag 2220
ttcggcgaca tccagagccg gacccccgag agcaaggacg tgtacgccaa tacccagctg 2280
gtgctgcaga gacccgccgt gggcaccgtg cacgtgcctt acagccaggc ccccagcggc 2340
ttcaagtact ggctgaaaga gaggggcgcc agcctgcagc acaccgcccc cttcggctgc 2400
cagatcgcca ccaaccccgt gcgggccgtg aattgtgccg tgggcaacat gcccatcagc 2460
atcgacatcc ccgaggccgc cttcaccagg gtggtggacg cccccagcct gaccgacatg 2520
agctgcgagg tgcccgcctg cacccacagc agcgacttcg gcggcgtggc catcatcaag 2580
tacgccgcca gcaagaaagg caagtgcgcc gtgcacagca tgaccaatgc cgtgaccatc 2640
cgggaggccg agatcgaggt ggagggcaac agccagctgc agatcagctt cagcaccgcc 2700
ctggccagcg ccgagttccg ggtgcaggtc tgcagcaccc aggtgcactg tgccgccgag 2760
tgtcaccccc ccaaggacca catcgtgaac taccccgcca gccacaccac cctgggcgtg 2820
caggacatca gcgccaccgc catgagctgg gtgcagaaga tcacaggcgg cgtcggcctg 2880
gtggtggccg tggccgccct gatcctgatc gtggtgctgt gcgtgagctt cagccggcac 2940
tgatgagcgg ccgc 2954

<210> 97
<211> 2223
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic acid sequence encoding CHIKV1-IgG

<400> 97

ggatccgcca ccatggactg gacttggatt ctgtttctgg tcgccgccgc tacccgagtg 60

cattcacagg tgcagctgca gcagcctggg gccgctctgg tgaagccagg agctagcgca 120

atgatgtcct gcaaagcctc tggctacact ttcacctcct attggatcac ctgggtgaag 180

cagcgacctg gacagggact ggagtggatc ggcgacatct acccaggcac cgggagaaca 240

atctacaagg aaaaattcaa gacaaaagcc acactgactg tggacaccag ctcctctaca 300

gcttttatgc agctgaacag cctgacttcc gaggatagcg ccgtgtacta ttgcgcaaga 360

ggatacggct ctccttacta tgccctggac tattgggggc agggaactag cgtcaccgtg 420

agttcagcat ctaccaaggg accaagcgtg ttcccactgg cacctagctc caaatccact 480

tctggcggga ccgccgctct gggatgtctg gtgaaggatt acttccctga gccagtcaca 540

gtgagttgga actcaggggc tctgaccagc ggagtccaca catttcctgc agtgctgcag 600

tctagtggac tgtactccct gtcaagcgtg gtcactgtcc catcctctag tctgggcacc 660

cagacatata tctgcaacgt gaatcacaag ccatccaata ccaaagtcga taagaaagtg 720

gagcccaagt cttgtgacaa aactcatacc tgccctccct gtccagcacc tgaactgctg 780

ggaggcccaa gcgtgttcct gtttccaccc aagcctaaag acaccctgat gattagcagg 840

acaccagagg tcacttgcgt ggtcgtggac gtgagccacg aagaccccga ggtcaagttc 900

aactggtacg tggatggcgt cgaagtgcat aatgccaaga caaaaccccg ggaggaacag 960

tacaactcaa cctatcgggt cgtgagcgtc ctgacagtgc tgcaccagga ctggctgaac 1020

ggaaaggagt acaagtgcaa agtgtctaat aaggccctgc cagctcccat cgaaaaaacc 1080

attagcaagg ctaaaggcca gccaagagag ccccaggtgt acacactgcc tccatcaagg 1140

gacgaactga caaagaacca ggtcagcctg acttgtctgg tgaaaggctt ctatcccagc 1200

gatatcgcag tggaatggga gtccaatggg cagcctgaga acaattacaa gaccacaccc 1260

cctgtgctgg acagcgatgg gtccttcttt ctgtattcca agctgacagt ggataaatct 1320

cggtggcagc agggaaacgt ctttagttgc tcagtgatgc acgaagccct gcacaatcat 1380

tacactcaga agagcctgtc cctgtctccc ggaaagaggg gccgcaaacg gagaagtggc 1440

tcaggggcaa ccaacttctc tctgctgaaa caggccggcg atgtggagga aaatcctggg 1500

ccaatggact ggacatggat tctgttcctg gtggcagccg ctacaagggt ccattccgac 1560

attgtgctga ctcagtctcc tgcaagtctg gccgtgtctc agggacagcg agcaaccatc 1620

agttgtaagg ctagccagtc cgtcgactac gatggggaca gttacgtgaa ctggtatcag 1680

cagaagcctg gacagtcccc aaaactgctg atctatgatg ctagtaatct ggagtcaggc 1740

attcccgcac gattctctgg aagtggctca gggacagact tcaccctgaa cattcaccct 1800

gtcgaggaag aggacgtggc tacctactat tgccaggaaa gcaatgagga cccccgcact 1860

ttcgggggag gcaccaagct ggagatcaaa cgaactgtcg cagcccccag cgtgttcatc 1920

tttccaccct cagacgaaca gctgaagagc ggaaccgcat ccgtggtgtg cctgctgaac 1980

aacttctacc cccgcgaggc caaggtccag tggaaagtgg ataacgctct gcagtcaggc 2040

aatagccagg aatccgtgac tgagcaggat tctaaggaca gtacctattc actgtcaagc 2100

acactgactc tgagcaaagc agactacgaa aagcataaag tgtatgcctg cgaagtcacc 2160

caccaggggc tgaggtctcc agtcactaag tctttcaaca gaggggaatg ctgataactc 2220

gag 2223

<210> 98
<211> 2217
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence encoding CHIKV2-IgG

<400> 98
ggatccgcca ccatggattg gacatggatt ctgtttctgg tcgccgccgc cacaagggtc 60

cactctcagg tgcagctggt gcagtcaggc tccgaactga agaaacccgg agcttctgtc 120

aaggtgagtt gcaaagcatc agggtacact ctgaccagat atgcaatgac ctgggtgcgg 180

caggcacctg gacagggact ggagtggatg ggctggatca acacatacac tggaaatcca 240

acttatgtgc agggcttcac cggacggttc gtcttttctc tggacacaag cgtgtccact 300

gcctttctgc acattacaag cctgaaggca gaggacactg ccgtgtactt ctgcgcccga 360

gaaggcggag ctaggggctt tgattattgg gggcagggca cactggtcac tgtgagctcc 420

gcttctacaa agggacctag cgtgttccca ctggcaccct ctagtaaatc taccagtggg 480

ggcacagccg ctctgggatg tctggtgaag gattacttcc ccgagcctgt caccgtgtca 540

tggaacagcg gggcactgac ctccggagtc catacatttc ccgccgtgct gcagtcaagc 600

ggactgtaca gcctgtcctc tgtggtcact gtgcctagtt caagcctggg gacccagaca 660

tatatctgca acgtgaatca caagccttct aataccaagg tcgacaaaag ggtggaacca 720

aagagctgtg ataaaactca tacctgccct ccctgtccag ctccagagct gctgggaggg 780

ccatccgtgt tcctgtttcc acccaagcct aaagacacac tgatgatttc cagaactcca 840

gaagtcacct gcgtggtcgt ggacgtgtct cacgaggacc ccgaagtcaa gttcaactgg 900

tacgtggatg gcgtcgaggt gcataatgcc aagaccaaac ccagggagga acagtacaac 960

tcaacatata gagtcgtgag cgtcctgact gtgctgcacc aggactggct gaacggcaag 1020

gagtataagt gcaaagtgag caataaggcc ctgcctgctc caatcgagaa aacaatttcc 1080

aaggctaaag gccagcctcg ggaaccacag gtgtacactc tgcctccaag tcgcgacgag 1140

ctgaccaaga accaggtctc tctgacatgt ctggtgaaag gcttttatcc cagtgatatc 1200

gccgtggagt gggaatcaaa tggacagcct gaaaacaatt acaagaccac acccccctgtg 1260

ctggactccg atggatcttt ctttctgtat tccaagctga cagtggataa atctcgctgg 1320

cagcagggga acgtcttctc atgcagcgtg atgcacgagg ccctgcacaa tcattacact 1380

cagaagtccc tgtctctgag tcctgggaag cggggccgca aaaggagatc aggaagcggg 1440

gccaccaact ttagcctgct gaaacaggct ggggacgtgg aggaaaatcc cggccctatg 1500

gactggacct ggattctgtt cctggtggca gccgctaccc gagtccattc ccagtctgtg 1560

ctgacacagc cacccagtgt ctcaggagca ccaggacagc gagtgacaat cagctgtact 1620

ggcagcagca gcaacattgg ggcctcccac gacgtgcatt ggtaccagca gctgcccggc 1680

accgctccta cactgctgat ctatgtcaac agcaatcgcc catccggagt gcccgatcga 1740

ttcagcggct ccaagtctgg aactagtgca tcactggcca ttaccggcct gcaggctgag 1800

gacgaagcag attactattg ccagagttac gactcaaacc tgagcgggtc cgccgtcttc 1860

ggcggaggga ctaagctgac cgtgctgggc cagcctaaag cagccccatc cgtgaccctg 1920

tttcctccat caagcgagga actgcaggct aataaggcca ccctggtgtg cctgatcagc 1980

gacttctacc caggagcagt caccgtggca tggaaggctg attcctctcc agtcaaagcc 2040

ggcgtggaaa ctaccacacc cagcaagcag tccaacaaca agtacgctgc aagttcatat 2100

ctgtccctga cccccgagca gtggaagtct cacaaatctt atagttgcca ggtgacccat 2160

gaaggctcaa ctgtggaaaa aactgtcgct cctactgaat gctcatgata actcgag 2217

<210> 99
<211> 2220
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence encoding CHIKV3-IgG

<400> 99
ggatccgcca ccatggattg gacatggatt ctgtttctgg tcgctgctgc cacacgggtg 60

cattctcagg tccagctgca ggagtcaggg ccagggctgg tcaagccttc cgaaaccctg 120

tctctgacat gcaccgtgag cggcgacagt atcagctcct actcatggag ctggattcgg 180

cagccccctg gcaaaggact ggagtggatc ggctacattc actatacagg aagcactaac 240

tataatccat cactgaagag ccgcctgacc atcagtgtgg acgcctcaaa aaaccagttc 300

tccctgaagc tgtctagtgt cactgccgct gacaccgccg tgtactattg cgcacgggat 360

tggggcggat actcaagctc ctggacatat gggatggacg tgtgggggca gggcaccaca 420

gtcacagtgt ctagtgcaag cactaaaggc ccctccgtgt ttccactggc cccctcaagc 480

aagtccacat ctgggggcac tgcagccctg ggatgtctgg tgaaggatta cttccccgag 540
cctgtcaccg tgtcctggaa ctctggagcc ctgacttccg gggtccatac ctttcccgct 600
gtgctgcagt cctctgggct gtactctctg agttcagtgg tcacagtgcc tagctcctct 660
ctgggcaccc agacatatat ctgcaacgtg aatcacaagc ctagcaatac taaggtcgac 720
aaaagggtgg aaccaaaaag ctgtgataag actcatacct gcccaccctg tccagcacca 780
gagctgctgg gagggccaag cgtgttcctg tttcctccaa agcccaaaga caccctgatg 840
atttccagaa ccccagaagt cacatgcgtg gtcgtggacg tgtctcacga ggaccccgaa 900
gtcaagttca actggtacgt ggatggcgtc gaggtgcata atgctaagac aaaaccacgc 960
gaggaacagt acaattctac atatcgagtc gtgagtgtcc tgactgtgct gcaccaggac 1020
tggctgaacg gaaaggagta caagtgcaaa gtgagcaaca aggccctgcc tgccccaatc 1080
gagaagacaa ttagcaaggc taaagggcag cctagggaac cacaggtgta cactctgccc 1140
ccttccagag acgagctgac caaaaaccag gtctctctga catgtctggt gaagggcttc 1200
tatcccagcg atatcgcagt ggagtgggaa agcaatggac agcctgaaaa caattacaag 1260
actaccccac ccgtgctgga cagtgatggc tcattctttc tgtattcaaa actgaccgtg 1320
gataagagcc ggtggcagca gggaaacgtc tttagttgct cagtgatgca cgaggccctg 1380
cacaatcatt acacacagaa aagcctgtcc ctgtctcctg ggaaacgggg ccgcaagagg 1440
agaagtggat caggggccac taacttcagc ctgctgaagc aggctgggga cgtggaggaa 1500
aatcccggcc ctatggattg gacctggatt ctgttcctgg tcgctgcagc cactcgcgtg 1560
cattccgaca ttcagatgac ccagtctccc agttcactga gcgcctccgt cggagatcga 1620
gtgacaatca cttgtagggc aagccagggg atttctaaca gtctggcctg gtaccagcag 1680
aagcccggaa aagctcctaa gctgctgctg tatgctgcaa gcagactgga atccggggtg 1740
ccttctcggt tctcaggcag cggcagcgga accgactaca ccctgacaat tagctccctg 1800
cagcctgagg atttcgccac atactattgc cagcagtact attccacccc atatacattt 1860
ggccagggaa ctaaactgga aatcaagcga accgtcgccg ctccaagcgt gttcatcttt 1920
cctccatctg acgagcagct gaagagtgga accgcttcag tggtgtgcct gctgaacaac 1980
ttctaccccc gcgaggcaaa agtccagtgg aaggtggata acgccctgca gagcggcaat 2040
tcccaggagt ctgtgaccga acaggacagt aaagattcaa catatagcct gtctagtact 2100
ctgaccctga gcaaggctga ctacgagaag cacaaagtgt atgcatgcga agtgacccac 2160
caggggctga gttctccagt gactaaatct ttcaacagag gcgaatgttg ataactcgag 2220

<210> 100
<211> 2208
<212> DNA

<213> Artificial Sequence

<220>
<223> Nucleic Acid Sequence encoding CHIKV4-IgG

<400> 100
ggatccgcca ccatggactg gacatggatt ctgttcctgg tcgctgctgc tactcgggtg 60

catagcgaag tgaggctggt cgaaagtggg ggcgggctgg agcagcccgg cggcagcctg 120

aagctgtctt gcgccgctag tggcttcacc tttagcgact acttcatgta ttgggtcaga 180

cagacacctg agaagcggct ggaatgggtg gcctacatca gcaacggcgg aatttcaaca 240

ttctatagcg acgccgtgaa aggccggttt accatctccc gagataacgc taggaataca 300

ctgtacctgc agatgtcccg gctgaagtct gaagacacag caatctacta ttgcgtccgc 360

caggtgtatg ggcagggcta cttcgattat tggggacagg ggaccacact ggctgtcagc 420

tccgcaagca ctaagggacc ctccgtgttt cccctggccc cttctagtaa aagtacctca 480

ggagggacag cagccctggg gtgtctggtg aaggactact tccctgagcc agtcaccgtg 540

tcatggaaca gcggagctct gacatccggg gtccacactt ttcctgcagt gctgcagtca 600

agcggactgt actctctgtc ctctgtggtc accgtgccaa gttcaagcct ggggacacag 660

acttatatct gcaacgtgaa tcacaagcca tccaatacaa aagtcgacaa gaaagtggaa 720

cccaagtctt gtgataaaac ccatacatgc cctccctgtc cagctcctga gctgctgggc 780

ggaccatccg tgttcctgtt tccacccaag cctaaagaca cactgatgat tagccggact 840

cccgaagtca cctgcgtggt cgtggacgtg tcccacgagg accccgaagt caagttcaac 900

tggtacgtgg atggcgtcga ggtgcataat gccaagacca aacctcgcga ggaacagtac 960

aactctactt atcgagtcgt gagtgtcctg accgtgctgc accaggactg gctgaacggc 1020

aaggagtata agtgcaaagt gtctaataag gcactgccag cccccatcga gaaaactatt 1080

agcaaggcta aaggacagcc aagggaaccc caggtgtaca ccctgcctcc atctagagac 1140

gagctgacca agaaccaggt cagcctgaca tgtctggtga aagggttcta tccttctgat 1200

atcgcagtgg agtgggaaag taatggccag ccagaaaaca attacaagac taccctccc 1260

gtgctggact ccgatgggtc tttctttctg tattcaaagc tgaccgtgga taaaagccgc 1320

tggcagcagg gcaacgtctt tagctgctcc gtgatgcatg aggccctgca caatcattac 1380

actcagaaat ctctgagtct gtcaccaggg aagcgaggac gaaaaaggag aagcggctcc 1440

ggagctacca acttcagcct gctgaagcag gcaggcgacg tggaggaaaa tcctggacca 1500

atggattgga cttggattct gttcctggtg gctgcagcca cccgagtcca ctcccagatc 1560

gtgctgattc agtctccagc cattatgtct gctagtctgg gcgagcgcgt cactatgacc 1620

tgtacagcca gcagcagcgt gagcagcagc tacctgcatt ggtatcagca gaagcctggc 1680

tctagtccaa aactgtggat ctactcaagc ttcagtctgg catcaggagt gccagcaagg 1740

ttttcaggga gcggctccgg aacatcttac agtctgacaa ttagcactat ggaggctgaa 1800

gacgctgcaa cttactattg ccaccagtat ctgagaagcc catggacctt cggcggcggc 1860

agcaagctgg aaatcaaaac tgtcgccgct cccagcgtgt tcatctttcc accctcagac 1920

gagcagctga agagtgggac cgcctcagtg gtgtgcctgc tgaacaactt ctaccctaga 1980

gaagccaagg tccagtggaa agtggataac gctctgcaga gcggaaattc ccaggagtct 2040

gtgacagaac aggacagtaa ggattcaact tatagcctgt cctctactct gaccctgtcc 2100

aaagcagatt acgagaagca taaagtgtat gcctgcgagg tcacccacca ggggctgcgg 2160

tctcccgtca caaagagctt caacaggggc gaatgttgat aactcgag 2208

<210> 101
<211> 133
<212> PRT
<213> Artificial Sequence

<220>
<223> ZIKV-3F12E9-VH

<400> 101

Met Asn Phe Gly Leu Ser Leu Ile Phe Leu Ala Leu Ile Leu Lys Gly
1 5 10 15

Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Lys
20 25 30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Arg Tyr Gly Met Ser Trp Gly Arg Gln Thr Pro Asp Lys Arg Leu
50 55 60

Glu Trp Val Ala Thr Ile Ser Ser Gly Gly Thr Tyr Thr Tyr Tyr Pro
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met
100 105 110

Tyr Tyr Cys Ala Arg Ser Trp Phe Ala Tyr Trp Gly Arg Gly Thr Leu
115 120 125

Val Thr Val Ser Ala
130

<210> 102
<211> 132
<212> PRT
<213> Artificial Sequence

<220>
<223> ZIKV-3F12E9-VL

<400> 102

```
Met Met Ser Pro Ala Gln Phe Leu Phe Leu Leu Val Leu Trp Ile Arg
1               5                   10                  15

Glu Thr Asn Gly Asp Val Val Met Thr Gln Thr Pro Leu Thr Leu Ser
            20                  25                  30

Val Thr Ile Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser
        35                  40                  45

Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Leu Gln Arg
    50                  55                  60

Pro Gly Gln Ser Pro Lys Arg Leu Ile Tyr Leu Val Ser Lys Leu Asp
65                  70                  75                  80

Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe
                85                  90                  95

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

Cys Trp Gln Gly Thr His Phe Pro His Thr Phe Gly Gly Gly Thr Lys
        115                 120                 125

Leu Glu Ile Lys
    130
```

<210> 103
<211> 134
<212> PRT
<213> Artificial Sequence

<220>
<223> ZIKV-8A9F9-VH

<400> 103

```
Met Asn Phe Gly Leu Ser Leu Ile Phe Leu Val Leu Ile Leu Lys Gly
1               5                   10                  15

Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
            20                  25                  30
```

```
Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu
    50                  55                  60

Glu Trp Val Ala Glu Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Pro
65                  70                  75                  80

Asp Thr Val Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
                85                  90                  95

Thr Leu Tyr Leu Glu Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met
            100                 105                 110

Tyr Tyr Cys Ala Ser Asp Gly Tyr Tyr Ser His Trp Gly Gln Gly Thr
        115                 120                 125

Ser Val Thr Val Ser Ser
    130
```

<210> 104
<211> 131
<212> PRT
<213> Artificial Sequence

<220>
<223> ZIKV-8A9F9-VL

<400> 104

```
Met Lys Leu Pro Val Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala
1               5                   10                  15

Ser Arg Ser Asp Val Val Met Thr Gln Ile Pro Leu Ser Leu Pro Val
            20                  25                  30

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
        35                  40                  45

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
    50                  55                  60

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
65                  70                  75                  80

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
                85                  90                  95
```

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
100 105 110

Phe Gln Ser Thr His Val Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu
115 120 125

Glu Ile Lys
130

<210> 105
<211> 82
<212> PRT
<213> Artificial Sequence

<220>
<223> ZIKV-8D10F4-VH

<400> 105

Met Asn Phe Gly Leu Ser Leu Ile Phe Leu Val Leu Ile Leu Lys Gly
1 5 10 15

Val Lys Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
20 25 30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu
50 55 60

Glu Trp Val Ala Glu Ile Ser Ser Gly Gly Ser Tyr Ile Tyr Tyr Pro
65 70 75 80

Asp Thr

<210> 106
<211> 131
<212> PRT
<213> Artificial Sequence

<220>
<223> ZIKV-8D10F4-VL

<400> 106

Met Lys Leu Pro Val Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala
1 5 10 15

Ser Ser Ser Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val
20 25 30

```
Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
        35                  40                  45

Val His Ser Asn Gly Asn Thr Tyr Phe His Trp Tyr Leu Gln Lys Pro
    50                  55                  60

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
65                  70                  75                  80

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
                85                  90                  95

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Leu Tyr Phe Cys
            100                 105                 110

Ser Gln Ser Thr His Val Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu
        115                 120                 125

Glu Ile Lys
    130
```

<210> 107
<211> 134
<212> PRT
<213> Artificial Sequence

<220>
<223> ZIKV-IC2A6-VH

<400> 107

```
Met Asn Phe Gly Leu Ser Leu Ile Phe Leu Val Leu Ile Leu Lys Gly
1               5                   10                  15

Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
            20                  25                  30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu
    50                  55                  60

Glu Trp Val Ala Glu Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Pro
65                  70                  75                  80

Asp Thr Val Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
                85                  90                  95
```

Thr Leu Tyr Leu Glu Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met
100 105 110

Tyr Tyr Cys Ala Ser Asp Gly Tyr Tyr Ser His Trp Gly Gln Gly Thr
115 120 125

Ser Val Thr Val Ser Ser
130

<210> 108
<211> 131
<212> PRT
<213> Artificial Sequence

<220>
<223> ZIKV-IC2A6-VH

<400> 108

Met Lys Leu Pro Val Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala
1 5 10 15

Ser Ser Ser Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val
20 25 30

Cys Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu
35 40 45

Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro
50 55 60

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser
65 70 75 80

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
85 90 95

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys
100 105 110

Phe Gln Ser Thr His Val Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu
115 120 125

Glu Ile Lys
130

<210> 109
<211> 146
<212> PRT
<213> Artificial Sequence

<220>
<223> ZIKV-ID4G7-VH

<400> 109

Met Ala Trp Val Trp Thr Leu Leu Phe Leu Met Ala Ala Ala Gln Ser
1 5 10 15

Ala Gln Ala Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys
20 25 30

Pro Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asn Tyr Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu
50 55 60

Lys Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala
65 70 75 80

Asp Asp Phe Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser
85 90 95

Thr Ala Tyr Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr
100 105 110

Tyr Phe Cys Ala Arg Glu Ile Ser Lys Ile Tyr Tyr Tyr Gly Ser Ser
115 120 125

Tyr Glu Asn Gly Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
130 135 140

Ser Ser
145

<210> 110
<211> 131
<212> PRT
<213> Artificial Sequence

<220>
<223> ZIKV-ID4G7-VL

<400> 110

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1 5 10 15

Gly Ser Thr Gly Asn Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala
20 25 30

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
35 40 45

Val Asp Ser Phe Gly Asn Ser Phe Met His Trp Phe Gln Gln Lys Pro
50 55 60

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Ser
65 70 75 80

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
85 90 95

Leu Thr Ile Asp Pro Val Glu Ala Asp Asp Ala Ala Thr Tyr Tyr Cys
100 105 110

Gln Gln Asn Asn Glu Tyr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu
115 120 125

Glu Ile Lys
130

<210> 111
<211> 728
<212> PRT
<213> Artificial Sequence

<220>
<223> Human anti-Zika (3F12E9)-IgG4: Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 111

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Lys
20 25 30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Arg Tyr Gly Met Ser Trp Gly Arg Gln Thr Pro Asp Lys Arg Leu
50 55 60

Glu Trp Val Ala Thr Ile Ser Ser Gly Gly Thr Tyr Thr Tyr Tyr Pro
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn

```
                85                  90                  95

Thr Leu Tyr Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met
            100                 105                 110

Tyr Tyr Cys Ala Arg Ser Trp Phe Ala Tyr Trp Gly Arg Gly Thr Leu
        115                 120                 125

Val Thr Val Ser Ala Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
    130                 135                 140

Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys
145                 150                 155                 160

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
                165                 170                 175

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
            180                 185                 190

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
        195                 200                 205

Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn
    210                 215                 220

Thr Lys Val Asp Lys Arg Val Ser Pro Asn Met Val Pro His Ala His
225                 230                 235                 240

His Ala Gln Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe
                245                 250                 255

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
            260                 265                 270

Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe
        275                 280                 285

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
    290                 295                 300

Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
305                 310                 315                 320

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
                325                 330                 335
```

```
Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala
            340                 345                 350

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln
        355                 360                 365

Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
    370                 375                 380

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
385                 390                 395                 400

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
                405                 410                 415

Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
            420                 425                 430

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
        435                 440                 445

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys Arg Gly Arg Lys
    450                 455                 460

Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala
465                 470                 475                 480

Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr Gln Val
                485                 490                 495

Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Asp Val Val
            500                 505                 510

Met Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly Gln Pro Ala
        515                 520                 525

Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser Asp Gly Lys
    530                 535                 540

Thr Tyr Leu Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser Pro Lys Arg
545                 550                 555                 560

Leu Ile Tyr Leu Val Ser Lys Leu Asp Ser Gly Val Pro Asp Arg Phe
                565                 570                 575

Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val
            580                 585                 590
```

```
Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly Thr His Phe
        595                 600                 605

Pro His Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val
    610                 615                 620

Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys
625                 630                 635                 640

Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
                645                 650                 655

Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
            660                 665                 670

Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
        675                 680                 685

Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
    690                 695                 700

Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
705                 710                 715                 720

Lys Ser Phe Asn Arg Gly Glu Cys
                725
```

<210> 112
<211> 731
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 112

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                   10                  15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Lys
            20                  25                  30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45

Ser Arg Tyr Gly Met Ser Trp Gly Arg Gln Thr Pro Asp Lys Arg Leu
    50                  55                  60
```

```
Glu Trp Val Ala Thr Ile Ser Ser Gly Gly Thr Tyr Thr Tyr Tyr Pro
65                  70                  75                  80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
                85                  90                  95

Thr Leu Tyr Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met
            100                 105                 110

Tyr Tyr Cys Ala Arg Ser Trp Phe Ala Tyr Trp Gly Arg Gly Thr Leu
        115                 120                 125

Val Thr Val Ser Ala Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
    130                 135                 140

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
145                 150                 155                 160

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
                165                 170                 175

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
            180                 185                 190

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
        195                 200                 205

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
    210                 215                 220

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
225                 230                 235                 240

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
                245                 250                 255

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
            260                 265                 270

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
        275                 280                 285

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
    290                 295                 300

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
```

```
305                 310                 315                 320

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
                325                 330                 335

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
            340                 345                 350

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
        355                 360                 365

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
    370                 375                 380

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
385                 390                 395                 400

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
                405                 410                 415

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
            420                 425                 430

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
        435                 440                 445

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg
    450                 455                 460

Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu
465                 470                 475                 480

Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu Gln
                485                 490                 495

Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly
            500                 505                 510

Asp Val Val Met Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly
        515                 520                 525

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
    530                 535                 540

Asp Gly Lys Thr Tyr Leu Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser
545                 550                 555                 560
```

```
Pro Lys Arg Leu Ile Tyr Leu Val Ser Lys Leu Asp Ser Gly Val Pro
                565                 570                 575

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
            580                 585                 590

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly
        595                 600                 605

Thr His Phe Pro His Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
    610                 615                 620

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
625                 630                 635                 640

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
                645                 650                 655

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
            660                 665                 670

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
        675                 680                 685

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
    690                 695                 700

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
705                 710                 715                 720

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
                725                 730
```

<210> 113
<211> 729
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 113

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                   10                  15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
            20                  25                  30
```

```
Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu
    50                  55                  60

Glu Trp Val Ala Glu Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Pro
65                  70                  75                  80

Asp Thr Val Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
                85                  90                  95

Thr Leu Tyr Leu Glu Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met
            100                 105                 110

Tyr Tyr Cys Ala Ser Asp Gly Tyr Tyr Ser His Trp Gly Gln Gly Thr
        115                 120                 125

Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
    130                 135                 140

Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly
145                 150                 155                 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                165                 170                 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            180                 185                 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser
    210                 215                 220

Asn Thr Lys Val Asp Lys Arg Val Ser Pro Asn Met Val Pro His Ala
225                 230                 235                 240

His His Ala Gln Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu
                245                 250                 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270

Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln
        275                 280                 285
```

```
Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
    290                 295                 300

Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        435                 440                 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys Arg Gly Arg
    450                 455                 460

Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln
465                 470                 475                 480

Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr Gln
                485                 490                 495

Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Asp Val
            500                 505                 510

Val Met Thr Gln Ile Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln
        515                 520                 525

Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly
```

530 535 540

Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys
545 550 555 560

Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg
565 570 575

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg
580 585 590

Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Phe Gln Ser Thr His
595 600 605

Val Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr
610 615 620

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
625 630 635 640

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
645 650 655

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
660 665 670

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
675 680 685

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
690 695 700

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
705 710 715 720

Thr Lys Ser Phe Asn Arg Gly Glu Cys
725

<210> 114
<211> 732
<212> PRT
<213> Artificial Sequence

<220>
<223> Human anti-Zika (8A9F9)-IgG1: Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 114

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                  10                  15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
            20                  25                  30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu
    50                  55                  60

Glu Trp Val Ala Glu Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Pro
65                  70                  75                  80

Asp Thr Val Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
                85                  90                  95

Thr Leu Tyr Leu Glu Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met
            100                 105                 110

Tyr Tyr Cys Ala Ser Asp Gly Tyr Tyr Ser His Trp Gly Gln Gly Thr
        115                 120                 125

Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
    130                 135                 140

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145                 150                 155                 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                165                 170                 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            180                 185                 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    210                 215                 220

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
225                 230                 235                 240

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
                245                 250                 255
```

```
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            260                 265                 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
        275                 280                 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    290                 295                 300

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
305                 310                 315                 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
                325                 330                 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
            340                 345                 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
        355                 360                 365

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
    370                 375                 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385                 390                 395                 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
                405                 410                 415

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
            420                 425                 430

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
        435                 440                 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455                 460

Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu
465                 470                 475                 480

Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu
                485                 490                 495

Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr
```

500 505 510

Gly Asp Val Val Met Thr Gln Ile Pro Leu Ser Leu Pro Val Ser Leu
515 520 525

Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His
530 535 540

Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln
545 550 555 560

Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val
565 570 575

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys
580 585 590

Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Phe Gln
595 600 605

Ser Thr His Val Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
610 615 620

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
625 630 635 640

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
645 650 655

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
660 665 670

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
675 680 685

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
690 695 700

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
705 710 715 720

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
725 730

<210> 115
<211> 728
<212> PRT
<213> Artificial Sequence

<220>
<223> Human anti-Zika (8D10F4)-IgG4: Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 115

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
20 25 30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu
50 55 60

Glu Trp Val Ala Glu Ile Ser Ser Gly Gly Ser Tyr Ile Tyr Tyr Pro
65 70 75 80

Asp Thr Val Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
85 90 95

Thr Leu Tyr Leu Glu Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met
100 105 110

Tyr Tyr Cys Ala Ser Asp Gly Tyr Tyr Ser His Trp Gly Gln Gly Thr
115 120 125

Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
130 135 140

Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly
145 150 155 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
165 170 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
180 185 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
195 200 205

Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser
210 215 220

```
Asn Thr Lys Val Asp Lys Arg Val Ser Pro Asn Met Val Pro His Ala
225                 230                 235                 240

His His Ala Gln Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu
                245                 250                 255

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
            260                 265                 270

Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln
        275                 280                 285

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
    290                 295                 300

Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu
305                 310                 315                 320

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
                325                 330                 335

Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys
            340                 345                 350

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
        355                 360                 365

Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
    370                 375                 380

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
385                 390                 395                 400

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                405                 410                 415

Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln
            420                 425                 430

Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        435                 440                 445

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys Arg Gly Arg
    450                 455                 460

Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln
```

```
465                 470                 475                 480

Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr Gln
                485                 490                 495

Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Asp Val
            500                 505                 510

Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly Asp Gln
        515                 520                 525

Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly
    530                 535                 540

Asn Thr Tyr Phe His Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys
545                 550                 555                 560

Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg
                565                 570                 575

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg
            580                 585                 590

Val Glu Ala Glu Asp Leu Gly Leu Tyr Phe Cys Ser Gln Ser Thr His
        595                 600                 605

Val Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Thr Val
    610                 615                 620

Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys
625                 630                 635                 640

Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
                645                 650                 655

Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
            660                 665                 670

Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
        675                 680                 685

Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
    690                 695                 700

Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
705                 710                 715                 720
```

Lys Ser Phe Asn Arg Gly Glu Cys
725

<210> 116
<211> 732
<212> PRT
<213> Artificial Sequence

<220>
<223> Human anti-Zika (8D10F4)-IgG1: Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 116

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
20 25 30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu
50 55 60

Glu Trp Val Ala Glu Ile Ser Ser Gly Gly Ser Tyr Ile Tyr Tyr Pro
65 70 75 80

Asp Thr Val Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
85 90 95

Thr Leu Tyr Leu Glu Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met
100 105 110

Tyr Tyr Cys Ala Ser Asp Gly Tyr Tyr Ser His Trp Gly Gln Gly Thr
115 120 125

Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
130 135 140

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145 150 155 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
165 170 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
180 185 190

```
Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    210                 215                 220

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
225                 230                 235                 240

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
                245                 250                 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            260                 265                 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
        275                 280                 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    290                 295                 300

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
305                 310                 315                 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
                325                 330                 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
            340                 345                 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
        355                 360                 365

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
    370                 375                 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385                 390                 395                 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
                405                 410                 415

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
            420                 425                 430

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
```

435 440 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
450 455 460

Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu
465 470 475 480

Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu
485 490 495

Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr
500 505 510

Gly Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu
515 520 525

Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His
530 535 540

Ser Asn Gly Asn Thr Tyr Phe His Trp Tyr Leu Gln Lys Pro Gly Gln
545 550 555 560

Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val
565 570 575

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys
580 585 590

Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Leu Tyr Phe Cys Ser Gln
595 600 605

Ser Thr His Val Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
610 615 620

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
625 630 635 640

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
645 650 655

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
660 665 670

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
675 680 685

```
Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
    690                 695                 700

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
705                 710                 715                 720

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
                725                 730
```

<210> 117
<211> 740
<212> PRT
<213> Artificial Sequence

<220>
<223> Human anti-Zika (1D4G7)-IgG4: Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 117

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                   10                  15

Thr His Ala Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys
            20                  25                  30

Pro Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe
        35                  40                  45

Thr Asn Tyr Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu
    50                  55                  60

Lys Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala
65                  70                  75                  80

Asp Asp Phe Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser
                85                  90                  95

Thr Ala Tyr Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr
            100                 105                 110

Tyr Phe Cys Ala Arg Glu Ile Ser Lys Ile Tyr Tyr Tyr Gly Ser Ser
        115                 120                 125

Tyr Glu Asn Gly Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
    130                 135                 140

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys
145                 150                 155                 160
```

```
Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys
                165                 170                 175

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
            180                 185                 190

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
        195                 200                 205

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
    210                 215                 220

Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val
225                 230                 235                 240

Asp Lys Arg Val Ser Pro Asn Met Val Pro His Ala His His Ala Gln
                245                 250                 255

Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
            260                 265                 270

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
        275                 280                 285

Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr
    290                 295                 300

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
305                 310                 315                 320

Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                325                 330                 335

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            340                 345                 350

Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        355                 360                 365

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met
    370                 375                 380

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
385                 390                 395                 400

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
```

405 410 415

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
420 425 430

Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val
435 440 445

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
450 455 460

Lys Ser Leu Ser Leu Ser Leu Gly Lys Arg Gly Arg Lys Arg Arg Ser
465 470 475 480

Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
485 490 495

Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr Gln Val Phe Ile Ser
500 505 510

Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Asn Ile Val Leu Thr Gln
515 520 525

Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala Thr Ile Ser
530 535 540

Cys Arg Ala Ser Glu Ser Val Asp Ser Phe Gly Asn Ser Phe Met His
545 550 555 560

Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Leu
565 570 575

Ala Ser Asn Leu Glu Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly
580 585 590

Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp Pro Val Glu Ala Asp Asp
595 600 605

Ala Ala Thr Tyr Tyr Cys Gln Gln Asn Asn Glu Tyr Pro Tyr Thr Phe
610 615 620

Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro Ser
625 630 635 640

Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala
645 650 655

```
Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val
            660                 665                 670

Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser
        675                 680                 685

Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr
    690                 695                 700

Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys
705                 710                 715                 720

Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn
                725                 730                 735

Arg Gly Glu Cys
            740
```

<210> 118
<211> 743
<212> PRT
<213> Artificial Sequence

<220>
<223> Human anti-Zika (1D4G7)-IgG1: Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 118

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                   10                  15

Thr His Ala Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys
            20                  25                  30

Pro Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe
        35                  40                  45

Thr Asn Tyr Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu
    50                  55                  60

Lys Trp Met Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala
65                  70                  75                  80

Asp Asp Phe Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser
                85                  90                  95

Thr Ala Tyr Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr
            100                 105                 110
```

```
Tyr Phe Cys Ala Arg Glu Ile Ser Lys Ile Tyr Tyr Tyr Gly Ser Ser
        115                 120                 125

Tyr Glu Asn Gly Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
    130                 135                 140

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
145                 150                 155                 160

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
                165                 170                 175

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
            180                 185                 190

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
        195                 200                 205

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
    210                 215                 220

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
225                 230                 235                 240

Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro
                245                 250                 255

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
            260                 265                 270

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
        275                 280                 285

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
    290                 295                 300

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
305                 310                 315                 320

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
                325                 330                 335

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
            340                 345                 350

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
```

```
        355                 360                 365

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
    370                 375                 380

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
385                 390                 395                 400

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
                405                 410                 415

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
            420                 425                 430

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
        435                 440                 445

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
    450                 455                 460

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys
465                 470                 475                 480

Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala
                485                 490                 495

Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr Gln Val
            500                 505                 510

Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Asn Ile Val
        515                 520                 525

Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala
    530                 535                 540

Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Asp Ser Phe Gly Asn Ser
545                 550                 555                 560

Phe Met His Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu
                565                 570                 575

Ile Tyr Leu Ala Ser Asn Leu Glu Ser Gly Val Pro Ala Arg Phe Ser
            580                 585                 590

Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp Pro Val Glu
        595                 600                 605
```

```
Ala Asp Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Asn Asn Glu Tyr Pro
    610                 615                 620

Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala
625                 630                 635                 640

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
                645                 650                 655

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
            660                 665                 670

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
        675                 680                 685

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
    690                 695                 700

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
705                 710                 715                 720

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
                725                 730                 735

Ser Phe Asn Arg Gly Glu Cys
            740
```

<210> 119
<211> 732
<212> PRT
<213> Artificial Sequence

<220>
<223> Human anti-Zika (8A9F9)-IgG1: Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2 (with LALA variant at 4th and 5th residue)-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 119

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                   10                  15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
            20                  25                  30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu
    50                  55                  60
```

```
Glu Trp Val Ala Glu Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Pro
65                  70                  75                  80

Asp Thr Val Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
                85                  90                  95

Thr Leu Tyr Leu Glu Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met
            100                 105                 110

Tyr Tyr Cys Ala Ser Asp Gly Tyr Tyr Ser His Trp Gly Gln Gly Thr
        115                 120                 125

Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
    130                 135                 140

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
145                 150                 155                 160

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
                165                 170                 175

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
            180                 185                 190

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
        195                 200                 205

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
    210                 215                 220

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
225                 230                 235                 240

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser
                245                 250                 255

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
            260                 265                 270

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
        275                 280                 285

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
    290                 295                 300

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
```

305 310 315 320

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
325 330 335

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
340 345 350

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
355 360 365

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
370 375 380

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
385 390 395 400

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
405 410 415

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
420 425 430

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
435 440 445

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
450 455 460

Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu
465 470 475 480

Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu
485 490 495

Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr
500 505 510

Gly Asp Val Val Met Thr Gln Ile Pro Leu Ser Leu Pro Val Ser Leu
515 520 525

Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His
530 535 540

Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln
545 550 555 560

```
Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val
                565                 570                 575

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys
            580                 585                 590

Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Phe Gln
        595                 600                 605

Ser Thr His Val Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
    610                 615                 620

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
625                 630                 635                 640

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
                645                 650                 655

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
            660                 665                 670

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
        675                 680                 685

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
    690                 695                 700

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
705                 710                 715                 720

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
                725                 730
```

<210> 120
<211> 731
<212> PRT
<213> Artificial Sequence

<220>
<223> Human anti-Zika (3F12E9)-IgG1: Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2 (with LALA variant at 4th and 5th residue)-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 120

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                   10                  15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Lys
            20                  25                  30
```

```
Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45

Ser Arg Tyr Gly Met Ser Trp Gly Arg Gln Thr Pro Asp Lys Arg Leu
    50                  55                  60

Glu Trp Val Ala Thr Ile Ser Ser Gly Gly Thr Tyr Thr Tyr Tyr Pro
65                  70                  75                  80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
                85                  90                  95

Thr Leu Tyr Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met
            100                 105                 110

Tyr Tyr Cys Ala Arg Ser Trp Phe Ala Tyr Trp Gly Arg Gly Thr Leu
        115                 120                 125

Val Thr Val Ser Ala Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
    130                 135                 140

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
145                 150                 155                 160

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
                165                 170                 175

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
            180                 185                 190

Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
        195                 200                 205

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
    210                 215                 220

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
225                 230                 235                 240

Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro Ser Val
                245                 250                 255

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
            260                 265                 270

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
```

```
        275                 280                 285

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
    290                 295                 300

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
305                 310                 315                 320

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
                325                 330                 335

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
            340                 345                 350

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
        355                 360                 365

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
    370                 375                 380

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
385                 390                 395                 400

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
                405                 410                 415

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
            420                 425                 430

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
        435                 440                 445

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg
    450                 455                 460

Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu
465                 470                 475                 480

Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu Gln
                485                 490                 495

Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly
            500                 505                 510

Asp Val Val Met Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly
        515                 520                 525
```

```
Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
    530                 535                 540

Asp Gly Lys Thr Tyr Leu Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser
545                 550                 555                 560

Pro Lys Arg Leu Ile Tyr Leu Val Ser Lys Leu Asp Ser Gly Val Pro
                565                 570                 575

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
            580                 585                 590

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly
        595                 600                 605

Thr His Phe Pro His Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
    610                 615                 620

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
625                 630                 635                 640

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
                645                 650                 655

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
            660                 665                 670

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
        675                 680                 685

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
    690                 695                 700

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
705                 710                 715                 720

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
                725                 730
```

<210> 121
<211> 780
<212> PRT
<213> Artificial Sequence

<220>
<223> Human anti-Zika (IC2A6)-IgG4: Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 121

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                  10                  15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
            20                  25                  30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu
    50                  55                  60

Glu Trp Val Ala Glu Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Pro
65                  70                  75                  80

Asp Thr Val Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
                85                  90                  95

Thr Leu Tyr Leu Glu Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met
            100                 105                 110

Tyr Tyr Cys Ala Ser Asp Gly Tyr Tyr Ser His Trp Gly Gln Gly Thr
        115                 120                 125

Ser Val Thr Val Ser Ser Val Thr Gly Arg Phe Thr Ile Ser Arg Asp
    130                 135                 140

Asn Ala Lys Asn Thr Leu Tyr Leu Glu Met Ser Ser Leu Arg Ser Glu
145                 150                 155                 160

Asp Thr Ala Met Tyr Tyr Cys Ala Ser Asp Gly Tyr Tyr Ser His Trp
                165                 170                 175

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
            180                 185                 190

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
        195                 200                 205

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
    210                 215                 220

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
225                 230                 235                 240

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
```

```
                245                 250                 255

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
            260                 265                 270

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Ser Pro Asn Met
        275                 280                 285

Val Pro His Ala His His Ala Gln Ala Pro Glu Phe Leu Gly Gly Pro
    290                 295                 300

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
305                 310                 315                 320

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp
                325                 330                 335

Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
            340                 345                 350

Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val
        355                 360                 365

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
    370                 375                 380

Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys
385                 390                 395                 400

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
                405                 410                 415

Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
            420                 425                 430

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
        435                 440                 445

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
    450                 455                 460

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys
465                 470                 475                 480

Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu
                485                 490                 495
```

```
Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
            500                 505                 510

Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser
        515                 520                 525

Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val
    530                 535                 540

Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala
545                 550                 555                 560

Tyr Gly Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Cys
                565                 570                 575

Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val
            580                 585                 590

His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly
        595                 600                 605

Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly
    610                 615                 620

Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
625                 630                 635                 640

Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Phe
                645                 650                 655

Gln Ser Thr His Val Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu
            660                 665                 670

Ile Lys Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
        675                 680                 685

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
    690                 695                 700

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
705                 710                 715                 720

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
                725                 730                 735

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
            740                 745                 750
```

```
Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
        755                 760                 765

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    770                 775                 780
```

<210> 122
<211> 784
<212> PRT
<213> Artificial Sequence

<220>
<223> Human anti-Zika (IC2A6)-IgG1: Human IgG heavy signal peptide-VH-CH1-Hinge Region-CH2-CH3-custom Furin cleavage site-'GSG' Linker and P2A Peptide-human kappa light chain signal peptide-VL-CL (kappa)

<400> 122

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                   10                  15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
            20                  25                  30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ser Pro Glu Lys Arg Leu
    50                  55                  60

Glu Trp Val Ala Glu Ile Ser Ser Gly Gly Ser Tyr Thr Tyr Tyr Pro
65                  70                  75                  80

Asp Thr Val Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
                85                  90                  95

Thr Leu Tyr Leu Glu Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met
            100                 105                 110

Tyr Tyr Cys Ala Ser Asp Gly Tyr Tyr Ser His Trp Gly Gln Gly Thr
        115                 120                 125

Ser Val Thr Val Ser Ser Val Thr Gly Arg Phe Thr Ile Ser Arg Asp
    130                 135                 140

Asn Ala Lys Asn Thr Leu Tyr Leu Glu Met Ser Ser Leu Arg Ser Glu
145                 150                 155                 160

Asp Thr Ala Met Tyr Tyr Cys Ala Ser Asp Gly Tyr Tyr Ser His Trp
```

```
                165                 170                 175

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
            180                 185                 190

Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
        195                 200                 205

Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
    210                 215                 220

Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
225                 230                 235                 240

Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
                245                 250                 255

Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
            260                 265                 270

His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser
        275                 280                 285

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
    290                 295                 300

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
305                 310                 315                 320

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
                325                 330                 335

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
            340                 345                 350

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
        355                 360                 365

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
    370                 375                 380

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
385                 390                 395                 400

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
                405                 410                 415
```

```
Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
            420                 425                 430

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
        435                 440                 445

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
    450                 455                 460

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
465                 470                 475                 480

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
                485                 490                 495

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
            500                 505                 510

Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr
        515                 520                 525

Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly
    530                 535                 540

Pro Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile
545                 550                 555                 560

Ser Gly Ala Tyr Gly Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu
                565                 570                 575

Pro Val Cys Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln
            580                 585                 590

Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln
        595                 600                 605

Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg
    610                 615                 620

Phe Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
625                 630                 635                 640

Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr
                645                 650                 655

Phe Cys Phe Gln Ser Thr His Val Pro Pro Thr Phe Gly Gly Gly Thr
            660                 665                 670
```

```
Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe
        675                 680                 685

Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys
    690                 695                 700

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
705                 710                 715                 720

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
                725                 730                 735

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
            740                 745                 750

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
        755                 760                 765

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    770                 775                 780
```

<210> 123
<211> 702
<212> PRT
<213> Artificial Sequence

<220>
<223> consensus Zika IgE Leader-prME

<400> 123

```
Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1               5                   10                  15

His Ser Gly Ile Ile Gly Leu Leu Leu Thr Thr Ala Met Ala Ala Glu
            20                  25                  30

Ile Thr Arg Arg Gly Ser Ala Tyr Tyr Met Tyr Leu Asp Arg Asn Asp
        35                  40                  45

Ala Gly Glu Ala Ile Ser Phe Pro Thr Thr Leu Gly Met Asn Lys Cys
    50                  55                  60

Tyr Ile Gln Ile Met Asp Leu Gly His Met Cys Asp Ala Thr Met Ser
65                  70                  75                  80

Tyr Glu Cys Pro Met Leu Asp Glu Gly Val Glu Pro Asp Asp Val Asp
                85                  90                  95
```

```
Cys Trp Cys Asn Thr Thr Ser Thr Trp Val Val Tyr Gly Thr Cys His
            100                 105                 110

His Lys Lys Gly Glu Ala Arg Arg Ser Arg Arg Ala Val Thr Leu Pro
        115                 120                 125

Ser His Ser Thr Arg Lys Leu Gln Thr Arg Ser Gln Thr Trp Leu Glu
    130                 135                 140

Ser Arg Glu Tyr Thr Lys His Leu Ile Arg Val Glu Asn Trp Ile Phe
145                 150                 155                 160

Arg Asn Pro Gly Phe Ala Leu Ala Ala Ala Ala Ile Ala Trp Leu Leu
                165                 170                 175

Gly Ser Ser Thr Ser Gln Lys Val Ile Tyr Leu Val Met Ile Leu Leu
            180                 185                 190

Ile Ala Pro Ala Tyr Ser Ile Arg Cys Ile Gly Val Ser Asn Arg Asp
        195                 200                 205

Phe Val Glu Gly Met Ser Gly Gly Thr Trp Val Asp Val Val Leu Glu
    210                 215                 220

His Gly Gly Cys Val Thr Val Met Ala Gln Asp Lys Pro Thr Val Asp
225                 230                 235                 240

Ile Glu Leu Val Thr Thr Thr Val Ser Asn Met Ala Glu Val Arg Ser
                245                 250                 255

Tyr Cys Tyr Glu Ala Ser Ile Ser Asp Met Ala Ser Asp Ser Arg Cys
            260                 265                 270

Pro Thr Gln Gly Glu Ala Tyr Leu Asp Lys Gln Ser Asp Thr Gln Tyr
        275                 280                 285

Val Cys Lys Arg Thr Leu Val Asp Arg Gly Trp Gly Asn Gly Cys Gly
    290                 295                 300

Leu Phe Gly Lys Gly Ser Leu Val Thr Cys Ala Lys Phe Thr Cys Ser
305                 310                 315                 320

Lys Lys Met Thr Gly Lys Ser Ile Gln Pro Glu Asn Leu Glu Tyr Arg
                325                 330                 335

Ile Met Leu Ser Val His Gly Ser Gln His Ser Gly Met Ile Val Asn
            340                 345                 350
```

```
Asp Ile Gly His Glu Thr Asp Glu Asn Arg Ala Lys Val Glu Val Thr
        355                 360                 365

Pro Asn Ser Pro Arg Ala Glu Ala Thr Leu Gly Gly Phe Gly Ser Leu
    370                 375                 380

Gly Leu Asp Cys Glu Pro Arg Thr Gly Leu Asp Phe Ser Asp Leu Tyr
385                 390                 395                 400

Tyr Leu Thr Met Asn Asn Lys His Trp Leu Val His Lys Glu Trp Phe
                405                 410                 415

His Asp Ile Pro Leu Pro Trp His Ala Gly Ala Asp Thr Gly Thr Pro
            420                 425                 430

His Trp Asn Asn Lys Glu Ala Leu Val Glu Phe Lys Asp Ala His Ala
        435                 440                 445

Lys Arg Gln Thr Val Val Val Leu Gly Ser Gln Glu Gly Ala Val His
    450                 455                 460

Thr Ala Leu Ala Gly Ala Leu Glu Ala Glu Met Asp Gly Ala Lys Gly
465                 470                 475                 480

Arg Leu Phe Ser Gly His Leu Lys Cys Arg Leu Lys Met Asp Lys Leu
                485                 490                 495

Arg Leu Lys Gly Val Ser Tyr Ser Leu Cys Thr Ala Ala Phe Thr Phe
            500                 505                 510

Thr Lys Val Pro Ala Glu Thr Leu His Gly Thr Val Thr Val Glu Val
        515                 520                 525

Gln Tyr Ala Gly Thr Asp Gly Pro Cys Lys Val Pro Ala Gln Met Ala
    530                 535                 540

Val Asp Met Gln Thr Leu Thr Pro Val Gly Arg Leu Ile Thr Ala Asn
545                 550                 555                 560

Pro Val Ile Thr Glu Ser Thr Glu Asn Ser Lys Met Met Leu Glu Leu
                565                 570                 575

Asp Pro Pro Phe Gly Asp Ser Tyr Ile Val Ile Gly Val Gly Asp Lys
            580                 585                 590

Lys Ile Thr His His Trp His Arg Ser Gly Ser Thr Ile Gly Lys Ala
        595                 600                 605
```

```
Phe Glu Ala Thr Val Arg Gly Ala Lys Arg Met Ala Val Leu Gly Asp
    610                 615                 620

Thr Ala Trp Asp Phe Gly Ser Val Gly Gly Val Phe Asn Ser Leu Gly
625                 630                 635                 640

Lys Gly Ile His Gln Ile Phe Gly Ala Ala Phe Lys Ser Leu Phe Gly
                645                 650                 655

Gly Met Ser Trp Phe Ser Gln Ile Leu Ile Gly Thr Leu Leu Val Trp
            660                 665                 670

Leu Gly Leu Asn Thr Lys Asn Gly Ser Ile Ser Leu Thr Cys Leu Ala
        675                 680                 685

Leu Gly Gly Val Met Ile Phe Leu Ser Thr Ala Val Ser Ala
    690                 695                 700
```

<210> 124
<211> 2112
<212> DNA
<213> Artificial Sequence

<220>
<223> consensus Zika IgE Leader-prME (construct 1)

<400> 124

```
atggactgga cctggattct gtttctggtc gctgctgcta caagagtgca ttctgggatt       60

attggactgc tgctgactac tgccatggca gcagagatca ccaggagagg cagcgcctac      120

tatatgtacc tggaccggtc tgatgccggc aaggccatca gctttgccac cacactgggc      180

gtgaataagt gccacgtgca gatcatggac ctgggccaca tgtgcgatgc caccatgtcc      240

tacgagtgtc caatgctgga cgagggcgtg gagcccgacg atgtggattg ctggtgtaac      300

accacatcta catgggtggt gtatggcacc tgtcaccaca agaagggaga ggcacggcgc      360

agcaggagag cagtgacact gccctctcac agcaccagga agctgcagac aagaagccag      420

acctggctgg agtcccggga gtatacaaag cacctgatca aggtggagaa ctggatcttt      480

cgcaatccag gattcgcact ggtggcagtg gcaatcgcat ggctgctggg cagctccacc      540

tcccagaaag tgatctacct ggtcatgatc ctgctgatcg cccctgccta ttccatcagg      600

tgcatcggcg tgtctaatag agacttcgtg gagggcatgt ctggcggcac ctgggtggat      660

gtggtgctgg agcacggcgg atgcgtgaca gtgatggccc aggacaagcc aaccgtggat      720

atcgagctgg tgaccacaac cgtgagcaac atggccgagg tgaggtccta ctgctatgag      780

gcctccatct ctgacatggc cagcgattcc agatgtccca cccagggcga ggcctacctg      840
```

gacaagcagt ccgatacaca gtacgtgtgc aagcggaccc tggtggacag gggatgggga 900

aatggatgtg gcctgtttgg caagggctct ctggtgacat gcgccaagtt cacctgttct 960

aagaagatga ccggcaagag catccagccc gagaacctgg agtacaggat catgctgagc 1020

gtgcacggca gccagcactc cggcatgaca gtgaacgaca tcggctatga gaccgatgag 1080

aatagggcca aggtggaggt gacacctaac agcccaagag ccgaggccac cctgggcggc 1140

tttggctccc tgggactgga ctgcgagcct agaacaggcc tggacttctc cgatctgtac 1200

tatctgacca tgaacaataa gcactggctg gtgcacaagg agtggtttca cgacatccca 1260

ctgccatggc acgcaggagc agatacagga accccacact ggaacaataa ggaggccctg 1320

gtggagttca aggatgccca cgccaagcgc cagacagtgg tggtgctggg cagccaggag 1380

ggagcagtgc acaccgccct ggcaggcgcc ctggaggccg agatggacgg cgccaagggc 1440

aagctgtttt ccggccacct gaagtgccgg ctgaagatgg ataagctgcg cctgaagggc 1500

gtgtcttaca gcctgtgcac agccgccttc accttcacca aggtgcctgc cgagaccctg 1560

cacggcacag tgaccgtgga ggtgcagtat gccggcacag acggcccctg taagatccct 1620

gtgcagatgg ccgtggatat gcagacactg acccctgtgg gccggctgat caccgcaaat 1680

ccagtgatca cagagtccac cgagaactct aagatgatgc tggagctgga ccctcccttc 1740

ggcgacagct acatcgtgat cggcgtgggc gacaagaaga tcacacacca ctggcaccgc 1800

tccggctcta caatcggcaa ggccttcgag gcaaccgtgc ggggcgccaa gaggatggcc 1860

gtgctgggcg acaccgcatg ggattttggc tccgtgggcg gcgtgttcaa ctctctgggc 1920

aagggcatcc accagatctt cggcgccgcc tttaagtctc tgttcggcgg aatgtcttgg 1980

ttcagccaga tcctgatcgg cacactgctg gtgtggctgg gcctgaacac caagaatggc 2040

agcatctctc tgacttgtct ggccctggga ggcgtgatga ttttcctgtc cactgccgtg 2100

tctgcctgat aa 2112

<210> 125
<211> 702
<212> PRT
<213> Artificial Sequence

<220>
<223> consensus Zika IgE Leader-prME (construct 1)

<400> 125

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1 5 10 15

His Ser Gly Ile Ile Gly Leu Leu Leu Thr Thr Ala Met Ala Ala Glu
20 25 30

```
Ile Thr Arg Arg Gly Ser Ala Tyr Tyr Met Tyr Leu Asp Arg Ser Asp
        35                  40                  45

Ala Gly Lys Ala Ile Ser Phe Ala Thr Thr Leu Gly Val Asn Lys Cys
    50                  55                  60

His Val Gln Ile Met Asp Leu Gly His Met Cys Asp Ala Thr Met Ser
65                  70                  75                  80

Tyr Glu Cys Pro Met Leu Asp Glu Gly Val Glu Pro Asp Asp Val Asp
                85                  90                  95

Cys Trp Cys Asn Thr Thr Ser Thr Trp Val Val Tyr Gly Thr Cys His
            100                 105                 110

His Lys Lys Gly Glu Ala Arg Arg Ser Arg Arg Ala Val Thr Leu Pro
        115                 120                 125

Ser His Ser Thr Arg Lys Leu Gln Thr Arg Ser Gln Thr Trp Leu Glu
    130                 135                 140

Ser Arg Glu Tyr Thr Lys His Leu Ile Lys Val Glu Asn Trp Ile Phe
145                 150                 155                 160

Arg Asn Pro Gly Phe Ala Leu Val Ala Val Ala Ile Ala Trp Leu Leu
                165                 170                 175

Gly Ser Ser Thr Ser Gln Lys Val Ile Tyr Leu Val Met Ile Leu Leu
            180                 185                 190

Ile Ala Pro Ala Tyr Ser Ile Arg Cys Ile Gly Val Ser Asn Arg Asp
        195                 200                 205

Phe Val Glu Gly Met Ser Gly Gly Thr Trp Val Asp Val Val Leu Glu
    210                 215                 220

His Gly Gly Cys Val Thr Val Met Ala Gln Asp Lys Pro Thr Val Asp
225                 230                 235                 240

Ile Glu Leu Val Thr Thr Thr Val Ser Asn Met Ala Glu Val Arg Ser
                245                 250                 255

Tyr Cys Tyr Glu Ala Ser Ile Ser Asp Met Ala Ser Asp Ser Arg Cys
            260                 265                 270

Pro Thr Gln Gly Glu Ala Tyr Leu Asp Lys Gln Ser Asp Thr Gln Tyr
        275                 280                 285
```

```
Val Cys Lys Arg Thr Leu Val Asp Arg Gly Trp Gly Asn Gly Cys Gly
    290                 295                 300

Leu Phe Gly Lys Gly Ser Leu Val Thr Cys Ala Lys Phe Thr Cys Ser
305                 310                 315                 320

Lys Lys Met Thr Gly Lys Ser Ile Gln Pro Glu Asn Leu Glu Tyr Arg
                325                 330                 335

Ile Met Leu Ser Val His Gly Ser Gln His Ser Gly Met Thr Val Asn
            340                 345                 350

Asp Ile Gly Tyr Glu Thr Asp Glu Asn Arg Ala Lys Val Glu Val Thr
        355                 360                 365

Pro Asn Ser Pro Arg Ala Glu Ala Thr Leu Gly Gly Phe Gly Ser Leu
    370                 375                 380

Gly Leu Asp Cys Glu Pro Arg Thr Gly Leu Asp Phe Ser Asp Leu Tyr
385                 390                 395                 400

Tyr Leu Thr Met Asn Asn Lys His Trp Leu Val His Lys Glu Trp Phe
                405                 410                 415

His Asp Ile Pro Leu Pro Trp His Ala Gly Ala Asp Thr Gly Thr Pro
            420                 425                 430

His Trp Asn Asn Lys Glu Ala Leu Val Glu Phe Lys Asp Ala His Ala
        435                 440                 445

Lys Arg Gln Thr Val Val Val Leu Gly Ser Gln Glu Gly Ala Val His
    450                 455                 460

Thr Ala Leu Ala Gly Ala Leu Glu Ala Glu Met Asp Gly Ala Lys Gly
465                 470                 475                 480

Lys Leu Phe Ser Gly His Leu Lys Cys Arg Leu Lys Met Asp Lys Leu
                485                 490                 495

Arg Leu Lys Gly Val Ser Tyr Ser Leu Cys Thr Ala Ala Phe Thr Phe
            500                 505                 510

Thr Lys Val Pro Ala Glu Thr Leu His Gly Thr Val Thr Val Glu Val
        515                 520                 525

Gln Tyr Ala Gly Thr Asp Gly Pro Cys Lys Ile Pro Val Gln Met Ala
    530                 535                 540
```

```
Val Asp Met Gln Thr Leu Thr Pro Val Gly Arg Leu Ile Thr Ala Asn
545                 550                 555                 560

Pro Val Ile Thr Glu Ser Thr Glu Asn Ser Lys Met Met Leu Glu Leu
                565                 570                 575

Asp Pro Pro Phe Gly Asp Ser Tyr Ile Val Ile Gly Val Gly Asp Lys
            580                 585                 590

Lys Ile Thr His His Trp His Arg Ser Gly Ser Thr Ile Gly Lys Ala
        595                 600                 605

Phe Glu Ala Thr Val Arg Gly Ala Lys Arg Met Ala Val Leu Gly Asp
    610                 615                 620

Thr Ala Trp Asp Phe Gly Ser Val Gly Gly Val Phe Asn Ser Leu Gly
625                 630                 635                 640

Lys Gly Ile His Gln Ile Phe Gly Ala Ala Phe Lys Ser Leu Phe Gly
                645                 650                 655

Gly Met Ser Trp Phe Ser Gln Ile Leu Ile Gly Thr Leu Leu Val Trp
            660                 665                 670

Leu Gly Leu Asn Thr Lys Asn Gly Ser Ile Ser Leu Thr Cys Leu Ala
        675                 680                 685

Leu Gly Gly Val Met Ile Phe Leu Ser Thr Ala Val Ser Ala
    690                 695                 700
```

<210> 126
<211> 1119
<212> DNA
<213> Artificial Sequence

<220>
<223> consensus Zika IgE Leader-NS1

<400> 126

```
atggactgga cttggattct gttcctggtg gctgccgcta caagagtgca tagcgtggga       60

tgcagcgtgg acttcagcaa gaaggagacc cgctgcggaa caggcgtgtt cgtgtacaac      120

gacgtggagg cttggagaga ccggtacaag taccaccccg atagccctag aagactggcc      180

gcagccgtga aacaggcttg ggaagaggga atttgcggca tcagcagcgt gtcccggatg      240

gagaacatca tgtggaagag cgtggagggc gagctgaacg ctatcctgga ggagaacggc      300

gtgcagctga cagtggtcgt gggatcagtg aagaacccca tgtggagagg ccctcagagg      360
```

ctgccagtgc cagtgaacga actgcctcac ggttggaagg cttggggcaa gagctacttc 420

gtgagggccg ccaagaccaa caacagcttc gtggtggacg gcgataccct caaggagtgt 480

cctctgaagc accgggcttg gaacagcttc ctggtggaag accacggctt tggcgtgttc 540

cacacaagcg tctggctgaa ggtccgcgaa gactacagcc tggagtgcga tccagcagtg 600

atcggcacag ccgtgaaggg aaaagaggcc gctcacagcg acctgggcta ttggatcgag 660

agcgagaaga acgacacttg gaggctgaag cgggcccacc tgatcgagat gaagacttgc 720

gagtggccca agagccacac tctgtggaca gacggcgtgg aagagagcga cctgatcatc 780

cctaagagcc tggccggacc tctgtctcat cacaacacca gggagggcta cagaacccag 840

gtgaagggac cttggcacag cgaagagctg gagatccgct tcgaggagtg tccaggaacc 900

aaggtgcacg tggaggagac ttgcggaacc agaggcccta gcctgagaag cacaacagcc 960

agcggacgcg tgatcgagga gtggtgttgt agggagtgca ccatgcctcc tctgagcttc 1020

agggccaagg acggttgttg gtacggcatg gagatcaggc ccagaaagga gccagagagc 1080

aacctcgtgc ggtctatggt gacagccgga agctgataa 1119

<210> 127
<211> 371
<212> PRT
<213> Artificial Sequence

<220>
<223> consensus Zika IgE Leader-NS1

<400> 127

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1 5 10 15

His Ser Val Gly Cys Ser Val Asp Phe Ser Lys Lys Glu Thr Arg Cys
20 25 30

Gly Thr Gly Val Phe Val Tyr Asn Asp Val Glu Ala Trp Arg Asp Arg
35 40 45

Tyr Lys Tyr His Pro Asp Ser Pro Arg Arg Leu Ala Ala Ala Val Lys
50 55 60

Gln Ala Trp Glu Glu Gly Ile Cys Gly Ile Ser Ser Val Ser Arg Met
65 70 75 80

Glu Asn Ile Met Trp Lys Ser Val Glu Gly Glu Leu Asn Ala Ile Leu
85 90 95

Glu Glu Asn Gly Val Gln Leu Thr Val Val Val Gly Ser Val Lys Asn
100 105 110

```
Pro Met Trp Arg Gly Pro Gln Arg Leu Pro Val Pro Val Asn Glu Leu
        115                 120                 125

Pro His Gly Trp Lys Ala Trp Gly Lys Ser Tyr Phe Val Arg Ala Ala
    130                 135                 140

Lys Thr Asn Asn Ser Phe Val Val Asp Gly Asp Thr Leu Lys Glu Cys
145                 150                 155                 160

Pro Leu Lys His Arg Ala Trp Asn Ser Phe Leu Val Glu Asp His Gly
                165                 170                 175

Phe Gly Val Phe His Thr Ser Val Trp Leu Lys Val Arg Glu Asp Tyr
            180                 185                 190

Ser Leu Glu Cys Asp Pro Ala Val Ile Gly Thr Ala Val Lys Gly Lys
        195                 200                 205

Glu Ala Ala His Ser Asp Leu Gly Tyr Trp Ile Glu Ser Glu Lys Asn
    210                 215                 220

Asp Thr Trp Arg Leu Lys Arg Ala His Leu Ile Glu Met Lys Thr Cys
225                 230                 235                 240

Glu Trp Pro Lys Ser His Thr Leu Trp Thr Asp Gly Val Glu Glu Ser
                245                 250                 255

Asp Leu Ile Ile Pro Lys Ser Leu Ala Gly Pro Leu Ser His His Asn
            260                 265                 270

Thr Arg Glu Gly Tyr Arg Thr Gln Val Lys Gly Pro Trp His Ser Glu
        275                 280                 285

Glu Leu Glu Ile Arg Phe Glu Glu Cys Pro Gly Thr Lys Val His Val
    290                 295                 300

Glu Glu Thr Cys Gly Thr Arg Gly Pro Ser Leu Arg Ser Thr Thr Ala
305                 310                 315                 320

Ser Gly Arg Val Ile Glu Glu Trp Cys Cys Arg Glu Cys Thr Met Pro
                325                 330                 335

Pro Leu Ser Phe Arg Ala Lys Asp Gly Cys Trp Tyr Gly Met Glu Ile
            340                 345                 350

Arg Pro Arg Lys Glu Pro Glu Ser Asn Leu Val Arg Ser Met Val Thr
```

355 360 365

Ala Gly Ser
370

<210> 128
<211> 438
<212> DNA
<213> Artificial Sequence

<220>
<223> consensus Zika IgE Leader-capsid

<400> 128
atggactgga cttggatcct gtttctggtg gccgccgcca caagagtgca tagcaagaac 60

cccaagaaga agagcggcgg cttcaggatc gtgaacatgc tgaagcgggg cgtggctaga 120

gtgaaccctc tgggaggcgg actgaagaga ctgccagcag gactgctcct gggacacgga 180

cctattcgca tggtgctggc catcctggct ttcctgaggt tcaccgccat caagcccagc 240

ctgggactga tcaaccgctg gggttcagtc ggcaagaagg aggccatgga gatcatcaag 300

aagttcaaga aggacctggc cgccatgctg aggatcatca acgcccggaa ggagcggaag 360

agaagaggag ccgacaccag catcggcatc atcggactgc tgctgacaac cgccatggct 420

gccgagatct gatgatga 438

<210> 129
<211> 143
<212> PRT
<213> Artificial Sequence

<220>
<223> consensus Zika IgE Leader-capsid

<400> 129

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1 5 10 15

His Ser Lys Asn Pro Lys Lys Lys Ser Gly Gly Phe Arg Ile Val Asn
20 25 30

Met Leu Lys Arg Gly Val Ala Arg Val Asn Pro Leu Gly Gly Gly Leu
35 40 45

Lys Arg Leu Pro Ala Gly Leu Leu Leu Gly His Gly Pro Ile Arg Met
50 55 60

Val Leu Ala Ile Leu Ala Phe Leu Arg Phe Thr Ala Ile Lys Pro Ser
65 70 75 80

Leu Gly Leu Ile Asn Arg Trp Gly Ser Val Gly Lys Lys Glu Ala Met
85 90 95

Glu Ile Ile Lys Lys Phe Lys Lys Asp Leu Ala Ala Met Leu Arg Ile
100 105 110

Ile Asn Ala Arg Lys Glu Arg Lys Arg Arg Gly Ala Asp Thr Ser Ile
115 120 125

Gly Ile Ile Gly Leu Leu Leu Thr Thr Ala Met Ala Ala Glu Ile
130 135 140

<210> 130
<211> 2130
<212> DNA
<213> Artificial Sequence

<220>
<223> Zika IgE Leader-prME MR766

<400> 130
atggactgga cttggattct gttcctggtg gctgccgcta caagagtgca ttcaggagcc 60

gacacctcta tcggcatcgt gggactgctg ctgaccacag ccatggccgc cgaaattacc 120

aggaggggca gcgcctacta catgtacctg gacagaagcg acgccggaaa agccatcagc 180

ttcgccacaa ccctgggcgt caacaagtgc cacgtgcaga tcatggacct gggccacatg 240

tgcgacgcca caatgagcta cgagtgccct atgctggacg agggagtgga accagacgac 300

gtcgactgtt ggtgcaacac cacctccact tgggtcgtgt acggcacttg ccaccacaag 360

aagggcgagg ccagaagaag cagaagagcc gtgaccctgc ctagccacag caccagaaag 420

ctgcagacca ggagccagac ttggctggaa agccgcgagt acaccaagca cctgatcaag 480

gtggagaatt ggatcttccg gaaccccggc ttcacactgg tggccgtggc aatcgcttgg 540

ctgctgggat ctagcaccag ccagaaagtg atctacctgg tcatgatcct gctgatcgcc 600

ccagcctaca gcatccgctg tatcggagtg agcaaccggg acttcgtgga gggaatgagc 660

ggaggaactt gggtggacgt ggtgctggaa cacggaggtt gcgtgacagt gatggctcag 720

gacaagccca ccgtggatat cgagctggtg accaccaccg tgtccaacat ggccgaagtg 780

cgcagctact gctacgaggc cagtatctcc gacatggcca gcgatagccg ctgtcctaca 840

cagggagagg cctatctgga caagcagagc gacacccagt acgtctgcaa gaggaccctc 900

gtggatagag gctggggaaa cggttgcgga ctgttcggaa agggcagcct cgtgacttgc 960

gccaagttca cttgcagcaa gaagatgacc ggcaagtcta tccagcccga gaacctggag 1020

taccggatca tgctgagcgt gcacggaagc cagcacagcg gcatgatcgt gaacgacgag 1080

ggatacgaga ccgacgagaa cagggccaag gtggaagtga cccctaacag ccctagagcc 1140

gaagccacac tgggaggatt tggcagcctg ggactggatt gcgagcctag aacaggcctg 1200

gacttcagcg acctgtacta cctgaccatg aacaacaagc attggctggt gcacaaggag 1260

tggttccacg acatccctct gccttggcac gcaggagccg atacaggcac acctcattgg 1320

aacaacaagg aggccctggt ggagttcaag gacgctcacg ccaagagaca gacagtggtg 1380

gtgctgggaa gccaggaagg agcagtgcat acagccctgg caggagctct ggaagcagaa 1440

atggacggcg ctaagggcag actgttcagc ggacacctca agtgccggct gaagatggac 1500

aagctgcggc tgaagggcgt gtcttacagc ctctgcaccg cagccttcac cttcaccaag 1560

gtgccagcag agacactgca cggaacagtg accgtggaag tgcagtacgc cggaacagac 1620

ggaccttgca aagtgccagc ccagatggca gtggacatgc agacactgac cccagtggga 1680

aggctgatca ccgctaaccc cgtcatcacc gagagcaccg agaacagcaa gatgatgctg 1740

gagctggacc ccccccttcgg cgatagctac atcgtgatcg gcgtgggcga caagaagatc 1800

acccaccatt ggcacagaag cggcagcaca atcggcaagg ctttcgaggc caccgtgaga 1860

ggagctaaga gaatggccgt gctgggagac accgcttggg attttggcag cgtgggagga 1920

gtgttcaaca gcctgggcaa gggcatccac cagatcttcg gagccgcctt caagagcctg 1980

ttcggcggca tgtcttggtt cagccagatc ctgatcggaa cactcctcgt ctggctggga 2040

ctgaacacca agaacggcag catcagcctg acttgtctgg ccctgggagg cgtgatgatc 2100

ttcctgagca ccgccgtgtc cgcttgataa 2130

<210> 131
<211> 708
<212> PRT
<213> Artificial Sequence

<220>
<223> Zika IgE Leader-prME MR766

<400> 131

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1 5 10 15

His Ser Gly Ala Asp Thr Ser Ile Gly Ile Val Gly Leu Leu Leu Thr
20 25 30

Thr Ala Met Ala Ala Glu Ile Thr Arg Arg Gly Ser Ala Tyr Tyr Met
35 40 45

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

Leu Gly Val Asn Lys Cys His Val Gln Ile Met Asp Leu Gly His Met
65 70 75 80

```
Cys Asp Ala Thr Met Ser Tyr Glu Cys Pro Met Leu Asp Glu Gly Val
                85                  90                  95

Glu Pro Asp Asp Val Asp Cys Trp Cys Asn Thr Thr Ser Thr Trp Val
            100                 105                 110

Val Tyr Gly Thr Cys His His Lys Lys Gly Glu Ala Arg Arg Ser Arg
        115                 120                 125

Arg Ala Val Thr Leu Pro Ser His Ser Thr Arg Lys Leu Gln Thr Arg
    130                 135                 140

Ser Gln Thr Trp Leu Glu Ser Arg Glu Tyr Thr Lys His Leu Ile Lys
145                 150                 155                 160

Val Glu Asn Trp Ile Phe Arg Asn Pro Gly Phe Thr Leu Val Ala Val
                165                 170                 175

Ala Ile Ala Trp Leu Leu Gly Ser Ser Thr Ser Gln Lys Val Ile Tyr
            180                 185                 190

Leu Val Met Ile Leu Leu Ile Ala Pro Ala Tyr Ser Ile Arg Cys Ile
        195                 200                 205

Gly Val Ser Asn Arg Asp Phe Val Glu Gly Met Ser Gly Gly Thr Trp
    210                 215                 220

Val Asp Val Val Leu Glu His Gly Gly Cys Val Thr Val Met Ala Gln
225                 230                 235                 240

Asp Lys Pro Thr Val Asp Ile Glu Leu Val Thr Thr Thr Val Ser Asn
                245                 250                 255

Met Ala Glu Val Arg Ser Tyr Cys Tyr Glu Ala Ser Ile Ser Asp Met
            260                 265                 270

Ala Ser Asp Ser Arg Cys Pro Thr Gln Gly Glu Ala Tyr Leu Asp Lys
        275                 280                 285

Gln Ser Asp Thr Gln Tyr Val Cys Lys Arg Thr Leu Val Asp Arg Gly
    290                 295                 300

Trp Gly Asn Gly Cys Gly Leu Phe Gly Lys Gly Ser Leu Val Thr Cys
305                 310                 315                 320

Ala Lys Phe Thr Cys Ser Lys Lys Met Thr Gly Lys Ser Ile Gln Pro
```

```
                325                 330                 335

Glu Asn Leu Glu Tyr Arg Ile Met Leu Ser Val His Gly Ser Gln His
            340                 345                 350

Ser Gly Met Ile Val Asn Asp Glu Gly Tyr Glu Thr Asp Glu Asn Arg
        355                 360                 365

Ala Lys Val Glu Val Thr Pro Asn Ser Pro Arg Ala Glu Ala Thr Leu
    370                 375                 380

Gly Gly Phe Gly Ser Leu Gly Leu Asp Cys Glu Pro Arg Thr Gly Leu
385                 390                 395                 400

Asp Phe Ser Asp Leu Tyr Tyr Leu Thr Met Asn Asn Lys His Trp Leu
                405                 410                 415

Val His Lys Glu Trp Phe His Asp Ile Pro Leu Pro Trp His Ala Gly
            420                 425                 430

Ala Asp Thr Gly Thr Pro His Trp Asn Asn Lys Glu Ala Leu Val Glu
        435                 440                 445

Phe Lys Asp Ala His Ala Lys Arg Gln Thr Val Val Val Leu Gly Ser
    450                 455                 460

Gln Glu Gly Ala Val His Thr Ala Leu Ala Gly Ala Leu Glu Ala Glu
465                 470                 475                 480

Met Asp Gly Ala Lys Gly Arg Leu Phe Ser Gly His Leu Lys Cys Arg
                485                 490                 495

Leu Lys Met Asp Lys Leu Arg Leu Lys Gly Val Ser Tyr Ser Leu Cys
            500                 505                 510

Thr Ala Ala Phe Thr Phe Thr Lys Val Pro Ala Glu Thr Leu His Gly
        515                 520                 525

Thr Val Thr Val Glu Val Gln Tyr Ala Gly Thr Asp Gly Pro Cys Lys
    530                 535                 540

Val Pro Ala Gln Met Ala Val Asp Met Gln Thr Leu Thr Pro Val Gly
545                 550                 555                 560

Arg Leu Ile Thr Ala Asn Pro Val Ile Thr Glu Ser Thr Glu Asn Ser
                565                 570                 575
```

```
Lys Met Met Leu Glu Leu Asp Pro Pro Phe Gly Asp Ser Tyr Ile Val
            580                 585                 590

Ile Gly Val Gly Asp Lys Lys Ile Thr His His Trp His Arg Ser Gly
        595                 600                 605

Ser Thr Ile Gly Lys Ala Phe Glu Ala Thr Val Arg Gly Ala Lys Arg
    610                 615                 620

Met Ala Val Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser Val Gly Gly
625                 630                 635                 640

Val Phe Asn Ser Leu Gly Lys Gly Ile His Gln Ile Phe Gly Ala Ala
                645                 650                 655

Phe Lys Ser Leu Phe Gly Gly Met Ser Trp Phe Ser Gln Ile Leu Ile
            660                 665                 670

Gly Thr Leu Leu Val Trp Leu Gly Leu Asn Thr Lys Asn Gly Ser Ile
        675                 680                 685

Ser Leu Thr Cys Leu Ala Leu Gly Gly Val Met Ile Phe Leu Ser Thr
    690                 695                 700

Ala Val Ser Ala
705
```

<210> 132
<211> 2130
<212> DNA
<213> Artificial Sequence

<220>
<223> Zika IgE Leader-prME Brazil

<400> 132

```
atggactgga cttggattct gttcctggtg gctgccgcta caagagtgca ttcaggagcc        60

gacacatcag tgggcatcgt gggactgctg ctgacaacag ctatggccgc cgaagtgacc       120

agaagaggca gcgcctacta catgtacctg gaccggaacg acgccggaga ggccattagc       180

tttcctacca ccctgggcat gaacaagtgc tacatccaga tcatggacct gggccacatg       240

tgcgacgcta caatgagcta cgagtgcccc atgctggacg aaggagtgga gccagacgac       300

gtggattgtt ggtgcaacac cacctccact tgggtcgtgt acggcacctg tcaccacaaa       360

aagggcgaag ccaggagaag cagaagagcc gtgaccctgc ctagccactc taccaggaag       420

ctgcagacca ggagccagac ttggctggag agcagggagt acaccaagca cctgatccgc       480

gtggagaatt ggatcttcag aaaccccggc ttcgccctgg cagccgcagc aattgcttgg       540
```

ctgctgggat ctagcaccag ccagaaggtc atctacctgg tcatgatcct gctgatcgcc 600

cccgcttaca gcatccgctg tatcggcgtg tccaacaggg acttcgtgga gggcatgagc 660

ggaggaactt gggtggacgt ggtgctggaa cacggaggtt gtgtgaccgt gatggctcag 720

gacaagccta ccgtggacat cgagctggtg accacaaccg tgtccaacat ggccgaggtc 780

cgcagctatt gctacgaggc cagcatcagc gatatggcca gcgatagcag gtgtcccacc 840

cagggtgaag cttacctgga caagcagagc gacacccagt acgtgtgcaa gcggacactg 900

gtggatagag gctggggaaa cggttgcggc ctgtttggca agggaagcct ggtgacctgc 960

gccaagttcg catgcagcaa gaagatgacc ggcaagagca tccagcccga gaacctggag 1020

taccggatca tgctgagcgt gcacggatct cagcatagcg gaatgatcgt gaacgacacc 1080

ggccacgaga ccgacgaaaa cagggccaag gtggaaatca cccccaactc tcctagagcc 1140

gaggccacac tgggaggttt tggaagcctg ggcctggatt gcgagcctag aacaggcctg 1200

gacttcagcg acctgtacta cctgaccatg aacaacaagc attggctggt gcacaaggag 1260

tggttccacg acatccctct gccttggcac gcaggagcag atacaggaac cccccattgg 1320

aacaacaagg aggccctggt ggagttcaag gacgctcacg ccaagagaca gacagtggtg 1380

gtgctgggaa gccaggaagg agcagtgcac acagctctgg caggagctct ggaagccgaa 1440

atggacggag ccaagggcag actgtcctcc ggacacctca agtgccggct gaagatggac 1500

aagctgcggc tgaagggcgt gtcttatagc ctctgcacag ccgctttcac cttcaccaag 1560

atccccgcag agaccctgca cggaacagtg accgtggaag tgcagtacgc cggaacagac 1620

ggaccttgca aggtgccagc tcagatggca gtggacatgc agaccctgac cccagtggga 1680

agactgatca ccgctaaccc cgtcatcacc gagagcaccg agaacagcaa gatgatgctg 1740

gagctggacc ccccccttcgg cgatagctac atcgtgatcg gcgtgggcga gaaaaagatc 1800

acccaccatt ggcacaggag cggcagcaca atcggcaagg cctttgaggc caccgtgaga 1860

ggagccaaga gaatggccgt gctgggagat accgcttggg atttcggcag cgtgggaggc 1920

gccctgaaca gcctgggcaa gggcattcac cagatcttcg gagccgcctt caagagcctg 1980

ttcggcggca tgtcttggtt cagccagatc ctgatcggca cactgctcat gtggctgggc 2040

ctgaacacca agaacggcag catcagcctg atgtgtctgg ctctgggagg cgtgctgatc 2100

ttcctgagca ccgctgtgtc cgcttgataa 2130

<210> 133
<211> 708
<212> PRT
<213> Artificial Sequence

<220>
<223> Zika IgE Leader-prME Brazil

<400> 133

```
Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1               5                  10                  15

His Ser Gly Ala Asp Thr Ser Val Gly Ile Val Gly Leu Leu Leu Thr
            20                  25                  30

Thr Ala Met Ala Ala Glu Val Thr Arg Arg Gly Ser Ala Tyr Tyr Met
        35                  40                  45

Tyr Leu Asp Arg Asn Asp Ala Gly Glu Ala Ile Ser Phe Pro Thr Thr
    50                  55                  60

Leu Gly Met Asn Lys Cys Tyr Ile Gln Ile Met Asp Leu Gly His Met
65                  70                  75                  80

Cys Asp Ala Thr Met Ser Tyr Glu Cys Pro Met Leu Asp Glu Gly Val
                85                  90                  95

Glu Pro Asp Asp Val Asp Cys Trp Cys Asn Thr Thr Ser Thr Trp Val
            100                 105                 110

Val Tyr Gly Thr Cys His His Lys Lys Gly Glu Ala Arg Arg Ser Arg
        115                 120                 125

Arg Ala Val Thr Leu Pro Ser His Ser Thr Arg Lys Leu Gln Thr Arg
    130                 135                 140

Ser Gln Thr Trp Leu Glu Ser Arg Glu Tyr Thr Lys His Leu Ile Arg
145                 150                 155                 160

Val Glu Asn Trp Ile Phe Arg Asn Pro Gly Phe Ala Leu Ala Ala Ala
                165                 170                 175

Ala Ile Ala Trp Leu Leu Gly Ser Ser Thr Ser Gln Lys Val Ile Tyr
            180                 185                 190

Leu Val Met Ile Leu Leu Ile Ala Pro Ala Tyr Ser Ile Arg Cys Ile
        195                 200                 205

Gly Val Ser Asn Arg Asp Phe Val Glu Gly Met Ser Gly Gly Thr Trp
    210                 215                 220

Val Asp Val Val Leu Glu His Gly Gly Cys Val Thr Val Met Ala Gln
225                 230                 235                 240

Asp Lys Pro Thr Val Asp Ile Glu Leu Val Thr Thr Thr Val Ser Asn
```

```
                245                 250                 255

Met Ala Glu Val Arg Ser Tyr Cys Tyr Glu Ala Ser Ile Ser Asp Met
            260                 265                 270

Ala Ser Asp Ser Arg Cys Pro Thr Gln Gly Glu Ala Tyr Leu Asp Lys
        275                 280                 285

Gln Ser Asp Thr Gln Tyr Val Cys Lys Arg Thr Leu Val Asp Arg Gly
    290                 295                 300

Trp Gly Asn Gly Cys Gly Leu Phe Gly Lys Gly Ser Leu Val Thr Cys
305                 310                 315                 320

Ala Lys Phe Ala Cys Ser Lys Lys Met Thr Gly Lys Ser Ile Gln Pro
                325                 330                 335

Glu Asn Leu Glu Tyr Arg Ile Met Leu Ser Val His Gly Ser Gln His
            340                 345                 350

Ser Gly Met Ile Val Asn Asp Thr Gly His Glu Thr Asp Glu Asn Arg
        355                 360                 365

Ala Lys Val Glu Ile Thr Pro Asn Ser Pro Arg Ala Glu Ala Thr Leu
    370                 375                 380

Gly Gly Phe Gly Ser Leu Gly Leu Asp Cys Glu Pro Arg Thr Gly Leu
385                 390                 395                 400

Asp Phe Ser Asp Leu Tyr Tyr Leu Thr Met Asn Asn Lys His Trp Leu
                405                 410                 415

Val His Lys Glu Trp Phe His Asp Ile Pro Leu Pro Trp His Ala Gly
            420                 425                 430

Ala Asp Thr Gly Thr Pro His Trp Asn Asn Lys Glu Ala Leu Val Glu
        435                 440                 445

Phe Lys Asp Ala His Ala Lys Arg Gln Thr Val Val Val Leu Gly Ser
    450                 455                 460

Gln Glu Gly Ala Val His Thr Ala Leu Ala Gly Ala Leu Glu Ala Glu
465                 470                 475                 480

Met Asp Gly Ala Lys Gly Arg Leu Ser Ser Gly His Leu Lys Cys Arg
                485                 490                 495
```

Leu Lys Met Asp Lys Leu Arg Leu Lys Gly Val Ser Tyr Ser Leu Cys
500 505 510

Thr Ala Ala Phe Thr Phe Thr Lys Ile Pro Ala Glu Thr Leu His Gly
515 520 525

Thr Val Thr Val Glu Val Gln Tyr Ala Gly Thr Asp Gly Pro Cys Lys
530 535 540

Val Pro Ala Gln Met Ala Val Asp Met Gln Thr Leu Thr Pro Val Gly
545 550 555 560

Arg Leu Ile Thr Ala Asn Pro Val Ile Thr Glu Ser Thr Glu Asn Ser
565 570 575

Lys Met Met Leu Glu Leu Asp Pro Pro Phe Gly Asp Ser Tyr Ile Val
580 585 590

Ile Gly Val Gly Glu Lys Lys Ile Thr His His Trp His Arg Ser Gly
595 600 605

Ser Thr Ile Gly Lys Ala Phe Glu Ala Thr Val Arg Gly Ala Lys Arg
610 615 620

Met Ala Val Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser Val Gly Gly
625 630 635 640

Ala Leu Asn Ser Leu Gly Lys Gly Ile His Gln Ile Phe Gly Ala Ala
645 650 655

Phe Lys Ser Leu Phe Gly Gly Met Ser Trp Phe Ser Gln Ile Leu Ile
660 665 670

Gly Thr Leu Leu Met Trp Leu Gly Leu Asn Thr Lys Asn Gly Ser Ile
675 680 685

Ser Leu Met Cys Leu Ala Leu Gly Gly Val Leu Ile Phe Leu Ser Thr
690 695 700

Ala Val Ser Ala
705

<210> 134
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> IgE leader

<400> 134

Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val
1 5 10 15

His Ser

<210> 135
<211> 732
<212> PRT
<213> Artificial Sequence

<220>
<223> DMAb-2G4

<400> 135

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Glu Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Met Gln
20 25 30

Pro Gly Gly Ser Met Lys Leu Ser Cys Val Ala Ser Gly Phe Thr Phe
35 40 45

Ser Asn Tyr Trp Met Asn Trp Val Arg Gln Ser Pro Glu Lys Gly Leu
50 55 60

Glu Trp Val Ala Glu Ile Arg Leu Lys Ser Asn Asn Tyr Ala Thr His
65 70 75 80

Tyr Ala Glu Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser
85 90 95

Lys Arg Ser Val Tyr Leu Gln Met Asn Thr Leu Arg Ala Glu Asp Thr
100 105 110

Gly Ile Tyr Tyr Cys Thr Arg Gly Asn Gly Asn Tyr Arg Ala Met Asp
115 120 125

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys
130 135 140

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
145 150 155 160

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
165 170 175

```
Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
            180                 185                 190

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
        195                 200                 205

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
    210                 215                 220

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro
225                 230                 235                 240

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
                245                 250                 255

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
            260                 265                 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
        275                 280                 285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
    290                 295                 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305                 310                 315                 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
                325                 330                 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
            340                 345                 350

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
        355                 360                 365

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
    370                 375                 380

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
385                 390                 395                 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
                405                 410                 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
```

420 425 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
435 440 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
450 455 460

Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly
465 470 475 480

Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn
485 490 495

Pro Gly Pro Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu
500 505 510

Trp Ile Ser Gly Ala Tyr Gly Asp Ile Gln Met Thr Gln Ser Pro Ala
515 520 525

Ser Leu Ser Val Ser Val Gly Glu Thr Val Ser Ile Thr Cys Arg Ala
530 535 540

Ser Glu Asn Ile Tyr Ser Ser Leu Ala Trp Tyr Gln Gln Lys Gln Gly
545 550 555 560

Lys Ser Pro Gln Leu Leu Val Tyr Ser Ala Thr Ile Leu Ala Asp Gly
565 570 575

Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Gln Tyr Ser Leu
580 585 590

Lys Ile Asn Ser Leu Gln Ser Glu Asp Phe Gly Thr Tyr Tyr Cys Gln
595 600 605

His Phe Trp Gly Thr Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu
610 615 620

Ile Lys Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
625 630 635 640

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
645 650 655

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
660 665 670

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
675 680 685

Ser Thr Tyr Ser Leu Ser Asn Thr Leu Thr Leu Ser Lys Ala Asp Tyr
690 695 700

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
705 710 715 720

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
725 730

<210> 136
<211> 2202
<212> DNA
<213> Artificial Sequence

<220>
<223> PGX9226, DMAb-2G4

<400> 136
atggattgga catggaggat tctgtttctg gtcgccgccg caactggaac ccacgctgaa 60

gtgcagctgc aggagtcagg aggaggactg atgcagcccg gcggaagcat gaagctgtcc 120

tgcgtggcat ctggcttcac ctttagtaac tactggatga attgggtccg ccagtcacct 180

gagaagggac tggaatgggt ggctgagatc cgactgaaaa gcaacaatta cgccacccac 240

tatgctgagt cagtgaaggg gcgattcaca attagcaggg acgattctaa aagaagtgtg 300

tatctgcaga tgaacactct gagagccgaa gacaccggaa tctactattg cacacggggc 360

aacggaaatt accgcgctat ggattattgg gggcagggca cttccgtcac cgtgagctcc 420

gcaagcacaa agggaccctc cgtgtttccc ctggcccctt ctagtaaaag cacctccgga 480

ggaacagcag ctctgggatg tctggtgaag gactacttcc ctgagccagt caccgtgtca 540

tggaacagcg gagccctgac ctctggggtc catacatttc ctgctgtgct gcagtcaagc 600

gggctgtact ccctgtcctc tgtggtcact gtgccaagtt caagcctggg cactcagacc 660

tatatctgca acgtgaatca caagcccagc aataccaaag tcgacaagaa agtggagcct 720

aagtcctgtg ataaaacaca tacttgccca ccttgtccag cacctgaact gctgggagga 780

cctagcgtgt tcctgtttcc acccaagcca aaagacacac tgatgatttc ccgcactcct 840

gaggtcacct gtgtggtcgt ggacgtgtct cacgaggacc ccgaagtcaa gttcaactgg 900

tacgtggatg gcgtcgaagt gcataatgcc aagaccaaac ccagggagga acagtacaac 960

tctacctata gggtcgtgag tgtcctgaca gtgctgcacc aggactggct gaacggcaag 1020

gagtataagt gcaaagtgag caataaggct ctgccagcac ccatcgaaaa aactatttcc 1080

aaggccaaag gacagccaag agagccccag gtgtacaccc tgcctccatc tcgggacgaa 1140

ctgacaaaga accaggtcag tctgacttgt ctggtgaaag gcttctatcc atccgatatc 1200

gctgtggagt gggaatctaa tggacagccc gagaacaatt acaagaccac acccccctgtg 1260

ctggactccg atgggtcttt ctttctgtat agtaagctga ccgtggataa atcacggtgg 1320

cagcagggca acgtcttttc ttgcagtgtg atgcatgaag ccctgcacaa tcattacaca 1380

cagaagtcac tgagcctgtc cccaggcaag cgaggacgaa aaaggagatc tggaagtggg 1440

gctactaact tcagcctgct gaaacaggca ggcgacgtgg aggaaaatcc tggaccaatg 1500

gtcctgcaga cccaggtgtt tatctcactg ctgctgtgga ttagcggggc ttacggcgat 1560

attcagatga cacagtcccc agcatcactg agcgtctccg tgggagaaac agtgtccatc 1620

acttgtcgcg cctctgagaa catctacagc agcctggctt ggtatcagca gaagcaggga 1680

aaaagccccc agctgctggt ctactccgca acaatcctgg ccgacggggt gccttctagg 1740

ttctctggca gtggatcagg gacacagtat agcctgaaga ttaatagtct gcagtcagag 1800

gattttggga cttactattg ccagcacttc tggggcacac catacacttt tggcggaggg 1860

actaagctgg agatcaaaac cgtcgcagcc ccctctgtgt tcatttttcc acccagtgac 1920

gaacagctga agagtggcac cgcctcagtc gtgtgtctgc tgaacaattt ctaccctaga 1980

gaggcaaagg tccagtggaa agtggataac gccctgcaga gcggcaattc ccaggaatct 2040

gtgactgagc aggacagtaa ggattcaacc tatagcctgt ccaacaccct gacactgagc 2100

aaagctgact acgaaaagca caaagtctat gcatgcgagg tgacacatca gggactgagt 2160

tcaccagtga ctaagtcctt taatcggggg gagtgttgat aa 2202

<210> 137
<211> 711
<212> PRT
<213> Artificial Sequence

<220>
<223> DMAb-4G7

<400> 137

Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Glu Met Pro Gly Ala
1 5 10 15

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

Ser Met Asn Trp Val Lys Gln Ser Asn Gly Lys Ser Leu Glu Trp Ile
35 40 45

Gly Asn Ile Asp Thr Tyr Tyr Gly Gly Thr Thr Tyr Asn Gln Lys Phe
50 55 60

```
Lys Gly Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

Met Gln Leu Lys Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Ala Tyr Tyr Gly Ser Thr Phe Ala Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
        115                 120                 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
    130                 135                 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
145                 150                 155                 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
                165                 170                 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
            180                 185                 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
        195                 200                 205

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
    210                 215                 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
225                 230                 235                 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
                245                 250                 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
            260                 265                 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
        275                 280                 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
    290                 295                 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
305                 310                 315                 320
```

```
Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
                325                 330                 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
            340                 345                 350

Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
        355                 360                 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
    370                 375                 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
385                 390                 395                 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
                405                 410                 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
            420                 425                 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
        435                 440                 445

Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser
    450                 455                 460

Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val
465                 470                 475                 480

Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala
                485                 490                 495

Tyr Gly Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser
            500                 505                 510

Val Gly Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr
        515                 520                 525

Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu
    530                 535                 540

Leu Val Tyr Asn Ala Lys Thr Leu Ile Glu Gly Val Pro Ser Arg Phe
545                 550                 555                 560

Ser Gly Ser Gly Ser Gly Thr Gln Phe Ser Leu Lys Ile Asn Ser Leu
                565                 570                 575
```

```
Gln Pro Glu Asp Phe Gly Ser Tyr Phe Cys Gln His His Phe Gly Thr
            580                 585                 590

Pro Phe Thr Phe Gly Ser Gly Thr Glu Leu Glu Ile Lys Thr Val Ala
        595                 600                 605

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
    610                 615                 620

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
625                 630                 635                 640

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
                645                 650                 655

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
            660                 665                 670

Ser Asn Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
        675                 680                 685

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
    690                 695                 700

Ser Phe Asn Arg Gly Glu Cys
705                 710
```

<210> 138
<211> 2196
<212> DNA
<213> Artificial Sequence

<220>
<223> pGX9229, DMAb-4G7

<400> 138

```
atggattgga catggaggat tctgtttctg gtcgccgccg ccactggaac ccacgcccag       60

gtgcagctgc agcagtcagg gcctgagctg gaaatgcctg gcgcttctgt gaaaatcagt      120

tgcaaggcat caggaagctc cttcacaggg tttagcatga actgggtgaa acagagcaat      180

gggaagtccc tggagtggat cggcaacatt gacacctact atggcggaac cacatacaat      240

cagaagttca aaggcaaggc tacactgact gtggacaaat ctagttcaac cgcatatatg      300

cagctgaaga gcctgacatc cgaggattct gcagtgtact attgcgctag atcagcatac      360

tatggcagca ctttcgccta ctggggccag ggaaccctgg tcacagtgag ctccgcctcc      420

accaaaggac catctgtgtt tcccctggct ccttctagta agagtacatc aggaggaact      480
```

gcagctctgg gatgtctggt gaaggattat ttccctgagc cagtcaccgt gagttggaac 540

tcaggcgcac tgacttctgg agtccacacc tttcctgccg tgctgcagtc aagcggcctg 600

tacagcctgt cctctgtggt caccgtgcca agttcaagcc tgggaaccca gacatatatc 660

tgcaacgtga atcacaaacc ctctaataca aaggtcgaca agaaagtgga acctaaaagc 720

tgtgataaga ctcatacctg cccaccttgt ccagcacctg agctgctggg agggccttcc 780

gtgttcctgt ttccacccaa accaaaggac acactgatga ttagcagaac ccctgaagtc 840

acatgtgtgg tcgtggacgt gtcccacgag gaccccgaag tcaagttcaa ctggtacgtg 900

gatggcgtcg aggtgcataa tgctaaaacc aagccccgag aggaacagta caactctact 960

tatagggtcg tgagtgtcct gaccgtgctg caccaggact ggctgaacgg caaggagtat 1020

aaatgcaagg tgtctaacaa ggccctgcca gctcccatcg agaagacaat tagcaaagct 1080

aagggacagc caagagaacc ccaggtgtac actctgcctc catctcggga cgagctgacc 1140

aaaaaccagg tcagtctgac atgtctggtg aagggattct atccaagcga tatcgcagtg 1200

gagtgggaat ccaatgggca gcccgaaaac aattacaaga ctacccccc tgtgctggac 1260

agcgatggca gcttcttcct gtattccaaa ctgacagtgg ataagtctcg gtggcagcag 1320

gggaacgtct ttagctgctc cgtgatgcat gaggccctgc acaatcatta cactcagaag 1380

tctctgagtc tgtcaccagg caaacgagga cgaaagagga gaagcgggtc cggagcaacc 1440

aacttctccc tgctgaagca ggctggagac gtggaggaaa atcctgggcc aatggtcctg 1500

cagacacagg tgtttatctc actgctgctg tggattagcg gggcctacgg cgatattcag 1560

atgactcaga gccccgcatc tctgagtgcc tcagtcggcg agacagtgac tatcacctgt 1620

cgcgcaagtg aaaacatcta ctcatatctg gcctggtacc agcagaaaca ggggaagagc 1680

ccccagctgc tggtctataa tgctaaaacc ctgatcgaag gagtgccttc ccgattcagc 1740

ggcagcgggt ctggcacaca gtttagcctg aagattaact ccctgcagcc agaggacttc 1800

ggcagctact tttgccagca ccatttcgga actcccttca cctttggcag cgggacagag 1860

ctggaaatca aaactgtcgc agcccccagt gtgttcattt ttccaccctc agacgaacag 1920

ctgaagtctg ggaccgccag tgtcgtgtgt ctgctgaaca atttttaccc tcgggaggct 1980

aaagtccagt ggaaggtgga taacgcactg cagtctggaa atagtcagga gtcagtgaca 2040

gaacaggaca gcaaagattc cacttatagt ctgtcaaaca cactgactct gtctaaggcc 2100

gactacgaga aacacaaggt ctatgcttgc gaagtgactc atcaggggct gtcctctcct 2160

gtgaccaaga gcttcaatcg cggcgagtgt tgataa 2196

<210> 139
<211> 733
<212> PRT
<213> Artificial Sequence

<220>
<223> DMAB4

<400> 139

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                  10                  15

Thr His Ala Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Lys
            20                  25                  30

Pro Ser Gln Thr Leu Ser Leu Thr Cys Ser Leu Ser Gly Phe Ser Leu
        35                  40                  45

Ser Thr Ser Gly Val Gly Val Gly Trp Phe Arg Gln Pro Ser Gly Lys
    50                  55                  60

Gly Leu Glu Trp Leu Ala Leu Ile Trp Trp Asp Asp Asp Lys Tyr Tyr
65                  70                  75                  80

Asn Pro Ser Leu Lys Ser Gln Leu Ser Ile Ser Lys Asp Phe Ser Arg
                85                  90                  95

Asn Gln Val Phe Leu Lys Ile Ser Asn Val Asp Ile Ala Asp Thr Ala
            100                 105                 110

Thr Tyr Tyr Cys Ala Arg Arg Asp Pro Phe Gly Tyr Asp Asn Ala Met
        115                 120                 125

Gly Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr
    130                 135                 140

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
145                 150                 155                 160

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
                165                 170                 175

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
            180                 185                 190

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
        195                 200                 205

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
    210                 215                 220

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu
```

```
225                 230                 235                 240

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
                245                 250                 255

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
            260                 265                 270

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
        275                 280                 285

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
    290                 295                 300

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
305                 310                 315                 320

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
                325                 330                 335

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
            340                 345                 350

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
        355                 360                 365

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
    370                 375                 380

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
385                 390                 395                 400

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
                405                 410                 415

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
            420                 425                 430

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
        435                 440                 445

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
    450                 455                 460

Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser
465                 470                 475                 480
```

```
Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu
                485                 490                 495

Asn Pro Gly Pro Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu
            500                 505                 510

Leu Trp Ile Ser Gly Ala Tyr Gly Asp Ile Val Met Thr Gln Ser Gln
        515                 520                 525

Lys Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Leu Thr Cys Lys
    530                 535                 540

Ala Ser Gln Asn Val Gly Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro
545                 550                 555                 560

Gly Gln Ser Pro Lys Leu Leu Ile Tyr Ser Ala Ser Asn Arg Tyr Thr
                565                 570                 575

Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr
            580                 585                 590

Leu Thr Ile Ser Asn Met Gln Ser Glu Asp Leu Ala Asp Tyr Phe Cys
        595                 600                 605

Gln Gln Tyr Ser Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu
    610                 615                 620

Glu Ile Lys Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser
625                 630                 635                 640

Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn
                645                 650                 655

Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala
            660                 665                 670

Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys
        675                 680                 685

Asp Ser Thr Tyr Ser Leu Ser Asn Thr Leu Thr Leu Ser Lys Ala Asp
    690                 695                 700

Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu
705                 710                 715                 720

Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
                725                 730
```

<210> 140
<211> 2226
<212> DNA
<213> Artificial Sequence

<220>
<223> pGX9230, DMAb4

<400> 140
ggatccgccg ccaccatgga ctggacttgg agaattctgt tcctggtcgc agcagccact 60

gggacacacg cacaggtgac actgaaagag agcggacccg gaatcctgaa accaagccag 120

actctgtccc tgacctgcag cctgtccggc ttctctctga gtacctcagg agtcggagtg 180

ggatggtttc gacagccaag cggaaaggga ctggagtggc tggccctgat ctggtgggac 240

gatgacaagt actataaccc ttcactgaaa agccagctga gcatttccaa ggatttctct 300

cgcaaccagg tctttctgaa gatcagtaat gtggatattg ccgacactgc tacctactat 360

tgcgctagga gagatccatt cggctacgac aatgcaatgg gatattgggg ccagggaacc 420

tccgtcacag tgagctccgc atccacaaaa gggccctctg tgtttccccc ggcccccttct 480

agtaagtcta caagtggcgg aactgccgct ctgggctgtc tggtgaagga ctacttccct 540

gagccagtca ccgtgtcctg gaactctgga gccctgactt ctggggtcca cacctttcct 600

gctgtgctgc agtcaagcgg actgtacagc ctgtcctctg tggtcaccgt gccaagttca 660

agcctgggga cacagactta tatctgcaac gtgaatcaca agccatctaa tacaaaagtc 720

gataagaaag tggaacccaa gagctgtgac aaaacccata catgcccacc ttgtccagca 780

cctgagctgc tgggaggacc aagcgtgttc ctgtttccac ccaagcctaa agatacactg 840

atgatttcca ggacccccga agtgacatgt gtggtcgtgg atgtgtctca cgaggaccct 900

gaagtcaagt tcaactggta cgtggacggc gtcgaggtgc ataatgctaa gaccaaacct 960

cgcgaggaac agtacaacag tacatatcga gtcgtgtcag tgctgaccgt cctgcaccag 1020

gactggctga acggaaagga gtataagtgc aaagtgagca acaaggcact gccagccccc 1080

atcgagaaga ctatttccaa ggcaaaaggg cagccaaggg aaccccaggt gtacaccctg 1140

cctccaagca gagatgagct gactaaaaac caggtctccc tgacctgtct ggtgaagggg 1200

ttctatccta gtgacatcgc tgtggagtgg gaatcaaatg gccagccaga aaacaattac 1260

aagaccacac cccctgtgct ggatagtgac ggctcattct ttctgtattc aaagctgacc 1320

gtggataaaa gcagatggca gcagggaaac gtcttctcat gcagcgtgat gcatgaggcc 1380

ctgcacaatc attacactca gaaatccctg tctctgagtc ccggcaagcg aggaaggaaa 1440

cggcgctcag ggagcggcgc tacaaacttt tccctgctga agcaggcagg ggacgtggag 1500

gaaaatcctg gcccaatggt cctgcagacc caggtgttca tcagcctgct gctgtggatt 1560

tccggggcct acggcgatat tgtgatgacc cagagccaga agttcatgtc cacatctgtc 1620

ggcgaccggg tgtctctgac ctgtaaggcc agtcagaacg tcggaactgc tgtggcatgg 1680

tatcagcaga agcctgggca gtccccaaaa ctgctgatct acagtgcttc aaacagatat 1740

accggcgtgc ctgatcggtt caccggaagc gggtccggca cagactttac tctgaccatt 1800

tctaatatgc agagtgaaga tctggctgac tacttctgcc agcagtactc ctcttatcca 1860

ctgacatttg gagcagggac taagctggaa atcaaaacag tcgcagcccc ctccgtgttc 1920

atttttccac cctctgatga gcagctgaag tcaggcactg ccagcgtcgt gtgtctgctg 1980

aacaatttct accccaggga ggccaaggtc cagtggaaag tggacaacgc tctgcagagc 2040

ggaaattccc aggagtctgt gactgaacag gatagtaaag actcaaccta ttctctgagt 2100

aacacactga ctctgtccaa ggcagactac gagaagcaca aagtctatgc ctgcgaagtg 2160

acccatcagg gcctgagttc accagtgaca aagtctttta atcgcggaga gtgttgataa 2220

ctcgag 2226

<210> 141
<211> 729
<212> PRT
<213> Artificial Sequence

<220>
<223> DMAb-10

<400> 141

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Arg Ser Tyr Asp Met His Trp Val Arg Gln Ala Thr Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Ala Ile Gly Thr Ala Gly Asp Thr Tyr Tyr Pro Gly
65 70 75 80

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Glu Asn Ala Lys Asn Ser
85 90 95

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
100 105 110

Tyr Cys Ala Arg Val Arg Phe Gly Asp Thr Ala Val Asp Tyr Trp Gly

```
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
    130                 135                 140

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
145                 150                 155                 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
                165                 170                 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
            180                 185                 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
        195                 200                 205

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
    210                 215                 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
225                 230                 235                 240

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
                245                 250                 255

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
            260                 265                 270

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        275                 280                 285

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    290                 295                 300

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
305                 310                 315                 320

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                325                 330                 335

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            340                 345                 350

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        355                 360                 365
```

```
Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
    370                 375                 380

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
385                 390                 395                 400

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                405                 410                 415

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            420                 425                 430

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        435                 440                 445

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    450                 455                 460

Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn
465                 470                 475                 480

Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro
                485                 490                 495

Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser
            500                 505                 510

Gly Ala Tyr Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
        515                 520                 525

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
    530                 535                 540

Ile Ser Ser Phe Leu Asn Trp His Gln Gln Lys Pro Gly Lys Ala Pro
545                 550                 555                 560

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
                565                 570                 575

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
            580                 585                 590

Ser Leu Gln Pro Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Ser Tyr
        595                 600                 605

Ile Ser Pro Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Thr
    610                 615                 620
```

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
625 630 635 640

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
645 650 655

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
660 665 670

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
675 680 685

Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
690 695 700

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
705 710 715 720

Thr Lys Ser Phe Asn Arg Gly Glu Cys
725

<210> 142
<211> 2214
<212> DNA
<213> Artificial Sequence

<220>
<223> pGX9244, DMAb-10

<400> 142
ggatccgccg ccaccatgga ctggacttgg agaatcctgt tcctggtcgc cgccgctact 60

gggactcatg ccgaggtgca gctggtcgaa tctggagggg gcctggtgca gcctggcggc 120

agcctgaggc tgtcctgcgc agcatctggc ttcaccttta ggagctacga catgcactgg 180

gtgcgccagg caacaggcaa gggactggag tgggtgtctg ccatcggaac cgcaggcgat 240

acatactatc caggctccgt gaagggcagg ttcaccatct cccgcgagaa cgccaagaat 300

tctctgtacc tgcagatgaa cagcctgaga gccgaggaca ccgccgtgta ctattgcgcc 360

agggtgcgct tcggcgacac agcagtggat tattggggcc agggcaccct ggtgacagtg 420

agctccgcct ccaccaaggg accaagcgtg ttcccactgg caccttctag caagtccacc 480

tctggcggca cagccgccct gggctgtctg gtgaaggatt acttccctga gccagtgaca 540

gtgtcctgga actctggcgc cctgaccagc ggagtgcaca catttcctgc cgtgctgcag 600

tcctctggcc tgtactccct gagctccgtg gtgaccgtgc catctagctc cctgggcacc 660

cagacatata tctgcaacgt gaatcacaag cctagcaata caaaggtgga caagaaggtg 720

gagccaaagt cctgtgataa gacccacaca tgccctccct gtccagcacc tgagctgctg 780

ggcggcccaa gcgtgttcct gtttccaccc aagcccaagg acaccctgat gatcagccgg 840

accccagagg tgacatgcgt ggtggtggac gtgtcccacg aggaccccga ggtgaagttt 900

aactggtacg tggatggcgt ggaggtgcac aatgccaaga ccaagccccg ggaggagcag 960

tacaacagca cctatagagt ggtgtccgtg ctgacagtgc tgcaccagga ctggctgaac 1020

ggcaaggagt ataagtgcaa ggtgagcaat aaggccctgc cagccccccat cgagaagacc 1080

atctccaagg caaagggaca gccaagggag ccacaggtgt acacactgcc tccatcccgc 1140

gacgagctga ccaagaacca ggtgtctctg acatgtctgg tgaagggctt ctatccctct 1200

gatatcgccg tggagtggga gagcaatggc cagcctgaga acaattacaa gaccacaccc 1260

cctgtgctgg acagcgatgg ctccttcttt ctgtattcca agctgaccgt ggacaagtct 1320

cggtggcagc agggcaacgt gtttagctgc tccgtgatgc acgaggccct gcacaatcac 1380

tacacccaga agtctctgag cctgtcccca ggcaagaggg gaagaaagcg gagatctggc 1440

agcggcgcca caaacttcag cctgctgaag caggccggcg atgtggagga gaatcctggc 1500

ccaatggtgc tgcagaccca ggtgtttatc tctctgctgc tgtggatcag cggcgcctat 1560

ggcgacatcc agatgacaca gtccccttct agcctgtccg cctctgtggg cgatcgggtg 1620

accatcacat gtagagccag ccagtccatc tcctctttcc tgaactggca ccagcagaag 1680

cctggcaagg ccccaaagct gctgatctac gcagccagct ccctgcagag cggagtgccc 1740

tccaggttct ctggcagcgg ctccggaacc gactttaccc tgacaatctc tagcctgcag 1800

cctgaggatt ttgccatcta ctattgccag cagtcttata tcagcccctt caccttggc 1860

cctggcacaa aggtggacat caagaccgtg gccgccccaa gcgtgttcat ctttccaccc 1920

tccgatgagc agctgaagtc tggcacagcc agcgtggtgt gcctgctgaa caatttctac 1980

ccccgcgagg ccaaggtgca gtggaaggtg gacaacgccc tgcagtccgg caattctcag 2040

gagagcgtga ccgagcagga ctccaaggat tctacatatt ctctgagctc taccctgaca 2100

ctgagcaagg ccgattacga gaagcacaag gtgtatgcct gcgaggtcac ccaccagggg 2160

ctgtcaagtc cagtcactaa gtccttcaat cggggcgaat gctgataact cgag 2214

<210> 143
<211> 739
<212> PRT
<213> Artificial Sequence

<220>
<223> DMAb-11

<400> 143

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

```
Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ile Gln
            20                  25                  30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ala Val
        35                  40                  45

Arg Ser Asn Tyr Leu Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    50                  55                  60

Glu Trp Val Ser Leu Ile Tyr Ser Gly Gly Leu Thr Ala Tyr Ala Asp
65                  70                  75                  80

Ser Val Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr
                85                  90                  95

Leu Tyr Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr
            100                 105                 110

Tyr Cys Ala Arg Val Ala Ser Ser Ala Gly Thr Phe Tyr Tyr Gly Met
        115                 120                 125

Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr
    130                 135                 140

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
145                 150                 155                 160

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
                165                 170                 175

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
            180                 185                 190

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
        195                 200                 205

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
    210                 215                 220

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu
225                 230                 235                 240

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
                245                 250                 255

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
            260                 265                 270
```

```
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
        275                 280                 285

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
    290                 295                 300

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
305                 310                 315                 320

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
                325                 330                 335

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
            340                 345                 350

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
        355                 360                 365

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
    370                 375                 380

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
385                 390                 395                 400

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
                405                 410                 415

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
            420                 425                 430

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
        435                 440                 445

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
    450                 455                 460

Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser
465                 470                 475                 480

Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu
                485                 490                 495

Asn Pro Gly Pro Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu
            500                 505                 510

Leu Trp Ile Ser Gly Ala Tyr Gly Asp Ile Val Met Thr Gln Ser Pro
```

515 520 525

Arg Ser Leu Ser Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg
530 535 540

Ser Ser Gln Ser Leu Leu His Arg Asn Gly Tyr Asn Tyr Leu Asp Trp
545 550 555 560

Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly
565 570 575

Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser
580 585 590

Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val
595 600 605

Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Ser Trp Thr Phe
610 615 620

Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Val Ala Ala Pro Ser Val
625 630 635 640

Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser
645 650 655

Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln
660 665 670

Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val
675 680 685

Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu
690 695 700

Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu
705 710 715 720

Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg
725 730 735

Gly Glu Cys

<210> 144
<211> 2244
<212> DNA
<213> Artificial Sequence

<220>
<223> pGX9256, DMAb-11

<400> 144
ggatccgccg ccaccatgga ctggacctgg agaatcctgt tcctggtggc agcagcaacc 60

ggaacacacg cagaggtgca gctggtggag agcggcggcg gcctgatcca gccaggcggc 120

agcctgaggc tgtcctgcgc agcatctgga tttgccgtga ggagcaacta cctgtcctgg 180

gtgagacagg caccaggcaa gggactggag tgggtgtctc tgatctacag cggcggcctg 240

accgcatatg cagacagcgt ggagggcagg ttcaccatct ccagagataa ctctaagaat 300

acactgtatc tgcagatgaa ttccctgcgg gtggaggaca ccgccctgta ctattgcgcc 360

cgcgtggcca gctccgccgg cacattctac tatggcatgg acgtgtgggg ccagggcacc 420

acagtgaccg tgtctagcgc ctccacaaag ggaccaagcg tgttcccact ggcaccttcc 480

tctaagtcca cctctggcgg cacagccgcc ctgggctgtc tggtgaagga ttacttccct 540

gagccagtga ccgtgtcttg gaacagcggc gccctgacca gcggagtgca cacatttcct 600

gccgtgctgc agagctccgg cctgtactcc ctgtctagcg tggtgaccgt gccatcctct 660

agcctgggca cccagacata tatctgcaac gtgaatcaca agcctagcaa tacaaaggtg 720

gacaagaagg tggagccaaa gtcctgtgat aagacccaca catgccctcc ctgtccagca 780

cctgagctgc tgggcggccc aagcgtgttc ctgtttccac ccaagcccaa ggacacactg 840

atgatctcta ggaccccaga ggtgacatgc gtggtggtgg acgtgagcca cgaggacccc 900

gaggtgaagt ttaactggta cgtggatggc gtggaggtgc acaatgccaa gaccaagcca 960

agggaggagc agtacaacag cacctataga gtggtgtccg tgctgacagt gctgcaccag 1020

gactggctga acggcaagga gtataagtgc aaggtgtcca ataaggccct gccagccccc 1080

atcgagaaga ccatctctaa ggcaaaggga cagccaaggg agccacaggt gtacacactg 1140

cctccatcca gagacgagct gaccaagaac caggtgtctc tgacatgtct ggtgaagggc 1200

ttctatccct ctgatatcgc cgtggagtgg gagagcaatg gccagcctga gaacaattac 1260

aagaccacac cccctgtgct ggactccgat ggctctttct ttctgtattc caagctgacc 1320

gtggataagt ctcggtggca gcagggcaac gtgtttagct gctccgtgat gcacgaggcc 1380

ctgcacaatc actacaccca gaagtctctg agcctgtccc ctggcaagag gggaaggaag 1440

aggagatctg gcagcggcgc cacaaacttc agcctgctga agcaggcagg cgacgtggag 1500

gagaatcctg gaccaatggt gctgcagacc caggtgttta tctctctgct gctgtggatc 1560

agcggcgcct acggcgatat cgtgatgacc cagtcccctc gctccctgtc tgtgacacct 1620

ggcgagccag ccagcatctc ctgtcggtcc tctcagtctc tgctgcaccg caacggctac 1680

aattatctgg actggtacct gcagaagccc ggccagtccc ctcagctgct gatctatctg 1740

ggcagcaaca gggcatccgg agtgccagac cgcttctctg gcagcggctc cggaaccgac 1800

ttcaccctga agatcagcag ggtggaggcc gaggatgtgg gcgtgtacta ttgcatgcag 1860

gccctgcaga ccccctcctg gacattcggc cagggcacca aggtggagat caagacagtg 1920

gccgccccta gcgtgttcat ctttccaccc tccgacgagc agctgaagtc tggcaccgcc 1980

agcgtggtgt gcctgctgaa caacttctac cccagagagg ccaaggtgca gtggaaggtg 2040

gataacgccc tgcagagcgg caattcccag gagtctgtga ccgagcagga cagcaaggat 2100

tccacatatt ctctgagctc caccctgaca ctgagcaagg ccgactacga gaagcacaag 2160

gtgtatgcct gcgaggtgac ccaccagggc ctgtctagcc ctgtgacaaa gtccttcaac 2220

agaggcgagt gttgataact cgag 2244

<210> 145
<211> 741
<212> PRT
<213> Artificial Sequence

<220>
<223> DMAb12

<400> 145

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30

Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Ala Thr Phe
35 40 45

Gly Ser Asp Thr Val Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60

Glu Trp Met Gly Gly Ile Ile Pro Phe Phe Gly Glu Ala Asn Tyr Ala
65 70 75 80

Gln Arg Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Asn
85 90 95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val
100 105 110

Tyr Phe Cys Ala Arg Gln Ile Asn Glu Met Ala Thr Phe Gly Glu Ile
115 120 125

His Tyr Tyr Thr Tyr Met Asp Val Trp Gly Gln Gly Thr Leu Val Thr
130 135 140

```
Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
145                 150                 155                 160

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                165                 170                 175

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
            180                 185                 190

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
        195                 200                 205

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
    210                 215                 220

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
225                 230                 235                 240

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
                245                 250                 255

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
            260                 265                 270

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        275                 280                 285

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
    290                 295                 300

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
305                 310                 315                 320

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
                325                 330                 335

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            340                 345                 350

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        355                 360                 365

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
    370                 375                 380

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
```

385 390 395 400

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
405 410 415

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
420 425 430

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
435 440 445

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
450 455 460

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg
465 470 475 480

Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln
485 490 495

Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr Gln
500 505 510

Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Gly Ser
515 520 525

Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Val
530 535 540

Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Asn Tyr Tyr Ala Ser Trp
545 550 555 560

Tyr Gln Gln Lys Pro Arg Gln Ala Pro Val Leu Val Phe Tyr Gly Lys
565 570 575

Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser
580 585 590

Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Ala Gln Ala Glu Asp Glu
595 600 605

Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Ser Asn His Leu Val
610 615 620

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Ser Thr Val Ala Ala Pro
625 630 635 640

```
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
                645                 650                 655

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
            660                 665                 670

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
        675                 680                 685

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Asn
    690                 695                 700

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
705                 710                 715                 720

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
                725                 730                 735

Asn Arg Gly Glu Cys
            740
```

<210> 146
<211> 2232
<212> DNA
<213> Artificial Sequence

<220>
<223> pGX9260, DMAb12

<400> 146

```
catggactgg acctggagaa tcctgttcct ggtggcagca gcaaccggaa cacacgcaca       60

ggtgcagctg gtgcagagcg gagcagaggt gaagaagcca ggcagctccg tgaaggtgtc      120

ctgcaaggca tctggagcca ccttcggctc cgataccgtg acatgggtgc gccaggcacc      180

aggacaggga ctggagtgga tgggcggcat catccctttc tttggcgagg ccaactacgc      240

ccagcggttt cagggcagag tgaccatcac agccgacaag tccaccaata cagcctacat      300

ggagctgtct agcctgcggt ctgaggatac cgccgtgtat ttctgcgcca gacagatcaa      360

cgagatggcc acctttggcg agatccacta ctatacatac atggacgtgt ggggacaggg      420

caccctggtg acagtgtcct ctgcctccac caagggacct agcgtgttcc cactggcacc      480

tagctccaag tctaccagcg gcggcacagc cgccctggga tgtctggtga aggattattt      540

ccctgagcca gtgacagtgt cctggaactc tggcgccctg accagcggag tgcacacatt      600

tcccgccgtg ctgcagtcta gcggcctgta ctccctgtcc tctgtggtga ccgtgcctag      660

ctcctctctg ggcacccaga catatatctg caacgtgaat cacaagcctt ctaatacaaa      720

ggtggacaag aaggtggagc caaagagctg tgataagacc cacacatgcc ctccctgtcc      780
```

agcacctgag ctgctgggcg gcccaagcgt gttcctgttt ccacccaagc ccaaggacac 840

cctgatgatc agcaggaccc ctgaggtgac atgcgtggtg gtggacgtgt cccacgagga 900

ccccgaggtg aagttcaact ggtacgtgga tggcgtggag gtgcacaatg ccaagaccaa 960

gccccgggag gagcagtaca acagcaccta tagagtggtg tccgtgctga cagtgctgca 1020

ccaggactgg ctgaacggca aggagtataa gtgcaaggtg tctaataagg ccctgccagc 1080

ccccatcgag aagaccatct ccaaggcaaa gggacagcca agggagccac aggtgtacac 1140

actgcctcca agccgcgacg agctgaccaa gaaccaggtg tccctgacat gtctggtgaa 1200

gggcttctat ccatccgata tcgccgtgga gtgggagtct aatggccagc ccgagaacaa 1260

ttacaagacc acacccccctg tgctggacag cgatggctcc ttctttctgt attccaagct 1320

gaccgtggac aagtctcggt ggcagcaggg caacgtgttt tcctgctctg tgatgcacga 1380

ggccctgcac aatcactaca cccagaagag cctgtccctg tctcctggca agaggggaag 1440

gaagcggaga agcggctccg gagccacaaa cttcagcctg ctgaagcagg ccggcgatgt 1500

ggaggagaat cctggcccaa tggtgctgca gacccaggtg tttatctctc tgctgctgtg 1560

gatcagcgga gcatacggcg gctccgagct gacacaggac ccagccgtga gcgtggccct 1620

gggacagacc gtgaggatca catgtcaggg cgatagcctg cgcaactact atgcctcctg 1680

gtaccagcag aagcctcggc aggccccagt gctggtgttc tatggcaaga acaataggcc 1740

ctctggcatc cctgaccgct ttagcggcag ctcctctggc aataccgcaa gcctgacaat 1800

ctccggagca caggcagagg acgaggcaga ttactattgc aacagcagag atagctcctc 1860

taatcacctg gtgttcggcg gcggaaccaa gctgacagtg ctgtctaccg tggccgcccc 1920

aagcgtgttc atctttccac cctccgacga gcagctgaag tctggcacag ccagcgtggt 1980

gtgcctgctg aacaacttct acccccggga ggccaaggtg cagtggaagg tggataacgc 2040

cctgcagtct ggcaatagcc aggagtccgt gaccgagcag gactctaagg atagcacata 2100

ttctctgagc aacaccctga cactgagcaa ggccgactac gagaagcaca aggtgtatgc 2160

atgcgaggtg acccaccagg gactgagctc cccagtgaca aagtccttca atagaggcga 2220

gtgttgataa ct 2232

<210> 147
<211> 735
<212> PRT
<213> Artificial Sequence

<220>
<223> DMAb13

<400> 147

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

```
Thr His Ala Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
            20                  25                  30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Glu Val Ser Gly Leu Thr Phe
        35                  40                  45

Ser Asn Phe Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    50                  55                  60

Glu Trp Val Ala Phe Ile Arg Phe Asp Gly Ser Asn Lys Tyr Tyr Ala
65                  70                  75                  80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
                85                  90                  95

Thr Val Tyr Leu Gln Met Gly Ser Leu Arg Ala Glu Asp Thr Ala Val
            100                 105                 110

Tyr Phe Cys Gly Arg Val Leu Tyr Gly Ala Ala Ala Asp Phe Trp Gly
        115                 120                 125

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
    130                 135                 140

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
145                 150                 155                 160

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
                165                 170                 175

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
            180                 185                 190

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
        195                 200                 205

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
    210                 215                 220

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
225                 230                 235                 240

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
                245                 250                 255

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
```

```
            260                 265                 270

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        275                 280                 285

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    290                 295                 300

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
305                 310                 315                 320

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                325                 330                 335

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            340                 345                 350

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        355                 360                 365

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
    370                 375                 380

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
385                 390                 395                 400

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                405                 410                 415

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            420                 425                 430

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        435                 440                 445

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    450                 455                 460

Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn
465                 470                 475                 480

Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro
                485                 490                 495

Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser
            500                 505                 510
```

```
Gly Ala Tyr Gly Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala
        515                 520                 525

Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Thr Ser Ser His Ser
    530                 535                 540

Leu Leu Tyr Ser Ser Asp Asn Lys Asn Tyr Leu Thr Trp Tyr Gln Gln
545                 550                 555                 560

Lys Ala Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg
                565                 570                 575

Gln Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu
            580                 585                 590

Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
        595                 600                 605

Tyr Cys Gln Gln Tyr Tyr Thr Lys Ser Phe Thr Phe Gly Gln Gly Thr
    610                 615                 620

Lys Val Glu Ile Lys Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
625                 630                 635                 640

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
                645                 650                 655

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
            660                 665                 670

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
        675                 680                 685

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Asn Thr Leu Thr Leu Ser Lys
    690                 695                 700

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
705                 710                 715                 720

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
                725                 730                 735
```

<210> 148
<211> 2214
<212> DNA
<213> Artificial Sequence

<220>
<223> pGX9261, DMAb13

<400> 148
catggactgg acctggagaa tcctgttcct ggtggcagca gcaaccggaa cacacgcaca 60

ggtgcagctg gtggagagcg gcggcggcgt ggtgcagcct ggcggctctc tgagactgag 120

ctgcgaggtg tccggcctga ccttcagcaa ctttggaatg cagtgggtga ggcaggcacc 180

aggcaaggga ctggagtggg tggccttcat ccgctttgac ggctctaata agtactatgc 240

cgatagcgtg aagggccggt tcaccatctc tagagacaac agcaagaata cagtgtacct 300

gcagatgggc agcctgaggg cagaggacac cgccgtgtac ttctgcggac gcgtgctgta 360

tggagcagca gcagattttt ggggacaggg caccctggtg acagtgagct ccgcctctac 420

aaagggacca agcgtgtttc cactggcacc ctctagcaag tccacctctg gcggcacagc 480

cgccctgggc tgtctggtga aggattactt ccccgagcct gtgaccgtga gctggaactc 540

cggcgccctg acctccggag tgcacacatt tccagccgtg ctgcagtcct ctggcctgta 600

cagcctgagc tccgtggtga ccgtgccctc tagctccctg ggcacccaga catatatctg 660

caacgtgaat cacaagccaa gcaatacaaa ggtggacaag aaggtggagc ccaagtcctg 720

tgataagacc cacacatgcc ctccctgtcc agcaccagag ctgctgggcg gcccaagcgt 780

gttcctgttt ccacccaagc ctaaggacac cctgatgatc tctagaaccc ccgaggtgac 840

atgcgtggtg gtggacgtga gccacgagga ccccgaggtg aagttcaact ggtacgtgga 900

tggcgtggag gtgcacaatg ccaagacaaa gcctcgggag gagcagtaca actccaccta 960

tagagtggtg tctgtgctga cagtgctgca ccaggactgg ctgaacggca aggagtataa 1020

gtgcaaggtg tccaataagg ccctgcctgc cccaatcgag aagaccatct ctaaggcaaa 1080

gggacagcct cgggagccac aggtgtacac actgcctcca tccagagacg agctgaccaa 1140

gaaccaggtg tctctgacat gtctggtgaa gggcttctat ccttctgata tcgccgtgga 1200

gtgggagagc aatggccagc cagagaacaa ttacaagacc acacccccctg tgctggactc 1260

tgatggcagc ttctttctgt attccaagct gaccgtggac aagtctcggt ggcagcaggg 1320

caacgtgttt agctgctccg tgatgcacga ggccctgcac aatcactaca cccagaagtc 1380

tctgagcctg tccccaggca agaggggaag gaagcggaga tctggcagcg gagccacaaa 1440

cttctccctg ctgaagcagg caggcgatgt ggaggagaat ccaggaccta tggtgctgca 1500

gacccaggtg tttatcagcc tgctgctgtg gatctccggc gcctatggcg acatcgtgat 1560

gacacagtcc ccagattctc tggccgtgtc cctgggagag agggcaacca tcaactgtac 1620

atctagccac agcctgctgt actcctctga caacaagaat tacctgacct ggtatcagca 1680

gaaggccggc cagccaccca agctgctgat ctattgggca tccaccaggc agtctggagt 1740

gccagaccgc ttctccggct ctggcagcgg cacagagttt accctgacaa tcagctccct 1800

gcaggccgag gatgtggccg tgtactattg ccagcagtac tataccaaga gcttcacatt 1860

tggccagggc accaaggtgg agatcaagac agtggccgcc cccagcgtgt tcatctttcc 1920

tccatccgac gagcagctga agagcggaac cgcatccgtg gtgtgcctgc tgaacaattt 1980

ctaccctagg gaggccaagg tgcagtggaa ggtggataac gccctgcaga gcggcaattc 2040

ccaggagtct gtgaccgagc aggacagcaa ggattccaca tattccctgt ctaacaccct 2100

gacactgtcc aaggccgatt acgagaagca caaggtgtat gcctgcgagg tgacccacca 2160

gggcctgtct agccctgtga caaagagctt taatcgcggc gagtgttgat aact 2214

<210> 149
<211> 2067
<212> DNA
<213> Artificial Sequence

<220>
<223> Marburg GP1 Consensus

<400> 149
ggatccgcca ccatgaagac cacatgcctg ttcatcagcc tgatcctgat ccagggcgtg 60

aagaccctgc caatcctgga gatcgcctcc aacaatcagc cccagaacgt ggacagcgtg 120

tgctctggca ccctgcagaa gacagaggat gtgcacctga tgggcttcac actgagcgga 180

cagaaggtgg cagactcccc actggaggcc tctaagaggt gggcctttag aaccggcgtg 240

ccccctaaga acgtggagta caccgagggc gaggaggcca agacatgcta taatatctcc 300

gtgaccgatc ccagcggcaa gtccctgctg ctggacccac ccacaaacat cagggattac 360

cctaagtgta agaccatcca ccacatccag ggccagaatc cacacgcaca gggaatcgcc 420

ctgcacctgt ggggcgcctt ctttctgtac gacaggatcg ccagcaccac aatgtataga 480

ggcaaggtgt tcacagaggg caacatcgcc gccatgatcg tgaataagac cgtgcacaag 540

atgatctttt ctaggcaggg ccagggctac agacacatga acctgacaag caccaataag 600

tattggacaa gctccaacgg cacacagacc aatgacaccg gatgcttcgg cgccctgcag 660

gagtacaact ccaccaagaa tcagacatgt gccccatcta agatccctct gccactgcca 720

acagcaaggc cagaggtgaa gctgacatct accagcacag acgccaccaa gctgaacacc 780

acagacccca attccgacga tgaggatctg accacatccg gctctggcag cggagagcag 840

gagccttata ccacatctga tgccgccacc aagcagggcc tgtctagcac catgcctcca 900

acacctagcc cacagccctc cacacctcag caggagggca acaataccaa ccactctcag 960

ggagcagtga ccgagcctgg caagacaaac accacagccc agccaagcat gccccctcac 1020

aataccacag ccatcagcac caacaataca tccaagcaca acttttctac ccctagcgtg 1080

ccactgcaga atgccaccaa ctacaataca cagtccaccg ccacagagaa cgagcagaca 1140

tccgcccccc ctaagaccac actgccaccc accgagaacc ctaccacagc caagagcacc 1200

aattccacaa agtctccaac cacaaccgtg cccaacacaa ccaataagca ctccacctct 1260

cctagcccaa cccccaaccc tacagcccag cacctggtgt atttcaggag aaagcggaat 1320

atcctgtggc gcgagggcga catgttcccc tttctggatg gcctgatcaa cgcccctatc 1380

gacttcgatc cagtgcccaa taccaagaca atctttgacg agtcctctag ctccggagca 1440

agcgccgagg aggatcagca cgcctctcct aacatcagcc tgacactgtc ctactttcca 1500

aagatcaacg agaataccgc ctattccggc gagaacgaga atgactgcga tgccgagctg 1560

aggatctgga gcgtgcagga ggacgatctg gcagcaggac tgtcctggat tcccttcttc 1620

ggacctggaa tcgagggact gtacaccgca ggactgatca agaaccagaa caacctggtg 1680

tgcagactgc ggcgcctggc caatcagaca gccaagtccc tggagctgct gctgcgggtg 1740

acaaccgagg agcgcacctt ctctctgatc aaccggcacg ccatcgactt tctgctggca 1800

agatggggcg gcacctgcaa ggtgctggga ccagactgct gtatcggcat cgaggatctg 1860

tctcggaata tcagcgagca gatcgaccag atcaagaagg atgagcagaa ggagggaacc 1920

ggatggggac tgggcggcaa gtggtggaca agcgattggg gcgtgctgac caacctgggc 1980

atcctgctgc tgctgtctat cgccgtgctg atcgccctga gctgcatctg tcgcatcttc 2040

accaagtata tcggctgata actcgag 2067

<210> 150
<211> 681
<212> PRT
<213> Artificial Sequence

<220>
<223> Marburg GP1 Consensus

<400> 150

Met Lys Thr Thr Cys Leu Phe Ile Ser Leu Ile Leu Ile Gln Gly Val
1 5 10 15

Lys Thr Leu Pro Ile Leu Glu Ile Ala Ser Asn Asn Gln Pro Gln Asn
20 25 30

Val Asp Ser Val Cys Ser Gly Thr Leu Gln Lys Thr Glu Asp Val His
35 40 45

Leu Met Gly Phe Thr Leu Ser Gly Gln Lys Val Ala Asp Ser Pro Leu
50 55 60

Glu Ala Ser Lys Arg Trp Ala Phe Arg Thr Gly Val Pro Pro Lys Asn
65 70 75 80

Val Glu Tyr Thr Glu Gly Glu Glu Ala Lys Thr Cys Tyr Asn Ile Ser
85 90 95

```
Val Thr Asp Pro Ser Gly Lys Ser Leu Leu Leu Asp Pro Pro Thr Asn
            100                 105                 110

Ile Arg Asp Tyr Pro Lys Cys Lys Thr Ile His His Ile Gln Gly Gln
        115                 120                 125

Asn Pro His Ala Gln Gly Ile Ala Leu His Leu Trp Gly Ala Phe Phe
    130                 135                 140

Leu Tyr Asp Arg Ile Ala Ser Thr Thr Met Tyr Arg Gly Lys Val Phe
145                 150                 155                 160

Thr Glu Gly Asn Ile Ala Ala Met Ile Val Asn Lys Thr Val His Lys
                165                 170                 175

Met Ile Phe Ser Arg Gln Gly Gln Gly Tyr Arg His Met Asn Leu Thr
            180                 185                 190

Ser Thr Asn Lys Tyr Trp Thr Ser Ser Asn Gly Thr Gln Thr Asn Asp
        195                 200                 205

Thr Gly Cys Phe Gly Ala Leu Gln Glu Tyr Asn Ser Thr Lys Asn Gln
    210                 215                 220

Thr Cys Ala Pro Ser Lys Ile Pro Leu Pro Leu Pro Thr Ala Arg Pro
225                 230                 235                 240

Glu Val Lys Leu Thr Ser Thr Ser Thr Asp Ala Thr Lys Leu Asn Thr
                245                 250                 255

Thr Asp Pro Asn Ser Asp Asp Glu Asp Leu Thr Thr Ser Gly Ser Gly
            260                 265                 270

Ser Gly Glu Gln Glu Pro Tyr Thr Thr Ser Asp Ala Ala Thr Lys Gln
        275                 280                 285

Gly Leu Ser Ser Thr Met Pro Pro Thr Pro Ser Pro Gln Pro Ser Thr
    290                 295                 300

Pro Gln Gln Glu Gly Asn Asn Thr Asn His Ser Gln Gly Ala Val Thr
305                 310                 315                 320

Glu Pro Gly Lys Thr Asn Thr Thr Ala Gln Pro Ser Met Pro Pro His
                325                 330                 335

Asn Thr Thr Ala Ile Ser Thr Asn Asn Thr Ser Lys His Asn Phe Ser
```

```
            340                 345                 350

Thr Pro Ser Val Pro Leu Gln Asn Ala Thr Asn Tyr Asn Thr Gln Ser
        355                 360                 365

Thr Ala Thr Glu Asn Glu Gln Thr Ser Ala Pro Ser Lys Thr Thr Leu
    370                 375                 380

Pro Pro Thr Glu Asn Pro Thr Thr Ala Lys Ser Thr Asn Ser Thr Lys
385                 390                 395                 400

Ser Pro Thr Thr Thr Val Pro Asn Thr Thr Asn Lys His Ser Thr Ser
                405                 410                 415

Pro Ser Pro Thr Pro Asn Pro Thr Ala Gln His Leu Val Tyr Phe Arg
            420                 425                 430

Arg Lys Arg Asn Ile Leu Trp Arg Glu Gly Asp Met Phe Pro Phe Leu
        435                 440                 445

Asp Gly Leu Ile Asn Ala Pro Ile Asp Phe Asp Pro Val Pro Asn Thr
    450                 455                 460

Lys Thr Ile Phe Asp Glu Ser Ser Ser Ser Gly Ala Ser Ala Glu Glu
465                 470                 475                 480

Asp Gln His Ala Ser Pro Asn Ile Ser Leu Thr Leu Ser Tyr Phe Pro
                485                 490                 495

Lys Ile Asn Glu Asn Thr Ala Tyr Ser Gly Glu Asn Glu Asn Asp Cys
            500                 505                 510

Asp Ala Glu Leu Arg Ile Trp Ser Val Gln Glu Asp Asp Leu Ala Ala
        515                 520                 525

Gly Leu Ser Trp Ile Pro Phe Phe Gly Pro Gly Ile Glu Gly Leu Tyr
    530                 535                 540

Thr Ala Gly Leu Ile Lys Asn Gln Asn Asn Leu Val Cys Arg Leu Arg
545                 550                 555                 560

Arg Leu Ala Asn Gln Thr Ala Lys Ser Leu Glu Leu Leu Leu Arg Val
                565                 570                 575

Thr Thr Glu Glu Arg Thr Phe Ser Leu Ile Asn Arg His Ala Ile Asp
            580                 585                 590
```

Phe Leu Leu Ala Arg Trp Gly Gly Thr Cys Lys Val Leu Gly Pro Asp
595 600 605

Cys Cys Ile Gly Ile Glu Asp Leu Ser Arg Asn Ile Ser Glu Gln Ile
610 615 620

Asp Gln Ile Lys Lys Asp Glu Gln Lys Glu Gly Thr Gly Trp Gly Leu
625 630 635 640

Gly Gly Lys Trp Trp Thr Ser Asp Trp Gly Val Leu Thr Asn Leu Gly
645 650 655

Ile Leu Leu Leu Leu Ser Ile Ala Val Leu Ile Ala Leu Ser Cys Ile
660 665 670

Cys Arg Ile Phe Thr Lys Tyr Ile Gly
675 680

<210> 151
<211> 2067
<212> DNA
<213> Artificial Sequence

<220>
<223> Marburg GP2 Consensus

<400> 151
ggatccgcca ccatgcggac cacatgcttc tttatcagcc tgatcctgat ccagggcatc 60

aagaccctgc caatcctgga gatcgcctcc aacgaccagc cccagaatgt ggatagcgtg 120

tgctccggca ccctgcagaa gacagaggac gtgcacctga tgggcttcac actgtctggc 180

cagaaggtgg ccgatagccc cctggaggcc tctaagaggt gggcctttag aaccggcgtg 240

ccccctaaga acgtggagta caccgagggc gaggaggcca agacatgcta taatatcagc 300

gtgaccgacc cttctggcaa gagcctgctg ctggacccac ccacaaacgt gcgcgattac 360

cctaagtgta agaccatcca ccacatccag ggccagaatc cacacgcaca gggaatcgcc 420

ctgcacctgt ggggcgcctt ctttctgtac gataggatcg cctccaccac aatgtataga 480

ggcaaggtgt tcacagaggg caacatcgcc gccatgatcg tgaataagac cgtgcacaag 540

atgatctttt ccaggcaggg ccagggctac agacacatga acctgacatc taccaataag 600

tattggacca gctccaacgg cacacagacc aatgacaccg gctgcttcgg cacactgcag 660

gagtacaact ccaccaagaa tcagacatgt gccccttcta agaccccctcc acccccctcca 720

acagcaaggc cagagatcaa gcctacaagc accccaacag acgccaccag actgaacacc 780

acaaacccca attccgacga tgaggatctg accacaagcg gctccggctc tggagagcag 840

gagccttata ccacatccga cgccgtgacc aagcagggcc tgtctagcac catgcccccct 900

acaccttccc cacagccagg aacacctcag cagggcggca acaataccaa ccactctcag 960

gacgccacca cagagctgga taacacaaat accacagccc agccacccat gccaagccac 1020

aataccacaa ccatcagcac caacaataca tccaagcaca acctgtccac cctgtctgag 1080

cctccacaga atacaaccaa cccaaatacc cagagcatgg tgacagagaa cgagaagacc 1140

agcgcccctc ccaaggccac cctgccaccc acagagaatc ccacaaccga gaagtctacc 1200

aacaatacaa agagccctac aaccctggag ccaaacaaga caaatggcca cttcaccagc 1260

ccctcctcta cacctaactc cacaacccag cacctgatct actttaggag aaagcggtcc 1320

atcctgtggc gcgagggcga catgttcccc tttctggatg gcctgatcaa cgcccctatc 1380

gacttcgatc ctgtgccaaa taccaagaca atctttgacg agagctcctc tagcggagca 1440

agcgccgagg aggatcagca cgcctcctct aacatcagcc tgaccctgtc ctacctgcca 1500

cacacctccg agaatacagc ctattctggc gagaacgaga atgactgcga tgccgagctg 1560

cggatctggt ctgtgcagga ggacgatctg gcagcaggac tgagctggat tcccctgttc 1620

ggaccaggaa tcgagggact gtataccgcc ggcctgatca agaaccagaa caacctggtg 1680

tgcaggctgc ggcgcctggc aaatcagaca gccaagtctc tggagctgct gctgcgggtg 1740

acaaccgagg agcgcacctt cagcctgatc aaccggcacg ccatcgactt tctgctgacc 1800

cgctggggcg gcacatgcaa ggtgctggga ccagactgct gtatcggcat cgaggatctg 1860

tctaggaaca tcagcgagca gatcgaccag atcaagaagg atgagcagaa ggagggaacc 1920

ggatggggac tgggcggcaa gtggtggaca agcgattggg gcgtgctgac caacctgggc 1980

atcctgctgc tgctgtctat cgccgtgctg atcgccctga gctgcatctg tagaatcttt 2040

accaagtata tcggctgata actcgag 2067

<210> 152
<211> 681
<212> PRT
<213> Artificial Sequence

<220>
<223> Marburg GP2 Consensus

<400> 152

Met Arg Thr Thr Cys Phe Phe Ile Ser Leu Ile Leu Ile Gln Gly Ile
1 5 10 15

Lys Thr Leu Pro Ile Leu Glu Ile Ala Ser Asn Asp Gln Pro Gln Asn
20 25 30

Val Asp Ser Val Cys Ser Gly Thr Leu Gln Lys Thr Glu Asp Val His
35 40 45

```
Leu Met Gly Phe Thr Leu Ser Gly Gln Lys Val Ala Asp Ser Pro Leu
    50                  55                  60

Glu Ala Ser Lys Arg Trp Ala Phe Arg Thr Gly Val Pro Pro Lys Asn
65                  70                  75                  80

Val Glu Tyr Thr Glu Gly Glu Glu Ala Lys Thr Cys Tyr Asn Ile Ser
                85                  90                  95

Val Thr Asp Pro Ser Gly Lys Ser Leu Leu Leu Asp Pro Pro Thr Asn
            100                 105                 110

Val Arg Asp Tyr Pro Lys Cys Lys Thr Ile His His Ile Gln Gly Gln
        115                 120                 125

Asn Pro His Ala Gln Gly Ile Ala Leu His Leu Trp Gly Ala Phe Phe
    130                 135                 140

Leu Tyr Asp Arg Ile Ala Ser Thr Thr Met Tyr Arg Gly Lys Val Phe
145                 150                 155                 160

Thr Glu Gly Asn Ile Ala Ala Met Ile Val Asn Lys Thr Val His Lys
                165                 170                 175

Met Ile Phe Ser Arg Gln Gly Gln Gly Tyr Arg His Met Asn Leu Thr
            180                 185                 190

Ser Thr Asn Lys Tyr Trp Thr Ser Ser Asn Gly Thr Gln Thr Asn Asp
        195                 200                 205

Thr Gly Cys Phe Gly Thr Leu Gln Glu Tyr Asn Ser Thr Lys Asn Gln
    210                 215                 220

Thr Cys Ala Pro Ser Lys Thr Pro Pro Pro Pro Pro Thr Ala Arg Pro
225                 230                 235                 240

Glu Ile Lys Pro Thr Ser Thr Pro Thr Asp Ala Thr Arg Leu Asn Thr
                245                 250                 255

Thr Asn Pro Asn Ser Asp Asp Glu Asp Leu Thr Thr Ser Gly Ser Gly
            260                 265                 270

Ser Gly Glu Gln Glu Pro Tyr Thr Thr Ser Asp Ala Val Thr Lys Gln
        275                 280                 285

Gly Leu Ser Ser Thr Met Pro Pro Thr Pro Ser Pro Gln Pro Gly Thr
    290                 295                 300
```

```
Pro Gln Gln Gly Gly Asn Asn Thr Asn His Ser Gln Asp Ala Thr Thr
305                 310                 315                 320

Glu Leu Asp Asn Thr Asn Thr Thr Ala Gln Pro Pro Met Pro Ser His
                325                 330                 335

Asn Thr Thr Thr Ile Ser Thr Asn Asn Thr Ser Lys His Asn Leu Ser
            340                 345                 350

Thr Leu Ser Glu Pro Pro Gln Asn Thr Thr Asn Pro Asn Thr Gln Ser
        355                 360                 365

Met Val Thr Glu Asn Glu Lys Thr Ser Ala Pro Pro Lys Ala Thr Leu
    370                 375                 380

Pro Pro Thr Glu Asn Pro Thr Thr Glu Lys Ser Thr Asn Asn Thr Lys
385                 390                 395                 400

Ser Pro Thr Thr Leu Glu Pro Asn Lys Thr Asn Gly His Phe Thr Ser
                405                 410                 415

Pro Ser Ser Thr Pro Asn Ser Thr Thr Gln His Leu Ile Tyr Phe Arg
            420                 425                 430

Arg Lys Arg Ser Ile Leu Trp Arg Glu Gly Asp Met Phe Pro Phe Leu
        435                 440                 445

Asp Gly Leu Ile Asn Ala Pro Ile Asp Phe Asp Pro Val Pro Asn Thr
    450                 455                 460

Lys Thr Ile Phe Asp Glu Ser Ser Ser Ser Gly Ala Ser Ala Glu Glu
465                 470                 475                 480

Asp Gln His Ala Ser Ser Asn Ile Ser Leu Thr Leu Ser Tyr Leu Pro
                485                 490                 495

His Thr Ser Glu Asn Thr Ala Tyr Ser Gly Glu Asn Glu Asn Asp Cys
            500                 505                 510

Asp Ala Glu Leu Arg Ile Trp Ser Val Gln Glu Asp Asp Leu Ala Ala
        515                 520                 525

Gly Leu Ser Trp Ile Pro Leu Phe Gly Pro Gly Ile Glu Gly Leu Tyr
    530                 535                 540

Thr Ala Gly Leu Ile Lys Asn Gln Asn Asn Leu Val Cys Arg Leu Arg
545                 550                 555                 560
```

```
Arg Leu Ala Asn Gln Thr Ala Lys Ser Leu Glu Leu Leu Leu Arg Val
                565                 570                 575

Thr Thr Glu Glu Arg Thr Phe Ser Leu Ile Asn Arg His Ala Ile Asp
            580                 585                 590

Phe Leu Leu Thr Arg Trp Gly Gly Thr Cys Lys Val Leu Gly Pro Asp
        595                 600                 605

Cys Cys Ile Gly Ile Glu Asp Leu Ser Arg Asn Ile Ser Glu Gln Ile
    610                 615                 620

Asp Gln Ile Lys Lys Asp Glu Gln Lys Glu Gly Thr Gly Trp Gly Leu
625                 630                 635                 640

Gly Gly Lys Trp Trp Thr Ser Asp Trp Gly Val Leu Thr Asn Leu Gly
                645                 650                 655

Ile Leu Leu Leu Leu Ser Ile Ala Val Leu Ile Ala Leu Ser Cys Ile
            660                 665                 670

Cys Arg Ile Phe Thr Lys Tyr Ile Gly
        675                 680
```

<210> 153
<211> 2067
<212> DNA
<213> Artificial Sequence

<220>
<223> Marburg GP3 Consensus

<400> 153

```
ggatccgcca ccatgaagac aatctacttc ctgatctctc tgatcctgat ccagagcatc       60

aagaccctgc cagtgctgga gatcgcctcc aactctcagc cccaggacgt ggatagcgtg      120

tgctctggca ccctgcagaa gacagaggac gtgcacctga tgggcttcac actgtccggc      180

cagaaggtgg ccgattcccc tctggaggcc tctaagaggt gggcctttag aaccggcgtg      240

ccccctaaga acgtggagta caccgagggc gaggaggcca agacatgcta taatatctcc      300

gtgaccgacc caagcggcaa gtccctgctg ctggacccac cctctaacat cagggattac      360

cccaagtgta agaccgtgca ccacatccag ggccagaatc ctcacgcaca gggaatcgcc      420

ctgcacctgt ggggcgcctt ctttctgtac gatcgggtgg ccagcaccac aatgtatcgc      480

ggcaaggtgt tcacagaggg caacatcgcc gccatgatcg tgaataagac cgtgcaccgg      540

atgatctttt ctcgccaggg ccagggctac aggcacatga acctgaccag cacaaataag      600
```

tattggacaa gctccaacga gacccagaga aatgacacag gctgctttgg catcctgcag 660

gagtataact ccaccaacaa tcagacatgt cctccaagcc tgaagccccc ttccctgcct 720

accgtgacac catctatcca cagcaccaac acacagatca ataccgccaa gagcggcaca 780

atgaaccctt ctagcgacga tgaggacctg atgatcagcg gctccggctc tggagagcag 840

ggaccacaca ccacactgaa tgtggtgacc gagcagaagc agtcctctac catcctgtcc 900

acaccatctc tgcacctgag cacatcccag cacgagcaga actctaccaa tcccagccgg 960

cacgcagtga ccgagcacaa cggcacagac cccaccacac agcctgccac cctgctgaac 1020

aatacaaata ccacacctac ctacaacaca ctgaagtata atctgagcac accatcccca 1080

cccaccagga acatcacaaa caatgatacc cagagagagc tggccgagtc cgagcagacc 1140

aacgcccagc tgaataccac actggaccca acagagaacc ccaccacagg ccaggatacc 1200

aactctacca caaatatcat catgaccaca tccgacatca cctctaagca cccaacaaat 1260

agctcccctg attctagccc aaccacacgc cctccaatct acttcaggaa gaagaggagc 1320

atcttttgga aggagggcga catcttcccc tttctggatg gcctgatcag caccgagatc 1380

gacttcgatc caatccccaa caccgagaca atcttcgacg agtctcccag ctttaacacc 1440

tccacaaatg aggagcagca cacacccccc aacatcagcc tgaccttctc ctactttcct 1500

gacaagaatg gcgataccgc ctatagcggc gagaacgaga atgactgcga tgccgagctg 1560

cggatctgga gcgtgcagga ggacgatctg gcagcaggac tgtcctggat tcccttcttc 1620

ggccctggca tcgagggcct gtataccgcc ggcctgatca agaaccagaa caacctggtg 1680

tgccgcctga ggagactggc caatcagaca gccaagagcc tggagctgct gctgagggtg 1740

accacagagg agagaacctt ctccctgatc aaccggcacg ccatcgactt tctgctgacc 1800

cgctggggcg gcacatgcaa ggtgctggga ccagactgct gtatcggcat cgaggatctg 1860

tctaagaata tcagcgagca gatcgacaag atcaggaagg atgagcagaa ggaggagacc 1920

ggatggggac tgggcggcaa gtggtggaca agcgattggg gcgtgctgac caacctgggc 1980

atcctgctgc tgctgtccat cgccgtgctg atcgccctgt cttgcatctg tagaatcttc 2040

accaagtaca tcggctgata actcgag 2067

<210> 154
<211> 681
<212> PRT
<213> Artificial Sequence

<220>
<223> Marburg GP3 Consensus

<400> 154

Met Lys Thr Ile Tyr Phe Leu Ile Ser Leu Ile Leu Ile Gln Ser Ile
1 5 10 15

```
Lys Thr Leu Pro Val Leu Glu Ile Ala Ser Asn Ser Gln Pro Gln Asp
            20                  25                  30

Val Asp Ser Val Cys Ser Gly Thr Leu Gln Lys Thr Glu Asp Val His
        35                  40                  45

Leu Met Gly Phe Thr Leu Ser Gly Gln Lys Val Ala Asp Ser Pro Leu
    50                  55                  60

Glu Ala Ser Lys Arg Trp Ala Phe Arg Thr Gly Val Pro Pro Lys Asn
65                  70                  75                  80

Val Glu Tyr Thr Glu Gly Glu Glu Ala Lys Thr Cys Tyr Asn Ile Ser
                85                  90                  95

Val Thr Asp Pro Ser Gly Lys Ser Leu Leu Leu Asp Pro Pro Ser Asn
            100                 105                 110

Ile Arg Asp Tyr Pro Lys Cys Lys Thr Val His His Ile Gln Gly Gln
        115                 120                 125

Asn Pro His Ala Gln Gly Ile Ala Leu His Leu Trp Gly Ala Phe Phe
    130                 135                 140

Leu Tyr Asp Arg Val Ala Ser Thr Thr Met Tyr Arg Gly Lys Val Phe
145                 150                 155                 160

Thr Glu Gly Asn Ile Ala Ala Met Ile Val Asn Lys Thr Val His Arg
                165                 170                 175

Met Ile Phe Ser Arg Gln Gly Gln Gly Tyr Arg His Met Asn Leu Thr
            180                 185                 190

Ser Thr Asn Lys Tyr Trp Thr Ser Ser Asn Glu Thr Gln Arg Asn Asp
        195                 200                 205

Thr Gly Cys Phe Gly Ile Leu Gln Glu Tyr Asn Ser Thr Asn Asn Gln
    210                 215                 220

Thr Cys Pro Pro Ser Leu Lys Pro Pro Ser Leu Pro Thr Val Thr Pro
225                 230                 235                 240

Ser Ile His Ser Thr Asn Thr Gln Ile Asn Thr Ala Lys Ser Gly Thr
                245                 250                 255

Met Asn Pro Ser Ser Asp Asp Glu Asp Leu Met Ile Ser Gly Ser Gly
```

```
            260                 265                 270

Ser Gly Glu Gln Gly Pro His Thr Thr Leu Asn Val Val Thr Glu Gln
        275                 280                 285

Lys Gln Ser Ser Thr Ile Leu Ser Thr Pro Ser Leu His Leu Ser Thr
    290                 295                 300

Ser Gln His Glu Gln Asn Ser Thr Asn Pro Ser Arg His Ala Val Thr
305                 310                 315                 320

Glu His Asn Gly Thr Asp Pro Thr Thr Gln Pro Ala Thr Leu Leu Asn
                325                 330                 335

Asn Thr Asn Thr Thr Pro Thr Tyr Asn Thr Leu Lys Tyr Asn Leu Ser
            340                 345                 350

Thr Pro Ser Pro Pro Thr Arg Asn Ile Thr Asn Asn Asp Thr Gln Arg
        355                 360                 365

Glu Leu Ala Glu Ser Glu Gln Thr Asn Ala Gln Leu Asn Thr Thr Leu
    370                 375                 380

Asp Pro Thr Glu Asn Pro Thr Thr Gly Gln Asp Thr Asn Ser Thr Thr
385                 390                 395                 400

Asn Ile Ile Met Thr Thr Ser Asp Ile Thr Ser Lys His Pro Thr Asn
                405                 410                 415

Ser Ser Pro Asp Ser Ser Pro Thr Thr Arg Pro Pro Ile Tyr Phe Arg
            420                 425                 430

Lys Lys Arg Ser Ile Phe Trp Lys Glu Gly Asp Ile Phe Pro Phe Leu
        435                 440                 445

Asp Gly Leu Ile Ser Thr Glu Ile Asp Phe Asp Pro Ile Pro Asn Thr
    450                 455                 460

Glu Thr Ile Phe Asp Glu Ser Pro Ser Phe Asn Thr Ser Thr Asn Glu
465                 470                 475                 480

Glu Gln His Thr Pro Pro Asn Ile Ser Leu Thr Phe Ser Tyr Phe Pro
                485                 490                 495

Asp Lys Asn Gly Asp Thr Ala Tyr Ser Gly Glu Asn Glu Asn Asp Cys
            500                 505                 510
```

```
Asp Ala Glu Leu Arg Ile Trp Ser Val Gln Glu Asp Asp Leu Ala Ala
        515                 520                 525

Gly Leu Ser Trp Ile Pro Phe Phe Gly Pro Gly Ile Glu Gly Leu Tyr
    530                 535                 540

Thr Ala Gly Leu Ile Lys Asn Gln Asn Asn Leu Val Cys Arg Leu Arg
545                 550                 555                 560

Arg Leu Ala Asn Gln Thr Ala Lys Ser Leu Glu Leu Leu Leu Arg Val
                565                 570                 575

Thr Thr Glu Glu Arg Thr Phe Ser Leu Ile Asn Arg His Ala Ile Asp
            580                 585                 590

Phe Leu Leu Thr Arg Trp Gly Gly Thr Cys Lys Val Leu Gly Pro Asp
        595                 600                 605

Cys Cys Ile Gly Ile Glu Asp Leu Ser Lys Asn Ile Ser Glu Gln Ile
    610                 615                 620

Asp Lys Ile Arg Lys Asp Glu Gln Lys Glu Glu Thr Gly Trp Gly Leu
625                 630                 635                 640

Gly Gly Lys Trp Trp Thr Ser Asp Trp Gly Val Leu Thr Asn Leu Gly
                645                 650                 655

Ile Leu Leu Leu Leu Ser Ile Ala Val Leu Ile Ala Leu Ser Cys Ile
            660                 665                 670

Cys Arg Ile Phe Thr Lys Tyr Ile Gly
        675                 680


<210>  155
<211>  735
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Influenza A DMAb

<400>  155

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                   10                  15

Thr His Ala Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys
            20                  25                  30

Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val
```

```
        35                  40                  45

Ser Ser Asn Asn Ala Val Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg
    50                  55                  60

Gly Leu Glu Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn
65                  70                  75                  80

Asp Tyr Ala Glu Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr
                85                  90                  95

Ser Lys Asn Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp
            100                 105                 110

Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly His Ile Thr Val Phe Gly
        115                 120                 125

Val Asn Val Asp Ala Phe Asp Met Trp Gly Gln Gly Thr Thr Val Thr
    130                 135                 140

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
145                 150                 155                 160

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                165                 170                 175

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
            180                 185                 190

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
        195                 200                 205

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
    210                 215                 220

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
225                 230                 235                 240

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
                245                 250                 255

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
            260                 265                 270

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        275                 280                 285
```

```
Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
    290                 295                 300

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
305                 310                 315                 320

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
                325                 330                 335

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            340                 345                 350

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        355                 360                 365

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
    370                 375                 380

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
385                 390                 395                 400

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                405                 410                 415

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
            420                 425                 430

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
        435                 440                 445

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
    450                 455                 460

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg
465                 470                 475                 480

Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln
                485                 490                 495

Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr Gln
            500                 505                 510

Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Asp Ile
        515                 520                 525

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
    530                 535                 540
```

```
Val Thr Ile Thr Cys Arg Thr Ser Gln Ser Leu Ser Ser Tyr Leu His
545                 550                 555                 560

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala
                565                 570                 575

Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
            580                 585                 590

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
        595                 600                 605

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Arg Thr Phe Gly Gln Gly Thr
    610                 615                 620

Lys Val Glu Ile Lys Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro
625                 630                 635                 640

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu
                645                 650                 655

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp
            660                 665                 670

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp
        675                 680                 685

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Asn Thr Leu Thr Leu Ser Lys
    690                 695                 700

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln
705                 710                 715                 720

Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
                725                 730                 735


<210>  156
<211>  745
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Influenza B DMAb

<400>  156

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                   10                  15
```

```
Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys
            20                  25                  30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Leu Thr Phe
        35                  40                  45

Leu Asn Ala Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    50                  55                  60

Glu Trp Val Gly Arg Ile Lys Ser Asn Thr Asp Gly Gly Thr Thr Asp
65                  70                  75                  80

Tyr Ala Ala Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Thr Thr Asp Gly Pro Tyr Ser Asp Asp Phe Arg
        115                 120                 125

Ser Gly Tyr Ala Ala Arg Tyr Arg Tyr Phe Gly Met Asp Val Trp Gly
    130                 135                 140

Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
145                 150                 155                 160

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
                165                 170                 175

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
            180                 185                 190

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
        195                 200                 205

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
    210                 215                 220

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
225                 230                 235                 240

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
                245                 250                 255

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
            260                 265                 270
```

```
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
        275                 280                 285

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
    290                 295                 300

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
305                 310                 315                 320

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
                325                 330                 335

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
            340                 345                 350

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
        355                 360                 365

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
    370                 375                 380

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
385                 390                 395                 400

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
                405                 410                 415

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
            420                 425                 430

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
        435                 440                 445

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
    450                 455                 460

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
465                 470                 475                 480

Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn
                485                 490                 495

Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro
            500                 505                 510

Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser
        515                 520                 525
```

```
Gly Ala Tyr Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser
    530                 535                 540

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp
545                 550                 555                 560

Ile Ser Thr Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
                565                 570                 575

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
            580                 585                 590

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
        595                 600                 605

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn
    610                 615                 620

Ser Phe Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr
625                 630                 635                 640

Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
                645                 650                 655

Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
            660                 665                 670

Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
        675                 680                 685

Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
    690                 695                 700

Ser Leu Ser Asn Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
705                 710                 715                 720

Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
                725                 730                 735

Thr Lys Ser Phe Asn Arg Gly Glu Cys
            740                 745
```

<210> 157
<211> 736
<212> PRT
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 157

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                  10                  15

Thr His Ala Glu Val Gln Leu Val Glu Ser Gly Pro Gly Leu Val Lys
            20                  25                  30

Pro Ser Asp Ile Leu Ser Leu Thr Cys Ala Val Ser Gly Tyr Ser Ile
        35                  40                  45

Ser Ser Asn Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly
    50                  55                  60

Leu Glu Trp Ile Gly Ser Ile Tyr His Ser Gly Ser Thr Tyr Tyr Lys
65                  70                  75                  80

Pro Ser Leu Glu Ser Arg Leu Gly Ile Ser Val Asp Thr Ser Lys Asn
                85                  90                  95

Gln Phe Ser Leu Lys Leu Ser Phe Val Ser Ala Ala Asp Thr Ala Val
            100                 105                 110

Tyr Tyr Cys Ala Arg His Val Arg Ser Gly Tyr Pro Asp Thr Ala Tyr
        115                 120                 125

Tyr Phe Asp Lys Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
    130                 135                 140

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
145                 150                 155                 160

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
                165                 170                 175

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
            180                 185                 190

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
        195                 200                 205

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
    210                 215                 220

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys
225                 230                 235                 240
```

```
Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
                245                 250                 255

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
            260                 265                 270

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
        275                 280                 285

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
    290                 295                 300

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
305                 310                 315                 320

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                325                 330                 335

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            340                 345                 350

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        355                 360                 365

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
    370                 375                 380

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
385                 390                 395                 400

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                405                 410                 415

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            420                 425                 430

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
        435                 440                 445

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
    450                 455                 460

Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly Arg Lys Arg Arg Ser
465                 470                 475                 480

Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
```

485 490 495

Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr Gln Val Phe Ile Ser
500 505 510

Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Ser Tyr Val Leu Thr Gln
515 520 525

Pro Pro Ser Val Ser Val Ala Pro Gly Glu Thr Ala Arg Ile Ser Cys
530 535 540

Gly Gly Asn Asn Ile Gly Thr Lys Val Leu His Trp Tyr Gln Gln Thr
545 550 555 560

Pro Gly Gln Ala Pro Val Leu Val Val Tyr Asp Asp Ser Asp Arg Pro
565 570 575

Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala
580 585 590

Thr Leu Thr Ile Ser Arg Val Glu Val Gly Asp Glu Ala Asp Tyr Tyr
595 600 605

Cys Gln Val Trp Asp Ile Ser Thr Asp Gln Ala Val Phe Gly Gly Gly
610 615 620

Thr Lys Leu Thr Val Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr
625 630 635 640

Leu Phe Pro Pro Ser Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu
645 650 655

Val Cys Leu Ile Ser Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp
660 665 670

Lys Ala Asp Ser Ser Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro
675 680 685

Ser Lys Gln Ser Asn Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu
690 695 700

Thr Pro Glu Gln Trp Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr
705 710 715 720

His Glu Gly Ser Thr Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
725 730 735

<210> 158
<211> 744
<212> PRT
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 158

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Thr Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Val Ile Ser Tyr Asp Ala Asn Tyr Lys Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Lys Asp Ser Gln Leu Arg Ser Leu Leu Tyr Phe Glu
115 120 125

Trp Leu Ser Gln Gly Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
130 135 140

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
145 150 155 160

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu
165 170 175

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
180 185 190

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
195 200 205

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu

```
    210                 215                 220

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
225                 230                 235                 240

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr
                245                 250                 255

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
            260                 265                 270

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
        275                 280                 285

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
    290                 295                 300

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
305                 310                 315                 320

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
                325                 330                 335

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
            340                 345                 350

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
        355                 360                 365

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
    370                 375                 380

Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
385                 390                 395                 400

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
                405                 410                 415

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
            420                 425                 430

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
        435                 440                 445

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
    450                 455                 460
```

```
Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Arg Gly
465                 470                 475                 480

Arg Lys Arg Arg Ser Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys
                485                 490                 495

Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Val Leu Gln Thr
            500                 505                 510

Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser Gly Ala Tyr Gly Asp
        515                 520                 525

Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly Glu
    530                 535                 540

Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Thr Phe Asn Tyr
545                 550                 555                 560

Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys
                565                 570                 575

Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg
            580                 585                 590

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
        595                 600                 605

Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln His Tyr Arg
    610                 615                 620

Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Val
625                 630                 635                 640

Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys
                645                 650                 655

Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
            660                 665                 670

Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
        675                 680                 685

Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
    690                 695                 700

Leu Ser Asn Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
705                 710                 715                 720
```

```
Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
                725                 730                 735

Lys Ser Phe Asn Arg Gly Glu Cys
            740
```

<210> 159
<211> 477
<212> PRT
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 159

```
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1               5                   10                  15

Thr His Ala Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys
            20                  25                  30

Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val
        35                  40                  45

Ser Ser Asn Asn Ala Val Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg
    50                  55                  60

Gly Leu Glu Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn
65                  70                  75                  80

Asp Tyr Ala Glu Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr
                85                  90                  95

Ser Lys Asn Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp
            100                 105                 110

Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly His Ile Thr Val Phe Gly
        115                 120                 125

Val Asn Val Asp Ala Phe Asp Met Trp Gly Gln Gly Thr Thr Val Thr
    130                 135                 140

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
145                 150                 155                 160

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                165                 170                 175
```

```
Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
            180                 185                 190

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
        195                 200                 205

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
    210                 215                 220

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
225                 230                 235                 240

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
                245                 250                 255

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
            260                 265                 270

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        275                 280                 285

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
    290                 295                 300

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
305                 310                 315                 320

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
                325                 330                 335

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            340                 345                 350

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        355                 360                 365

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
    370                 375                 380

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
385                 390                 395                 400

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                405                 410                 415

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
            420                 425                 430
```

```
Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
        435                 440                 445

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
    450                 455                 460

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
465                 470                 475

<210>  160
<211>  229
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Influenza A DMAb

<400>  160

Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser
1               5                   10                  15

Gly Ala Tyr Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
            20                  25                  30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Thr Ser Gln Ser
        35                  40                  45

Leu Ser Ser Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
    50                  55                  60

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
65                  70                  75                  80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
                85                  90                  95

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Arg
            100                 105                 110

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Val Ala Ala Pro
        115                 120                 125

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
    130                 135                 140

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
145                 150                 155                 160
```

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
165 170 175

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Asn
180 185 190

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
195 200 205

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
210 215 220

Asn Arg Gly Glu Cys
225

<210> 161
<211> 477
<212> PRT
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 161

Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
1 5 10 15

Thr His Ala Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys
20 25 30

Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val
35 40 45

Ser Ser Asn Asn Ala Val Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg
50 55 60

Gly Leu Glu Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn
65 70 75 80

Asp Tyr Ala Glu Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr
85 90 95

Ser Lys Asn Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp
100 105 110

Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly His Ile Thr Val Phe Gly
115 120 125

Val Asn Val Asp Ala Phe Asp Met Trp Gly Gln Gly Thr Thr Val Thr

```
    130                 135                 140

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
145                 150                 155                 160

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                165                 170                 175

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
            180                 185                 190

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
        195                 200                 205

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
    210                 215                 220

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
225                 230                 235                 240

Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
                245                 250                 255

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
            260                 265                 270

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        275                 280                 285

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
    290                 295                 300

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
305                 310                 315                 320

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
                325                 330                 335

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            340                 345                 350

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        355                 360                 365

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
    370                 375                 380
```

```
Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
385                 390                 395                 400

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                405                 410                 415

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
            420                 425                 430

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
        435                 440                 445

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
    450                 455                 460

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
465                 470                 475
```

<210> 162
<211> 229
<212> PRT
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 162

```
Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser
1               5                   10                  15

Gly Ala Tyr Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
            20                  25                  30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Thr Ser Gln Ser
        35                  40                  45

Leu Ser Ser Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
    50                  55                  60

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
65                  70                  75                  80

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
                85                  90                  95

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Arg
            100                 105                 110

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Val Ala Ala Pro
```

115 120 125

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
130 135 140

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
145 150 155 160

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
165 170 175

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Asn
180 185 190

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
195 200 205

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
210 215 220

Asn Arg Gly Glu Cys
225

<210> 163
<211> 2211
<212> DNA
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 163
atggattgga cttggaggat tctgtttctg gtcgccgccg ctactggaac tcacgctcag 60

gtgcagctgc agcagtctgg acccggactg gtgaagcctt cacagactct gagcctgacc 120

tgcgccatct ccggcgactc tgtgagctcc aacaatgctg tctggaactg gattagacag 180

tccccatctc gggggctgga atggctggga cgaacatact ataggagcaa atggtacaat 240

gactatgctg agagtgtgaa gtcacgaatc acaattaacc cagatactag caagaatcag 300

ttctccctgc agctgaactc tgtgacaccc gaggatactg cagtctacta ttgcgcacgc 360

tccggacaca tcaccgtgtt cggagtcaat gtggacgcct ttgatatgtg gggacagggg 420

accacagtca cagtgtctag tgcaagtact aaaggcccat cagtgtttcc cctggccccc 480

tcaagcaaga gtacctcagg cggaacagcc gctctgggat gtctggtgaa ggactacttc 540

cctgagccag tcaccgtgag ctggaactcc ggagctctga ccagcggggt gcatacattt 600

cctgcagtcc tgcagtcctc tggcctgtac agcctgagtt cagtggtcac cgtgccaagc 660

tcctctctgg gaacacagac ttatatctgc aacgtgaatc acaaaccatc caatacaaag 720

gtcgacaaga aagtggaacc caaatcttgt gataagaccc atacatgccc tccctgtcca 780

gcacctgagc tgctgggcgg cccatccgtg ttcctgtttc cacccaagcc taaagacaca 840

ctgatgatta gccggactcc cgaagtgacc tgcgtggtcg tggacgtgag ccacgaggac 900

cccgaagtga agttcaactg gtacgtggat ggcgtcgagg tgcataatgc caagaccaaa 960

cctagggagg aacagtacaa cagcacttat agagtcgtgt ccgtcctgac cgtgctgcac 1020

caggattggc tgaacgggaa ggagtataag tgcaaagtgt ccaacaaggc cctgccagct 1080

cccatcgaga agaccatttc taaggccaaa ggccagccac gggaacccca ggtgtacaca 1140

ctgcctccaa gccgcgacga gctgaccaaa aaccaggtga gcctgacatg tctggtcaag 1200

ggattctatc ctagtgatat cgctgtggag tgggaatcta atgggcagcc agaaaacaat 1260

tacaagacta cccctcccgt gctggactct gatggaagtt tctttctgta ttcaaaactg 1320

accgtggaca agagccgctg gcagcagggg aacgtcttta gctgctccgt gatgcacgag 1380

gccctgcaca atcattacac tcagaaatct ctgagtctgt cacccggaaa acgaggacga 1440

aagaggagaa gcggctccgg agctaccaac ttctccctgc tgaagcaggc aggggatgtg 1500

gaggaaaatc ctggcccaat ggtcctgcag acacaggtgt ttatctctct gctgctgtgg 1560

attagtggcg cttacggaga catccagatg actcagtctc ctagttcact gtctgcaagt 1620

gtcggcgatc gcgtgactat tacctgtcga acctcacaga gcctgagctc ctacctgcat 1680

tggtatcagc agaagcctgg gaaagcacca aagctgctga tctatgcagc ctctagtctg 1740

cagtccggcg tgccctctag gttctccggg tctggcagtg gaactgactt tacactgact 1800

atttcaagcc tgcagcctga ggatttcgct acctactatt gccagcagag cagaactttt 1860

gggcagggca ccaaagtcga aatcaagaca gtggctgcac catccgtctt catttttcca 1920

ccctctgacg agcagctgaa gagtggaact gcctcagtgg tgtgcctgct gaacaatttc 1980

taccccccggg aagccaaagt ccagtggaag gtggataacg ctctgcagtc aggcaatagc 2040

caggagtccg tgacagaaca ggactctaaa gatagtactt attcactgag caacaccctg 2100

acactgagca aggcagacta cgagaagcac aaagtgtatg cctgcgaagt gacccaccag 2160

gggctgagca gtccagtgac caaatctttc aacaggggag aatgttgata a 2211

<210> 164
<211> 2241
<212> DNA
<213> Artificial Sequence

<220>
<223> Influenza B DMAb

<400> 164
atggactgga cttggaggat tctgtttctg gtggccgccg caactggcac tcatgccgag 60

gtgcagctgg tggaatcagg gggaggactg gtgaagcctg gcggatcact gcgactgagc 120

tgcgcagctt ccggactgac cttcctgaac gcttggatga gctgggtgcg acaggcacca 180

gggaaaggcc tggaatgggt cgggcgcatc aagagcaata cagacggcgg aaccacagat 240

tacgcagccc ccgtgaaagg caggttcacc atttctcggg acgatagtaa gaacacactg 300

tatctgcaga tgagctccct gaaaaccgag gacacagccg tgtactattg cactaccgat 360

ggcccctaca gcgacgattt ccgctccgga tatgctgcac ggtaccgcta ttttgggatg 420

gacgtgtggg gacaggggac aactgtcaca gtgtctagtg catctactaa gggacctagc 480

gtgttcccac tggcccctc aagcaaatca actagcggag ggaccgccgc tctgggatgt 540

ctggtgaagg attacttccc cgagcctgtc accgtgagct ggaactccgg ggccctgacc 600

tccggagtgc acacatttcc tgctgtcctg cagtcctctg ggctgtactc tctgagttca 660

gtggtcacag tgccaagctc ctctctgggc actcagacct atatctgcaa cgtgaatcac 720

aaacctagca atactaaggt cgacaagaaa gtggaaccaa aaagctgtga taagacacat 780

acttgccctc cctgtccagc tccagagctg ctgggcggac catccgtgtt cctgtttcca 840

cccaagccca aagacaccct gatgatttcc cggacaccag aagtgacttg cgtggtcgtg 900

gacgtgagcc acgaggaccc cgaagtgaag ttcaactggt acgtggatgg cgtcgaggtg 960

cataatgcca agacaaaacc cagggaggaa cagtacaact caacttatag agtcgtgagc 1020

gtcctgaccg tgctgcacca ggactggctg aacggcaagg agtataagtg caaagtgagc 1080

aacaaggccc tgcctgctcc aatcgagaag actattagca aggctaaagg acagcctcgg 1140

gaaccacagg tgtacaccct gcctccatcc cgcgacgagc tgaccaaaaa ccaggtgtct 1200

ctgacatgtc tggtcaaggg cttctatccc tctgatatcg ccgtggagtg ggaaagtaat 1260

ggacagcctg aaaacaatta caagaccaca ccccctgtgc tggactctga tggcagtttc 1320

tttctgtata gtaaactgac cgtggacaag tcaagatggc agcagggaaa cgtgttttcc 1380

tgctctgtca tgcatgaggc cctgcacaat cattacaccc agaagagtct gtcactgagc 1440

ccaggaaaac gagggaggaa gaggagatcc ggctctggag ccacaaactt ctccctgctg 1500

aagcaggctg gagacgtgga ggaaaatccc gggcctatgg tgctgcagac ccaggtcttt 1560

atctccctgc tgctgtggat ttctggcgct tacggagata tccagatgac acagtctccc 1620

agttcagtca gtgcatcagt gggcgaccgc gtcaccatca catgtcgagc atcacaggat 1680

attagcacct ggctggcctg gtaccagcag aagcccggaa aagctcctaa gctgctgatc 1740

tatgcagcca gctccctgca gtccggagtg ccctctaggt tcagcgggtc cggctctgga 1800

acagacttta ctctgaccat ttctagtctg cagcctgagg atttcgcaac ttactattgc 1860

cagcaggcca acagcttccc acccactttt gggcagggca ccaaactgga aatcaagact 1920

gtggctgcac ctagcgtctt catttttcct ccatccgacg agcagctgaa gagtggcacc 1980

gcctcagtgg tgtgcctgct gaacaacttc tacccaagag aagcaaaagt gcagtggaag 2040

gtcgataacg ccctgcagtc aggcaatagc caggagtccg tgacagaaca ggactctaag 2100

gatagtactt atagtctgtc aaatacactg actctgagca aagctgacta cgagaagcat 2160

aaagtgtatg catgcgaggt cactcaccag ggactgtctt cacccgtcac caaatctttc 2220

aatagaggag aatgctgata a 2241

<210> 165
<211> 2214
<212> DNA
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 165
atggactgga catggagaat cctgttcctg gtcgccgccg ctactgggac tcacgcagaa 60

gtgcagctgg tcgaatcagg gcctgggctg gtgaagccct cagacatcct gagcctgacc 120

tgcgccgtgt ctggctacag tatcagctcc aactactatt ggggatggat tcggcagccc 180

cctggcaagg gactggaatg gatcgggtcc atctaccact caggcagcac ctactataaa 240

ccttcactgg agagccgcct gggaatttcc gtggacacat ctaagaatca gttcagcctg 300

aaactgtcct ttgtctctgc cgctgatact gcagtgtact attgcgcccg acatgtcagg 360

tccggctacc cagacaccgc ttactatttt gataagtggg ggcagggcac cctggtcaca 420

gtgtctagtg ctagcaccaa gggcccctcc gtgttccctc tggcaccatc aagcaaatcc 480

acatctggcg gaactgcagc cctgggatgt ctggtgaagg attacttccc agagcccgtc 540

acagtgagtt ggaactcagg cgcactgact tctggagtcc acacctttcc cgccgtgctg 600

cagtcctctg gcctgtacag cctgagttca gtggtcacag tgcctagctc ctctctggga 660

actcagacct atatctgcaa cgtgaatcac aagccctcaa atactaaagt cgacaagaaa 720

gtggaaccta agtcttgtga taaaacacat acttgcccac catgtcctgc accagagctg 780

ctgggaggac caagcgtgtt cctgtttcct ccaaagccca aagacaccct gatgatctcc 840

agaaccctg aagtgacatg tgtggtcgtg gacgtctctc acgaggaccc cgaagtcaag 900

tttaactggt acgtggatgg cgtcgaggtg cataatgcta agacaaaacc ccgcgaggaa 960

cagtacaact caacctatcg agtcgtgagc gtcctgacag tgctgcacca ggactggctg 1020

aacggaaagg agtataagtg caaagtgagc aataaggcac tgcccgcccc tatcgagaaa 1080

actatttcca aggctaaagg gcagcccagg gaacctcagg tgtacaccct gccccttct 1140

agagacgagc tgacaaagaa ccaggtcagt ctgacttgtc tggtgaaagg attttatcca 1200

agtgatatcg cagtggagtg ggaatcaaat gggcagcccg aaaacaatta caagaccaca 1260

ccacccgtgc tggacagcga tggcagcttc ttcctgtatt ccaagctgac cgtggacaaa 1320

tctcggtggc agcaggggaa cgtcttcagt tgctcagtga tgcacgaggc cctgcacaat 1380

cattacaccc agaagagcct gtccctgtct ccaggcaagc ggggacgcaa aaggagaagt 1440

ggatcagggg ccacaaactt ttccctgctg aaacaggctg gagatgtgga ggaaaatcca 1500

gggcccatgg tcctgcagac tcaggtgttc atcagcctgc tgctgtggat ttctggggcc 1560

tacggcagtt atgtgctgac acagcctcca agcgtctccg tggctcctgg cgaaactgca 1620

cgaatctcct gtggagggaa caatattggg actaaggtgc tgcattggta ccagcagacc 1680

ccaggacagg ctccagtgct ggtcgtgtat gacgatagtg acagaccttc aggcatcccc 1740

gagcggttct ctggaagtaa ctcagggaat accgccacac tgactatttc ccgcgtcgaa 1800

gtgggcgacg aagctgatta ctattgccaa gtgtgggaca tctctaccga tcaggccgtc 1860

ttcggcggag ggactaagct gaccgtgctg ggccagccca aagctgcacc ttccgtgaca 1920

ctgtttcccc ctagttcaga ggaactgcag gctaacaagg caaccctggt gtgtctgatt 1980

agcgacttct acccaggagc agtcacagtg gcatggaagg ctgatagctc ccctgtcaaa 2040

gccggcgtgg aaactaccac accatctaag cagagtaaca acaagtacgc cgcttctagt 2100

tatctgagcc tgacacctga gcagtggaag tcccacagga gctattcctg ccaagtgact 2160

catgagggca gtactgtcga aaaaaccgtg gccccaacag agtgtagctg ataa 2214

<210> 166
<211> 2238
<212> DNA
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 166
atggactgga cttggaggat tctgtttctg gtcgccgccg ctactgggac acacgctcag 60

gtgcagctgg tcgagagtgg ggggggagtg gtccagccag ggcgatctct gaggctgagt 120

tgcgccgctt caggcttcac cttcagcact tacgcaatgc actgggtgcg gcaggctcca 180

ggaaagggac tggagtgggt cgccgtgatc tcttacgacg ctaactataa gtactatgca 240

gatagtgtga aaggcagatt caccattagc cgggacaact ccaagaatac actgtacctg 300

cagatgaatt ccctgcgagc agaagacacc gccgtgtact attgcgccaa agattctcag 360

ctgcgcagtc tgctgtattt cgagtggctg tctcaggggt actttgacta ttggggccag 420

ggaaccctgg tcacagtgag ctccgccagt accaagggcc catcagtgtt tcctctggct 480

ccatctagta aatctacaag tggcggaact gcagccctgg gctgtctggt gaaggattac 540

ttcccagagc ccgtcacagt gtcctggaac tctggagctc tgacttccgg ggtgcatacc 600

tttcctgcag tcctgcagtc aagcgggctg tactctctgt cctctgtggt caccgtgcca 660

agttcaagcc tgggcactca gacctatatc tgcaacgtga atcacaagcc ttccaataca 720
aaagtcgaca agaaagtgga accaaagtct tgtgataaaa cacatacttg ccccccttgt 780
cctgctccag agctgctggg aggaccaagc gtgttcctgt ttccacccaa gcccaaagac 840
accctgatga ttagcaggac cccagaagtg acatgtgtgg tcgtggacgt cagccacgag 900
gaccccgaag tgaagttcaa ctggtacgtg gatggcgtcg aggtgcataa tgccaagaca 960
aaacctaggg aggaacagta caacagcact tatagagtcg tgtccgtcct gaccgtgctg 1020
caccaggact ggctgaacgg aaaggagtat aagtgcaaag tgtccaataa ggccctgccc 1080
gctcctatcg agaaaaccat ttctaaggct aaagggcagc cccgggaacc tcaggtgtac 1140
acactgcctc caagccgcga cgagctgacc aagaaccagg tgtccctgac atgtctggtc 1200
aaaggcttct atcccagtga tatcgccgtg gagtgggaat caaatggaca gcctgaaaac 1260
aattacaaga ccacaccccc tgtgctggac agtgatggct cattctttct gtattcaaag 1320
ctgaccgtgg acaaaagccg gtggcagcag ggaaacgtct tttcatgcag cgtgatgcat 1380
gaggctctgc acaatcatta cactcagaag tccctgtctc tgagtcccgg caagcgggga 1440
cgcaaaagga gatcagggag cggcgctaca aacttctccc tgctgaagca ggcaggcgat 1500
gtggaggaaa atccaggacc catggtcctg cagacacagg tgtttatctc tctgctgctg 1560
tggattagtg gggcctatgg cgacatcgtg atgactcaga gccctgattc cctggcagtg 1620
agcctgggag agcgagcaac aattaactgt aagtcctctc agagcgtgac tttcaactac 1680
aaaaattatc tggcatggta ccagcagaag cccggacagc cacccaaact gctgatctat 1740
tgggcctcaa ctcgcgaaag cggggtgcct gaccgattct ccggatctgg gagtggcacc 1800
gattttaccc tgacaattag ttcactgcag gctgaggacg tcgcagtgta ctattgccag 1860
cagcactaca ggactcctcc aaccttcgga caggggacaa aggtcgaaat caaaactgtg 1920
gctgcacctt ccgtcttcat ttttccccct tctgacgagc agctgaagtc cggcaccgcc 1980
tctgtcgtgt gtctgctgaa caatttttac ccaagagaag ccaaggtcca gtggaaagtg 2040
gataacgctc tgcagtctgg aaatagtcag gagtcagtga cagaacagga cagcaaggat 2100
tccacttatt cactgagcaa cactctgacc ctgagcaaag cagattacga gaagcacaaa 2160
gtgtatgcct gcgaagtcac tcatcaggga ctgagctccc ccgtgaccaa gagctttaat 2220
agaggggagt gttgataa 2238

<210> 167
<211> 1437
<212> DNA
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 167
atggattgga cttggaggat tctgtttctg gtcgccgccg ctactggaac tcacgctcag 60

gtgcagctgc agcagtctgg acccggactg gtgaagcctt cacagactct gagcctgacc 120

tgcgccatct ccggcgactc tgtgagctcc aacaatgctg tctggaactg gattagacag 180

tccccatctc gggggctgga atggctggga cgaacatact ataggagcaa atggtacaat 240

gactatgctg agagtgtgaa gtcacgaatc acaattaacc cagatactag caagaatcag 300

ttctccctgc agctgaactc tgtgacaccc gaggatactg cagtctacta ttgcgcacgc 360

tccggacaca tcaccgtgtt cggagtcaat gtggacgcct ttgatatgtg gggacagggg 420

accacagtca cagtgtctag tgcaagtact aaaggcccat cagtgtttcc cctggccct 480

tcaagcaaga gtacctcagg cggaacagcc gctctgggat gtctggtgaa ggactacttc 540

cctgagccag tcaccgtgag ctggaactcc ggagctctga ccagcggggt gcatacattt 600

cctgcagtcc tgcagtcctc tggcctgtac agcctgagtt cagtggtcac cgtgccaagc 660

tcctctctgg gaacacagac ttatatctgc aacgtgaatc acaaaccatc caatacaaag 720

gtcgacaaga aagtggaacc caaatcttgt gataagaccc atacatgccc tccctgtcca 780

gcacctgagc tgctgggcgg cccatccgtg ttcctgtttc cacccaagcc taaagacaca 840

ctgatgatta gccggactcc cgaagtgacc tgcgtggtcg tggacgtgag ccacgaggac 900

cccgaagtga agttcaactg gtacgtggat ggcgtcgagg tgcataatgc caagaccaaa 960

cctagggagg aacagtacaa cagcacttat agagtcgtgt ccgtcctgac cgtgctgcac 1020

caggattggc tgaacgggaa ggagtataag tgcaaagtgt ccaacaaggc cctgccagct 1080

cccatcgaga agaccatttc taaggccaaa ggccagccac gggaacccca ggtgtacaca 1140

ctgcctccaa gccgcgacga gctgaccaaa aaccaggtga gcctgacatg tctggtcaag 1200

ggattctatc ctagtgatat cgctgtggag tgggaatcta atgggcagcc agaaaacaat 1260

tacaagacta cccctcccgt gctggactct gatggaagtt tctttctgta ttcaaaactg 1320

accgtggaca agagccgctg gcagcagggg aacgtcttta gctgctccgt gatgcacgag 1380

gccctgcaca atcattacac tcagaaatct ctgagtctgt cacccggaaa atgataa 1437

<210> 168
<211> 693
<212> DNA
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 168
atggtcctgc agacacaggt gtttatctct ctgctgctgt ggattagtgg cgcttacgga 60

gacatccaga tgactcagtc tcctagttca ctgtctgcaa gtgtcggcga tcgcgtgact 120

attacctgtc gaacctcaca gagcctgagc tcctacctgc attggtatca gcagaagcct 180

gggaaagcac caaagctgct gatctatgca gcctctagtc tgcagtccgg cgtgccctct 240

aggttctccg ggtctggcag tggaactgac tttacactga ctatttcaag cctgcagcct 300

gaggatttcg ctacctacta ttgccagcag agcagaactt ttgggcaggg caccaaagtc 360

gaaatcaaga cagtggctgc accatccgtc ttcatttttc caccctctga cgagcagctg 420

aagagtggaa ctgcctcagt ggtgtgcctg ctgaacaatt tctacccccg ggaagccaaa 480

gtccagtgga aggtggataa cgctctgcag tcaggcaata gccaggagtc cgtgacagaa 540

caggactcta aagatagtac ttattcactg agcaacaccc tgacactgag caaggcagac 600

tacgagaagc acaaagtgta tgcctgcgaa gtgacccacc aggggctgag cagtccagtg 660

accaaatctt tcaacagggg agaatgttga taa 693

<210> 169
<211> 1437
<212> DNA
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 169
atggattgga catggaggat tctgtttctg gtcgccgccg caactggaac tcacgctcag 60

gtgcagctgc agcagtcagg gcctggcctg gtgaagccca gccagaccct gtccctgaca 120

tgcgccatct ccggcgactc tgtgagctcc aacaatgccg tgtggaactg gatcaggcag 180

tccccttctc gcggcctgga gtggctggga aggacctact atagaagcaa gtggtacaat 240

gactatgccg agagcgtgaa gtccaggatc accatcaacc cagatacatc taagaatcag 300

ttcagcctgc agctgaactc cgtgaccccc gaggatacag ccgtgtacta ttgcgccaga 360

tccggccaca tcaccgtgtt cggcgtgaat gtggacgcct ttgatatgtg gggccagggc 420

accacagtga ccgtgtctag cgcctctaca aagggcccaa gcgtgtttcc actggcaccc 480

tcctctaaga gcacctccgg cggcacagcc gccctgggct gtctggtgaa ggactacttc 540

ccagagcccg tgaccgtgtc ttggaacagc ggcgccctga ccagcggagt gcacacattt 600

cctgccgtgc tgcagagctc cggcctgtac tccctgtcta gcgtggtgac cgtgccatcc 660

tctagcctgg gcacccagac atatatctgc aacgtgaatc acaagccaag caatacaaag 720

gtggacaaga aggtggagcc caagtcctgt gataagaccc acacatgccc tccctgtcct 780

gcaccagagc tgctgggcgg cccaagcgtg ttcctgtttc cacccaagcc taaggacacc 840

ctgatgatct ctcggacccc cgaggtgaca tgcgtggtgg tggacgtgag ccacgaggac 900

cccgaggtga agttcaactg gtacgtggat ggcgtggagg tgcacaatgc caagacaaag 960

cctagggagg agcagtacaa ctccacctat agagtggtgt ctgtgctgac agtgctgcac 1020

caggattggc tgaacggcaa ggagtataag tgcaaggtgt ccaataaggc cctgcccgcc 1080

cctatcgaga agaccatctc taaggcaaag ggacagcctc gggagccaca ggtgtacaca 1140

ctgcctccat cccgcgacga gctgaccaag aaccaggtgt ctctgacatg tctggtgaag 1200

ggcttctatc cttctgatat cgccgtggag tgggagagca atggccagcc agagaacaat 1260

tacaagacca cacccctgt gctggactcc gatggctctt tctttctgta tagcaagctg 1320

accgtggaca agtcccgctg gcagcagggc aacgtgtttt cttgtagcgt gatgcacgaa 1380

gcactgcaca accattacac ccagaagtca ctgtcactgt ccccaggaaa atgataa 1437

<210> 170
<211> 693
<212> DNA
<213> Artificial Sequence

<220>
<223> Influenza A DMAb

<400> 170
atggtgctgc agacccaggt gtttatttcc ctgctgctgt ggattagcgg cgcatacggc 60

gacattcaga tgactcagag cccttcaagc ctgtccgcct ctgtgggcga cagggtgacc 120

atcacatgca gaaccagcca gtccctgagc tcctacctgc actggtatca gcagaagcca 180

ggcaaggccc ccaagctgct gatctacgca gcctctagcc tgcagagcgg cgtgccttcc 240

cggttctctg gcagcggctc cggcaccgac tttaccctga caatctcctc tctgcagcca 300

gaggatttcg ccacatacta ttgccagcag tcccgcacct ttggccaggg cacaaaggtg 360

gagatcaaga ccgtggccgc cccctccgtg ttcatctttc ccccttctga cgagcagctg 420

aagtctggca cagccagcgt ggtgtgcctg ctgaacaatt tctaccctag ggaggccaag 480

gtgcagtgga aggtggataa cgccctgcag tccggcaatt ctcaggagag cgtgaccgag 540

caggactcca aggattctac atattctctg agcaacaccc tgacactgag caaggccgat 600

tacgagaagc acaaggtgta tgcctgtgag gtcactcacc aggggctgtc atcacccgtc 660

accaaatcct ttaatagggg agaatgttga taa 693

<210> 171
<211> 47
<212> PRT
<213> Artificial Sequence

<220>
<223> amyloid beta (X-Y) peptide

<400> 171

Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys
1 5 10 15

```
Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
            20                  25                  30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Val Ile Val Ile
        35                  40                  45
```