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(71) **Applicant**: **DUKE UNIVERSITY** [US/US]; 2812 Erwin Road, Suite 306, Durham, NC 27705 (US).

(72) **Inventors**: **HAYNES, Barton, F.**; C/o Duke University, 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). **LIAO, Hua-xin**; C/o Duke University, 2812 Erwin Road, Suite 306, Durham, NC 27705 (US). **GAO, Feng**; C/o Duke University, 2812 Erwin Road, Suite 306, Durham, NC 27705 (US).

(74) **Agents**: **WILLIAM, Kim W** et al.; Wilmer Cutler Pickering Hale And Dorr LLP, 60 State Street, Boston, MA 02109 (US).

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(54) **Title**: COMPOSITIONS COMPRISING CH505 SENSITIVE ENVELOPES

(57) **Abstract**:

Compositions comprising CH505 sensitive envelopes

[0001] This application claims the benefit of priority of U.S. Application Serial No. 62/027,427 filed July 22, 2014, the content of which application is herein incorporated by reference in its entirety.

[0002] This invention was made with government support under Center for HIV/AIDS Vaccine Immunology-Immunogen Design grant UM1-AI100645 from the NIH, NIAID, Division of AIDS. The government has certain rights in the invention.

FIELD OF THE INVENTION

[0003] The present invention relates in general, to a composition suitable for use in inducing anti-HIV-1 antibodies, and, in particular, to immunogenic compositions comprising envelope proteins and nucleic acids to induce cross-reactive neutralizing antibodies and increase their breadth of coverage. The invention also relates to methods of inducing such broadly neutralizing anti-HIV-1 antibodies using such compositions.

BACKGROUND

[0004] The development of a safe and effective HIV-1 vaccine is one of the highest priorities of the scientific community working on the HIV-1 epidemic. While anti-retroviral treatment (ART) has dramatically prolonged the lives of HIV-1 infected patients, ART is not routinely available in developing countries.

SUMMARY OF THE INVENTION

[0005] In certain aspects, the invention provides compositions comprising any one of the sequences of Figures 18-23 and Figures 24A-24B, or a combination thereof. In certain embodiments, the compositions comprise a variant of these sequence, for example but not limited to gp160, gp140 (cleaved or uncleaved), gp145, gp150, gp120, N-terminal deletion variants.

[0006] In certain embodiments, the HIV-1 envelopes of the invention are provided as nucleic acid sequences, including but not limited to nucleic acids optimized for expression in the desired vector and/or host cell. In other embodiments, the HIV-1 envelopes are provided as recombinantly expressed protein.

[0007] In certain aspects, the invention provides a composition comprising nucleic acids encoding 703010505.TF, 703010505.W4.03, 703010505.W4.26, 703010505.W14.21, 703010505.W20.14,

703010505.W30.28, 703010505.W30.13, 703010505.W53.31, 703010505.W78.15, and 703010505.W100.B4. In certain embodiments, the composition further comprises any one of 703010505.W14.3, 703010505.W14.8, 703010505.W20.7, 703010505.W20.26, 703010505.W20.9, 703010505.W30.12, 703010505.W30.19, 703010505.W53.19, 703010505.W53.13, and 703010505.W78.1, or the combination thereof.

[0008] In certain aspects, the invention provides a method of inducing an immune response in a subject comprising administering a composition comprising any one of the HIV-1 envelopes described herein. In certain embodiments, the induced immune response comprises CD4 binding site antibodies. In certain aspects, the invention provides a method of inducing an immune response in a subject comprising administering a composition comprising HIV-1 envelope T/F, w004.03 and/or w004.26 in an amount sufficient to induce an immune response. In certain embodiments, the method further comprises administering a composition of any one of the HIV-1 envelopes 703010505.W14.21, 703010505.W20.14, 703010505.W30.28, 703010505.W30.13, 703010505.W53.31, 703010505.W78.15, and 703010505.W100.B4, or any combination thereof in an amount sufficient to induce an immune response. In certain embodiments, the method further comprises administering a composition comprising any one of the HIV-1 envelopes 703010505.W14.3, 703010505.W14.8, 703010505.W20.7, 703010505.W20.26, 703010505.W20.9, 703010505.W30.12, 703010505.W30.19, 703010505.W53.19, 703010505.W53.13, and 703010505.W78.1, or any combination thereof in an amount sufficient to induce an immune response.

[0009] In certain embodiments, the HIV-1 envelopes are administered as a nucleic acid, a protein or any combination thereof. In certain embodiments, the nucleic acid encoding the envelope is operably linked to a promoter inserted in an expression vector. In certain embodiments, the protein is recombinant. In certain embodiments, the envelopes are administered as a prime, a boost, or both. In certain embodiments, the envelopes, or any combinations thereof are administered as a multiple boosts. In certain embodiments, the compositions and method further comprise an adjuvant. In certain embodiments, the HIV-1 envelopes are provided as nucleic acid sequences, including but not limited to nucleic acids optimized for expression in the desired vector and/or host cell. In other embodiments, the HIV-1 envelopes are provided as recombinantly expressed protein.

[0010] In certain embodiments, the invention provides compositions and method for induction of immune response, for example cross-reactive (broadly) neutralizing Ab induction. In certain embodiments, the methods use compositions comprising “swarms” of sequentially evolved envelope viruses that occur in the setting of bnAb generation in vivo in HIV-1 infection.

[0011] In certain aspects the invention provides compositions comprising a selection of HIV-1 envelopes or nucleic acids encoding these envelopes, for example but not limited to, as described herein. In certain embodiments, these compositions are used in immunization methods as a prime and/or boost, for example but not limited to, as described herein.

[0012] In certain embodiments, the compositions contemplate nucleic acid, as DNA and/or RNA, or protein immunogens either alone or in any combination. In certain embodiments, the methods contemplate genetic, as DNA and/or RNA, immunization either alone or in combination with envelope protein(s).

[0013] In certain embodiments the nucleic acid encoding an envelope is operably linked to a promoter inserted in an expression vector. In certain aspects the compositions comprise a suitable carrier. In certain aspects the compositions comprise a suitable adjuvant.

[0014] In certain embodiments the induced immune response includes induction of antibodies, including but not limited to autologous and/or cross-reactive (broadly) neutralizing antibodies against HIV-1 envelope. Various assays that analyze whether an immunogenic composition induces an immune response, and the type of antibodies induced are known in the art and are also described herein (e.g. Example 1).

[0015] In certain aspects the invention provides an expression vector comprising any of the nucleic acid sequences of the invention, wherein the nucleic acid is operably linked to a promoter. In certain aspects the invention provides an expression vector comprising a nucleic acid sequence encoding any of the polypeptides of the invention, wherein the nucleic acid is operably linked to a promoter. In certain embodiments, the nucleic acids are codon optimized for expression in a mammalian cell, in vivo or in vitro. In certain aspects the invention provides nucleic acid comprising any one of the nucleic acid sequences of invention. A nucleic acid consisting essentially of any one of the nucleic acid sequences of invention. A nucleic acid consisting of any one of the nucleic acid sequences of invention. In certain embodiments the nucleic acid of invention, is operably linked to a promoter and is inserted in an expression vector. In certain aspects the invention provides an immunogenic composition comprising the expression vector.

[0016] In certain aspects the invention provides a composition comprising at least one of the nucleic acid sequences of the invention. In certain aspects the invention provides a composition comprising any one of the nucleic acid sequences of invention. In certain aspects the invention provides a composition comprising a combination of one nucleic acid sequence encoding any one of the polypeptides of the invention. In certain embodiments, combining DNA and protein gives

higher magnitude of ab responses. See Pissani F. Vaccine 32: 507-13, 2013; Jalah R et al PLoS One 9: e91550, 2014.

[0017] In certain embodiments, the compositions and methods employ an HIV-1 envelope as polypeptide instead of a nucleic acid sequence encoding the HIV-1 envelope. In certain embodiments, the compositions and methods employ an HIV-1 envelope as polypeptide, a nucleic acid sequence encoding the HIV-1 envelope, or a combination thereof. The envelope can be a gp160, gp150, gp140, gp120, gp41, N-terminal deletion variants as described herein, cleavage resistant variants as described herein, or codon optimized sequences thereof. The polypeptide contemplated by the invention can be a polypeptide comprising any one of the polypeptides described herein. The polypeptide contemplated by the invention can be a polypeptide consisting essentially of any one of the polypeptides described herein. The polypeptide contemplated by the invention can be a polypeptide consisting of any one of the polypeptides described herein. In certain embodiments, the polypeptide is recombinantly produced. In certain embodiments, the polypeptides and nucleic acids of the invention are suitable for use as an immunogen, for example to be administered in a human subject.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] To conform to the requirements for PCT patent applications, many of the figures presented herein are black and white representations of images originally created in color. In the below descriptions and the examples, the colored images are described in terms of its appearance in black and white. Different colors are described by different shades of white to gray with an attempt to match the description the descriptions of the color as closely as possible to that of the figures. The original color versions of some of the Figures can be viewed in Gao, et al., *Cooperation of B Cell Lineages in Induction of HIV-1 Broadly Neutralizing Antibodies*, Cell 158: 481-491 (2014) (including the accompanying Supplementary Information). For the purposes of the PCT, contents of Gao, et al. (2014), including the accompanying "Supplementary Information," are herein incorporated by reference.

[0019] **Figure 1 shows neutralization activity of CH103 clonal lineage antibodies against autologous CH505 viruses.** Heat map analysis of neutralization data generated from 124 pseudoviruses (row) and 13 CH103 lineage mAbs (column). The neutralization potency (IC_{50}) is shown in different shades of colors as indicated in the histogram; from white (>50μg/ml) to black (0.079 μg/ml). The Env pseudoviruses were generated for the CH505 T/F virus and variants from weeks 4 – 100 and were all assayed against the unmutated common ancestor (UCA), intermediate

antibodies (IA8-1) and mature bnAbs (CH103-106) in the TZM-bl cell-based neutralization assay. The resistant viruses (shown in brackets along the right side of the data) were defined as those with the average IC_{50} values 1.8 fold higher than that of the T/F pseudoviruses for later IAs (IA3-IA1) and all mature Abs. The week 30 viruses that fully escaped from the early IAs (IA8-IA4) are also indicated by the bracket. See also Table S1; Figure 8 and Figures 11A-11F.

[0020] **Figures 2A-2B show association of insertions in V1 and V5 with neutralization escape from CH103 lineage mAbs.** The V1 (Figure 2A) and V5 (Figure 2B) amino acid sequences at week 30 were compared to the CH505 T/F sequence. The neutralization sensitive viruses to early IAs (IA8-4) and late IAs (IA3-1)/mature CH103 lineage mAbs (CH103-106) are indicated in gray and black, respectively. The potential N-linked glycosylation (PNLG) sites are indicated in light gray. The identical amino acids are shown as dashes and deletions are shown as dots. See also Figure 8 and Figures 9A-9D.

[0021] **Figures 3A-3D show mutations in loop D that rendered the Env mutants more sensitive to CH103 lineage bnAb neutralization with enhanced Env binding. (Figure 3A)** Alignment of nine amino acids (starting at position 275) in loop D of Env is shown. The amino acid sequences from week 4 to week 160 were compared to the CH505 T/F sequence. The number and frequency of each variant in loop D are shown at the right of the alignment. The two asparagines (N) whose side chains interact with the CH103 light chain are indicated in light gray. The loop D mutations that occurred early or predominated are indicated in gray, and Env mutants containing those mutations are indicated by arrows at the right of the alignment. (**Figure 3B**) Neutralization susceptibility of the loop D mutants by the CH103 lineage mAbs. Heatmap analysis was performed for the neutralization data of all CH103 lineage mAbs (column) against the CH505 T/F virus and the loop D variants (row). The neutralization potency (IC_{50}) is shown in different shades of colors as indicated; from white (>50 μg/ml) to black (0.12 μg/ml). (**Figure 3C**) Neutralization activity of the nAb CH235 were compared to that of the bnAb CH103 against the CH505 T/F virus and loop D mutants. (**Figure 3D**) The fold difference in binding to loop D mutant Envs versus the CH505 T/F Env by both CH103 and CH235 lineage Abs. Seven loop D mutant Envs ($M6^{V281A}$, $M10^{V281G}$, $M11^{N279D/V281G}$, $M7^{E275K/N279D/V281S}$, $M8^{N280S/V281A}$, $M9^{E275K/N279D/V281G}$ and $M21^{N280T/V281A}$) and the CH505 T/F Env were serially diluted and the log area under the curve (AUC) values for all members of the CH103 and CH235 lineage mAbs were determined by ELISA. The fold difference in log AUC between each loop D mutant Env versus the CH505 T/F Env is shown. See also Figures 10A-10D, Figures 11A-11F, and Figures 13A-13B; Tables S2, S3 and S6.

[0022] **Figure 4 shows neutralization activity of the CH235 clonal lineage antibodies against autologous CH505 viruses.** Heatmap analysis of neutralization data generated from 41 pseudoviruses (row) and 10 CH235 lineage mAbs (column). The neutralization potency (IC_{50}) is shown in different shades of colors as indicated in the histogram; from white (>50 μg/ml) to black (0.1 μg/ml) (see also Table S4). The CH505 T/F and select variant Env pseudoviruses from each time point (weeks 4-100) were assayed against the unmutated common ancestor (UCA), intermediate antibodies (IA4-1) and mature autologous neutralizing antibodies (CH235, CH236, CH239, CH240 and CH241) in the TZM-bl cell-based neutralization assay. The partially and fully resistant viruses are indicated by the brackets along the right side of the data. See also Figures 12A-12B and Table S4.

[0023] **Figure 5 shows neutralization activity of CH235 clonal lineage antibodies against CH505 Env loop D mutants.** Heat map analysis of neutralization data generated from 10 loop D mutants (row) and 10 CH235 lineage mAbs (column). The neutralization potency (IC_{50}) is shown in different shades of colors as indicated in the histogram; from white (>50 μg/ml) to black (0.1 μg/ml). The CH505 T/F and loop D mutant Env pseudoviruses were assayed against the unmutated common ancestor (UCA), intermediate antibodies (IA4-1) and mature autologous neutralizing antibodies (CH235, CH236, CH239, CH240 and CH241) in the TZM-bl cell-based neutralization assay. The partially and fully resistant viruses are indicated by the brackets on the left side of the data. See also Table S5.

[0024] **Figures 6A-6C show evolutionary mutations in the Loop D and antibody facilitate interactions between gp120 and CH103 lineage antibodies. (Figure 6A)** Model of CH505 T/F gp120 in complex with UCA of CH103. **(Figure 6B)** Model of loop D mutant $M7^{E275K/N279D/V281S}$ gp120 in complex with mature CH103. The gp120 is shown in semi-transparent electrostatic potential surface with gray for negative charge and dark gray for positive charge. The heavy and light chains of the CH103 bnAb are shown in light gray and lighter gray, respectively. All critical mutations in loop D and CDR L2 are highlighted in sticks and colored in different shades of white to black, such as a light shade of gray for residues (279 and 281) in loop D, lighter shade of gray for conserved CDR L2 Lys53, and dark gray for mutated CDR L2 residues 50-52. **(Figure 6C)** Estimated binding affinity change when specified residues were reverted back to the T/F or germline sequences for gp120 and CH103 light chain, respectively. "--" indicates the calculated binding energy was decreased by >1.0 kcal/mol, "-" indicates a decrease by 0.1-1.0 kcal/mol, and "+/-" indicates calculated energies were about the same. Reversion of residues, such as Loop D Asp279 and CDR L2 Tyr52, resulted in weaker binding suggesting that the evolution of both gp120

loop D and CDR L2 of CH103 facilitated the interaction between HIV-1 gp120 and mature CH103 antibodies.

[0025] **Figure 7 shows Schema of Cooperation of B Cell Lineages in Induction of HIV-1 Broadly Neutralizing Antibodies.** The T/F Env (red Env trimer) likely initiated both the CH235 and CH103 lineages by binding to their UCA. The CH235 lineage (dark black), selected viral escape mutations in loop D of the CH505 T/F virus (black Env timer) at week 53. The CH103 lineage gradually accumulated mutations that led to acquisition of bnAb activity as CH103 lineage affinity maturation progressed. The loop D mutant Envs more avidly bound CH103 IAs and mature antibodies than the T/F Env and thus cooperated with the T/F Env to drive CH103 bnAb B cell lineage development.

[0026] **Figure 8 shows Amino acid sequence alignment of regions in the *env* genes used to generate pseudoviruses,** Related to Figures 1 and 2. All sequences are compared to the CH505 T/F Env sequence. Only V1, V4, V5, loop D, CD4-binding loop regions in the *env* gene are shown. The identical amino acids are shown as dashes and deletions are shown as dots.

[0027] **Figures 9A-9D show characterization of the mutations in V1 and V5, Related with Figures 2A and 2B.** (**Figure 9A**) Insertion and extra glycosylation sites in the V1 loop may change the conformation of the V2 loop and therefore cause steric hindrance for CH103 binding. Antibody CH103 was modeled into the BG505-VRC-PG04 complex structure with the V1 loop of the CH103-bound protomer highlighted in dark gray (left). The boxed area was zoomed in to show the relative positions of V1, V2 and the heavy chain of CH103. Even though the V2 is not visible in the current trimeric BG505 structure, it is obvious from the model that V2 is sandwiched between gp120 V1 and CH103 heavy chain. The longer V1 with extra glycans (black dots, the four rightmost dots) in the CH505 variants may push V2 into positions incompatible with CH103 binding. BG505 glycans in V1 were shown in dark gray spheres (the two leftmost spheres). (**Figure 9B**) Sequence alignment of V1 loop of CH505 strains and BG505. Residue positions were marked according to HXB2 numbering. (**Figure 9C**) Loop V5 insertion push loop V5 and glycan at position 461 into possible clashing position with the light chain of CH103 antibodies and confer resistance. The gp120 with Asp-Thr insertion is shown in gray cartoon with Asp-Thr highlighted in dark gray. The likely positions of Asn461 (hence the glycan associated with it) were shown in sticks and colored medium gray. (**Figure 9D**) Resistance to CH103 lineage bnAbs due to a two-amino acid insertion in V5 of the CH505 T/F Env. The M28 mutant contains a 2-amino acid (DT) insertion in the V5 was fully resistant to the UCA and early intermediate antibodies (IA8-IA3) and

more resistant to the late intermediate antibodies (IA3-IA1) and mature antibodies (CH103, CH104, CH105 and CH106). The neutralization potency (IC_{50}; μg/ml) is shown.

[0028] **Figures 10A-10D show characterization of mutations in V4 and loop D, Related to Figures 3A-3D.** (**Figure 10A**) Amino acid alignment of nine amino acids in V4 of Env. The amino acid sequences from weeks 4-14 were compared to the CH505 T/F sequence. The number and frequency of each variant in the region are shown at the right of the alignment. The percentage of the viruses with the identical T/F sequences is shown in the boxed text. The T415K mutation (circled) at week 14 was tested for $CD8^+$ T cell responses. The variants that were tested for neutralization susceptibility to CH103 lineage mAbs are indicated by arrows. (**Figure 10B**) Mutations in V4 were driven by $CD8^+$ T cell response as determined by the ELISpot assay. The $CD8^+$ T cell responses were measured with autologous overlapping peptides that contained both wild type T/F and T425T mutations by the ELISpot assay. The numbers of spots above a threshold of 50 or more per 10^6 cells were considered positive. The CD8 T cell responses recognized the peptides from the CH505 T/F virus but not the mutant peptides. (**Figure 10C**) Similar neutralization susceptibility between the CH505 T/F virus and all V4 mutants. Heat map analysis was performed for the neutralization data of all CH103 lineage bnAbs against the CH505 T/F virus and the V4 variants. The neutralization potency (IC_{50}; μg/ml) is shown by different shades of gray. (**Figure 10D**) The loop D mutants are less fit than the CH505 T/F virus. The infectious molecular clone (IMC) for the CH505 T/F virus was chemically synthesized and cloned in pUC57 as previously described (Salazar-Gonzalez et al., 2009). The loop D mutations were introduced into the CH505 T/F IMC by site-directed mutagenesis. The virus stocks were generated by transfecting the IMCs into 293T cells. The mutant M5 (N279K), M6 (V281A), M7 (E275K, N279D and V281S) or M10 (V281G) each was compared to the CH505 T/F virus. Same amount (5 ng p24) of each compared virus was mixed to infect 10^6 of purified CD4+ T cells in triplicates. The viruses were cultured for five days and the culture supernatant were harvested daily by completely replacing the medium. The percentage of each virus in the inoculum stock and the culture supernatant was determined by parallel allele-specific sequencing (PASS) (Cai et al., 2007; Song et al., 2012). Mean ± standard deviations are shown. The relative fitness was determined by modeling the replication slope of each virus as previously described (Maree et al., 2000; Song et al., 2012). All mutants were less fit than the CH505 T/F virus.

[0029] **Figures 11A-11F show characterization of natural intermediate antibodies of the CH103 bnAb lineage , Related to Figure 1 and Figures 3A-3D.** (**Figure 11A**) Sequence alignment of natural intermediate antibodies of the bnAb CH103 lineage. The intermediate

members (CH186, CH187, CH188 and CH200) of the bnAb CH103 lineage were isolated from cultured memory B cells from the CH505 week 41 post-transmission sample. The V_H amino acid sequences of the bnAb CH103 natural intermediates were aligned to the inferred unmutated common ancestor (UCA), inferred intermediates (IA2, IA3, IA4 and IA8) and mature CH106 sequences as we reported before (Liao et al., 2013a). (**Figure 11B**) Maximum likelihood phylogram showing evolutionary relationships among the inferred intermediates (designated by an initial IA) and observed sequences (initial CH), and the inferred UCA. The dnaml routine of the PHYLIP software package was used for this analysis. All natural intermediate antibody sequences were closer to the inferred UCA than the mature bnAbs (CH103-106). (**Figure 11C**) Neutralization susceptibility of the loop D mutants by the natural intermediate antibodies of the bnAb CH103 lineage. Heatmap analysis was performed for the neutralization data of the bnAb CH103 natural intermediates (column) against the CH505 T/F virus and the loop D variants (row). The neutralization potency (IC_{50}) is shown in different colors as indicated; from white (>5 μg/ml) to black(<0.025 μg/ml). The loop D mutants were generally more sensitive to neutralization by the bnAb CH103 natural intermediates than the CH505 T/F virus. (**Figure 11D**) The fold difference in binding to loop D mutant Envs versus the CH505 T/F Env by the bnAb CH103 natural intermediates. Seven loop D mutant Envs ($M6^{V281A}$, $M10^{V281G}$, $M11^{N279D/V281G}$, $M7^{E275K/N279D/V281S}$, $M8^{N280S/V281A}$, $M9^{E275K/N279D/V281G}$ and $M21^{N280T/V281A}$) and CH505 T/F Env were serially diluted and log AUC binding to the bnAb CH103 natural intermediates were determined by ELISA. The fold difference in log AUC between each loop D mutant Env versus the CH505 T/F Env is shown. Like the mature bnAb CH106, the bnAb CH103 natural intermediates bound the loop D mutant Envs better than the CH505 T/F Env. (**Figure 11E**) Characteristics of the CH103 natural intermediate autologous neutralizing antibodies. The CH186, CH187, CH188 and CH200 intermediate antibody sequences were compared to the inferred UCA and mature CH106 bnAb sequences. The mutation frequencies of the natural intermediate antibodies were similar to those of inferred early intermediates (IA8, IA4 and IA3) as previously reported (Liao et al., 2013a). (**Figure 11F**) Neutralization activity of the CH103 natural intermediate antibodies. Neutralization activity of the natural intermediate antibodies (CH186, CH187, CH188 and CH200) of the CH103 bnAb lineage and the mature CH106 bnAb was determined against the autologous transmitted/founder virus (CH505.T/F) and 10 heterologous viruses in the pseudovirus neutralization assay using TZM-bl cells. Antibodies were serially diluted, starting at 50 μg/ml. Results are expressed as the half maximal inhibitory concentration (IC_{50}, μg/ml). Murine Leukemia Virus (MLV-SVA) served as a negative control. While CH106 displayed neutralization breadth, the natural intermediate

antibodies of the CH103 bnAb lineage only neutralized the autologous transmitted/founder virus, similar to the inferred intermediate antibodies of CH103.

[0030] **Figures 12A-12B show the phylogenetic tree of the CH235 lineage antibodies and inference of UCA and intermediate antibodies, Related to Figure 4. (Figure 12A)** The maximum likelihood phylogenetic tree was constructed with six members (CH235, Ch236, CH239, CH240 and CH241) of the CH235 antibody lineage. The unmutated common ancestor (UCA), and intermediate antibodies (IA) (indicated at each node) were inferred using methods as previously described (Kepler, 2013). **(Figure 12B)** Characteristics of the UCA, intermediate antibodies (IA4-IA1) and the mature antibodies (CH235, CH236, CH239, Ch240 and CH241) in the CH235 clonal lineage.

[0031] **Figures 13A-13B show binding of antibody members in the CH103 and CH235 lineages to the CH505 T/F and loop D mutant Envs, Related to Figures 3A-3D.** The UCA, intermediate antibody (IA) members from the CH103 **(Figure 13A)** and CH235 **(Figure 13B)** clonal lineages at concentrations ranging from 100 μg/ml to 0.0006 μg/ml were tested by ELISA for binding to the CH505 T/F and loop D mutant Envs. Shown are the data expressed as a log number of the area under a curve (AUC) in the y axis for the binding of individual antibodies on the x axis to the indicated CH505 T/F and loop D mutant Envs.

[0032] **Figures 14A-14E show neutralization activity of CH103 clonal lineage antibodies against autologous CH505 viruses, Related to Figure 1.** Values are the concentrations (μg/ml) of antibodies required for the 50% inhibition (IC_{50}).

[0033] **Figure15 shows neutralization susceptibility of the CH505 loop D mutants to CH103 lineage antibodies, Related to Figures 3A-3D.** Values are the concentrations (μg/ml) of antibodies required for the 50% inhibition (IC_{50}).

[0034] **Figure 16 shows neutralization activity of CH235 clonal lineage antibodies against autologous CH505 viruses, Related to Figure 4.** Values are the concentrations (μg/ml) of antibodies required for the 50% inhibition (IC_{50}).

[0035] **Figure 17 shows neutralization susceptibility of CH505 loop D mutants to CH235 lineage antibodies, Related to Figure 5.** Values are the concentrations (μg/ml) of antibodies required for the 50% inhibition (IC_{50}).

[0036] **Figure 18** shows nucleic acid sequences (gp160) of CH505 envelopes ("first ten envelopes").

[0037] **Figure 19** shows amino acid sequences (gp160) of CH505 envelopes (first ten envelopes).

[0038] **Figure 20** shows nucleic acid sequences (gp160) of CH505 envelopes ("second ten envelopes").

[0039] **Figure 21** shows amino acid sequences (gp160) of CH505 envelopes (second ten envelopes).

[0040] **Figure 22** shows sequence comparison of CH505 envelopes.

[0041] **Figure 23** shows sequence comparison of D loop mutant variants.

[0042] **Figure 24A** shows amino acid sequences of D loop mutant variants.

[0043] **Figure 24B** shows nucleic acid sequences of D loop mutant variants.

DETAILED DESCRIPTION

[0044] The development of a safe, highly efficacious prophylactic HIV-1 vaccine is of paramount importance for the control and prevention of HIV-1 infection. A major goal of HIV-1 vaccine development is the induction of broadly neutralizing antibodies (bnAbs) (Immunol. Rev. 254: 225-244, 2013). BnAbs are protective in rhesus macaques against SHIV challenge, but as yet, are not induced by current vaccines.

[0045] For the past 25 years, the HIV vaccine development field has used single or prime boost heterologous Envs as immunogens, but to date has not found a regimen to induce high levels of bnAbs.

[0046] Recently, a new paradigm for design of strategies for induction of broadly neutralizing antibodies was introduced, that of B cell lineage immunogen design (Nature Biotech. 30: 423, 2012) in which the induction of bnAb lineages is recreated. It was recently demonstrated the power of mapping the co-evolution of bnAbs and founder virus for elucidating the Env evolution pathways that lead to bnAb induction (Nature 496: 469, 2013). From this type of work has come the hypothesis that bnAb induction will require a selection of antigens to recreate the "swarms" of sequentially evolved viruses that occur in the setting of bnAb generation in vivo in HIV infection (Nature 496: 469, 2013).

[0047] A critical question is why the CH505 immunogens are better than other immunogens. This rationale comes from three recent observations. First, a series of immunizations of single putatively "optimized" or "native" trimers when used as an immunogen have not induced bnAbs as single immunogens. Second, in all the chronically infected individuals who do develop bnAbs, they develop them in plasma after ~2 years. When these individuals have been studied at the time soon after transmission, they do not make bnAbs immediately. Third, now that individual's virus and bnAb co-evolution has been mapped from the time of transmission to the development of

bnAbs, the identification of the specific Envs that lead to bnAb development have been identified-thus taking the guess work out of env choice.

[0048] Two other considerations are important. The first is that for the CH103 bnAb CD4 binding site lineage, the VH4-59 and Vλ3-1 genes are common as are the VDJ, VJ recombinations of the lineage (Liao, Nature 496: 469, 2013). In addition, the bnAb sites are so unusual, we are finding that the same VH and VL usage is recurring in multiple individuals. Thus, we can expect the CH505 Envs to induce CD4 binding site antibodies in many different individuals.

[0049] Finally, regarding the choice of gp120 vs. gp160, for the genetic immunization we would normally not even consider not using gp160. However, in acute infection, gp41 non-neutralizing antibodies are dominant and overwhelm gp120 responses (Tomaras, G et al. J. Virol. 82: 12449, 2008; Liao, HX et al. JEM 208: 2237, 2011). Recently we have found that the HVTN 505 DNA prime, rAd5 vaccine trial that utilized gp140 as an immunogen, also had the dominant response of non-neutralizing gp41 antibodies. Thus, we will evaluate early on the use of gp160 vs gp120 for gp41 dominance.

[0050] In certain aspects the invention provides a strategy for induction of bnAbs is to select and develop immunogens designed to recreate the antigenic evolution of Envs that occur when bnAbs do develop in the context of infection.

[0051] That broadly neutralizing antibodies (bnAbs) occur in nearly all sera from chronically infected HIV-1 subjects suggests anyone can develop some bnAb response if exposed to immunogens via vaccination. Working back from mature bnAbs through intermediates enabled understanding their development from the unmutated ancestor, and showed that antigenic diversity preceded the development of population breadth. See Liao et al. (2013) Nature 496, 469–476. In this study, an individual "CH505" was followed from HIV-1 transmission to development of broadly neutralizing antibodies. This individual developed antibodies targeted to CD4 binding site on gp120. In this individual the virus was sequenced over time, and broadly neutralizing antibody clonal lineage ("CH103") was isolated by antigen-specific B cell sorts, memory B cell culture, and amplified by VH/VL next generation pyrosequencing. See Liao et al. (2013) Nature 496, 469–476.

[0052] Further analysis of envelopes and antibodies from the CH505 individual indicated that a non-CH103 Lineage participates in driving CH103-BnAb induction (See Example 1). For example V1 loop, V5 loop and CD4 binding site loop mutations escape from CH103 and are driven by CH103 lineage (See Example 1). Loop D mutations *enhanced* neutralization by CH103 lineage and are driven by another lineage. Transmitted/founder Env, or another early envelope for example W004.03, and/or W004.26, triggers naïve B cell with CH103 Unmutated Common Ancestor (UCA)

which develop in to intermediate antibodies. Transmitted/founder Env, or another early envelope for example W004.03, and/or W004.26, also triggers non-CH103 autologous neutralizing Abs that drive loop D mutations in Env that have enhanced binding to intermediate and mature CH103 antibodies and drive remainder of the lineage.

[0053] The invention provides various methods to choose a subset of viral variants, including but not limited to envelopes, to investigate the role of antigenic diversity in serial samples. In other aspects, the invention provides compositions comprising viral variants, for example but not limited to envelopes, selected based on various criteria as described herein to be used as immunogens.

[0054] In other aspects, the invention provides immunization strategies using the selections of immunogens to induce cross-reactive neutralizing antibodies. In certain aspects, the immunization strategies as described herein are referred to as "swarm" immunizations to reflect that multiple envelopes are used to induce immune responses. The multiple envelopes in a swarm could be combined in various immunization protocols of priming and boosting.

[0055] Sequences/Clones

[0056] Described herein are nucleic and amino acids sequences of HIV-1 envelopes. In certain embodiments, the described HIV-1 envelope sequences are gp160s. In certain embodiments, the described HIV-1 envelope sequences are gp120s. Other sequences, for example but not limited to gp140s, both cleaved and uncleaved, gp150s, gp41s, which are readily derived from the nucleic acid and amino acid gp160 sequences. In certain embodiments the nucleic acid sequences are codon optimized for optimal expression in a host cell, for example a mammalian cell, a rBCG cell or any other suitable expression system.

[0057] In certain embodiments, the envelope design in accordance with the present invention involves deletion of residues (e.g., 5-11, 5, 6, 7, 8, 9, 10, or 11 amino acids) at the N-terminus. For delta N-terminal design, amino acid residues ranging from 4 residues or even fewer to 14 residues or even more are deleted. These residues are between the maturation (signal peptide, usually ending with CX, X can be any amino acid) and "VPVXXXX…". In case of CH505 T/F Env as an example, 8 amino acids (italicized and underlined in the below sequence) were deleted: MRVMGIQRNYPQWWIWSMLGFWMLMICNG*MWVTVYYG*VPVWKEAKTTLFCASDAKAY EKEVHNVWATHACVPTDPNPQE…(rest of envelope sequence is indicated as "…"). In other embodiments, the delta N-design described for CH505 T/F envelope can be used to make delta N-designs of other CH505 envelopes. In certain embodiments, the invention relates generally to an immunogen, gp160, gp120 or gp140, without an N-terminal Herpes Simplex gD tag substituted for amino acids of the N-terminus of gp120, with an HIV leader sequence (or other leader sequence),

and without the original about 4 to about 25, for example 11, amino acids of the N-terminus of the envelope (e.g. gp120). See WO2013/006688, e.g. at pages 10-12, the contents of which publication is hereby incorporated by reference in its entirety.

[0058] The general strategy of deletion of N-terminal amino acids of envelopes results in proteins, for example gpl20s, expressed in mammalian cells that are primarily monomeric, as opposed to dimeric, and, therefore, solves the production and scalability problem of commercial gp120 Env vaccine production. In other embodiments, the amino acid deletions at the N-terminus result in increased immunogenicity of the envelopes.

[0059] In certain embodiments, the invention provides envelope sequences, amino acid sequences and the corresponding nucleic acids, and in which the V3 loop is substituted with the following V3 loop sequence TRPNNNTRKSIRIGPGQTFY ATGDIIGNIRQAH. This substitution of the V3 loop reduced product cleavage and improves protein yield during recombinant protein production in CHO cells.

[0060] In certain embodiments, the CH505 envelopes will have added certain amino acids to enhance binding of various broad neutralizing antibodies. Such modifications could include but not limited to, mutations at W680G or modification of glycan sites for enhanced neutralization.

[0061] In certain aspects, the invention provides composition and methods which use a selection of sequential CH505 Envs, as gp120s, gp 140s cleaved and uncleaved and gp160s, as proteins, DNAs, RNAs, or any combination thereof, administered as primes and boosts to elicit immune response. Sequential CH505 Envs as proteins would be co-administered with nucleic acid vectors containing Envs to amplify antibody induction.

[0062] In certain embodiments, the compositions and methods include any immunogenic HIV-1 sequences to give the best coverage for T cell help and cytotoxic T cell induction. In certain embodiments, the compositions and methods include mosaic and/or consensus HIV-1 genes to give the best coverage for T cell help and cytotoxic T cell induction. In certain embodiments, the compositions and methods include mosaic group M and/or consensus genes to give the best coverage for T cell help and cytotoxic T cell induction. In some embodiments, the mosaic genes are any suitable gene from the HIV-1 genome. In some embodiments, the mosaic genes are Env genes, Gag genes, Pol genes, Nef genes, or any combination thereof. See e.g. US Patent No. 7951377. In some embodiments the mosaic genes are bivalent mosaics. In some embodiments the mosaic genes are trivalent. In some embodiments, the mosaic genes are administered in a suitable vector with each immunization with Env gene inserts in a suitable vector and/or as a protein. In some embodiments, the mosaic genes, for example as bivalent mosaic Gag group M consensus

genes, are administered in a suitable vector, for example but not limited to HSV2, would be administered with each immunization with Env gene inserts in a suitable vector, for example but not limited to HSV-2.

[0063] In certain aspects the invention provides compositions and methods of Env genetic immunization either alone or with Env proteins to recreate the swarms of evolved viruses that have led to bnAb induction. Nucleotide-based vaccines offer a flexible vector format to immunize against virtually any protein antigen. Currently, two types of genetic vaccination are available for testing—DNAs and mRNAs.

[0064] In certain aspects the invention contemplates using immunogenic compositions wherein immunogens are delivered as DNA. See Graham BS, Enama ME, Nason MC, Gordon IJ, Peel SA, et al. (2013) DNA Vaccine Delivered by a Needle-Free Injection Device Improves Potency of Priming for Antibody and CD8+ T-Cell Responses after rAd5 Boost in a Randomized Clinical Trial. PLoS ONE 8(4): e59340, page 9. Various technologies for delivery of nucleic acids, as DNA and/or RNA, so as to elicit immune response, both T-cell and humoral responses, are known in the art and are under developments. In certain embodiments, DNA can be delivered as naked DNA. In certain embodiments, DNA is formulated for delivery by a gene gun. In certain embodiments, DNA is administered by electroporation, or by a needle-free injection technologies, for example but not limited to Biojector® device. In certain embodiments, the DNA is inserted in vectors. The DNA is delivered using a suitable vector for expression in mammalian cells. In certain embodiments the nucleic acids encoding the envelopes are optimized for expression. In certain embodiments DNA is optimized, e.g. codon optimized, for expression. In certain embodiments the nucleic acids are optimized for expression in vectors and/or in mammalian cells. In non-limiting embodiments these are bacterially derived vectors, adenovirus based vectors, rAdenovirus (Barouch DH, et al. Nature Med. 16: 319-23, 2010), recombinant mycobacteria (i.e., rBCG or M smegmatis) (Yu, JS et al. Clinical Vaccine Immunol. 14: 886-093,2007; ibid 13: 1204-11,2006), and recombinant vaccinia type of vectors (Santra S. Nature Med. 16: 324-8, 2010), for example but not limited to ALVAC, replicating (Kibler KV et al., PLoS One 6: e25674, 2011 nov 9.) and non-replicating (Perreau M et al. J. virology 85: 9854-62, 2011) NYVAC, modified vaccinia Ankara (MVA)), adeno-associated virus, Venezuelan equine encephalitis (VEE) replicons, Herpes Simplex Virus vectors, and other suitable vectors.

[0065] In certain aspects the invention contemplates using immunogenic compositions wherein immunogens are delivered as DNA or RNA in suitable formulations. Various technologies which contemplate using DNA or RNA, or may use complexes of nucleic acid molecules and other

entities to be used in immunization. In certain embodiments, DNA or RNA is administered as nanoparticles consisting of low dose antigen-encoding DNA formulated with a block copolymer (amphiphilic block copolymer 704). See Cany et al., Journal of Hepatology 2011 vol. 54 j 115–121; Arnaoty et al., Chapter 17 in Yves Bigot (ed.), Mobile Genetic Elements: Protocols and Genomic Applications, Methods in Molecular Biology, vol. 859, pp293-305 (2012); Arnaoty et al. (2013) Mol Genet Genomics. 2013 Aug;288(7-8):347-63. Nanocarrier technologies called Nanotaxi® for immunogenic macromolecules (DNA, RNA, Protein) delivery are under development. See for example technologies by Incellart.

[0066] In certain aspects the invention contemplates using immunogenic compositions wherein immunogens are delivered as recombinant proteins. Various methods for production and purification of recombinant proteins suitable for use in immunization are known in the art.

[0067] The immunogenic envelopes can also be administered as a protein boost in combination with a variety of nucleic acid envelope primes (e.g., HIV -1 Envs delivered as DNA expressed in viral or bacterial vectors).

[0068] Dosing of proteins and nucleic acids can be readily determined by a skilled artisan. A single dose of nucleic acid can range from a few nanograms (ng) to a few micrograms (μg) or milligram of a single immunogenic nucleic acid. Recombinant protein dose can range from a few μg micrograms to a few hundred micrograms, or milligrams of a single immunogenic polypeptide.

[0069] Administration: The compositions can be formulated with appropriate carriers using known techniques to yield compositions suitable for various routes of administration. In certain embodiments the compositions are delivered via intramascular (IM), via subcutaneous, via intravenous, via nasal, via mucosal routes.

[0070] The compositions can be formulated with appropriate carriers and adjuvants using techniques to yield compositions suitable for immunization. The compositions can include an adjuvant, such as, for example but not limited to, alum, poly IC, MF-59 or other squalene-based adjuvant, ASOIB, or other liposomal based adjuvant suitable for protein or nucleic acid immunization. In certain embodiments, TLR agonists are used as adjuvants. In other embodiment, adjuvants which break immune tolerance are included in the immunogenic compositions.

[0071] There are various host mechanisms that control bNAbs. For example highly somatically mutated antibodies become autoreactive and/or less fit (Immunity 8: 751, 1998; PloS Comp. Biol. 6 e1000800 , 2010; J. Thoret. Biol. 164:37, 1993); Polyreactive/autoreactive naïve B cell receptors (unmutated common ancestors of clonal lineages) can lead to deletion of Ab precursors (Nature 373: 252, 1995; PNAS 107: 181, 2010; J. Immunol. 187: 3785, 2011); Abs with long HCDR3 can

be limited by tolerance deletion (JI 162: 6060, 1999; JCI 108: 879, 2001). BnAb knock-in mouse models are providing insights into the various mechanisms of tolerance control of MPER BnAb induction (deletion, anergy, receptor editing). Other variations of tolerance control likely will be operative in limiting BnAbs with long HCDR3s, high levels of somatic hypermutations. 2F5 and 4E10 BnAbs were induced in mature antibody knock-in mouse models with MPER peptide-liposome-TLR immunogens. Next step is immunization of germline mouse models and humans with the same immunogens.

Example 1

[0072] Example 1: Cooperation of B-cell lineages in induction of hIV-1 broad neutralizing antibodies

[0073] Development of strategies for induction of HIV-1 broadly neutralizing antibodies (bnAbs) by vaccines is a priority. Determining the steps of bnAb induction in HIV-1-infected individuals who make bnAbs is a key strategy for immunogen design. Here we study the B cell response in a bnAb-producing individual, and report cooperation between two B cell lineages to drive bnAb development. We isolated a virus-neutralizing antibody lineage that targeted an envelope region (loop D) and selected virus escape mutants that resulted in both enhanced bnAb lineage envelope binding and escape mutant neutralization—traits associated with increased B cell antigen drive. Thus, in this individual, two B cell lineages cooperated to induce the development of bnAbs. Design of vaccine immunogens that simultaneously drive both helper and broadly neutralizing B cell lineages may be important for vaccine-induced recapitulation of events that transpire during the maturation of neutralizing antibodies in HIV-1-infected individuals.

[0074] The development of a successful HIV-1 vaccine has been stymied by the inability to induce broadly neutralizing antibodies (bnAbs) to conserved regions of the HIV-1 envelope glycoprotein (Env) (Burton et al., 2012; Mascola and Haynes, 2013), that include the CD4-binding site (CD4bs), the membrane-proximal external region, and glycans and amino acid residues in the regions of the first (V1), second (V2) and third (V3) loops (Burton et al., 2012; Kwong and Mascola, 2012; Sattentau and McMichael, 2010; Stamatatos, 2012; Walker et al., 2011; Walker et al., 2009; Zhou et al., 2010). To date, all bnAbs isolated have one or more unusual characteristics: high levels of somatic hypermutations, long heavy chain third complementarity determining regions (HCDR3), or poly- or auto-reactivity to non-HIV-1 antigens (Haynes et al., 2005; Haynes et al., 2012; Kwong and Mascola, 2012; Mouquet and Nussenzweig, 2012; Scheid et al., 2009) —all antibody traits influenced by various host tolerance mechanisms (Haynes et al., 2012; Mascola and Haynes, 2013;

Mouquet and Nussenzweig, 2012). As a consequence of these antibody traits, bnAbs appear to be disfavored and difficult to induce with traditional immunization regimens (Haynes et al., 2012; Mascola and Haynes, 2013; Mascola and Montefiori, 2010; Montefiori et al., 2012). We and others have suggested strategies whereby immunogens are selected to react with bnAb lineage members at multiple stages in their development in an effort to drive otherwise unfavored antibody pathways (Haynes et al., 2012; Liao et al., 2013a; Mascola and Haynes, 2013).

[0075] One approach to dissect the mechanisms underlying bnAb development is to identify the drivers that are responsible for the sequential stimulation of HIV-1 reactive B cell lineages in chronically infected individuals over time (Bonsignori et al., 2011; Corti et al., 2010; Gray et al., 2011; Hraber et al., 2014; Klein et al., 2012; Lynch et al., 2012; Moore et al., 2009; Moore et al., 2011; Tomaras et al., 2011; Walker et al., 2011). We have recently identified an African individual (CH505) in whom HIV-1 infection was established by a single subtype C transmitted/founder (T/F) virus, and mapped the co-evolution of CD4bs bnAbs (the CH103 bnAb B cell lineage) and CH505 T/F virus over time (Liao et al., 2013a). The T/F Env continuously diversified over time under the selection pressure of bnAbs and, concurrently, the inferred unmutated common ancestor (UCA) of the CH103 B cell lineage accumulated somatic mutations leading to gradual acquisition of bnAb activity (Liao et al., 2013a). While the minimally mutated early members of this lineage neutralized only the T/F virus, the later, more mature members of the CH103 clonal lineage potently neutralized both the CH505 T/F and 55% of multi-clade heterologous HIV-1 strains (Liao et al., 2013a). These data engendered interest in determining the autologous virus Env variants that stimulated the development of this broadly neutralizing CH103 antibody lineage. Co-crystal structure of the CH103 antibody and the HIV-1 Env revealed antibody contacts in the V5, CD4-binding loop, and loop D regions in Env, and analysis of the *env* gene sequences obtained by single genome amplification demonstrated additional early mutations in the V1 and V4 loop regions (Liao et al., 2013a).

[0076] In this study, we have probed the mechanisms of selection of early CH505 Env mutations, and found that amino acid changes in the V1, V4, V5 and CD4-binding loops resulted in escape from neutralization by the CH103 lineage (V1, V5, CD4-binding loop) or from cytotoxic T cell pressure (V4). Surprisingly, however, the mutations in the Env loop D increased neutralization sensitivity to the CH103 bnAb lineage. We demonstrated a mechanism of bnAb induction wherein a second antibody lineage targeted a bnAb contact site, thus selecting Env variants with enhanced binding and neutralization sensitivity for bnAb B cell lineage antibodies. These results

demonstrated that cooperation between two B cell lineages early in HIV-1 infection can facilitate the induction of broadly neutralizing CD4bs antibodies.

[0077] **Early CH505 Env mutations in V1, V4, V5 and the CD4bs were associated with escape from CH103 bnAbs or T cell responses.**

[0078] To study the interplay between HIV-1 Env variants and bnAb development in the CH505 individual, we determined neutralization susceptibility of 124 Env pseudoviruses (~18 per time point) from seven time points after HIV-1 transmission (weeks 4, 14, 20, 30, 53, 78 and 100) to members of the CH103 bnAb lineage (**Fig. 1 and Fig. 8**). The CH103 UCA and intermediate antibody (IA) 8 through IA4 only neutralized the CH505 T/F virus. Over time (weeks 4-100), CH505 viruses gradually became more resistant to subsets of the CH103 bnAb lineage antibodies. By week 53, all virus variants were resistant to the early members of the CH103 antibody lineage (UCA and IA8-4). For lineage members that exhibited increased heterologous neutralization (IA3-IA1 and mature CH103, CH104, CH105 and CH106 CD4bs bnAbs), escape was less complete, with a spectrum of sensitive and resistant autologous virus variants isolated from each time point (**Fig. 1 and Table S1**). Thus, pseudoviruses were categorized into sensitive and resistant groups and analyzed for location of accumulated mutations in the *env* gene (**Fig. 1**).

[0079] Env sequence analysis showed that all but 1 of the 20 viruses resistant to early IAs (IA8-IA4) at week 30 contained insertions (3-12 amino acids) in V1 (**Fig. 2A**). Importantly, the V1 insertions also added 1-4 potential N-linked glycosylation (PNLG) sites (**Fig. 2A and Figs. 9A-9D**). Although V1 was not seen in the Env-CH103 co-crystal structure (Liao et al., 2013a), a recent cryo-EM structure of the fully glycosylated Env trimer showed that V1/V2 could significantly affect the binding and neutralization of CD4bs bnAbs (Lyumkis et al., 2013). Docking the CH103 bnAb and CH505 Env sequences on the cryo-EM structure showed that an enlarged V1 loop with potential extra glycan(s) might push V2 into positions incompatible with early IA binding (**Figs. 9A and 9B**). All but one of the 16 viruses resistant to later IAs (IA3-IA1) and mature CH103 mAbs had a 2 or 7-amino acid insertions in V5, which is a major Env contact site for the CH103 bnAb heavy chain (Liao et al., 2013a). All resistant viruses from weeks 53, 78 and 100 had insertions in V5 (**Fig. 1 and Fig. 8**). The 2-amino acid (Asp and Thr) insertions could push loop V5 and the glycan at position 461 into a possible clashing position with the light chain of CH103 antibodies (**Fig. 9C**). Introduction of the Asp and Thr into V5 in the T/F Env confirmed that this 2-amino acid insertion indeed conferred resistance to CH103 lineage mAbs (**Fig. 9D**). We also found one mutation (S365P) in the CD4-binding loop that resulted in a pseudovirus (w14.12) that completely escaped from all members of the CH103 lineage except for weak neutralization susceptibility to

mAb CH103 (**Fig. 1 and Fig. 8**). These results indicated that early insertions in the V1 and V5 loops as well as site mutations in the CD4-binding loop resulted from CH103 bnAb mediated selection pressure.

[0080] Mutations in V4 were found early on at week 7 and persisted throughout later time points, suggesting that they were strongly selected (**Fig. 8**). Viruses with mutations in a 9-amino acid region in V4 were predominant (78%) as early as week 7 and completely replaced the T/F virus population from week 14 onward (**Fig. 8 and 10A**). The N279K mutation in loop D was detected at as early as week 4 (10%), peaked at week 7 (57%), and disappeared from week w14 onward (**Fig. 3A and Fig. 8**). In addition, the V281A and V281G mutations were detected at week 7 and week 9, respectively, and both become predominant in later time points together with other mutations in a 9-amino acid region in loop D (**Fig. 3A**). Since the mutations in both regions occurred early and their patterns were typical for T cell escape mutations, we performed ELISpot analysis using autologous overlapping peptides to determine if those mutations were driven by $CD8^+$ T cell responses.

[0081] A $CD8^+$ T cell response was detected for a putative T cell epitope (NSTRTITIHC) in V4 (**Fig. 10B and Table S2**). The same peptides containing a T415K mutation, which were detected at week 14, could not be recognized by $CD8^+$ T cells. Four mutants containing individual V4 mutations, including the T415K, had similar neutralization susceptibility to CH103 lineage mAbs as the T/F virus (**Fig. 10C).** These results demonstrated that the predominant mutations in V4 were driven by $CD8^+$ T cell responses. In contrast, no T cell responses were found targeting the loop D or V1, V3 and V5 regions (**Table S2**).

[0082] **Selection of the loop D mutations in CH505 envelope by neutralizing non-CH103 Abs.**

[0083] Since the Env loop D region is a binding site for CH103 lineage bnAbs (Liao et al., 2013a), we next asked if loop D mutations might be due to the selection by CH103 lineage CD4bs antibodies. To test this hypothesis, we introduced loop D mutations at positions 275, 279, 280 and 281, individually or in combination as they occurred *in vivo*, into the T/F *env* gene to determine their effect on Env pseudovirus sensitivity to neutralization by the autologous CH103 lineage mAbs. Unexpectedly, all loop D mutations rendered the mutant Env pseudoviruses 4.5-fold (range, 0.4-20) more sensitive than the T/F virus to neutralization by CH103 lineage bnAbs **(Fig. 3B and Table S3**). In addition, when compared to the CH505 T/F virus, four loop D mutants ($M5^{N279K}$, $M6^{V281A}$, $M7^{E275K/N279D/V281S}$ and $M10^{V281G}$) with one or three mutations were less fit than the T/F virus (**Fig. 10D**). These results demonstrated that the loop D mutations were selected by an antibody lineage other than the CH103 bnAb lineage.

[0084] To isolate the antibodies responsible for the loop D mutations, we established limiting dilution cell cultures from peripheral blood memory B cells collected at week 41 in CH505 (Bonsignori et al., 2011). We chose week 41 to study because neutralization of heterologous tier 2 viruses was first detected at week 41, 21 weeks after the detection of the first autologous neutralization activity. We identified one mAb, CH235 (VH1-46, Vκ3-15), that neutralized the CH505 T/F but belonged to a clonal family distinct from CH103 lineage (VH4-59, Vλ3-1). MAb CH235 neutralized the CH505 T/F virus ~7 fold more potently than antibody CH103 (**Fig. 3C**). However, CH235 poorly neutralized loop D mutant $M11^{N279D/V281G}$ and could not neutralize five other loop D mutants ($M7^{E275K/N279D/V281S}$, $M8^{N280S/V281A}$, $M9^{E275K/N279D/V281G}$, $M20^{N280S/V281G}$ and $M21^{N280T/V281A}$). In contrast, CH103 neutralized the same five loop D mutants ~10-fold better than the CH505 T/F virus (**Fig. 3C**).

[0085] To identify antibody members of the CH235 lineage, we analyzed limiting dilution memory B cell cultures from week 41 and identified four additional CH235 lineage members (CH236, CH239, CH240, and CH241). The frequency of CH235 clonal lineage memory B cells at week 41 post-transmission was 0.018%, which was similar to that (0.014%) of the CH103 bnAb lineage. The four CH103 lineage antibodies isolated at week 41 were of similar mutation frequencies as inferred antibodies of the neutralization arm of the CH103 lineage (**Figs. 11A-11F**). To confirm the relevance of the inferred IAs of the CH103 lineage, we characterized these newly isolated four natural IAs (CH186, CH187, CH188 and CH200) of the CH103 bnAb lineage from week 41 and demonstrated that their neutralization specificity was similar to that of the inferred IAs with only neutralization of the autologous CH505 T/F virus and no neutralization of heterologous viruses (**Figs. 11A-11F**).

[0086] We inferred the CH235 lineage UCA and IAs, and expressed all CH235 lineage members as IgG1 recombinant antibodies (Liao et al., 2013a) (**Figs. 12A-12B**). We then determined the ability of the CH235 lineage antibodies to neutralize the CH505 T/F and its variants. Like CH103 lineage mAbs, the CH235 UCA did not neutralize the CH505 T/F virus, with neutralization capacity acquired at IA3 (**Fig. 4 and Table S4**). The CH235 lineage mAbs could partially neutralize week 30 viruses, but could not neutralize the majority of viruses from weeks 53-100 after these viruses acquired loop D mutations. These results demonstrated that CH235 lineage mAbs had an autologous neutralization profile distinct from the CH103 bnAb lineage, in that they potently neutralized early autologous viruses and then at week 53 selected viruses that completely escaped CH235 lineage neutralization.

[0087] To determine whether the escape from CH235 lineage mAbs was indeed due to loop D mutations, we determined the ability of CH235 lineage mAbs to neutralize the CH505 loop D mutants. CH235 lineage antibodies neutralized the early loop D mutants ($M5^{N279K}$, $M6^{V281A}$, $M10^{V281G}$) that occurred before week 30 equally well or better than the T/F virus (**Fig. 5 and Table S5**). These mutants have only one mutation at position 279 or 281. However, the CH235 lineage mAbs only partially neutralized loop D mutants $M19^{V281D}$ and $M11^{N279D/V281G}$ that were first detected at week 30, and could not neutralize the five loop D mutants representing CH505 variants at week 30 or later time points ($M8^{N280S/V281A}$, $M9^{E275K/N279D/V281G}$, $M7^{E275K/N279D/V281S}$, $M20^{N280S/V281G}$ and $M21^{N280T/V281A}$). Thus, we have identified a second clonal lineage (CH235) of neutralizing antibodies from the CH505 individual that selected early loop D Env mutations.

[0088] **Mutations in Loop D enhance interactions between Env gp120 and CH103 bnAbs.**

[0089] Based on our previous co-crystal structure of Env and CH103 (Liao et al., 2013a), the T/F Env favored the interaction with the CH103 UCA (**Fig. 6A**). However, the loop D mutant $M7^{E275K/N279D/V281S}$ that contained three mutations favorably bound the mature CH103, which contained three CDR L2 mutations (Q50E, D51N and S52Y) compared to the UCA (**Fig. 6B**). The E275K mutation in M7 rendered the Loop D positively charged at one side and this change is complementarily accommodated by a CDR L2 Q50E mutation in the mature CH103. Similarly, the N279D mutation makes the other side of loop D more negatively charged to better complement the CDR L2 Lys53. Computational reversion of critical mutations in loop D and CDR L2, such as gp120 Asp279 and CH103 Tyr52, back to those in the T/F Env and CH103 UCA, respectively, resulted in less favorable binding energy (**Fig. 6C**). This suggested that the coevolution of the CH505 loop D and CH103 lineage antibodies led to better binding between loop D mutants and mature CH103 antibodies, while the reversion mutations in either Env or CH103 bnAb resulted in reduced binding. In the CH505 Env evolution, analysis of longitudinal sequences demonstrated that single loop D Env mutations were selected early, followed by multiple loop D mutations at later time points; most of these mutations occurred at positions 279 and 281 (**Fig. 3A**). The sequential accumulation of mutations from simple to complex forms in loop D might have gradually selected the mutations at the binding site in CDR L2 with continuously increased binding affinity. Thus, the improved binding between the loop D mutants and CDR L2 of mature CH103 might have driven the further maturation of CH103 lineage mAbs.

[0090] **CH103 lineage bnAbs bound to the loop D mutant Envs more efficiently than the T/F Env.**

[0091] We next asked whether the CH505 Envs with the loop D mutants could bind to the CH103 lineage members better than the CH505 T/F Env, a trait thought to be necessary to drive antibody lineage maturation (Dal Porto et al., 2002; Dal Porto et al., 1998; Schwickert et al., 2011; Shih et al., 2002). Seven loop D mutant Envs were expressed as gp140s, $M6^{V281A}$ and $M10^{V281G}$ with individual mutations, $M8^{N280S/V281A}$, $M11^{N279D/V281G}$ and $M21^{N280T/V281A}$ with two mutations, and $M7^{E275K/N279D/V281S}$ and $M9^{E275K/N279D/V281G}$ with three mutations (**Fig. 3B**). We then determined their binding by ELISA to all members in the CH103 and CH235 lineages (**Figs. 13A and 13B**). The $M6^{V281A}$, $M10^{V281G}$ and $M11^{N279D/V281G}$ Loop D mutant Envs bound to nearly all CH103 clonal lineage members better than the T/F Env (**Fig. 3D**), while $M8^{N280S/V281A}$, $M9^{E275K/N279D/V281G}$ and $M21^{N280T/V281A}$ mutant Envs bound less well than the T/F Env to early CH103 lineage members (UCA through IA4) (**Fig. 3D**). All seven loop D mutant Envs also bound to four natural IAs (CH186, CH187, CH188 and CH200) of the CH103 bnAb lineage better than the T/F Env (**Fig. 11D**). Thus, it is likely that CH505 Env loop D mutant viruses drove the maturation of the CH103 lineage by targeting early lineage members through mutations at amino acid positions 281 and 279, and late CH103 lineage members by a combinations of mutations at amino acid positions 280, 281, 279 and/or 275 (**Figs. 3A and 3D**).

[0092] In contrast, when compared to the T/F Env, mature CH235 mAbs and IA3-IA1 bound loop D mutant Envs at least 100-fold lower than the T/F Env, except that they bound to $M6^{V281A}$ Env better than the T/F Env (**Fig. 3D**). While none of the loop D mutants or the CH505 T/F Env bound the CH235 UCA or IA4 by ELISA, the T/F Env did weakly react with the CH235 UCA at ~10μM as determined by surface plasmon resonance (**Table S6**). These results strongly supported the hypothesis that the CH235 lineage mAbs selected the loop D mutant Envs that had lower binding to the CH235 lineage mAbs, but higher binding to, and enhanced neutralization by, the CH103 lineage mAbs (**Fig. 7**).

[0093] One fundamental question in HIV-1 vaccine design is how immunogens can be optimized to drive the maturation of bnAbs *in vivo*. By studying the HIV-1 quasispecies evolution in an individual (CH505) with a single TF virus, and by mapping the neutralization susceptibility of early quasispecies members to the autologous CH103 lineage, we have shown that the maturation of the CD4bs bnAb lineage was driven by cooperation of two neutralizing antibody B cell lineages. This observation came from the surprising finding that one of the contact sites of the CH103 bnAb light chain (the Env loop D) contained mutations that did not lead to escape from the CH103 bnAb lineage, but in contrast, resulted in enhanced binding and neutralization of loop D mutant viruses by the CH103 bnAb lineage. These data demonstrated that the CH103 bnAb lineage members did not

select the loop D mutants in CH505 Env, but rather suggested the existence of antibodies that could neutralize the CH505 T/F virus, but not neutralize loop D mutant viruses. Thus, these observations led to the isolation of the CH235 lineage, and the demonstration that this neutralizing lineage indeed selected CH505 transmitted/founder virus loop D escape mutants.

[0094] The concept of bnAbs evolving from autologous neutralizing antibody lineages has been recently put forth (Doria-Rose et al., 2014; Liao et al., 2013a; Moore et al., 2012; Wibmer et al., 2013). Moore and colleagues demonstrated that autologous polyclonal plasma neutralizing antibodies targeted at subsequent sites of V1V2 bnAbs could be documented (Moore et al., 2012; Wibmer et al., 2013). Our studies differ from these studies in that we have used recombinant antibody techniques to isolate entire clonal lineages to directly demonstrate their cooperation in induction of CD4bs bnAbs. While it is clear that bnAbs develop heterologous broad neutralizing capacity by first neutralizing autologous virus Env mutant viruses (Doria-Rose et al., 2014; Liao et al., 2013a), our study directly demonstrates a mechanism of how this can happen at the B cell lineage level. These observations of two lineages cooperating to drive a bnAb lineage provide a view of how one lineage can be affected by another to accommodate autologous Env variation. Thus, the cooperation between the CH235 and CH103 lineages represents a novel molecular mechanism of bnAb development, wherein one neutralizing lineage (CH235) selected escape mutations in an Env contact site (loop D) that led to increased binding and neutralization of the other bnAb lineage (CH103), ultimately driving the maturation and development of broadly cross-reactive neutralizing antibodies (**Fig. 7**). It has been unclear how bnAbs can acquire heterologous breadth of neutralization in response to evolving T/F variants. Our studies show that one mechanism for achieving this is via cooperating lineages that select virus mutants with more bnAb lineage neutralization sensitivity than the T/F virus, thus potentiating bnAb affinity maturation. It has recently been demonstrated that CH103 antibody lineage mutations also resulted in bnAb conformational shifts that led to accommodations of mutational insertions in Env V5 (Fera et al., 2014).

[0095] The contrast in selection of autologous escape mutants by the CH103 bnAb lineage (**Fig. 1**) and the CH235 nAb lineage (**Fig. 4**) is striking and suggested a difference in their biology. Whereas the CH235 nAb lineage led to total escape from identified lineage members after 30 weeks of infection (**Fig. 4**), the CH103 bnAb lineage differed in that it was comprised of two components, the early autologous-only nAbs (UCA through IA4), and the more mature antibodies (IA3 through CH103, CH104, CH105 and CH106 bnAbs) with neutralization breadth (**Fig.1**). The early CH103 autologous-only nAbs also select total escape by week 53, but the later CH103

antibodies with neutralization breadth did not. Rather, the more mature CH103 bnAbs retained the ability to neutralize select autologous variants through week 100 (**Fig. 1**). These data suggested that a component of bnAb development is the retention of ability to neutralize autologous variants (**Fig. 1**). Thus, the cooperation between the nAb CH235 lineage and the CH103 bnAb lineage demonstrated the first step in bnAb lineage development in which CH103 lineage bnAb retained the ability to neutralize autologous virus variants as they matured to neutralize heterologous viruses. It is critical to determine if the types of cooperating lineages as seen in CH235-CH103 interactions are the key initiators of bnAb breadth, or if other additional Env-reactive B cell lineages are required. Against this latter notion was the observation that multiple loop D Env mutants can likely drive all stages of the CH103 lineage (**Figs. 3A-3D**).

[0096] It will be important to determine whether the interaction between CH235 and CH103 lineages only occurs during a short window early in viral evolution, or over a longer period of time. We note in this context that the heavy chain of CH235 derived from VH1-46, which has also been observed to produce broadly neutralizing CD4bs antibodies like 1B2530 and 8ANC131 (Scheid et al., 2011).

[0097] It is also important to note that the CH103 bnAb is a loop binding CD4bs bnAb in contrast to the VRC01-type class of CD4bs bnAb that recognizes the CD4 binding site in a manner similar to CD4 (Zhou et al., 2013). Whereas VRC01-class like mAbs derive from restricted VH1-2 paired with a V_LJ_L with a 5-amino acid LCDR3, new loop binding CD4bs bnAbs have been isolated and can utilize multiple V_HDJ_H/V_LJ_L pairs (Bonsignori et al., 2014; Corti et al., 2010; Liao et al., 2013a). It will be key to determine, with immunization of CH505 Envs, if either CH103-like VH4-59, Vλ3-1 CD4bs lineage Abs are induced, or if other VH usage can be induced with CD4bs bnAb signatures.

[0098] These findings have considerable importance for HIV-1 vaccine design for induction of CD4bs bnAbs. First, mapping of individual bnAb lineages over time in those individuals who make them may not be sufficient for obtaining the information needed for the design of protective immunogens for bnAb development. Rather, mapping of multiple neutralizing antibody lineages may be required for optimal choice of immunogen candidates. Second, these data suggest that induction of one or more neutralizing antibody lineages to select Env variants with enhanced affinity for bnAb lineage antibody members may be required to induce CH103-like CD4bs HIV-1 neutralizing antibodies. For example, for CH103-like lineage induction, priming with the transmitted/founder Env and additional Envs variants such as $M6^{V281A}$ with enhanced binding to

CH235 lineage antibodies, followed by boosting with Env mutants with enhanced binding to CH103 lineage members is likely to be important for experimental vaccine design.

[0099] **Experimental Procedures**

[0100] **Generation of pseudoviruses.** Env pseudoviruses were produced as described (Kirchherr et al., 2007).

[0101] **Neutralization assay.** Neutralization activity was measured as a reduction in luciferase activity after a single round infection of TZM-bl cells as previously described (Li et al., 2005; Montefiori, 2004).

[0102] **IFN-γ ELISpot assay**. The IFN-γ ELISpot assay was performed according to previous descriptions (Cox et al., 2006). The responses were considered positive if >50 SFC per 10^6 PBMCs were detected.

[0103] **Site-directed mutagenesis.** Mutants of CH0505.T/F envelope gene were constructed using the Quick Change II Site-Directed Mutagenesis kit (Agilent Technologies, Santa Clara, CA). All final *env* mutants were confirmed by sequencing.

[0104] **Viral fitness assay.** The fitness of the Env loop D mutants was determined by comparing to their cognate CH505 T/F virus in a competitive fitness assay as previous described (Cai et al., 2007; Song et al., 2012).

[0105] **Envelope glycoprotein expression.** The codon-optimized CH505 transmitted/founder and loop D mutant *env* genes were generated by de novo synthesis (GeneScript, Piscataway, NJ) or site-directed mutagenesis in mammalian expression plasmid pcDNA3.1/hygromycin (Invitrogen, Grand Island, NY) as described (Liao et al., 2013b), and stored at -80°C until use.

[0106] **B cell culture.** IgG^+ memory cells were isolated from PBMCs using a previously described protocol (Bonsignori et al., 2011). Cell culture supernatants were screened for binding to autologous CH505 T/F gp140 and neutralization of the autologous CH505 w4.3 Env pseudovirus. Culture supernatants that neutralized CH505 w4.3 were then screened for differential neutralization of the CH505 T/F and M10 mutant viruses.

[0107] **Isolation of immunoglobulin V(D)J and VL gene segments and expression of recombinant antibodies.** RNA from positive cultures was extracted by using standard procedures (RNeasy minikit; Qiagen, Valencia, CA), and the genes encoding Ig V_HDJ_H and V_LJ_L rearrangements were amplified by RT and nested PCR without cloning by use of a previously reported method (Liao et al., 2009). Sequence base calling was performed by using Phred. V, D, and J region genes and mutations were analyzed by using the SoDA information system (Volpe et al., 2006). The genetic information of the Ig V_HDJ_H and V_LJ_L were annotated using the method as

described (Liao et al., 2013a). For further characterization, the isolated V_HDJ_H/V_LJ_L genes of the observed antibodies from CH505 and inferred V_HDJ_H/V_LJ_L for UCAs and intermediate antibodies were synthesized (GenScript, Piscataway, NJ) and cloned into pcDNA3.1 plasmid (Invitrogen, Grand Island, NY) for production of purified recombinant IgG1 antibodies in 293F cells by transient transfection as described previously (Liao et al., 2011).

[0108] **Inference of UCA and IAs of CH235 lineage.** The five members of the CH235 antibody lineage were used to infer the UCA and IAs of both heavy and light chains simultaneously using methods described in (Kepler, 2013).

[0109] **Direct binding ELISA.** Direct binding ELISAs were performed in 384-well plates as previously described (Bonsignori et al., 2011).

[0110] **Surface plasmon resonance (SPR) affinity and kinetics measurements.** Binding K_d and rate constant (association rate k_a, dissociation rate k_d) measurements of mAbs to the autologous Env C. CH05 gp140 were carried out on BIAcore 3000 or BIAcore T200 instruments as described (Alam et al., 2007; Alam et al., 2009; Liao et al., 2013a).

[0111] **Structural alignment and loop modeling.** To visualize effects of evolutionary mutations in CH505 variants, such as sequence insertions and addition of potential glycosylation sites, in the trimeric viral spike context, the antibody CH103-gp120 complex structure (PGB ID: 4JAN) was aligned to the structure of BG505 SOSIP.664 HIV-1 Env trimer in complex with VRC-PG04 (PGB ID: 3J5M) by superposing the outer domains of gp120 in each structure using program package CCP4 (Winn et al., 2011). Based on the superposed CH103 gp120 structure, possible conformations of loop insertions in the HIV-1 V1-, V2- and V5-loop were modeled with program Loopy (Xiang et al., 2002). Relative positions and potential clashes between the HIV-1 V1-, V2- and V5-loop and the gp120-bound CH103 were depicted with program PyMOL available at pymol.org).

[0112] **Calculation of changes in binding affinity upon mutation.**

[0113] To evaluate the effects of evolutionary mutations in loop D of CH505 gp120 and affinity maturation mutations in antibody CH103 on binding affinity, we computationally estimated the changes in binding affinity caused by mutations on either loop D of gp120 or CHR L2 of antibody CH103 with the program BeAtMuSiC (Dehouck et al., 2013; Moretti et al., 2013). This program uses the known structure of a protein-protein complex to evaluates the change in binding affinity between two proteins caused by single-site mutations in their sequence; we observed a high concordance in prediction by this program and binding data for HIV-1 gp120-antibody complex structures for which binding data for single-site mutations had been previously determined

experimentally (Zhou et al., 2010). Single mutations were modeled using the structure of mature antibody CH103 in complex with gp120 (PDB ID: 4JAN) while keeping the protein backbone rigid. Calculations were carried out by reverting respective amino acid at each position (275, 279 and 281 in the HIV-1 loop D and 50-52 in CH103 CDR L2) to its counterpart in the T/F virus or germline antibody.

[0114] **Table S1 shows neutralization activity of CH103 clonal lineage antibodies against autologous CH505 viruses. Table S1 is presented as Figures 14A-14E, and is related to Figure 1.** Values are the concentrations (μg/ml) of antibodies required for the 50% inhibition (IC_{50}).

[0115] **Table S2. Detection of T cell responses targeting the V1, V2, V3, V4 and loop D regions by ELISpot, Related to Figures 3A-3D.** 15-mer peptides overlapping by 10 were designed for five regions (V1, V3, V4, V5 and loop D). Those regions showed evidence of positive selection in that mutations were recurrent in the earliest viral sequence data sets in CH505. For each region, both the T/F form and the most common early selected mutation were tested for both susceptibility and escape by the ELISpot assay. The spot counts were the average of the numbers from two independent wells. The targeted regions that were strongly selected are indicated between underscores or dashes (deletion). The amino acids affected in the CH505 T/F Env are enclosed in a dashed box and the mutations in the variants are enclosed in a dashed circle. Only two V4 peptides in the T/F Env were recognized by the CD8+ T cells. The same peptides containing the early T415K mutation was not recognized by the CD8+ T cells, confirming T cell mediated immune escape. All the peptides gave negative responses (≤50 Spots/106 cells) in the seronegative subjects (n=3); two of the seronegatives were HLA matched to CH505.

Table S2. Detection of T cell responses targeting V1, V2, V3, V4 and loop D regions by ELISpot, Related to Figures 3A-3D

Region containing selected mutations	tested overlapping peptide		SFC/10^6
STDMANSTETN_STRTITIH_CRIKQIINMWQ	V4_T/F	STDMANSTETNSTRT	3
		NSTETNSTRTITIHC	175
		NSTRTITIHCRIKQI	243
		ITIHCRIKQIINMWQ	3
	V4_variant	NSTETNSTRTKIHC	0
		NSTRTKIHCRIKQI	0
		IKIHCRIKQIINMWQ	3
LAEGEIIIRSENI_TNNA_KTIIVHLNESVKI	Loop D_T/F	LAEGEIIIRSENITN	0
		IIIRSENITNNVKTI	5
		ENITNNVKTIIVHLN	0
		NVKTIIVHLNESVKI	0
	Loop D_variant1	IIIRSENITNNGKTI	0
		ENITNNGKTIIVHLN	3
		NGKTIIVHLNESVKI	0
	Loop D_variant2	IIIRSENITNNDKTI	0
		ENITNNDKTIIVHLN	0
		NDKTIIVHLNESVKI	3
	Loop D_variant3	LAEGEIIIRSENITK	0
		IIIRSENITKNVKTI	0
		ENITKNVKTIIVHLN	3

Table S2 cont.

LCVTLNCTNA_TASNSSIIEG_MKNCSFNITT	V1_T/F	LCVTLNCTNATASNS	0
		NCTNATASNSSIIEG	0
		TASNSSIIEGMKNCS	8
		SIIEGMKNCSFNITT	3
	V1_variant	LCVTLNCTNATASNA	3
		NCTNATASNATASNS	3
		TASNATASNSSIIEG	0
AFYATGQVIG_DIREAYCNIN_ESKWNETLQR	V3_T/F	AFYATGQVIGDIREA	0
		GQVIGDIREAYCNIN	3
		DIREAYCNINESKWN	3
		YCNINESKWNETLQR	0
	V3_variant	GQVIGDIREAYCNIS	0
		DIREAYCNISESKWN	3
		YCNISESKWNETLQR	0
NITGLLLTRDGGKNNT--ETFRPGGGNMKDNW	V5_T/F	NITGLLLTRDGGKNN	0
		LLTRDGGKNNT--ETFR	0
		GGKNNT--ETFRPGGGN	0
		T--ETFRPGGGNMKDNW	3
	V5_variant	LLTRDGGKNNTDTET	0
		GGKNNTDTETFRPGG	3
		TDTETFRPGGGNMKD	3
		TETFRPGGGNMKDNW	3

15-mer peptides overlapping by 10 were designed for five regions (V1, V3, V4, V5 and loop D). Those regions showed evidence of positive selection in that mutations were recurrent in the earliest viral sequence data sets in CH505. For each region, both the T/F form and the most common early selected mutation were tested for both susceptibility and escape by the ELISpot assay. The spot counts were the average of the numbers from two independent wells. The targeted regions that were strongly selected are indicated between underscores or dashes (deletion). The amino acids affected in the CH505 T/F Env are indicated by green and the mutations in the variants are indicated by red. Only two V4 peptides in the T/F Env were recognized by the CD8+ T cells. The same peptides containing the early T415K mutation was not recognized by the CD8+ T cells, confirming T cell mediated immune escape. All the peptides gave negative responses (≤50 Spots/106 cells) in the seronegative subjects (n=3); two of the seronegatives were HLA matched to CH505.

[0116] **Table S3 shows neutralization susceptibility of the CH505 loop D mutants to CH103 lineage antibodies. Table S3 is presented as Figure 15 and is related to Figures 3A-3D.**

Values are the concentrations (μg/ml) of antibodies required for the 50% inhibition (IC_{50}).

[0117] **Table S4 shows neutralization activity of CH235 clonal lineage antibodies against autologous CH505 viruses. Table S4 is presented as Figure 16 and is related to Figure 4.**

Values are the concentrations (μg/ml) of antibodies required for the 50% inhibition (IC_{50}).

[0118] **Table S5 shows neutralization susceptibility of CH505 loop D mutants to CH235 lineage antibodies. Table S5 is presented as Figure 17 and is related to Figure 5.** Values are the concentrations (μg/ml) of antibodies required for the 50% inhibition (IC_{50}).

[0119] **Table S6 shows CH235 clonal lineage antibodies binding to CH505 gp140, Related to Figures 3A-3D.** *Binding detected at 200 μg/mL.

Table S6. CH235 clonal lineage antibodies binding to CH505 gp140, Related to Figure 3

mAb	k_a ($M^{-1}s^{-1}$)x 10^3	k_d (s^{-1}) x 10^{-3}	K_d (nM)
UCA	-	-	-*
IA4	-	-	-
IA3	-	-	>1 μM
IA2	0.57	0.153	270
IA1	2.9	0.0438	15.1
CH235	13	0.0095	0.73
CH236	0.473	0.0057	12
CH239	13.8	0.0128	0.93
CH240	2.79	0.0403	14.5
CH241	16.9	0.00233	0.14

*Binding detected at 200 μg/mL

[0120] **References for Example 1:**

Alam, S.M., McAdams, M., Boren, D., Rak, M., Scearce, R.M., Gao, F., Camacho, Z.T., Gewirth, D., Kelsoe, G., Chen, P., *et al.* (2007). The role of antibody polyspecificity and lipid reactivity in binding of broadly neutralizing anti-HIV-1 envelope human monoclonal antibodies 2F5 and 4E10 to glycoprotein 41 membrane proximal envelope epitopes. J Immunol *178*, 4424-4435.

Alam, S.M., Morelli, M., Dennison, S.M., Liao, H.X., Zhang, R., Xia, S.M., Rits-Volloch, S., Sun, L., Harrison, S.C., Haynes, B.F., *et al.* (2009). Role of HIV membrane in neutralization by two broadly neutralizing antibodies. Proceedings of the National Academy of Sciences of the United States of America *106*, 20234-20239.

Bonsignori, M., Hwang, K.K., Chen, X., Tsao, C.Y., Morris, L., Gray, E., Marshall, D.J., Crump, J.A., Kapiga, S.H., Sam, N.E., *et al.* (2011). Analysis of a clonal lineage of HIV-1 envelope V2/V3

conformational epitope-specific broadly neutralizing antibodies and their inferred unmutated common ancestors. Journal of virology *85*, 9998-10009.

Bonsignori, M., Wiehe, K., Grimm, S.K., Lynch, R., Yang, G., Kozink, D.M., Perrin, F., Cooper, A.J., Hwang, K.K., Chen, X., *et al.* (2014). An autoreactive antibody from an SLE/HIV-1 individual broadly neutralizes HIV-1. J Clin Invest *124*, 1835-1843.

Burton, D.R., Poignard, P., Stanfield, R.L., and Wilson, I.A. (2012). Broadly neutralizing antibodies present new prospects to counter highly antigenically diverse viruses. Science *337*, 183-186.

Cai, F., Chen, H., Hicks, C.B., Bartlett, J.A., Zhu, J., and Gao, F. (2007). Detection of minor drug-resistant populations by parallel allele-specific sequencing. Nat Methods *4*, 123-125.

Corti, D., Langedijk, J.P., Hinz, A., Seaman, M.S., Vanzetta, F., Fernandez-Rodriguez, B.M., Silacci, C., Pinna, D., Jarrossay, D., Balla-Jhagjhoorsingh, S., *et al.* (2010). Analysis of memory B cell responses and isolation of novel monoclonal antibodies with neutralizing breadth from HIV-1-infected individuals. PloS one *5*, e8805.

Cox, J.H., Ferrari, G., and Janetzki, S. (2006). Measurement of cytokine release at the single cell level using the ELISPOT assay. Methods *38*, 274-282.

Dal Porto, J.M., Haberman, A.M., Kelsoe, G., and Shlomchik, M.J. (2002). Very low affinity B cells form germinal centers, become memory B cells, and participate in secondary immune responses when higher affinity competition is reduced. The Journal of experimental medicine *195*, 1215-1221.

Dal Porto, J.M., Haberman, A.M., Shlomchik, M.J., and Kelsoe, G. (1998). Antigen drives very low affinity B cells to become plasmacytes and enter germinal centers. Journal of immunology *161*, 5373-5381.

Dehouck, Y., Kwasigroch, J.M., Rooman, M., and Gilis, D. (2013). BeAtMuSiC: Prediction of changes in protein-protein binding affinity on mutations. Nucleic acids research *41*, W333-339.

Doria-Rose, N.A., Schramm, C.A., Gorman, J., Moore, P.L., Bhiman, J.N., Dekosky, B.J., Ernandes, M.J., Georgiev, I.S., Kim, H.J., Pancera, M., *et al.* (2014). Developmental pathway for potent V1V2-directed HIV-neutralizing antibodies. Nature *509*, 55-62.

Fera, D., Schmidt, A.G., Haynes, B.F., Gao, F., Liao, H.X., Kepler, T.B., and Harrison, S.C. (2014). Affinity maturation in an HIV broadly neutralizing B-cell lineage through reorientation of variable domains. Proc Natl Acad Sci U S A. June 30 [Epub ahead of print].

Gray, E.S., Madiga, M.C., Hermanus, T., Moore, P.L., Wibmer, C.K., Tumba, N.L., Werner, L., Mlisana, K., Sibeko, S., Williamson, C., *et al.* (2011). The neutralization breadth of HIV-1

develops incrementally over four years and is associated with CD4+ T cell decline and high viral load during acute infection. Journal of virology *85*, 4828-4840.

Haynes, B.F., Fleming, J., St Clair, E.W., Katinger, H., Stiegler, G., Kunert, R., Robinson, J., Scearce, R.M., Plonk, K., Staats, H.F., *et al.* (2005). Cardiolipin polyspecific autoreactivity in two broadly neutralizing HIV-1 antibodies. Science *308*, 1906-1908.

Haynes, B.F., Kelsoe, G., Harrison, S.C., and Kepler, T.B. (2012). B-cell-lineage immunogen design in vaccine development with HIV-1 as a case study. Nature biotechnology *30*, 423-433.

Hraber, P., Seaman, M.S., Bailer, R.T., Mascola, J.R., Montefiori, D.C., and Korber, B.T. (2014). Prevalence of broadly neutralizing antibody responses during chronic HIV-1 infection. AIDS *28*, 163-169.

Kepler, T.B. (2013). Reconstructing a B-cell clonal lineage. I. Statistical inference of unobserved ancestors. F1000Res *2*, 103.

Kirchherr, J.L., Lu, X., Kasongo, W., Chalwe, V., Mwananyanda, L., Musonda, R.M., Xia, S.M., Scearce, R.M., Liao, H.X., Montefiori, D.C., *et al.* (2007). High throughput functional analysis of HIV-1 env genes without cloning. J Virol Methods *143*, 104-111.

Klein, F., Gaebler, C., Mouquet, H., Sather, D.N., Lehmann, C., Scheid, J.F., Kraft, Z., Liu, Y., Pietzsch, J., Hurley, A., *et al.* (2012). Broad neutralization by a combination of antibodies recognizing the CD4 binding site and a new conformational epitope on the HIV-1 envelope protein. The Journal of experimental medicine *209*, 1469-1479.

Kwong, P.D., and Mascola, J.R. (2012). Human antibodies that neutralize HIV-1: identification, structures, and B cell ontogenies. Immunity *37*, 412-425.

Li, M., Gao, F., Mascola, J.R., Stamatatos, L., Polonis, V.R., Koutsoukos, M., Voss, G., Goepfert, P., Gilbert, P., Greene, K.M., *et al.* (2005). Human immunodeficiency virus type 1 env clones from acute and early subtype B infections for standardized assessments of vaccine-elicited neutralizing antibodies. J Virol *79*, 10108-10125.

Liao, H.X., Chen, X., Munshaw, S., Zhang, R., Marshall, D.J., Vandergrift, N., Whitesides, J.F., Lu, X., Yu, J.S., Hwang, K.K., *et al.* (2011). Initial antibodies binding to HIV-1 gp41 in acutely infected subjects are polyreactive and highly mutated. The Journal of experimental medicine *208*, 2237-2249.

Liao, H.X., Levesque, M.C., Nagel, A., Dixon, A., Zhang, R., Walter, E., Parks, R., Whitesides, J., Marshall, D.J., Hwang, K.K., *et al.* (2009). High-throughput isolation of immunoglobulin genes from single human B cells and expression as monoclonal antibodies. J Virol Methods *158*, 171-179.

Liao, H.X., Lynch, R., Zhou, T., Gao, F., Alam, S.M., Boyd, S.D., Fire, A.Z., Roskin, K.M., Schramm, C.A., Zhang, Z., *et al.* (2013a). Co-evolution of a broadly neutralizing HIV-1 antibody and founder virus. Nature *496*, 469-476.

Liao, H.X., Tsao, C.Y., Alam, S.M., Muldoon, M., Vandergrift, N., Ma, B.J., Lu, X., Sutherland, L.L., Scearce, R.M., Bowman, C., *et al.* (2013b). Antigenicity and immunogenicity of transmitted/founder, consensus, and chronic envelope glycoproteins of human immunodeficiency virus type 1. Journal of virology *87*, 4185-4201.

Lynch, R.M., Tran, L., Louder, M.K., Schmidt, S.D., Cohen, M., Dersimonian, R., Euler, Z., Gray, E.S., Abdool Karim, S., Kirchherr, J., *et al.* (2012). The development of CD4 binding site antibodies during HIV-1 infection. Journal of virology *86*, 7588-7595.

Lyumkis, D., Julien, J.P., de Val, N., Cupo, A., Potter, C.S., Klasse, P.J., Burton, D.R., Sanders, R.W., Moore, J.P., Carragher, B., *et al.* (2013). Cryo-EM Structure of a Fully Glycosylated Soluble Cleaved HIV-1 Envelope Trimer. Science *342*, 1484-1490.

Mascola, J.R., and Haynes, B.F. (2013). HIV-1 neutralizing antibodies: understanding nature's pathways. Immunological reviews *254*, 225-244.

Mascola, J.R., and Montefiori, D.C. (2010). The role of antibodies in HIV vaccines. Annual review of immunology *28*, 413-444.

Montefiori, D.C. (2004). Evaluating neutralizing antibodies against HIV, SIV, and SHIV in luciferase reporter gene assays. In Current protocols in immunology, J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, and R. Coico, eds. (New York, NY: John Whiley & Sons), pp. 12.11.11-12.11.15.

Montefiori, D.C., Karnasuta, C., Huang, Y., Ahmed, H., Gilbert, P., de Souza, M.S., McLinden, R., Tovanabutra, S., Laurence-Chenine, A., Sanders-Buell, E., *et al.* (2012). Magnitude and breadth of the neutralizing antibody response in the RV144 and Vax003 HIV-1 vaccine efficacy trials. The Journal of infectious diseases *206*, 431-441.

Moore, P.L., Gray, E.S., and Morris, L. (2009). Specificity of the autologous neutralizing antibody response. Current opinion in HIV and AIDS *4*, 358-363.

Moore, P.L., Gray, E.S., Sheward, D., Madiga, M., Ranchobe, N., Lai, Z., Honnen, W.J., Nonyane, M., Tumba, N., Hermanus, T., *et al.* (2011). Potent and broad neutralization of HIV-1 subtype C by plasma antibodies targeting a quaternary epitope including residues in the V2 loop. Journal of virology *85*, 3128-3141.

Moore, P.L., Gray, E.S., Wibmer, C.K., Bhiman, J.N., Nonyane, M., Sheward, D.J., Hermanus, T., Bajimaya, S., Tumba, N.L., Abrahams, M.R., *et al.* (2012). Evolution of an HIV glycan-dependent broadly neutralizing antibody epitope through immune escape. Nature medicine *18*, 1688-1692.

Moretti, R., Fleishman, S.J., Agius, R., Torchala, M., Bates, P.A., Kastritis, P.L., Rodrigues, J.P., Trellet, M., Bonvin, A.M., Cui, M., *et al.* (2013). Community-wide evaluation of methods for predicting the effect of mutations on protein-protein interactions. Proteins *81*, 1980-1987.

Mouquet, H., and Nussenzweig, M.C. (2012). Polyreactive antibodies in adaptive immune responses to viruses. Cell Mol Life Sci *69*, 1435-1445.

Sattentau, Q.J., and McMichael, A.J. (2010). New templates for HIV-1 antibody-based vaccine design. F1000 Biol Rep *2*, 60.

Scheid, J.F., Mouquet, H., Feldhahn, N., Seaman, M.S., Velinzon, K., Pietzsch, J., Ott, R.G., Anthony, R.M., Zebroski, H., Hurley, A., *et al.* (2009). Broad diversity of neutralizing antibodies isolated from memory B cells in HIV-infected individuals. Nature *458*, 636-640.

Scheid, J.F., Mouquet, H., Ueberheide, B., Diskin, R., Klein, F., Oliveira, T.Y., Pietzsch, J., Fenyo, D., Abadir, A., Velinzon, K., *et al.* (2011). Sequence and structural convergence of broad and potent HIV antibodies that mimic CD4 binding. Science *333*, 1633-1637.

Schwickert, T.A., Victora, G.D., Fooksman, D.R., Kamphorst, A.O., Mugnier, M.R., Gitlin, A.D., Dustin, M.L., and Nussenzweig, M.C. (2011). A dynamic T cell-limited checkpoint regulates affinity-dependent B cell entry into the germinal center. The Journal of experimental medicine *208*, 1243-1252.

Shih, T.A., Meffre, E., Roederer, M., and Nussenzweig, M.C. (2002). Role of BCR affinity in T cell dependent antibody responses in vivo. Nat Immunol *3*, 570-575.

Song, H., Pavlicek, J.W., Cai, F., Bhattacharya, T., Li, H., Iyer, S.S., Bar, K.J., Decker, J.M., Goonetilleke, N., Liu, M.K., *et al.* (2012). Impact of immune escape mutations on HIV-1 fitness in the context of the cognate transmitted/founder genome. Retrovirology *9*, 89.

Stamatatos, L. (2012). HIV vaccine design: the neutralizing antibody conundrum. Curr Opin Immunol *24*, 316-323.

Tomaras, G.D., Binley, J.M., Gray, E.S., Crooks, E.T., Osawa, K., Moore, P.L., Tumba, N., Tong, T., Shen, X., Yates, N.L., *et al.* (2011). Polyclonal B cell responses to conserved neutralization epitopes in a subset of HIV-1-infected individuals. Journal of virology *85*, 11502-11519.

Volpe, J.M., Cowell, L.G., and Kepler, T.B. (2006). SoDA: implementation of a 3D alignment algorithm for inference of antigen receptor recombinations. Bioinformatics *22*, 438-444.

Walker, L.M., Huber, M., Doores, K.J., Falkowska, E., Pejchal, R., Julien, J.P., Wang, S.K., Ramos, A., Chan-Hui, P.Y., Moyle, M., *et al.* (2011). Broad neutralization coverage of HIV by multiple highly potent antibodies. Nature *477*, 466-470.

Walker, L.M., Phogat, S.K., Chan-Hui, P.Y., Wagner, D., Phung, P., Goss, J.L., Wrin, T., Simek, M.D., Fling, S., Mitcham, J.L., *et al.* (2009). Broad and potent neutralizing antibodies from an African donor reveal a new HIV-1 vaccine target. Science *326*, 285-289.

Wibmer, C.K., Bhiman, J.N., Gray, E.S., Tumba, N., Abdool Karim, S.S., Williamson, C., Morris, L., and Moore, P.L. (2013). Viral escape from HIV-1 neutralizing antibodies drives increased plasma neutralization breadth through sequential recognition of multiple epitopes and immunotypes. PLoS pathogens *9*, e1003738.

Winn, M.D., Ballard, C.C., Cowtan, K.D., Dodson, E.J., Emsley, P., Evans, P.R., Keegan, R.M., Krissinel, E.B., Leslie, A.G., McCoy, A., *et al.* (2011). Overview of the CCP4 suite and current developments. Acta Crystallogr D Biol Crystallogr *67*, 235-242.

Xiang, Z., Soto, C.S., and Honig, B. (2002). Evaluating conformational free energies: the colony energy and its application to the problem of loop prediction. Proceedings of the National Academy of Sciences of the United States of America *99*, 7432-7437.

Zhou, T., Georgiev, I., Wu, X., Yang, Z.-Y., Dai, K., Finzi, A., Do Kwon, Y., Scheid, J.F., Shi, W., Xu, L., *et al.* (2010). Structural basis for broad and potent neutralization of HIV-1 by antibody VRC01. Science *329*, 811-817.

Zhou, T., Zhu, J., Wu, X., Moquin, S., Zhang, B., Acharya, P., Georgiev, I.S., Altae-Tran, H.R., Chuang, G.Y., Joyce, M.G., *et al.* (2013). Multidonor analysis reveals structural elements, genetic determinants, and maturation pathway for HIV-1 neutralization by VRC01-class antibodies. Immunity *39*, 245-258.

Kepler, T.B. (2013). Reconstructing a B-cell clonal lineage. I. Statistical inference of unobserved ancestors. F1000Res *2*, 103.

Maree, A.F., Keulen, W., Boucher, C.A., and De Boer, R.J. (2000). Estimating relative fitness in viral competition experiments. J Virol *74*, 11067-11072.

Salazar-Gonzalez, J.F., Salazar, M.G., Keele, B.F., Learn, G.H., Giorgi, E.E., Li, H., Decker, J.M., Wang, S., Baalwa, J., Kraus, M.H., *et al.* (2009). Genetic identity, biological phenotype, and evolutionary pathways of transmitted/founder viruses in acute and early HIV-1 infection. J Exp Med *206*, 1273-1289..

Example 2

[0121] **Example 2:** Combination of antigens from CH505 envelope sequences for swam immunization

[0122] Provided herein are non-limiting examples of combinations of antigens derived from CH505 envelope sequences for a swarm immunization. The selection includes priming with a virus which binds to the UCA, for example a T/F virus or another early (e.g. but not limited to week 004.3, or 004.26) virus envelope. In certain embodiments the prime could include D-loop variants. In certain embodiments the boost could include D-loop variants.

[0123] Non-limiting embodiments of envelopes selected for swarm vaccination are shown as the selections described below. A skilled artisan would appreciate that a vaccination protocol can include a sequential immunization starting with the "prime" envelope(s) and followed by sequential boosts, which include individual envelopes or combination of envelopes. In another vaccination protocol, the sequential immunization starts with the "prime" envelope(s) and is followed with boosts of cumulative prime and/or boost envelopes. In certain embodiments, the prime does not include T/F sequence (W000.TF). In certain embodiments, the prime includes w004.03 envelope. In certain embodiments, the prime includes w004.26 envelope. In certain embodiments, the immunization methods do not include immunization with HIV-1 envelope T/F. In other embodiments for example the T/F envelope may not be included when w004.03 or w004.26 envelope is included. In certain embodiments, there is some variance in the immunization regimen; in some embodiments, the selection of HIV-1 envelopes may be grouped in various combinations of primes and boosts, either as nucleic acids, proteins, or combinations thereof.

[0124] In certain embodiments the immunization includes a prime administered as DNA, and MVA boosts. See Goepfert, et al. 2014; "Specificity and 6-Month Durability of Immune Responses Induced by DNA and Recombinant Modified Vaccinia Ankara Vaccines Expressing HIV-1 Virus-Like Particles" J Infect Dis. 2014 Feb 9. [Epub ahead of print].

[0125] **HIV-1 Envelope selection A (ten envelopes):** 703010505.TF, 703010505.W4.03, 703010505.W4.26, 703010505.W14.21, 703010505.W20.14, 703010505.W30.28, 703010505.W30.13, 703010505.W53.31, 703010505.W78.15, 703010505.W100.B4.

[0126] **HIV-1 Envelope selection B (twenty envelopes)**: 703010505.TF, 703010505.W4.03, 703010505.W4.26, 703010505.W14.3, 703010505.W14.8, 703010505.W14.21, 703010505.W20.7, 703010505.W20.26, 703010505.W20.9, 703010505.W20.14, 703010505.W30.28, 703010505.W30.12, 703010505.W30.19, 703010505.W30.13, 703010505.W53.19,

703010505.W53.13, 703010505.W53.31, 703010505.W78.1, 703010505.W78.15, 703010505.W100.B4.

Example 3

[0127] **Example 3**: immunization protocols in subjects with swarms of HIV-1 envelopes.

[0128] Immunization protocols contemplated by the invention include envelopes sequences as described herein including but not limited to nucleic acids and/or amino acid sequences of gp160s, gp150s, cleaved and uncleaved gp140s, gp120s, gp41s, N-terminal deletion variants as described herein, cleavage resistant variants as described herein, or codon optimized sequences thereof. A skilled artisan can readily modify the gp160 and gp120 sequences described herein to obtain these envelope variants. The swarm immunization protocols can be administered in any subject, for example monkeys, mice, guinea pigs, or human subjects.

[0129] In non-limiting embodiments, the immunization includes a nucleic acid is administered as DNA, for example in a modified vaccinia vector (MVA). In non-limiting embodiments, the nucleic acids encode gp160 envelopes. In other embodiments, the nucleic acids encode gp120 envelopes. In other embodiments, the boost comprises a recombinant gp120 envelope. The vaccination protocols include envelopes formulated in a suitable carrier and/or adjuvant, for example but not limited to alum. In certain embodiments the immnuzations include a prime, as a nucleic acid or a recombinant protein, followed by a boost, as a nucleic acid or a recombinant protein. A skilled artisan can readily determine the number of boosts and intervals between boosts.

[0130] In non-limiting embodiments, the prime includes a 703010505.TF envelope and a loop D variant as described herein (see Figures 3A-3D and Figures 24A-24B). In non-limiting embodiments, the prime includes a 703010505.TF envelope and/or 703010505.W4.03, 703010505.W4.26 envelope, and a loop D variant as described herein, or a combination of D loop mutant variants (see Figures 3A-3D and Figures 24A-24B). In certain embodiments, the loop D variant is M6. In certain embodiments, the loop D variant is M5. In certain embodiments, the loop D variant is M10. In certain embodiments, the loop D variant is M19. In certain embodiments, the loop D variant is M11. In certain embodiments, the loop D variant is M20. In certain embodiments, the loop D variant is M21. In certain embodiments, the loop D variant is M9. In certain embodiments, the loop D variant is M8. In certain embodiments, the loop D variant is M7.

[0131] Table S7 shows a non-limiting example of a sequential immunization protocol using a swarm of HIV1 envelopes (703010505.TF, 703010505.W4.03, 703010505.W4.26, 703010505.W14.21, 703010505.W20.14, 703010505.W30.28, 703010505.W30.13,

703010505.W53.31, 703010505.W78.15, 703010505.W100.B4). In a non-limiting embodiment, a suggested grouping for prime and boost is to begin with the CH505 TF + W4.03, then boost with a mixture of w4.26+ 14.21+ 20.14 , then boost with a mixture of w30.28+ 30.13+53.31, then boost with a mixture of w78.15 + 100.B4.

Envelope	Prime	Boost(s)	Boost(s)	Boost(s)
CH505 TF + W4.03	CH505 TF + W4.03 as a nucleic acid e.g. DNA/MVA vector and/or protein			
w4.26+ 14.21+ 20.14		w4.26+ 14.21+ 20.14 as a nucleic acid e.g. DNA/MVA vector and/or protein		
w30.28+ 30.13+53.31			w30.28+ 30.13+53.31 as a nucleic acid e.g. DNA/MVA vector and/or protein	
w78.15 + 100.B4				w78.15 + 100.B4 as a nucleic acid e.g. DNA/MVA vector and/or protein

[0132] A skilled artisan can readily determine the number and interval between boosts. .

[0133] Table S8 shows a non-limiting example of a sequential immunization protocol using a swarm of HIV1 envelopes

Envelope	Prime	Boost(s)
703010505.TF, 703010505.W4.03, 703010505.W4.26, 703010505.W14.21, 703010505.W20.14, 703010505.W30.28, 703010505.W30.13, 703010505.W53.31, 703010505.W78.15, 703010505.W100.B4.	703010505.TF (optionally 703010505.W4.03, 703010505.W4.26) as a nucleic acid e.g. DNA/MVA vector and/or protein	703010505.TF, 703010505.W4.03, 703010505.W4.26, 703010505.W14.21, 703010505.W20.14, 703010505.W30.28, 703010505.W30.13, 703010505.W53.31, 703010505.W78.15, 703010505.W100.B4 as a nucleic acid e.g. DNA/MVA vector and/or protein

[0134] A skilled artisan can readily determine the number and interval between boosts

[0135] For a 20mer immunization regimen (envelopes (703010505.TF, 703010505.W4.03, 703010505.W4.26, 703010505.W14.3, 703010505.W14.8, 703010505.W14.21, 703010505.W20.7, 703010505.W20.26, 703010505.W20.9, 703010505.W20.14, 703010505.W30.28, 703010505.W30.12, 703010505.W30.19, 703010505.W30.13, 703010505.W53.19, 703010505.W53.13, 703010505.W53.31, 703010505.W78.1, 703010505.W78.15, 703010505.W100.B4), in a non-limiting embodiment, one can prime with CH505 TF + W4.03, then boost with a mixture of w4.26+ 14.21+ 20.14 + 14.3 + 14.8 + 20.7 , then boost with a mixture of w 20.26+ 20.9 + 30.12+ w30.28+ 30.13+53.31, then boost with a mixture of w78.15 + 100.B4 + 30.19 + 53.19 + 53.13+ 78.1. Other combinations of envelopes are contemplated for boosts.

[0136] Table S9 shows a non-limiting example of a sequential immunization protocol using a swarm of HIV1 envelopes

Envelope	Prime	Boost(s)
703010505.TF, 703010505.W4.03, 703010505.W4.26, 703010505.W14.3, 703010505.W14.8, 703010505.W14.21,	703010505.TF, (optionally 703010505.W4.03, 703010505.W4.26, 703010505.W14.3, 703010505.W14.8, 703010505.W14.21), as a	703010505.TF, 703010505.W4.03, 703010505.W4.26, 703010505.W14.3, 703010505.W14.8, 703010505.W14.21,

703010505.W20.7, 703010505.W20.26, 703010505.W20.9, 703010505.W20.14, 703010505.W30.28, 703010505.W30.12, 703010505.W30.19, 703010505.W30.13, 703010505.W53.19, 703010505.W53.13, 703010505.W53.31, 703010505.W78.1, 703010505.W78.15, 703010505.W100.B4.	nucleic acid e.g. DNA/MVA vector and/or protein	703010505.W20.7, 703010505.W20.26, 703010505.W20.9, 703010505.W20.14, 703010505.W30.28, 703010505.W30.12, 703010505.W30.19, 703010505.W30.13, 703010505.W53.19, 703010505.W53.13, 703010505.W53.31, 703010505.W78.1, 703010505.W78.15, 703010505.W100.B4. as a nucleic acid e.g. DNA/MVA vector and/or protein

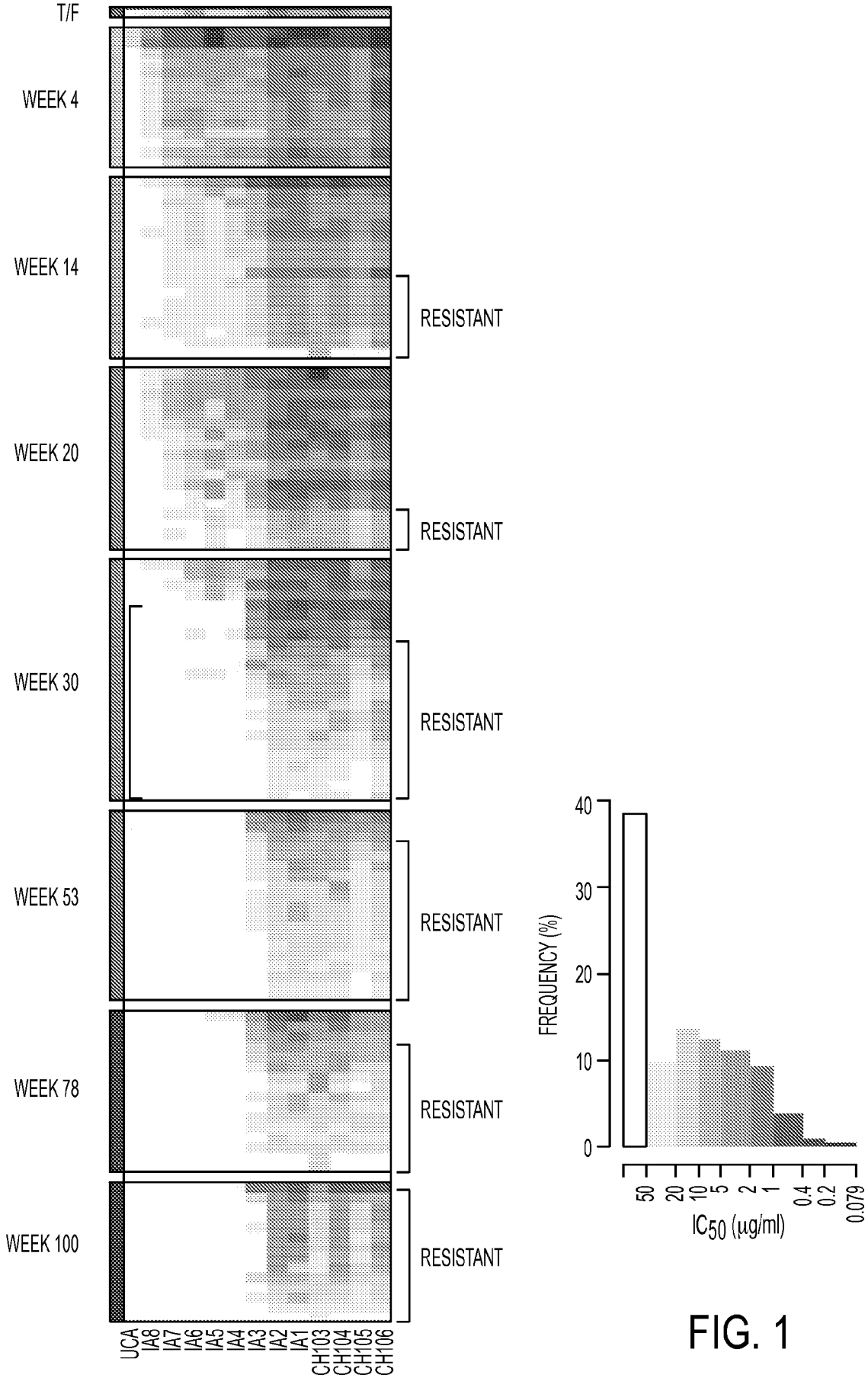
[0137] A skilled artisan can readily determine the number and interval between boosts.

[0138] The contents of all documents and other information sources cited herein are herein incorporated by reference in their entirety.

WHAT IS CLAIMED IS:

1. A composition comprising any one of the sequences of Figures 18-23 and Figures 24A-24B, or a combination thereof.
2. A composition comprising nucleic acids encoding 703010505.TF, 703010505.W4.03, 703010505.W4.26, 703010505.W14.21, 703010505.W20.14, 703010505.W30.28, 703010505.W30.13, 703010505.W53.31, 703010505.W78.15, and 703010505.W100.B4.
3. The composition of claim 2, further comprising any one of 703010505.W14.3, 703010505.W14.8, 703010505.W20.7, 703010505.W20.26, 703010505.W20.9, 703010505.W30.12, 703010505.W30.19, 703010505.W53.19, 703010505.W53.13, and 703010505.W78.1, or a combination thereof.
4. A method of inducing an immune response in a subject comprising administering a composition comprising HIV-1 envelope T/F, w004.03 or w004.26 in an amount sufficient to induce an immune response.
5. The method further comprising administering a composition any one of the HIV-1 envelopes 703010505.W14.21, 703010505.W20.14, 703010505.W30.28, 703010505.W30.13, 703010505.W53.31, 703010505.W78.15, and 703010505.W100.B4, or any combination thereof in an amount sufficient to induce an immune response.
6. The method further comprising administering a composition comprising any one of the HIV-1 envelopes 703010505.W14.3, 703010505.W14.8, 703010505.W20.7, 703010505.W20.26, 703010505.W20.9, 703010505.W30.12, 703010505.W30.19, 703010505.W53.19, 703010505.W53.13, and 703010505.W78.1, or any combination thereof in an amount sufficient to induce an immune response.
7. The method of claim 4, 5 or 6, wherein the HIV-1 envelopes are administered as a nucleic acid, a protein or any combination thereof.
8. The method of claim 7, wherein the nucleic acid encoding the envelope is operably linked to a promoter inserted in an expression vector.
9. The method of claim 7, wherein the protein is recombinant.
10. The method of claim 4, 5 or 6, wherein the HIV-1 envelopes are administered as a prime, a boost, or both.
11. The method of claim 4, 5 or 6, wherein the HIV-1 envelopes are administered as a multiple boosts.
12. The method of claim 4, 5 or 6, wherein the composition further comprises an adjuvant.

13. The composition of claim 2 or 3 further comprising a loop D mutant HIV-1 envelope (Figures 24A-24B).
14. The composition of claim 2 or 3, wherein the loop D mutant is M6.
15. The method of claim 4, 5 or 6 further comprising administering a loop D mutant HIV-1 envelope (Figures 24A-24B).
16. The method of claim 4, 5 or 6, wherein the loop D mutant is M6.


T/F
WEEK 4
WEEK 14
WEEK 20
WEEK 30
WEEK 53
WEEK 78
WEEK 100
RESISTANT
RESISTANT
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RESISTANT
UCA
IA8
IA7
IA6
IA5
IA4
IA3
IA2
IA1
CH103
CH104
CH105
CH106
FREQUENCY (%)
40
30
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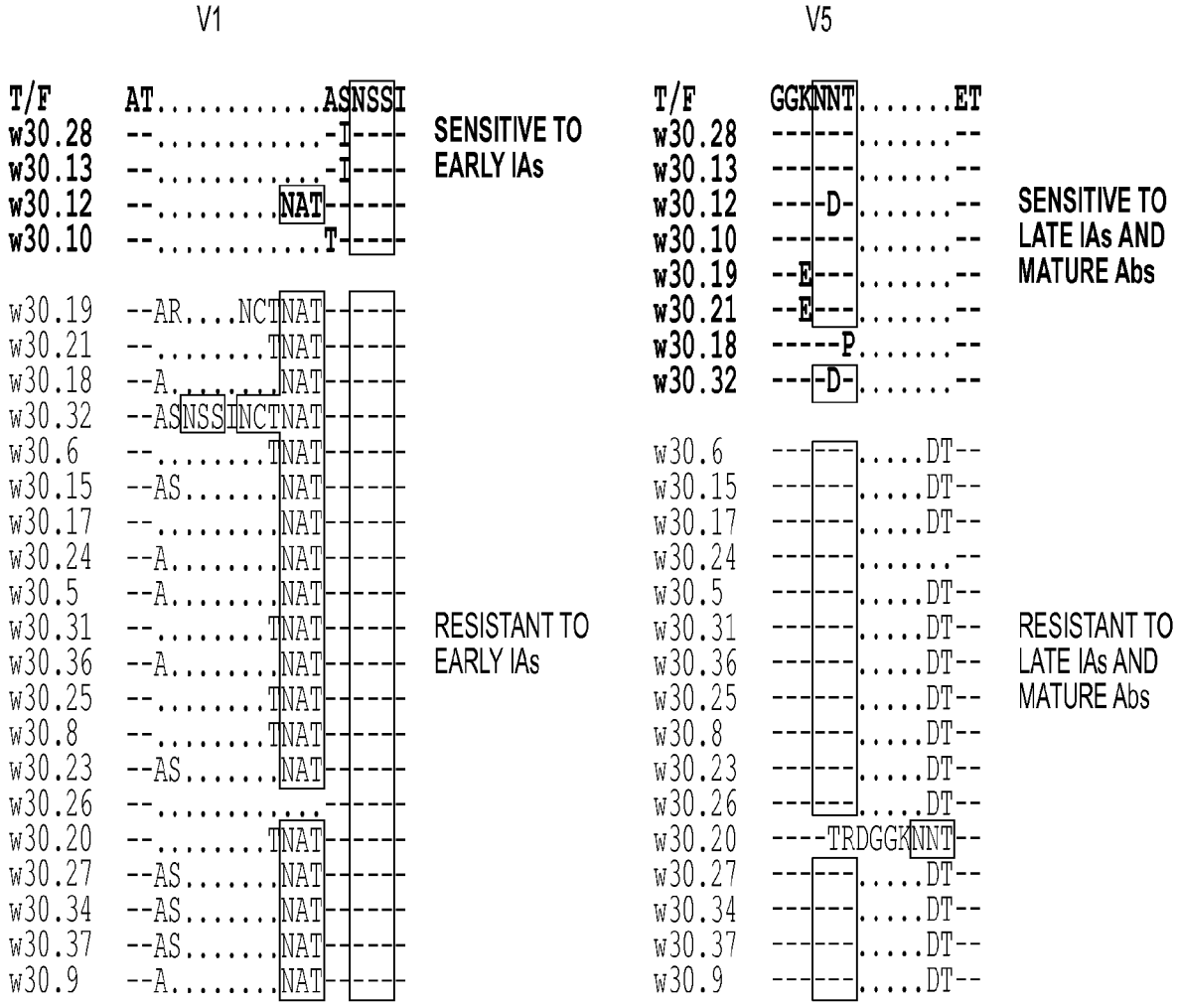
50
20
10
5
2
1
0.4
0.2
0.079
IC50 (µg/ml)

FIG. 1


V1
T/F AT.....ASNSSI
w30.28 --.....-I---- SENSITIVE TO
w30.13 --.....-I---- EARLY IAs
w30.12 --.....NAT-----
w30.10 --.....T-----
w30.19 --AR....NCTNAT-----
w30.21 --.....TNAT-----
w30.18 --A.....NAT-----
w30.32 --ASNSSINCTNAT-----
w30.6 --.....TNAT-----
w30.15 --AS.....NAT-----
w30.17 --.....NAT-----
w30.24 --A.....NAT-----
w30.5 --A.....NAT-----
w30.31 --.....TNAT----- RESISTANT TO
w30.36 --A.....NAT----- EARLY IAs
w30.25 --.....TNAT-----
w30.8 --.....TNAT-----
w30.23 --AS.....NAT-----
w30.26 --.....-----
w30.20 --.....TNAT-----
w30.27 --AS.....NAT-----
w30.34 --AS.....NAT-----
w30.37 --AS.....NAT-----
w30.9 --A.....NAT-----
V5
T/F GGKNNT.....ET
w30.28 ------.....--
w30.13 ------.....--
w30.12 ----D-.....-- SENSITIVE TO
w30.10 ------.....-- LATE IAs AND
w30.19 --E---.....-- MATURE Abs
w30.21 --E---.....--
w30.18 -----P.....--
w30.32 ----D-.....--
w30.6 ------.....DT--
w30.15 ------.....DT--
w30.17 ------.....DT--
w30.24 ------.....--
w30.5 ------.....DT--
w30.31 ------.....DT-- RESISTANT TO
w30.36 ------.....DT-- LATE IAs AND
w30.25 ------.....DT-- MATURE Abs
w30.8 ------.....DT--
w30.23 ------.....DT--
w30.26 ------.....DT--
w30.20 ----TRDGGKNNT--
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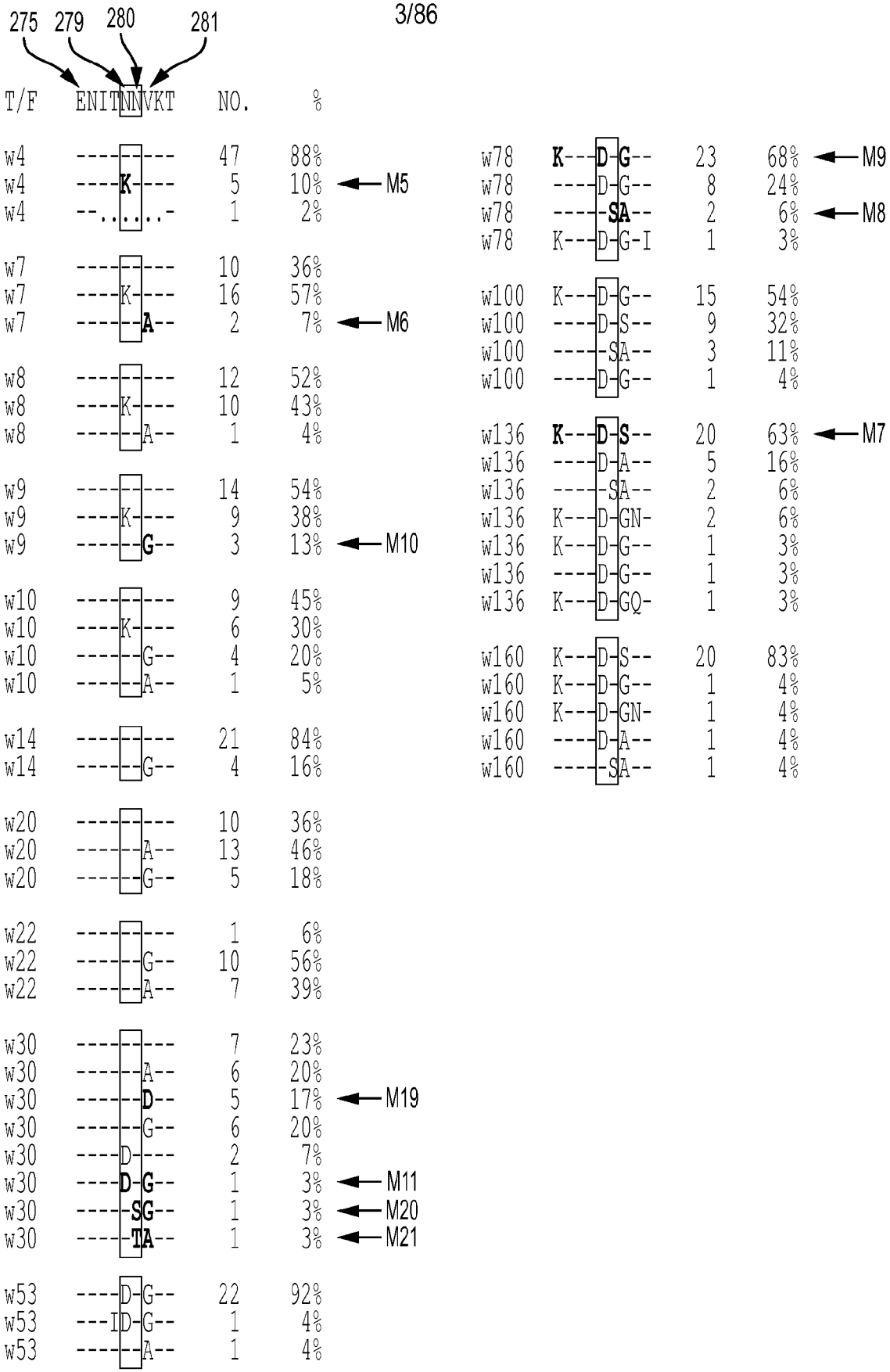
w30.37 ------.....DT--
w30.9 ------.....DT--

FIG. 2A FIG. 2B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w4 ----K----- 5 10% M5
w4 --.....- 1 2%
w7 ---------- 10 36%
w7 ----K----- 16 57%
w7 ------A-- 2 7% M6
w8 ---------- 12 52%
w8 ----K----- 10 43%
w8 ------A-- 1 4%
w9 ---------- 14 54%
w9 ----K----- 9 38%
w9 ------G-- 3 13% M10
w10 ---------- 9 45%
w10 ----K----- 6 30%
w10 ------G-- 4 20%
w10 ------A-- 1 5%
w14 ---------- 21 84%
w14 ------G-- 4 16%
w20 ---------- 10 36%
w20 ------A-- 13 46%
w20 ------G-- 5 18%
w22 ---------- 1 6%
w22 ------G-- 10 56%
w22 ------A-- 7 39%
w30 ---------- 7 23%
w30 ------A-- 6 20%
w30 ------D-- 5 17% M19
w30 ------G-- 6 20%
w30 ----D----- 2 7%
w30 ----D-G-- 1 3% M11
w30 -----SG-- 1 3% M20
w30 -----TA-- 1 3% M21
w53 ----D-G-- 22 92%
w53 ---ID-G-- 1 4%
w53 ------A-- 1 4%
w78 K---D-G-- 23 68% M9
w78 ----D-G-- 8 24%
w78 -----SA-- 2 6% M8
w78 K---D-G-I 1 3%
w100 K---D-G-- 15 54%
w100 ----D-S-- 9 32%
w100 -----SA-- 3 11%
w100 ----D-G-- 1 4%
w136 K---D-S-- 20 63% M7
w136 ----D-A-- 5 16%
w136 -----SA-- 2 6%
w136 K---D-GN- 2 6%
w136 K---D-G-- 1 3%
w136 ----D-G-- 1 3%
w136 K---D-GQ- 1 3%
w160 K---D-S-- 20 83%
w160 K---D-G-- 1 4%
w160 K---D-GN- 1 4%
w160 ----D-A-- 1 4%
w160 -----SA-- 1 4%

FIG. 3A

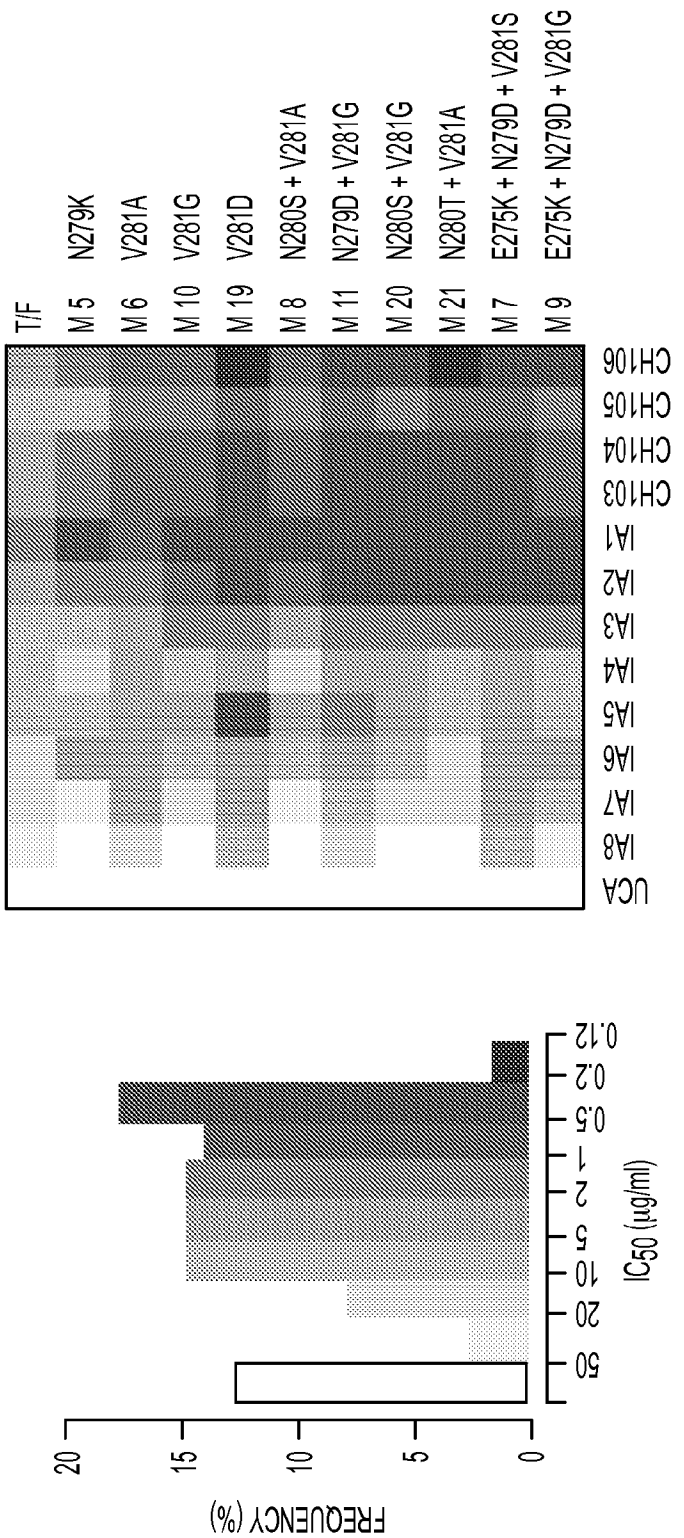

FIG. 3B

Ab	T/F	M5	M6	M10	M19	M11	M7	M8	M9	M20	M21
CH235	0.58	0.14	0.44	0.43	1.55	35.7	>50	**>50**	**>50**	**>50**	**>50**
CH103	4.14	1.21	0.54	0.56	0.31	0.46	0.38	0.53	0.72	0.34	0.39

FIG. 3C

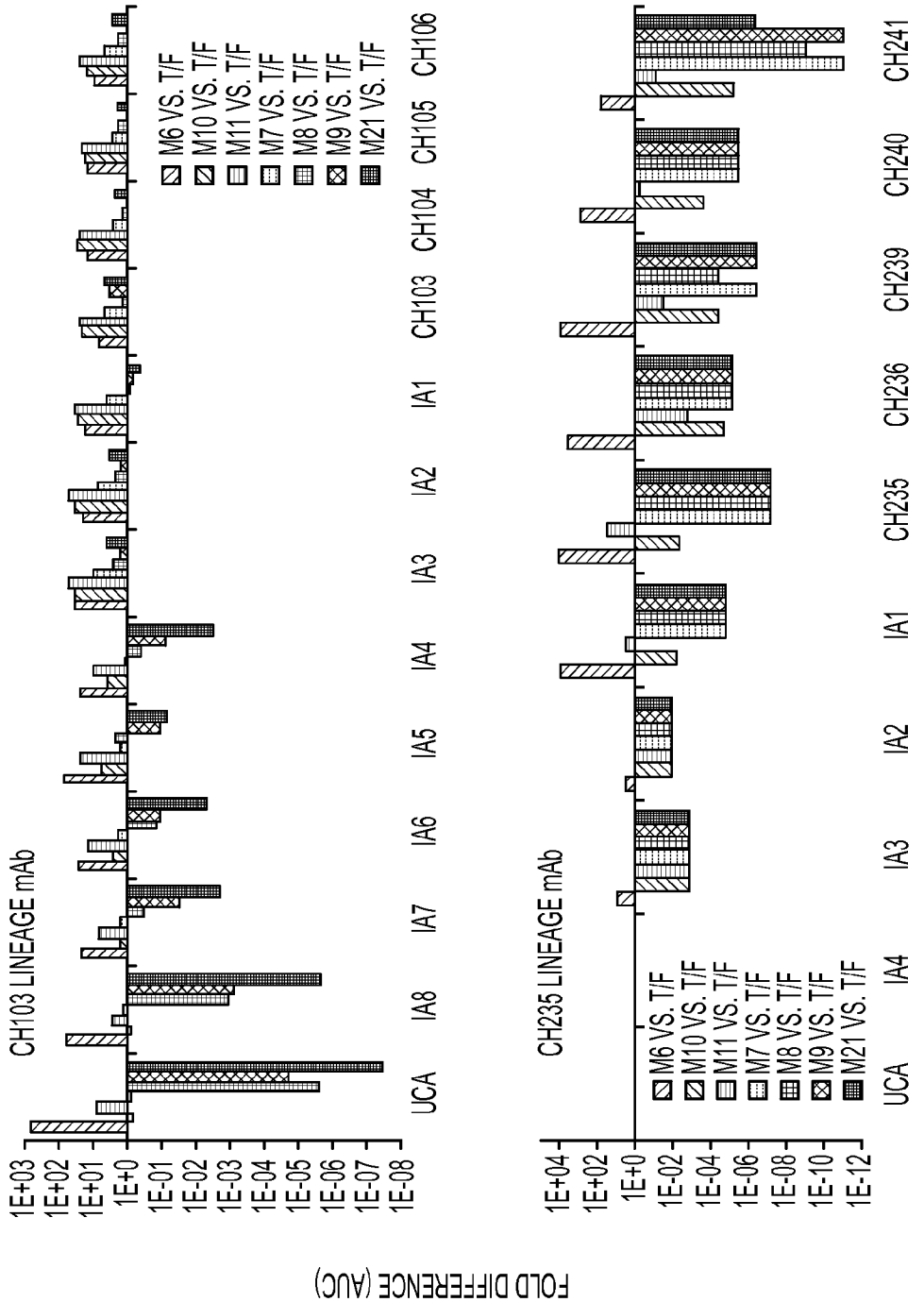
CH103 LINEAGE mAb
M6 VS. T/F
M10 VS. T/F
M11 VS. T/F
M7 VS. T/F
M8 VS. T/F
M9 VS. T/F
M21 VS. T/F
1E+03
1E+02
1E+01
1E+0
1E-01
1E-02
1E-03
1E-04
1E-05
1E-06
1E-07
1E-08
UCA
IA8
IA7
IA6
IA5
IA4
IA3
IA2
IA1
CH103
CH104
CH105
CH106
CH235 LINEAGE mAb
1E+04
1E+02
1E+0
1E-02
1E-04
1E-06
1E-08
1E-10
1E-12
UCA
IA4
IA3
IA2
IA1
CH235
CH236
CH239
CH240
CH241
mAb
FOLD DIFFERENCE (AUC)

FIG. 3D

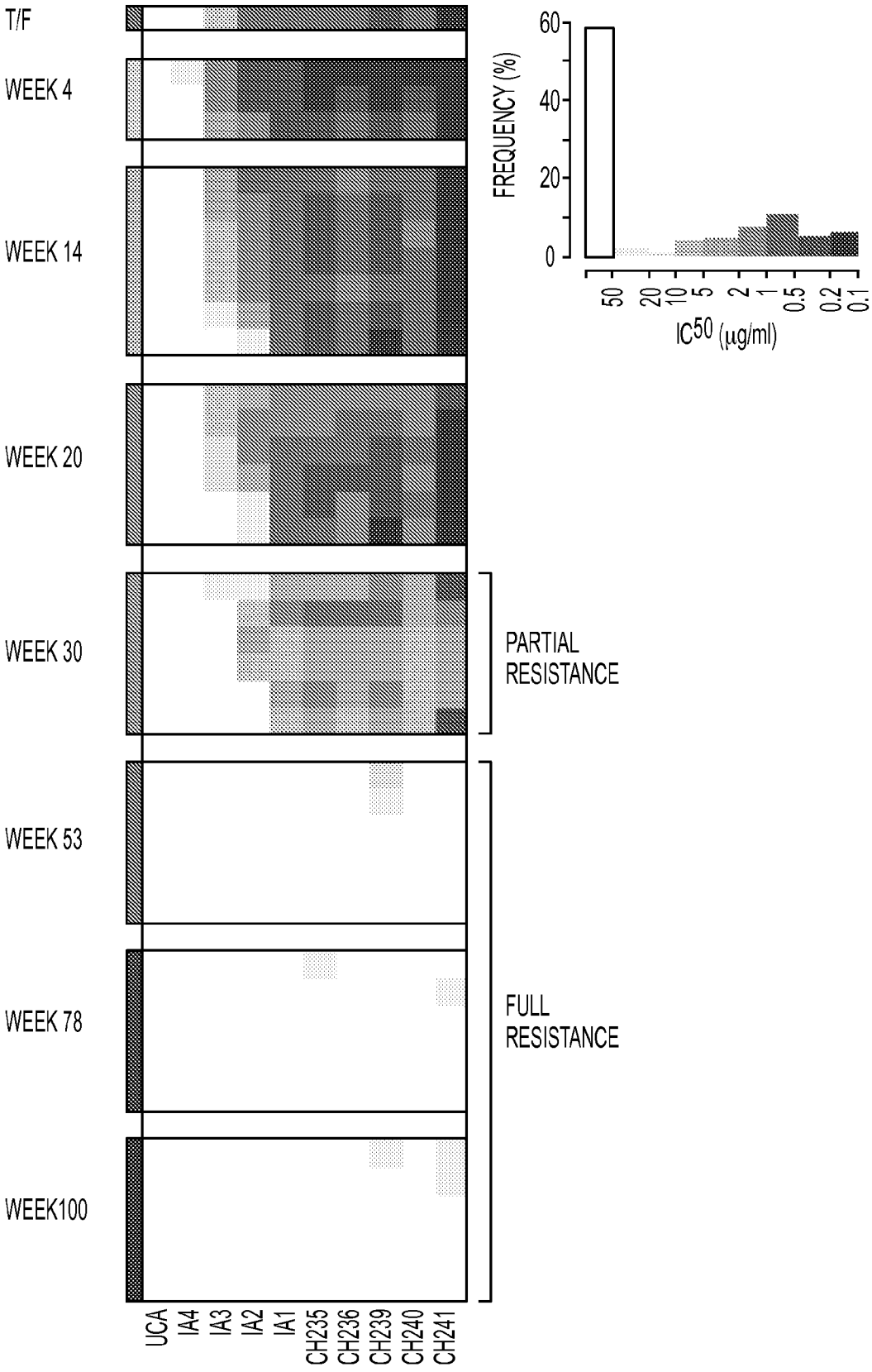
T/F
WEEK 4
WEEK 14
WEEK 20
WEEK 30
WEEK 53
WEEK 78
WEEK100
PARTIAL RESISTANCE
FULL RESISTANCE
UCA
IA4
IA3
IA2
IA1
CH235
CH236
CH239
CH240
CH241
FREQUENCY (%)
60
40
20
0
50
20
10
5
2
1
0.5
0.2
0.1
IC50 (μg/ml)

FIG. 4

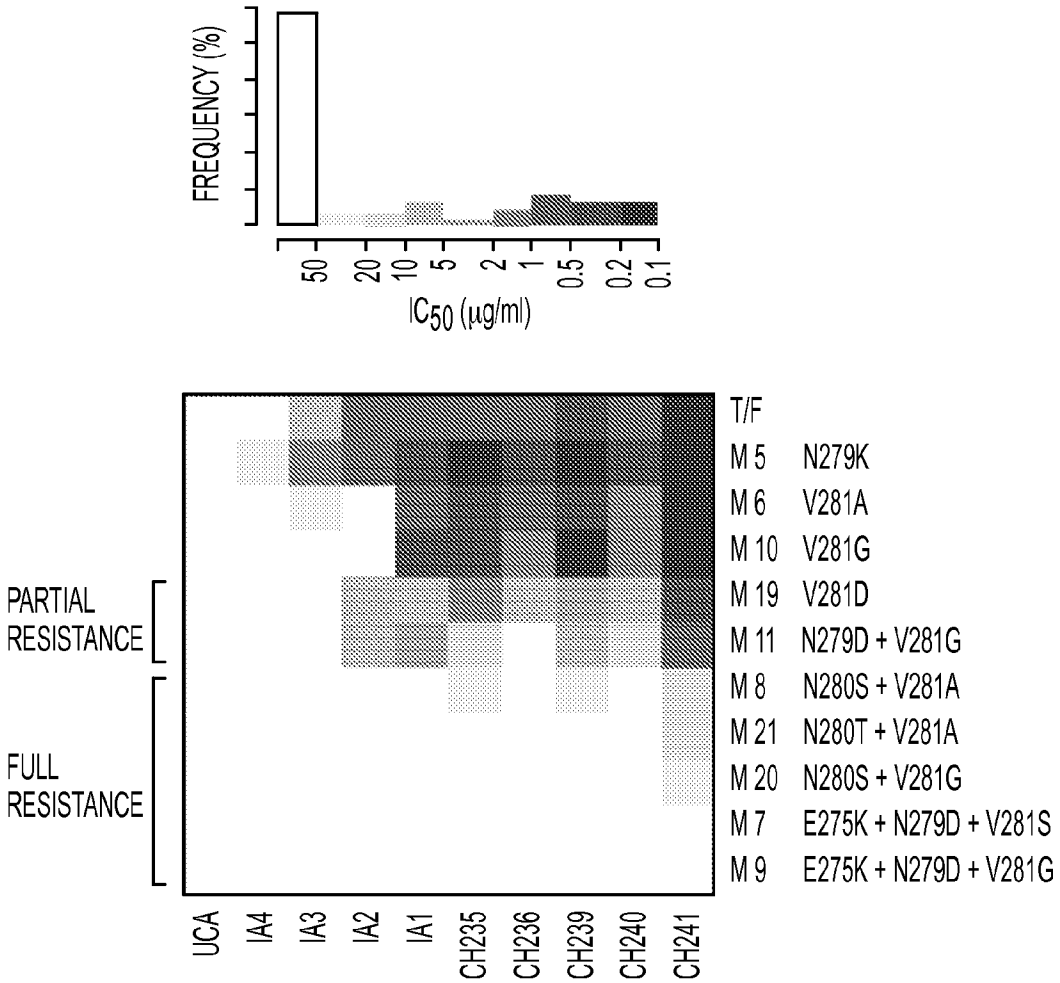
FREQUENCY (%)
50
20
10
5
2
1
0.5
0.2
0.1
IC50 (μg/ml)
T/F
M 5 N279K
M 6 V281A
M 10 V281G
M 19 V281D
M 11 N279D + V281G
M 8 N280S + V281A
M 21 N280T + V281A
M 20 N280S + V281G
M 7 E275K + N279D + V281S
M 9 E275K + N279D + V281G
PARTIAL RESISTANCE
FULL RESISTANCE
UCA
IA4
IA3
IA2
IA1
CH235
CH236
CH239
CH240
CH241

FIG. 5

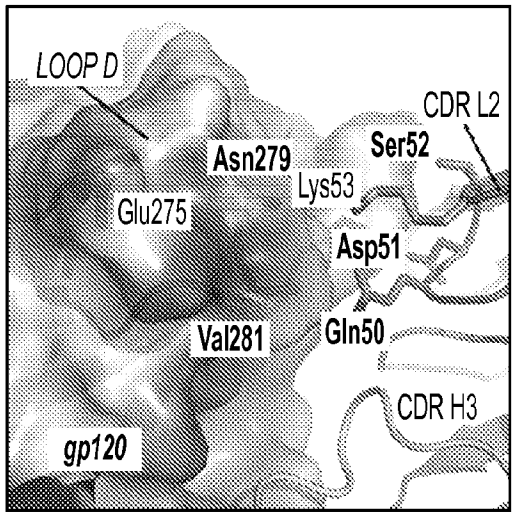

FIG. 6A

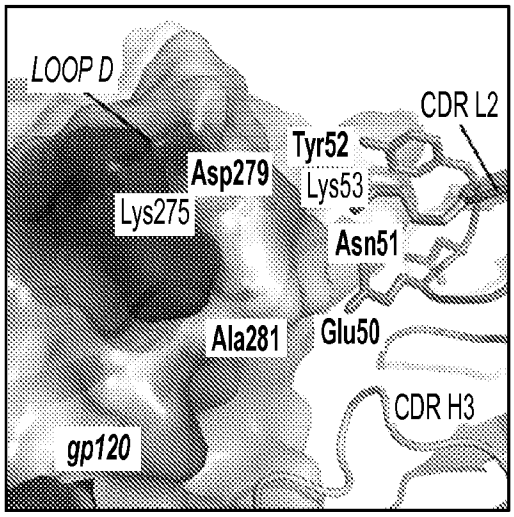

FIG. 6B

CHAIN(S)	POSITION	REVERTANT (LATE TO EARLY)	CALCULATED BINDING
gp120	275	K → E	+/-
gp120	279	D → N	-
gp120	281	A → V	-
gp120	281	S → V	-
gp120	281	G → V	-
LIGHT CHAIN	50	E → Q	-
LIGHT CHAIN	51	N → D	--
LIGHT CHAIN	52	Y → S	-

FIG. 6C

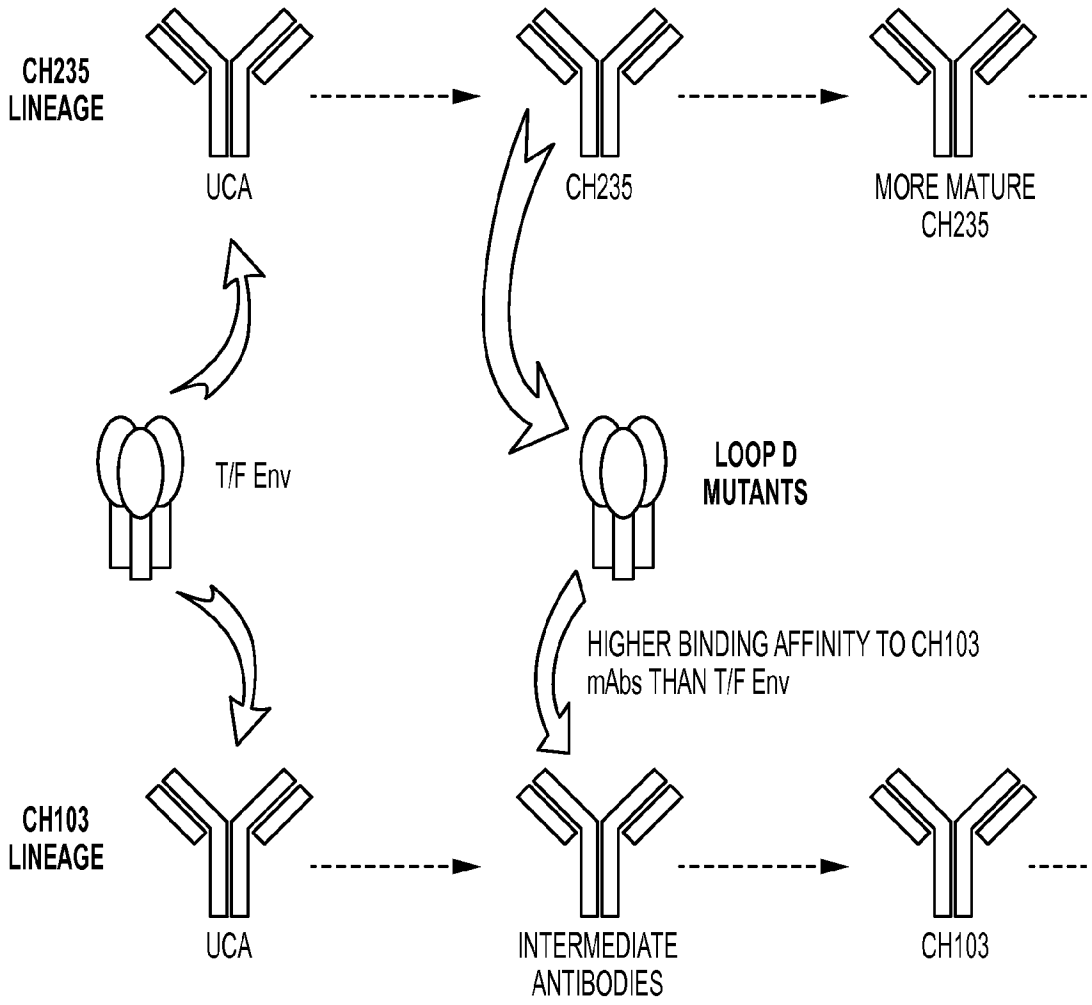
CH235
LINEAGE
UCA
CH235
MORE MATURE
CH235
T/F Env
LOOP D
MUTANTS
HIGHER BINDING AFFINITY TO CH103
mAbs THAN T/F Env
CH103
LINEAGE
UCA
INTERMEDIATE
ANTIBODIES
CH103

FIG. 7

	V1		LOOP D	CD4-BINDING LOOP
T?F	CTNATASN.....SSIIEGMKNC		ENITNNVKTIIVH	TFQPSSGGDLEITTH
w4.03	--------.....----------		----------	---------------
w4.26	--------.....----------		----------	---------------
w4.27	--------.....----------		----------	---------------
w4.29	--------.....----------		----------	---------------
w4.08	--------.....----------		----------	---------------
w4.37	--------.....----------		----------	---------------
w4.51	--------.....----------		----------	---------------
w4.56	--------.....----------		----------	---------------
w4.16	--------.....----------		----------	---------------
w4.13	--------.....----------		----------	---------------
w4.14	--------.....----------		----------	---------------
w4.11	--------.....----------		----------	---------------
w4.10	--------.....----------		----K-----	---------------
w4.15	--------.....----------		----R-----	---------------
w14.21	--------.....----------		------G------	---------------
w14.3	--------.....----------		----------	---------------
w14.19	--------.....----------		----------	---------------
w14.17	--------.....----------		----------	---------------
w14.20	--------.....----------		----------	---------------
w14.8	--------.....-----R----		----------	---------------
w14.2	--------.....----------		----------	---------------
w14.4	--------.....----------		----------	---------------
w14.6	--------.....----------		----------	---------------
w14.10	--------.....----------		------G------	---------------
w14.16	--------.....----------		----------	---------------
w14.30	--------.....-----E----		----------	---------------
w14.31	--------.....----------		----------	---------------
w14.32	--------.....----------		----------	---------------
w14.39	--------.....----------		----------	---------------
w14.29	--------.....----------		----------	---------------
w14.34	--------.....----------		----------	---------------
w14.12	--------.....----------		----------	-----P---------

FIG. 8

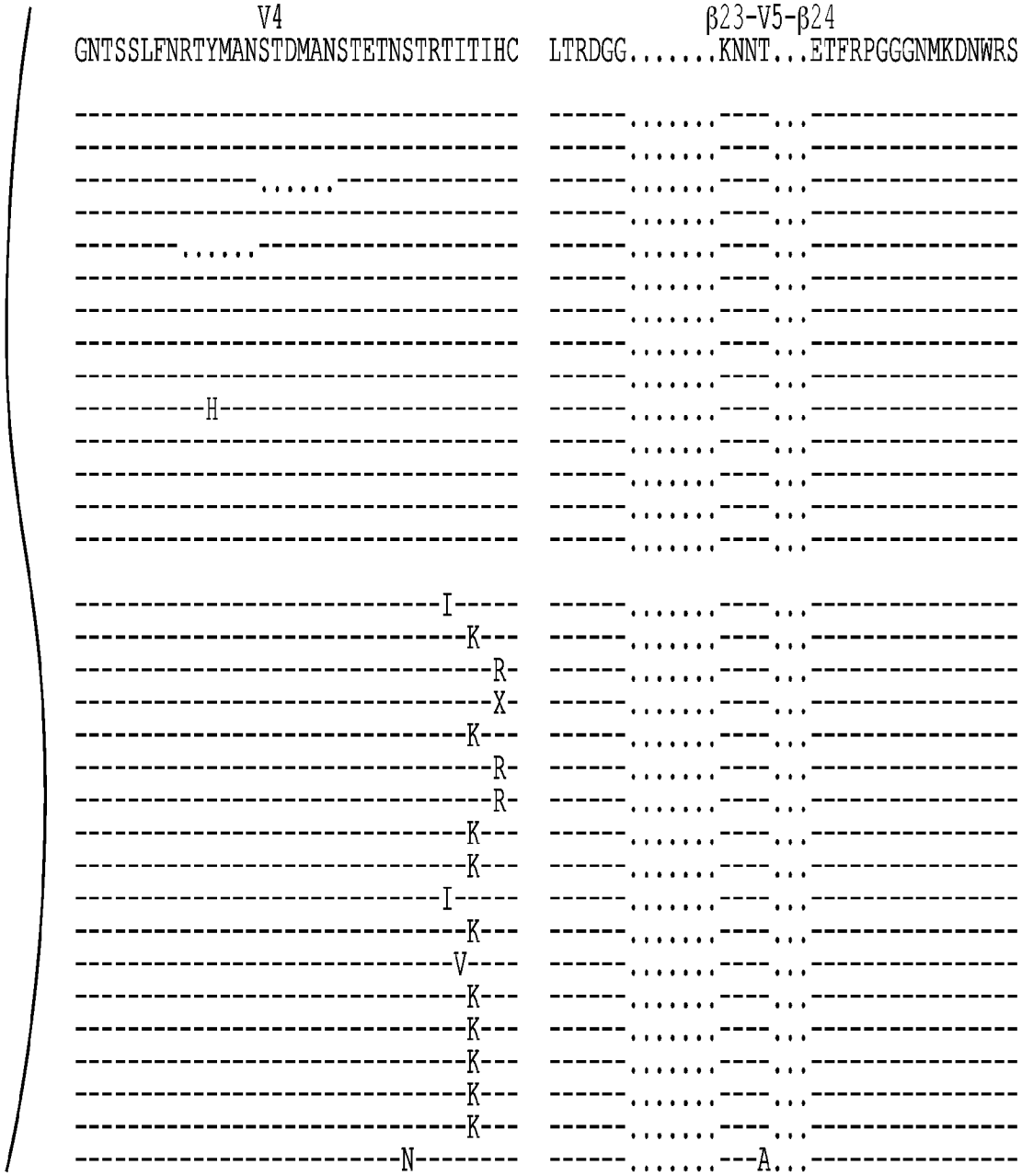

FIG. 8
CONTINUED

```
w20.14  --------.................N---------  ------A------  --------------
w20.7   ----N---.................N---------  ------G------  --------------
w20.9   ----.---.................----------  ------A------  --------------
w20.23  -----T--.................----------  ------A------  --------------
w20.24  -----T--.................----------  ------A------  --------------
w20.26  --------.................I---------  ------G------  --------------
w20.11  -----T--.................----------  ------------  --------------
w20.22  -----T--.................----------  ------------  --------------
w20.8   ------N-.................----------  ------A------  --------------
w20.2   ------N-.................-N---E----  ------------  --------------
w20.27  ------N-.................----------  ------A------  --------------
w20.4   ------N-.................----------  ------G------  --------------
w20.3   --------TNA.........TASN--T------   ------A------  --------------
w20.21  ----ASN.................----------  ------A------  --------------
w20.15  -----T--.................----------  ------------  --------------
w20.13  --------AT............ASN----------  ------------  --------------
w20.19  --------AT............ASN----------  ------------  --------------
w20.25  --------AT............ASN----------  ------------  --------------

w30.28  ------I-.................----------  ------D------  --------------
w30.13  ------I-.................----------  ------D------  --------------
w30.12  -----NATA..............SN----------  ------D------  --------------
w30.10  -----T--.................----------  ------D------  --------------
w30.19  ------R-CTNA.........TASN----------  -----SG------  --------------
w30.21  -----TNATA.............SN-----E----  -----TA------  --------------
w30.18  ------NATA.............SN----------  ------A------  --------------
w30.32  --------SSINCT.....NATASN----------  ------G------  --------------
w30.6   -----TNATA.............SN----------  ------A------  --------------
w30.15  --------AT............ASN----------  ------G------  --------------
w30.17  -----NATA.............SN----------  ----D-G------  --------------
w30.24  ------NATA.............SN----------  ------------  --------------
w30.5   ------NATA.............SN----------  ------G-----Q  --------------
w30.31  -----TNATA.............SN----------  ------A------  --------------
w30.36  ------NATA.............SN----------  ------------  --------------
w30.25  -----TNATA.............SN----------  ------A------  --------------
w30.8   -----TNATA.............SN----------  ------A------  --------------
w30.23  --------AT............ASN----------  ------G------  --------------
w30.26  -----SN.................-----E----  ------G------  --------------
w30.20  -----TNATA.............SN----------  ------A------  --------------
w30.27  --------AT............ASN----------  ------------  --------------
w30.34  --------AT............ASN----------  ------------  --------------
w30.37  --------AT............ASN----------  ------------  --------------
w30.9   ------NATA.............SN----------  ------------  --------------
```

FIG. 8
CONTINUED

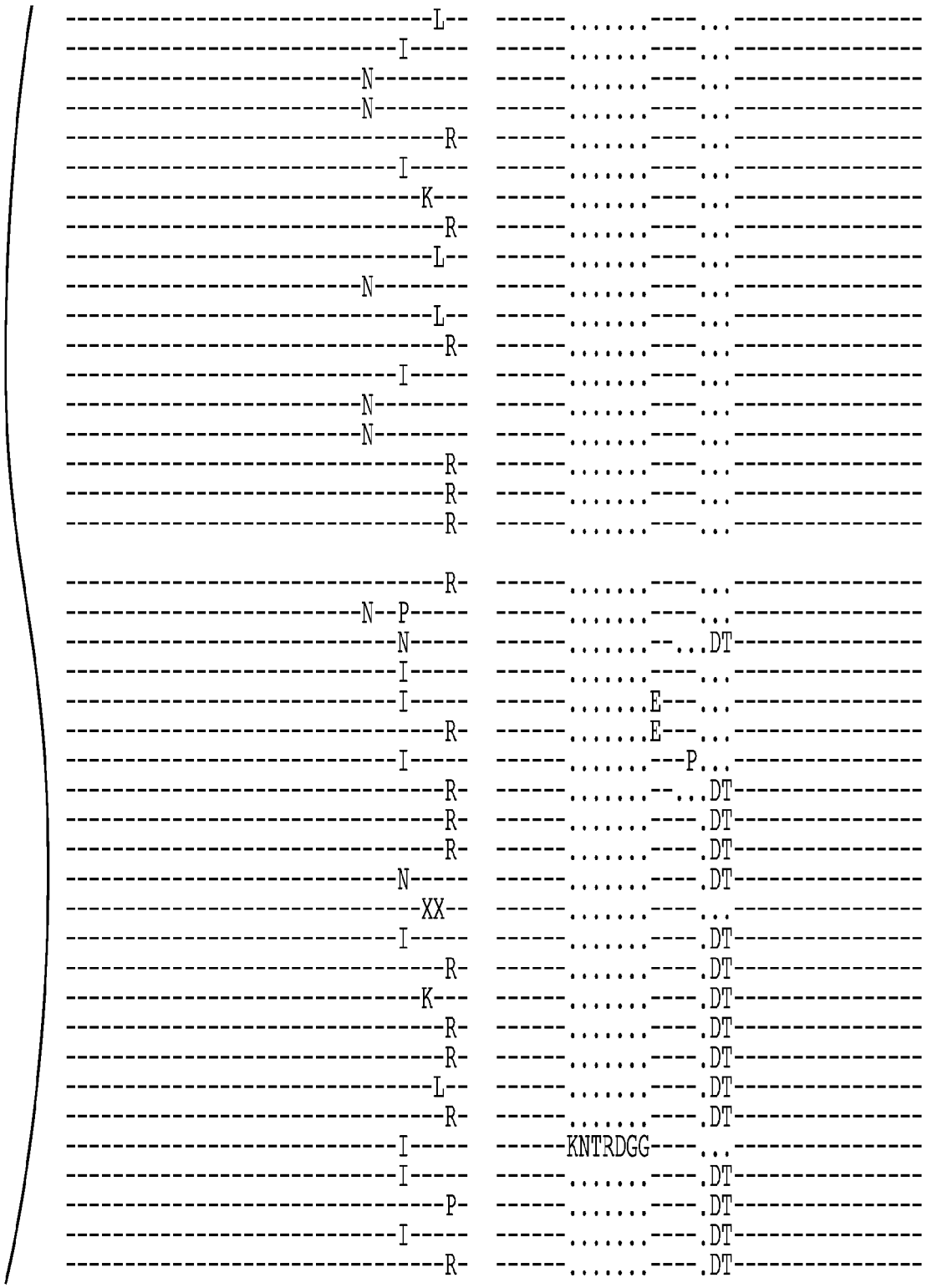

FIG. 8
CONTINUED

```
w53.31  --D-----ATASN.......ATASN----------  ----D-G------  --------------
w53.19  --D-----ATASN.......ATASN-----E----  ----D-G------  --------------
w53.13  --D-----ATASNS....SIIEGMN----------  ----D-G------  --------------
w53.14  --T-N-TAS..............N----------  ----D-G------  --------------
w53.32  ----N-TASNSSI.......IEGMN----------  ---ID-G------  --------------
w53.3   -----NATA..............SN---L------  ----D-G------  --------------
w53.25  --D-----ATASN.......ATASN----------  ----D-G------  --------------
w53.16  ----N-TASNSSI.......IEGMN----------  ----D-G------  --------------
w53.17  -----NATA..............SN---L------  ----D-G------  --------------
w53.15  -----NATA..............SN---L------  ----D-G------  --------------
w53.28  --D-----ATASNS....SIIEGMN----------  ----D-G------  --------------
w53.22  ----N-TASNSSI.......IEGMN----------  ----D-G------  --------------
w53.27  -----NATA..............SN---L------  ----D-G------  --------------
w53.8   --T-N-TAS..............N----------  ----D-G------  --------------
w53.10  --D-----ATASN.......ATASN----------  ----D-G------  --------------
w53.29  --D-----AT............AIN----------  ------A------  --------------
w53.6   -----NATA..............SN---L------  ----D-G------  --------------
w53.9   -I--N-TASNSSI.......IEGMN----------  ----D-G------  --------------
w53.11  ----N-TASNSSI.......IEGMN----------  ----D-G------  --------------
```

FIG. 8
CONTINUED

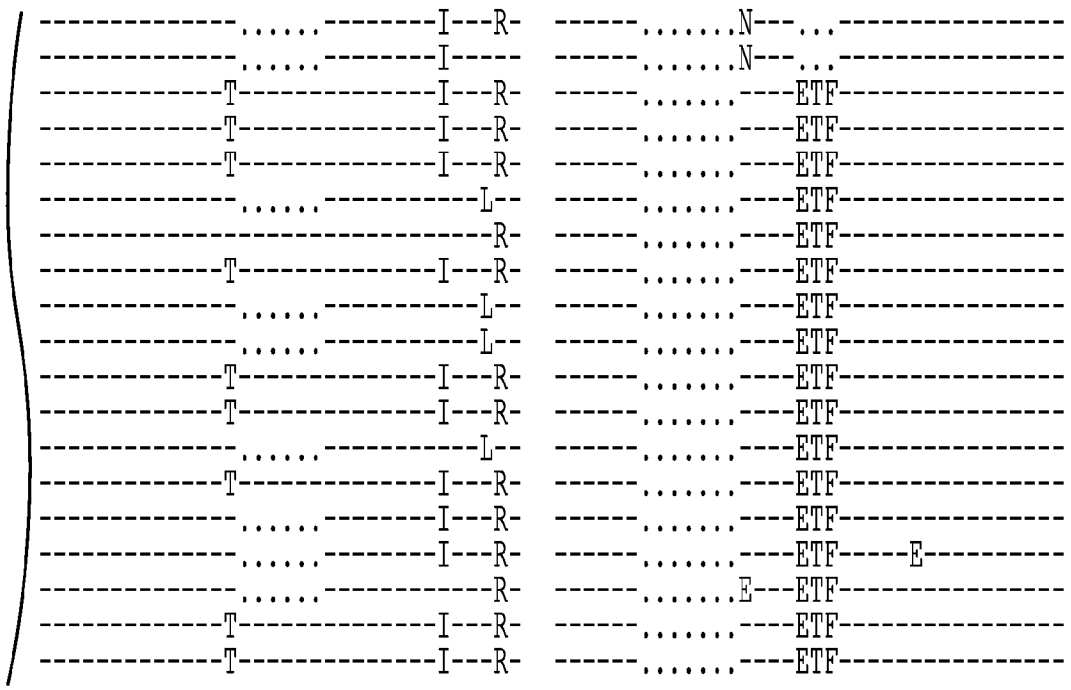

FIG. 8
CONTINUED

```
w78.15   -----NATA.............SN---L------  K---D-G------  --------------
w78.1    -I---NATA.............SNN--L------  K---D-G------  --------------
w78.3    -I---NATA.............SN---L------  K---D-G-I----  --------------
w78.10   -ID-----AT............AINI----E----  K---D-G------  --------------
w78.8    ---VN-TASNSSI.......IEGMN---L------  K---D-G------  --------------
w78.7    ---VN-TASNSSI.......IEGMN---L------  K---D-G------  --------------
w78.33   -ID-N-TASNA..........TASN----------  -----SA------  --------------
w78.6    --D-----ATASNATA.SNSSI.NS-.---E----  ----D-G------  ----------V---
w78.14   ---VN-TASNSSI.......IEGMN---L------  K---D-G------  --------------
w78.17   -I---NATA.............SN---L------  K---D-G------  --------------
w78.38   -ID-----AT............AINI----E----  K---D-G------  --------------
w78.25   --D-----ATASNATA.SNATASNS-I--------  K---D-G------  --------------
w78.4    --D-----ATASNAT..ASNATASN---L------  K---D-G------  --------------
w78.9    --D-----ATASNATA.SNATASNS-I--------  K---D-G------  --------------
w78.5    --D-N-TASNT.NATASNINATASN----------  ----D-G------  ----------V---
w78.16   --D--T.-ATASNATA.SNATASNS-.--------  ----D-G------  ----------V---

w100.B4  --D-N-TASNTNATAS.NINATASKN----E----  K---D-G------  ---S-----P-----
w100.A3  --D-N-TASNSSI.......IKGMN--M--E----  K---D-G------  --------------
w100.A11 --D-N-TASN..IN......ATASK-----E----  ----D-S------  ---------P-----
w100.B3  --D-N-TASNTNATAS.NINATASK-----E----  ----D-S------  ---------P-----
w100.b7  --D-N-TASN..IN......ATASK-----E----  ----D-S------  ---------P-----
w100.A5  --D-N-TASNTNATAS.NINATASK-----E----  ----D-S------  ---------P-----
w100.B6  --D-N-TASNTNATAS.NINATASK-----E----  ----D-S------  ---------P-----
w100.A2  --D-N-TASNTNATAS.NINATASK-----E----  ----D-S------  ---------P-----
w100.A13 --D-N-TASNANATAS.NTNATVSN-----E----  -----SA------  ---------P-----
w100.A6  -I---NATA.............SN---L------  K---D-G------  --------------
w100.A4  -I---NATA.............SN---L------  K---D-G------  --------------
w100.A12 -I---NATA.............SN---L------  K---D-G------  --------------
w100.A10 --D--NATA.............SN---LG-----  K---D-G------  --------------
w100.B8  --D-N-TASNSSI.......IKGMN--M--E----  K---D-G------  --------------
```

FIG. 8
CONTINUED

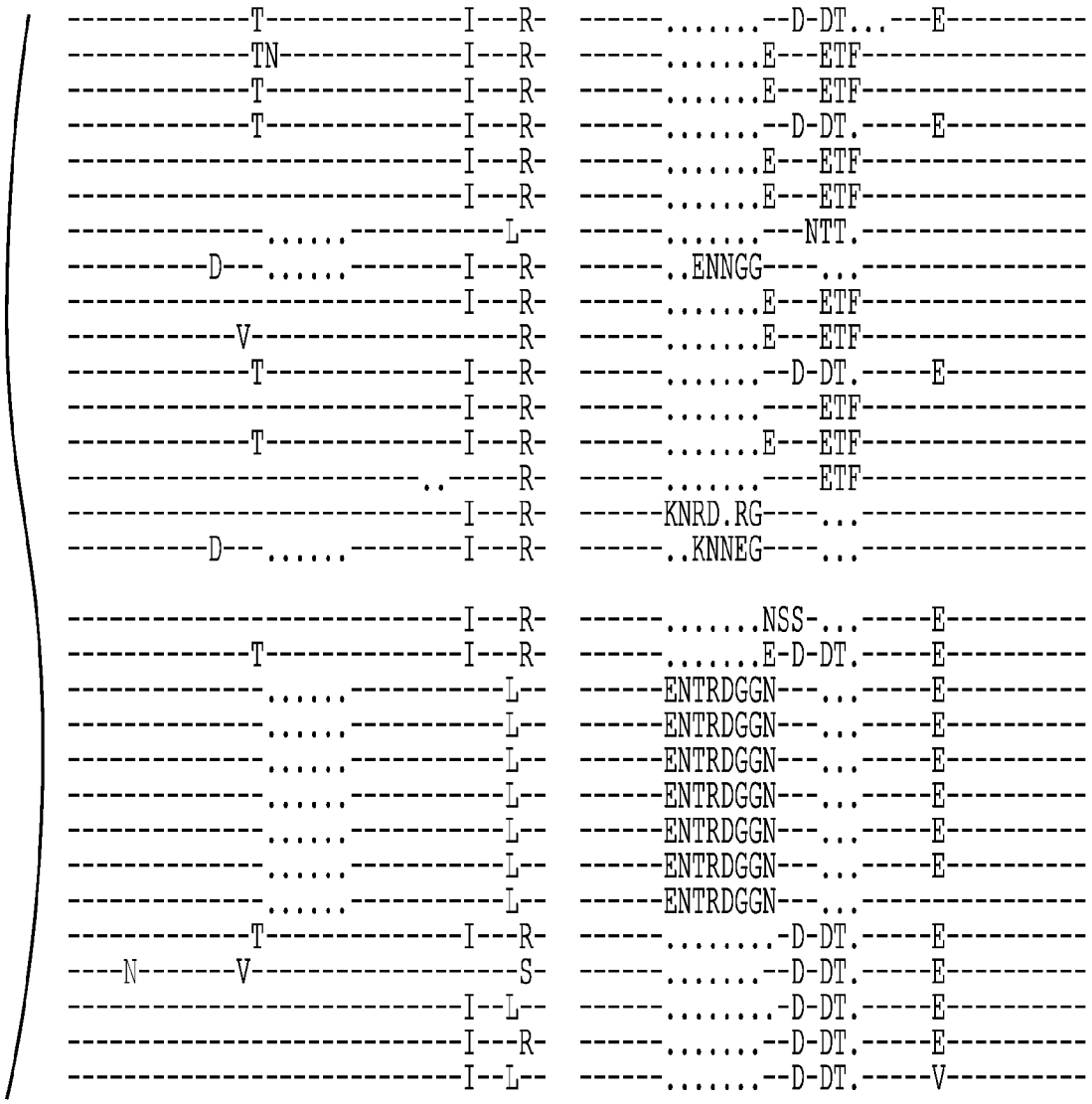

FIG. 8
CONTINUED

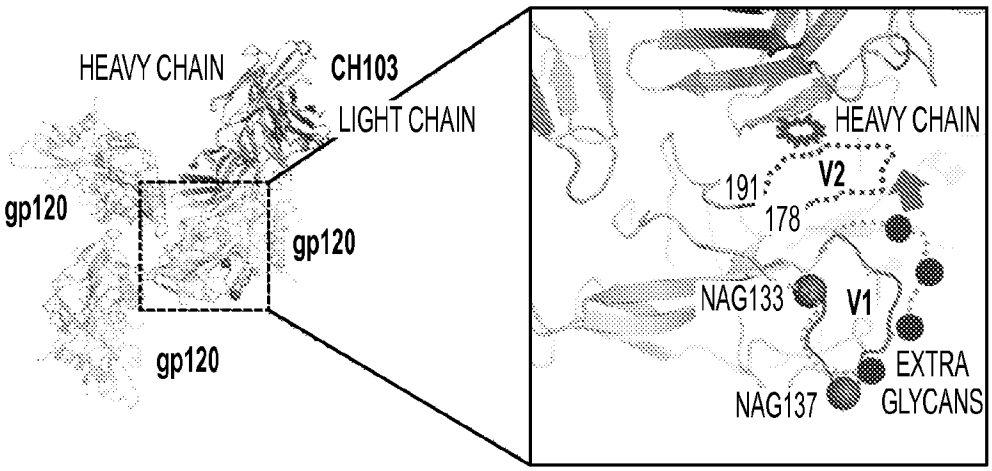
HEAVY CHAIN
CH103
LIGHT CHAIN
gp120
gp120
gp120
HEAVY CHAIN
191
V2
178
NAG133
V1
EXTRA
GLYCANS
NAG137

FIG. 9A

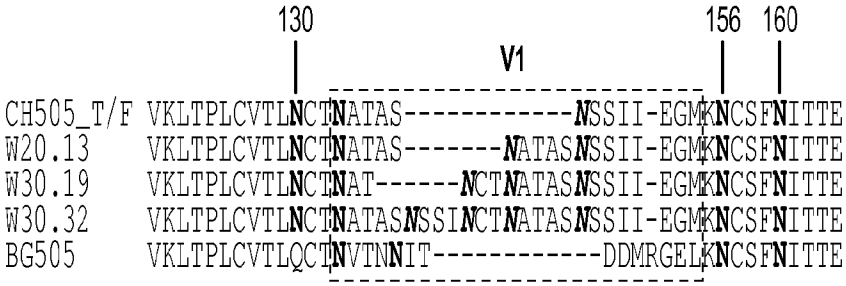
130
156
160
V1
CH505_T/F VKLTPLCVTLNCTNATAS----------NSSII-EGMKNCSFNITTE
W20.13 VKLTPLCVTLNCTNATAS-------NATASNSSII-EGMKNCSFNITTE
W30.19 VKLTPLCVTLNCTNAT------NCTNATASNSSII-EGMKNCSFNITTE
W30.32 VKLTPLCVTLNCTNATASNSSINCTNATASNSSII-EGMKNCSFNITTE
BG505 VKLTPLCVTLQCTNVTNNIT----------DDMRGELKNCSFNITTE

FIG. 9B

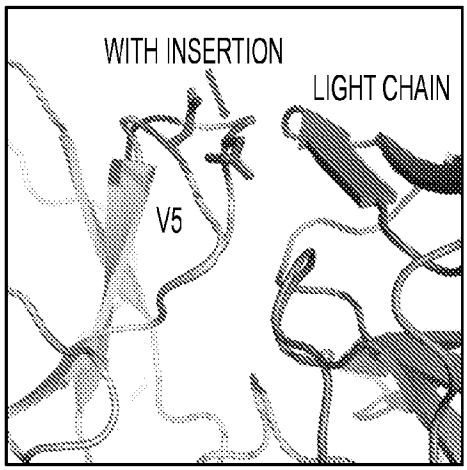

FIG. 9C

VIRUS	UCA	IA8	IA7	IA6	IA5	IA4	IA3	IA2	IA1	CH103	CH104	CH105	CH106
T/F	>50	44.67	10.17	10.17	6.82	9.72	6.62	2.73	1.42	4.14	3.08	5.1	2.29
M28	>50	>50	>50	>50	>50	>50	>50	11.19	8.99	10.89	9.95	22.63	4.89

FIG. 9D

T/F	STRTITIH	NO.	%
w4	--------	53	100%
w7	--------	8	27%
w7	-I------	7	23%
w7	-------R	5	17%
w7	-A------	4	13%
w7	------L-	1	3%
w7	-----I--	1	3%
w7	---I----	1	3%
w7	--Q-----	1	3%
w7	N-------	1	3%
w7	-X------	1	3%
w8	--------	5	22%
w8	-I------	9	39%
w8	------L-	2	9%
w8	-A------	2	9%
w8	-------Y	1	4%
w8	-------R	1	4%
w8	---I----	1	4%
w8	--Q-----	1	4%
w8	-K------	1	4%
w9	--------	3	12%
w9	-I------	8	31%
w9	N-------	5	19%
w9	---I----	4	15%
w9	-------R	2	8%
w9	--Q-----	2	8%
w9	-X------	2	8%
w10	--------	1	5%
w10	---I----	5	24%
w10	-------R	4	19%
w10	-------N	2	10%
w10	-A------	2	10%
w10	N-------	2	14%
w10	----V---	1	5%
w10	-I------	1	5%
w10	-K------	1	5%
w10	...-----	1	5%
w14	----(K)-	12	48% ←
w14	-------R	5	20% ←
w14	---I----	4	16%
w14	N-------	2	8% ←
w14	----V---	1	4% ←
w14	-------X	1	4%

FIG. 10A

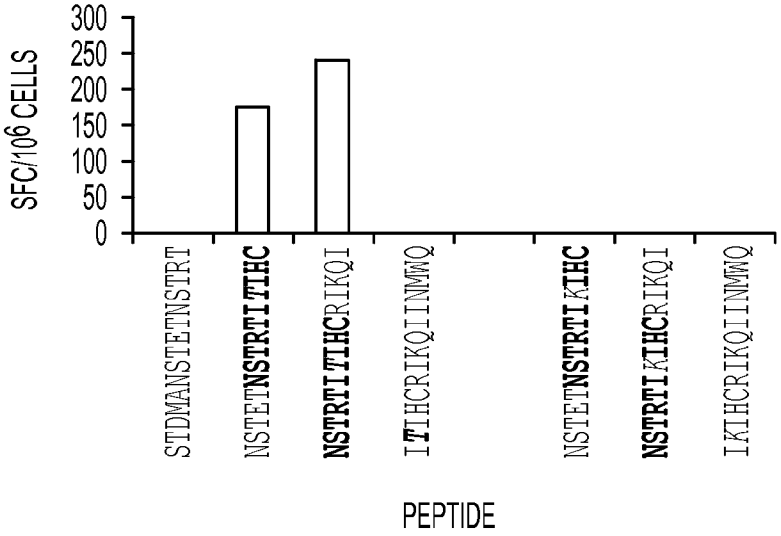

FIG. 10B

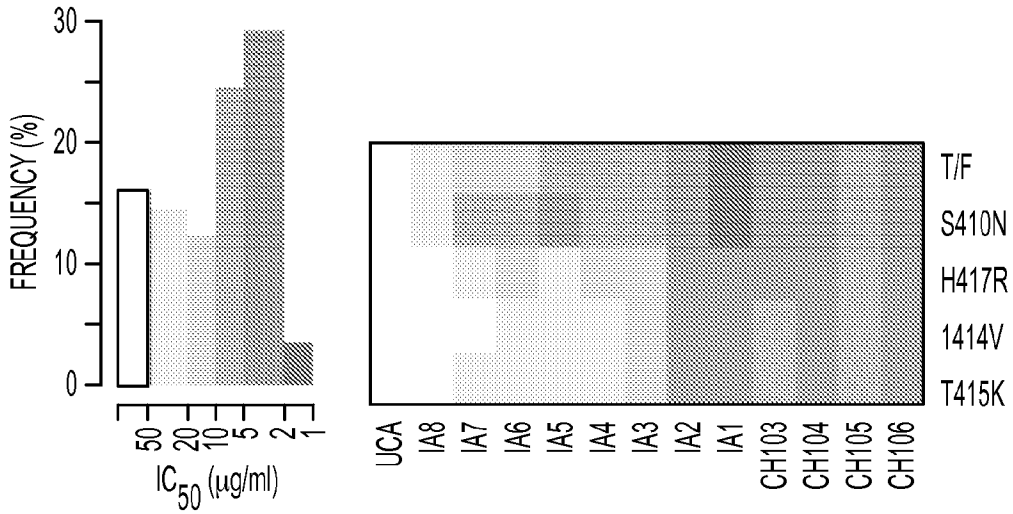

FIG. 10C

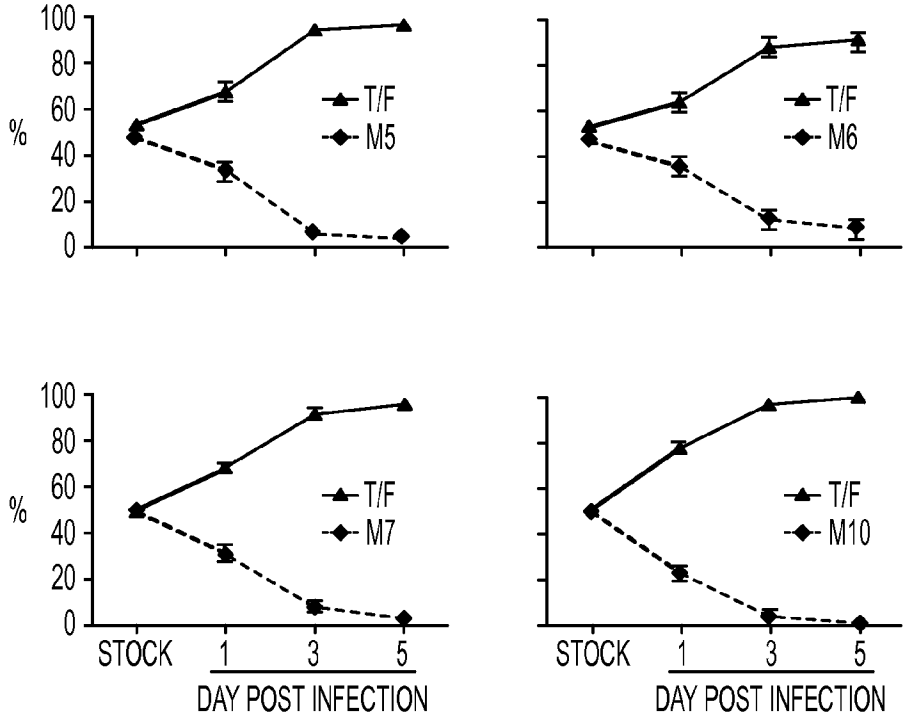
100
80
60
40
20
0
%
T/F
M5
T/F
M6
100
80
60
40
20
0
%
T/F
M7
T/F
M10
STOCK
1
3
5
DAY POST INFECTION
STOCK
1
3
5
DAY POST INFECTION

FIG. 10D

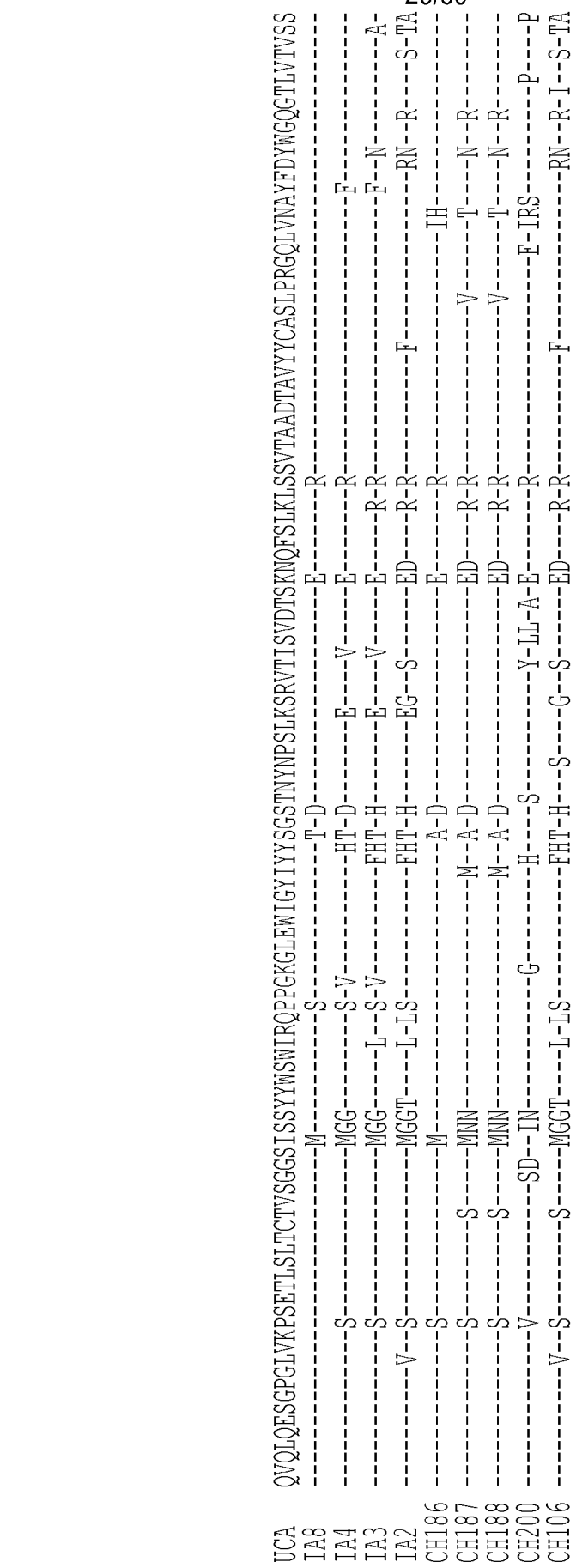
UCA QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIYYSGSTNYNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCASLPRGQLVNAYFDYWGQGTLVTVSS
IA8 ---------M---------S---------T-D---------E---------R---------
IA4 ---------S---------MGG---------S-V---------HT-D---------E---V---E---------R---------F---------
IA3 ---------S---------MGG---L-S-V---------FHT-H---------E---V---E---R-R---------F-N---------A-
IA2 ---V-S---------MGGT--L-LS---------FHT-H---------EG-S---------ED---R-R---------F---------RN-R---S-TA
CH186 ---------S---------M---------A-D---------E---------R---------IH---------
CH187 ---------S---------S---MNN---------M-A-D---------ED---R-R---------V---T---N-R---------
CH188 ---------S---------S---MNN---------M-A-D---------ED---R-R---------V---T---N-R---------
CH200 ---------V---------SD--IN---------G---------H---S---------Y-LL-A-E---------R---------E-IRS---------P---P
CH106 ---V-S---------S---MGGT---L-LS---------FHT-H---S---G-S---------ED---R-R---------F---------RN-R-I--S-TA

FIG. 11A

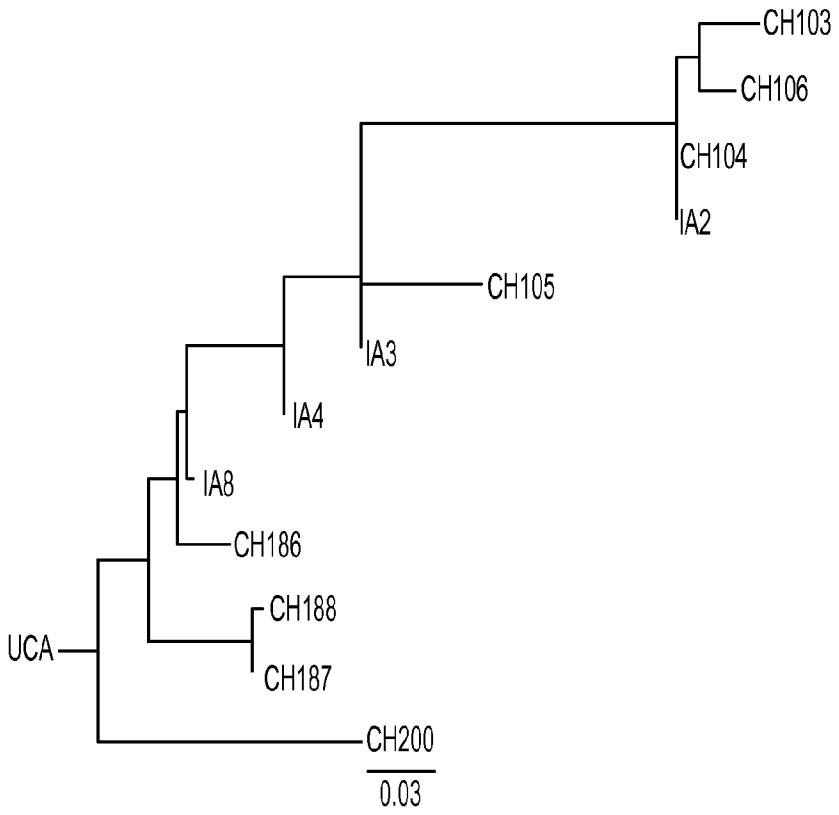
CH103
CH106
CH104
IA2
CH105
IA3
IA4
IA8
CH186
CH188
UCA
CH187
CH200
0.03

FIG. 11B

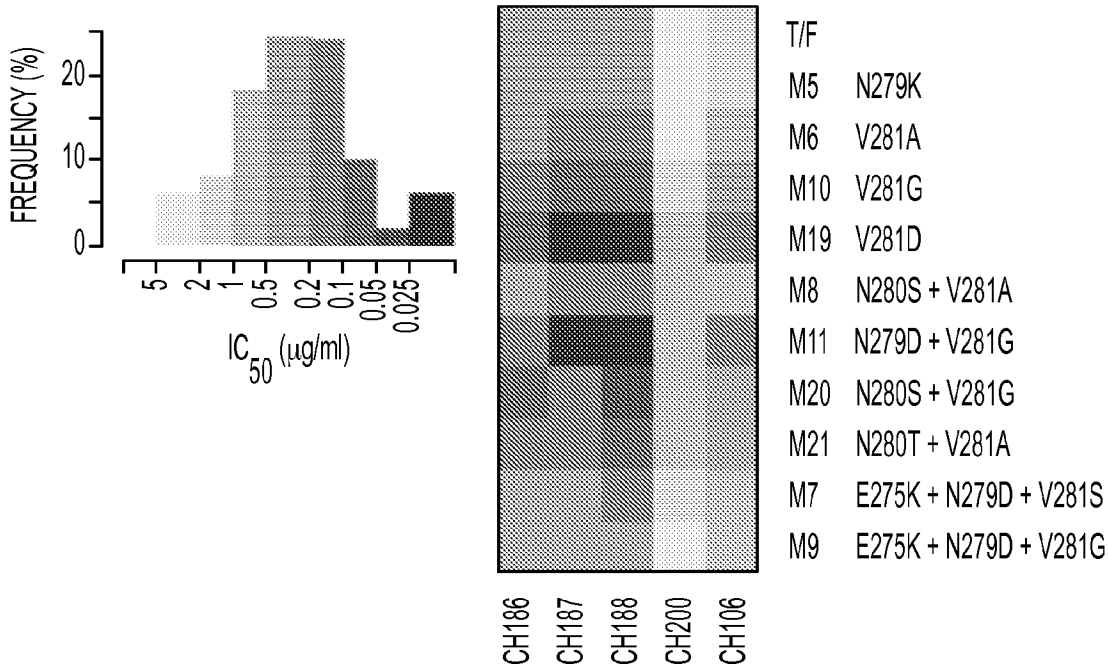

FIG. 11C

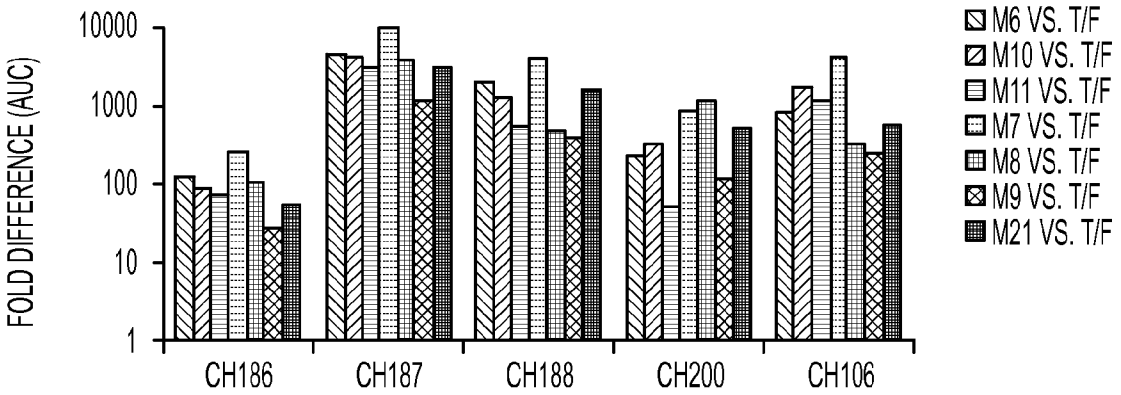

FIG. 11D

ANTIBODY	VH	DH	JH	MUTATION FREQUENCY	CDRH3 LENGTH	ISOTYPE	VL	JL	MUTATION FREQUENCY	CDRL3 LENGTH
UCA	4-59*01	3-16*01	4*02	0.0%	15	IgG1	3-1*01	1*01	0.0%	10
CH186	4-59*01	3-16*01	4*02	4.7%	15	IgG1	3-1*01	1*01	5.6%	10
CH187	4-59*01	3-16*01	4*02	5.8%	15	IgG1	3-1*01	1*01	6.5%	10
CH188	4-59*01	3-16*01	4*02	6.1%	15	IgG1	3-1*01	1*01	7.5%	10
CH200	4-59*01	3-16*01	4*02	9.1%	15	IgG1	3-1*01	1*01	6.2%	10
CH106	4-59*01	3-16*01	4*02	16.0%	15	IgG1	3-1*01	1*01	11.2%	10

FIG. 11E

ANTIBODY	CH505.T/F	B.SF162	A.Q769	A.Q168	A.Q842	B.6101	B.BaL	B.BX08	B.SS1196	B.BG1168	B.JRFL	MLV-SVA
CH186	0.46	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
CH187	0.21	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
CH188	0.29	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
CH200	2.41	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
CH106	3.12	0.08	1	2.53	1.46	1.8	0.68	1.15	1.34	21.7	0.02	>50

FIG. 11F

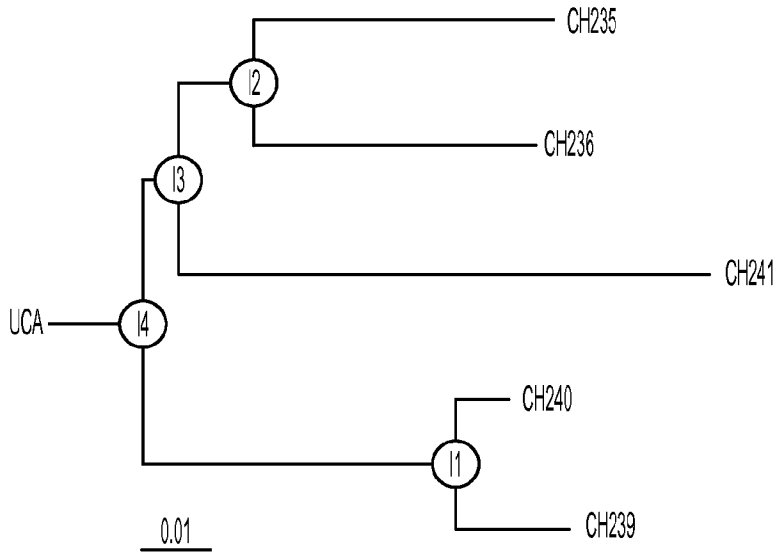

FIG. 12A

ANTIBODY ID	IgH ID	VH	DH	JH	MUTATION FREQUENCY	CDRH3 LENGTH	ISOTYPE	VL ID	VL	JL	MUTATION FREQUENCY	CDRL3 LENGTH
UCA	UCAVH	1-46*01	3-10*01	4*02	0.0%	15	IgG1	UCAVK	3-15*01	1*01	0.0%	8
IA4	I4VH	1-46*01	3-10*01	4*02	1.1%	15	IgG1	I4VK	3-15*01	1*01	0.3%	8
IA3	I3VH	1-46*01	3-10*01	4*02	1.6%	15	IgG1	I3VK	3-15*01	1*01	0.6%	8
IA2	I2VH	1-46*01	3-10*01	4*02	3.0%	15	IgG1	I2VK	3-15*01	1*01	0.6%	8
IA1	I1VH	1-46*01	3-10*01	4*02	6.6%	15	IgG1	I1VK	3-15*01	1*01	2.8%	8
CH235	CH235VH	1-46*01	3-10*01	4*02	7.9%	15	IgG1	CH235VK	3-15*01	1*01	3.8%	8
CH236	CH236VH	1-46*01	3-10*01	4*02	8.2%	15	IgG1	CH236VK	3-15*01	1*01	2.8%	8
CH239	CH239VH	1-46*01	3-10*01	4*02	7.9%	15	IgG1	CH239VK	3-15*01	1*01	4.7%	8
CH240	CH240VH	1-46*01	3-10*01	4*02	7.4%	15	IgG1	CH240VK	3-15*01	1*01	3.1%	8
CH241	CH241VH	1-46*01	3-10*01	4*02	11.2%	15	IgG1	CH241VK	3-15*01	1*01	3.5%	8

FIG. 12B

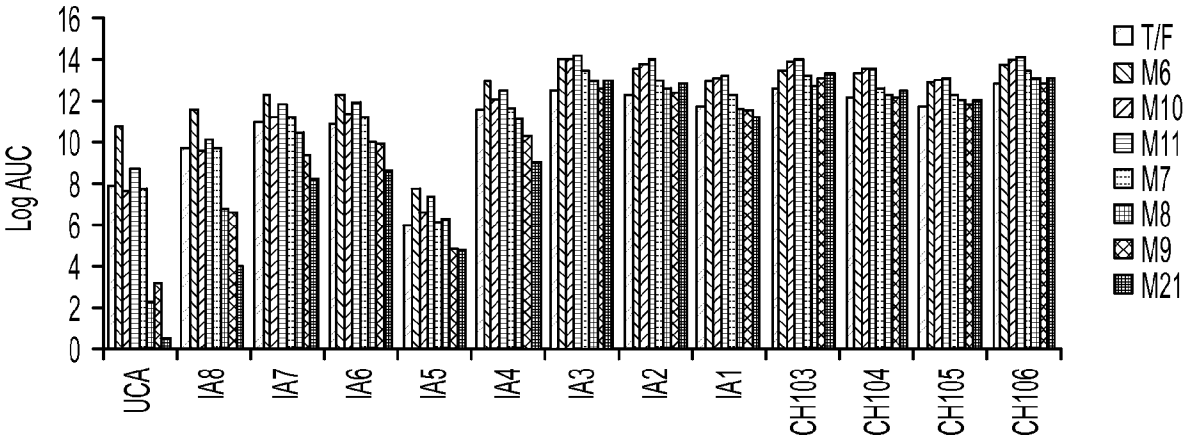

FIG. 13A

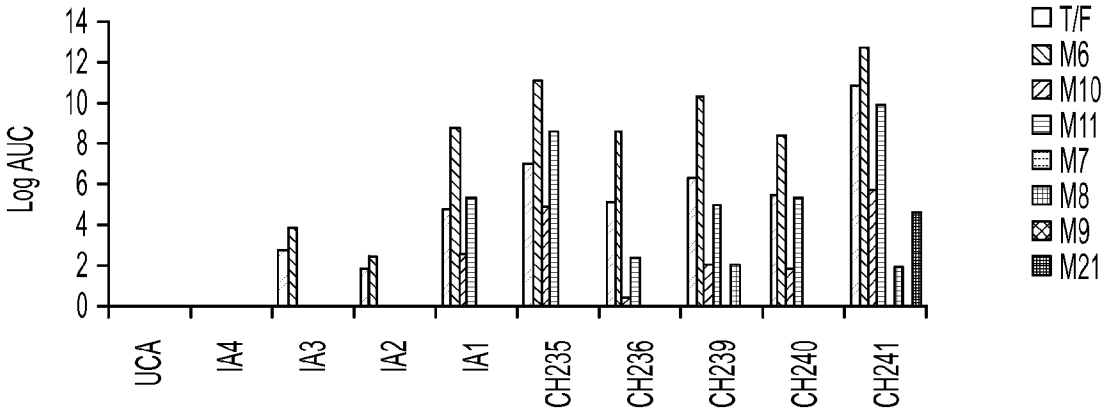

FIG. 13B

CH103 CLONAL IMAGE

TIME POINT	VIRUS	UCA	IA8	IA7	IA6	IA5	IA4	IA3	IA2	IA1	CH103	CH104	CH105	CH106	CD4bs bnAb CH31
T/F		>50	49.37	14.67	4.64	12.84	10.94	6.22	1.50	2.47	3.12	1.99	4.90	2.28	<0.023
WEEK 4	w4.3	15.12	2.05	0.71	0.99	0.13	0.67	0.85	0.29	0.16	0.13	0.29	0.38	0.16	<0.023
	w4.26	19.50	1.50	0.77	0.88	0.07	0.67	0.41	0.15	0.25	0.24	0.27	0.24	0.09	<0.023
	w4.27	>50	12.39	2.32	2.57	4.69	2.70	5.70	1.89	1.17	1.94	1.44	2.40	0.53	<0.023
	w4.29	>50	31.68	5.57	4.72	2.48	4.70	3.40	1.30	1.10	1.90	1.36	2.24	0.79	<0.023
	w4.8	>50	16.75	4.20	4.11	3.38	3.24	6.09	1.29	0.95	1.89	1.62	2.92	1.39	<0.023
	w4.37	>50	25.63	8.66	7.97	4.76	5.61	4.15	1.68	1.00	1.87	1.65	2.19	0.43	<0.023
	w4.51	>50	34.15	6.83	5.77	8.62	6.54	5.45	1.54	1.36	2.04	1.59	2.11	0.56	<0.023
	w4.56	>50	34.78	8.46	8.51	6.42	6.35	5.83	2.00	1.39	2.40	1.59	3.36	0.80	<0.023
	w4.16	>50	21.26	8.43	4.33	7.32	6.95	6.40	2.78	1.39	2.83	2.66	4.33	1.23	<0.023
	w4.13	>50	25.24	3.08	3.50	9.78	4.08	7.88	3.46	1.45	3.15	2.09	3.40	1.08	<0.023
	w4.14	>50	47.61	11.92	9.71	13.78	11.02	10.62	3.53	2.14	4.00	2.34	5.22	1.32	<0.023
	w4.11	>50	>50	14.35	10.32	8.17	8.76	7.71	2.79	1.71	2.37	2.32	3.62	1.20	<0.023
	w4.10	>50	41.36	8.66	5.32	5.66	3.80	3.68	1.17	0.74	1.10	1.31	2.44	0.71	>50
	w4.15	>50	>50	16.45	9.82	6.43	8.20	6.23	1.92	1.34	1.37	1.49	4.03	1.41	39.26
WEEK 14	w14.21	>50	24.97	11.01	5.22	4.07	3.36	0.94	0.39	0.24	0.53	0.37	0.60	0.41	0.05
	w14.3	>50	>50	23.50	13.51	8.13	10.07	5.83	1.18	1.84	2.57	1.69	3.64	1.45	<0.023
	w14.19	>50	>50	15.49	10.14	20.09	9.20	6.06	1.82	1.36	4.66	2.47	4.39	2.47	<0.023
	w14.17	>50	>50	23.66	11.66	21.81	12.23	8.12	2.13	1.41	3.70	2.63	4.98	2.58	<0.023
	w14.20	>50	>50	23.56	12.68	20.30	15.94	6.27	1.96	1.07	2.92	1.88	3.02	1.43	<0.023
	w14.8	>50	28.47	23.12	17.30	34.15	12.93	8.81	1.06	1.54	1.06	1.41	4.59	1.60	<0.023
	w14.2	>50	>50	26.66	14.92	25.33	13.63	10.30	2.28	2.87	4.01	3.24	6.84	2.86	<0.023
	w14.4	>50	>50	24.72	20.23	28.95	15.59	10.41	2.77	2.25	3.37	2.35	6.04	2.55	<0.023
	w14.6	>50	>50	26.84	25.13	32.85	20.88	12.23	3.37	3.07	4.14	3.14	6.99	3.02	0.03
	w14.10	>50	>50	28.28	29.42	25.98	28.93	4.98	1.72	1.27	1.60	1.90	2.82	0.98	0.24
	w14.16	>50	>50	42.21	27.23	32.29	18.85	11.75	4.30	4.08	6.27	4.48	8.42	4.45	0.04
	w14.30	>50	>50	>50	46.59	39.45	34.46	15.52	4.94	3.01	6.17	4.20	8.11	3.41	0.04
	w14.31	>50	>50	36.38	25.99	31.67	28.03	13.04	4.05	4.28	5.84	3.69	7.22	3.19	0.03
	w14.32	>50	>50	41.85	25.02	21.56	22.67	16.00	5.66	3.66	5.51	3.96	8.26	4.41	<0.023
	w14.39	>50	43.27	40.99	24.91	34.07	32.87	15.15	5.77	3.09	5.44	4.73	8.48	4.52	0.03
	w14.29	>50	>50	37.65	39.45	>50	22.36	14.88	5.66	4.02	6.91	6.14	12.54	6.33	0.04
	w14.34	>50	>50	>50	43.94	48.04	49.79	22.64	7.05	5.09	7.32	5.72	11.24	4.66	0.06
	w14.12	>50	>50	>50	>50	>50	>50	>50	>50	>50	6.03	>50	>50	>50	<0.023

FIG. 14A

WEEK 20													
w20.14	>50	42.47	10.13	5.45	6.33	4.88	1.99	1.22	0.72	0.08	0.67	1.04	0.46	<0.023
w20.7	>50	23.88	6.85	2.85	2.92	3.83	1.39	0.62	0.41	0.52	0.95	0.86	0.60	0.04
w20.9	>50	14.87	5.46	2.07	4.30	3.06	3.62	1.16	1.06	1.37	1.33	1.92	1.13	<0.023
w20.23	>50	26.79	8.07	4.74	10.60	3.45	2.65	1.12	0.54	0.87	0.87	1.48	0.68	<0.023
w20.24	>50	28.92	9.44	5.57	12.97	4.73	2.51	1.12	0.57	1.11	1.52	3.15	1.54	<0.023
w20.26	>50	48.25	10.45	7.31	8.65	6.79	2.06	0.90	0.51	0.88	1.29	1.23	0.77	0.05
w20.11	>50	32.68	21.45	13.04	4.41	12.53	5.97	1.14	1.17	0.43	0.85	1.82	0.61	<0.023
w20.22	>50	>50	20.77	12.38	14.10	8.22	3.48	1.25	0.53	1.45	0.88	2.21	1.01	<0.023
w20.8	>50	>50	14.67	8.41	3.78	7.53	3.34	1.37	1.14	2.02	1.63	3.54	1.70	<0.023
w20.2	>50	>50	20.17	18.40	7.09	19.49	11.80	4.08	2.12	3.50	3.29	6.20	2.78	<0.023
w20.27	>50	>50	20.82	14.21	25.37	9.51	5.70	2.24	1.20	1.81	1.85	3.89	1.22	<0.023
w20.4	>50	>50	25.99	9.46	3.98	11.83	2.77	0.88	0.55	0.67	0.60	1.36	0.67	0.07
w20.3	>50	>50	>50	24.06	4.17	22.41	4.93	1.63	0.77	1.41	1.46	2.35	1.04	<0.023
w20.21	>50	>50	>50	29.58	>50	21.02	6.36	1.88	1.23	2.54	1.81	3.64	1.56	<0.023
w20.15	>50	>50	42.09	21.00	19.46	29.54	16.25	6.41	3.12	6.91	5.90	11.42	6.16	0.05
w20.13	>50	>50	>50	>50	19.84	31.77	20.17	6.70	3.62	5.82	5.60	14.16	6.15	<0.023
w20.19	>50	>50	43.58	>50	43.43	>50	21.65	7.58	5.05	8.34	6.12	13.42	7.69	<0.023
w20.25	>50	>50	>50	>50	37.72	>50	23.37	11.15	6.41	7.95	9.01	14.00	7.96	<0.023

FIG. 14B

WEEK 30													
w30.28	>50	44.00	23.07	7.18	3.78	6.92	4.35	0.77	0.49	0.77	0.59	2.13	0.77	>50
w30.13	>50	>50	>50	8.43	2.77	9.64	5.19	1.00	1.06	1.43	0.43	3.86	1.08	>50
w30.12	>50	>50	36.65	25.87	6.44	18.39	1.92	0.52	0.65	1.11	0.95	1.88	0.62	>50
w31.10	>50	>50	>50	35.00	6.93	23.97	8.07	1.11	1.61	1.56	1.08	3.88	1.14	>50
w30.19	>50	>50	>50	>50	>50	>50	1.45	0.47	0.39	0.58	0.51	0.81	0.54	>50
w30.21	>50	>50	>50	>50	>50	>50	2.35	0.43	0.62	1.05	0.53	1.49	0.56	42.95
w30.18	>50	>50	>50	>50	>50	>50	2.92	1.12	1.08	1.36	1.16	2.10	0.88	<0.023
w30.32	>50	>50	>50	33.90	>50	40.93	2.56	1.09	0.54	1.03	1.52	2.89	1.25	0.31
w30.6	>50	>50	>50	>50	>50	>50	15.27	1.30	4.99	4.15	1.30	9.23	4.51	0.03
w30.15	>50	>50	>50	>50	>50	>50	11.44	3.50	4.60	3.98	5.79	7.43	2.80	0.12
w30.17	>50	>50	>50	>50	>50	>50	3.86	7.28	6.86	4.28	6.78	14.24	3.90	0.05
w30.24	>50	>50	>50	39.62	38.33	>50	19.21	4.81	8.91	6.07	7.64	12.52	7.64	1.20
w30.5	>50	>50	>50	>50	>50	>50	45.16	6.76	9.67	8.05	7.45	34.12	10.04	0.04
w30.31	>50	>50	>50	>50	>50	>50	43.08	11.73	6.71	8.79	9.79	27.73	10.00	0.04
w30.36	>50	>50	>50	>50	>50	>50	>50	10.96	8.12	9.24	11.07	21.15	8.13	0.26
w30.25	>50	>50	>50	>50	>50	>50	20.19	11.02	12.90	11.99	8.69	12.84	7.70	0.04
w30.8	>50	>50	>50	>50	>50	>50	>50	10.35	12.83	12.56	7.07	14.11	9.91	<0.023
w30.23	>50	>50	>50	>50	>50	>50	33.12	18.56	17.21	9.51	12.81	23.24	9.39	0.26
w30.26	>50	>50	>50	>50	>50	>50	>50	17.23	12.50	12.11	18.90	32.38	12.48	0.12
w30.20	>50	>50	>50	>50	>50	>50	>50	20.42	31.48	30.02	28.33	44.19	17.56	0.04
w30.27	>50	>50	>50	>50	>50	>50	>50	43.69	18.28	13.02	38.02	>50	31.87	0.17
w30.34	>50	>50	>50	>50	>50	>50	>50	44.85	49.72	26.37	47.07	>50	39.83	0.24
w30.37	>50	>50	>50	>50	>50	>50	>50	29.75	25.19	22.30	>50	>50	40.42	0.14
w30.9	>50	>50	>50	>50	>50	>50	>50	44.49	>50	49.94	42.98	>50	19.82	0.26

FIG. 14C

WEEK 53															
w53.31	>50	>50	>50	>50	>50	>50	2.38	1.06	0.43	1.24	1.09	2.06	1.68	>50
w53.19	>50	>50	>50	>50	>50	>50	4.58	2.59	1.91	3.16	2.66	2.84	2.55	>50
w53.13	>50	>50	>50	>50	>50	>50	12.38	4.78	3.60	5.30	4.47	6.64	4.66	5.61
w53.14	>50	>50	>50	>50	>50	>50	20.93	6.00	5.76	8.01	6.46	15.52	8.28	9.99
w53.32	>50	>50	>50	>50	>50	>50	22.80	7.53	6.09	6.76	6.29	13.89	10.78	>50
w53.3	>50	>50	>50	>50	>50	>50	49.31	10.51	4.42	8.37	8.82	27.54	9.46	7.24
w53.25	>50	>50	>50	>50	>50	>50	43.14	13.07	7.56	9.26	10.10	28.05	10.47	5.49
w53.16	>50	>50	>50	>50	>50	>50	>50	10.68	17.37	12.31	3.44	21.73	18.39	46.35
w53.17	>50	>50	>50	>50	>50	>50	43.24	10.62	10.32	10.61	7.25	20.89	13.80	6.54
w53.15	>50	>50	>50	>50	>50	>50	31.54	12.11	8.19	13.82	12.65	29.48	17.72	10.60
w53.28	>50	>50	>50	>50	>50	>50	46.24	14.19	7.67	12.65	14.45	21.84	15.86	8.89
w53.22	>50	>50	>50	>50	>50	>50	41.20	15.81	11.58	12.19	12.31	29.51	19.36	15.95
w53.27	>50	>50	>50	>50	>50	>50	>50	17.47	14.56	10.47	13.61	27.02	14.99	10.48
w53.8	>50	>50	>50	>50	>50	>50	>50	21.53	16.78	16.01	17.15	34.75	20.92	18.82
w53.10	>50	>50	>50	>50	>50	>50	>50	10.59	13.21	18.87	20.07	31.68	12.73	5.97
w53.29	>50	>50	>50	>50	>50	>50	>50	21.79	14.58	21.95	17.38	42.24	22.52	8.79
w53.6	>50	>50	>50	>50	>50	>50	>50	19.43	16.67	11.88	19.00	>50	12.57	1.29
w53.9	>50	>50	>50	>50	>50	>50	>50	31.44	22.70	28.81	32.21	>50	34.57	27.83
w53.11	>50	>50	>50	>50	>50	>50	>50	26.22	32.31	30.37	32.63	>50	37.41	19.14

FIG. 14D

WEEK 78	w78.15	>50	>50	>50	>50	21.97	49.04	2.97	0.76	0.25	1.51	0.96	2.55	2.08
	w78.1	>50	>50	>50	>50	>50	>50	7.06	1.30	3.31	2.69	1.68	4.07	4.63
	w78.3	>50	>50	>50	>50	>50	>50	7.14	2.28	1.41	3.74	3.11	5.34	5.17
	w78.10	>50	>50	>50	>50	>50	>50	15.43	4.42	3.04	7.08	6.10	8.67	5.49
	w78.8	>50	>50	>50	>50	>50	>50	17.56	6.07	5.27	6.41	4.85	9.70	9.33
	w78.7	>50	>50	>50	>50	>50	>50	43.42	2.58	6.67	6.79	4.40	18.53	15.23
	w78.33	>50	>50	>50	>50	>50	>50	>50	12.23	15.79	4.13	11.06	28.41	12.20
	w78.6	>50	>50	>50	>50	>50	>50	>50	22.34	20.68	3.80	23.56	>50	17.31
	w78.14	>50	>50	>50	>50	>50	>50	28.34	10.25	6.58	11.33	9.25	17.70	17.81
	w78.17	>50	>50	>50	>50	>50	>50	>50	16.62	9.56	15.23	14.81	30.44	26.32
	w78.38	>50	>50	>50	>50	>50	>50	33.25	13.81	13.26	12.32	12.51	15.49	12.85
	w78.25	>50	>50	>50	>50	>50	>50	30.45	21.40	29.85	17.72	22.67	10.50	15.19
	w78.4	>50	>50	>50	>50	>50	>50	>50	19.03	23.86	22.48	10.56	24.76	29.17
	w78.9	>50	>50	>50	>50	>50	>50	47.83	13.28	16.17	17.32	17.02	15.44	14.00
	w78.5	>50	>50	>50	>50	>50	>50	>50	>50	>50	10.90	>50	>50	>50
	w78.16	>50	>50	>50	>50	>50	>50	>50	>50	>50	12.73	>50	>50	>50

WEEK 100	w100.B4	>50	>50	>50	>50	>50	>50	1.64	1.13	0.91	3.46	0.64	0.75	0.74
	w100.A3	>50	>50	>50	>50	>50	>50	13.27	2.87	1.02	5.76	3.81	7.42	6.10
	w100.A1	>50	>50	>50	>50	>50	>50	>50	4.13	2.11	10.74	3.13	12.24	3.99
	w100.B3	>50	>50	>50	>50	>50	>50	>50	3.18	2.06	10.72	3.42	12.56	4.64
	w100.B7	>50	>50	>50	>50	>50	>50	41.77	4.89	2.38	11.33	3.66	14.31	5.38
	w100.A5	>50	>50	>50	>50	>50	>50	>50	3.70	1.85	15.63	3.34	20.69	5.64
	w100.B6	>50	>50	>50	>50	>50	>50	>50	2.77	3.15	10.97	3.00	13.02	3.41
	w100.A2	>50	>50	>50	>50	>50	>50	>50	4.85	3.42	21.36	7.63	25.34	9.21
	w100.A13	>50	>50	>50	>50	>50	>50	>50	3.96	10.36	26.34	3.49	17.24	6.63
	w100.A6	>50	>50	>50	>50	>50	>50	16.02	5.79	6.34	11.51	5.27	12.64	12.01
	w100.A4	>50	>50	>50	>50	>50	>50	>50	12.83	12.93	13.65	10.51	25.45	14.06
	w100.A12	>50	>50	>50	>50	>50	>50	33.48	13.17	5.98	18.02	10.77	20.53	17.72
	w100.A10	>50	>50	>50	>50	>50	>50	>50	25.12	27.54	36.75	21.80	48.74	37.29
	w100.B8	>50	>50	>50	>50	>50	>50	>50	>50	>50	44.90	>50	>50	>50

														>50
														>50
														>50
														>50
														>50
														>50
														>50
														>50
														>50
														>50
														12.69
														>50
														10.66
														15.61
														13.76

VALUES ARE THE CONCENTRATIONS (μg/ml) OF ANTIBODIES REQUIRED FOR THE 50% INHIBITION (IC_{50}).

FIG. 14E

VIRUS	MUTATION	UCA	IA8	IA7	IA6	IA5	IA4	IA3	IA2	IA1	CH103	CH104	CH105	CH106
T/F	NONE	>50	44.67	10.17	10.17	6.82	9.72	6.62	2.73	1.42	4.14	3.08	5.10	2.29
M5	N279K	>50	>50	21.53	4.48	8.57	10.58	5.05	1.43	0.41	1.21	1.99	5.00	1.62
M6	V281A	>50	13.81	3.31	4.32	2.09	3.36	3.08	1.57	0.91	0.54	0.61	1.30	0.95
M10	V281G	>50	>50	12.88	6.47	4.39	5.23	1.90	0.68	0.33	0.56	0.64	1.21	0.54
M19	V281D	>50	8.90	2.84	2.85	0.34	2.83	1.97	0.37	0.28	0.31	0.22	0.99	0.12
M8	N280S + V281A	>50	>50	27.61	6.75	3.48	10.83	3.95	0.81	0.41	0.53	0.64	1.25	0.50
M11	N279D + V281G	>50	15.34	5.10	3.92	1.48	2.78	1.48	0.34	0.20	0.46	0.42	0.99	0.36
M20	N280S + V281G	>50	>50	13.44	8.12	3.25	4.21	1.31	0.40	0.33	0.34	0.36	1.13	0.28
M21	N280T + V281A	>50	>50	16.78	13.52	6.03	8.12	1.47	0.37	0.36	0.39	0.39	0.59	0.13
M7	E275K + N279D + V281S	>50	6.63	2.52	2.39	2.26	2.14	1.75	0.37	0.27	0.38	0.37	0.95	0.23
M9	E275K + N279D + V281G	>50	27.11	7.87	4.42	5.32	5.81	1.71	0.49	0.23	0.72	0.67	1.17	0.48

VALUES ARE THE CONCENTRATIONS (μg/ml) OF ANTIBODIES REQUIRED FOR THE 50% INHIBITION (IC_{50}).

FIG. 15

TIME POINT	VIRUS	CH235 CLONAL LINAGE										CD4bs bnAb
		UCA	IA4	IA3	IA2	IA1	CH235	CH236	CH239	CH240	CH241	CH31
	T/F	>50	>50	5.22	0.97	0.91	0.63	0.61	0.48	0.94	0.41	<0.023
WEEK 4	w4.3	>50	>50	1.65	0.35	0.30	0.11	0.40	0.10	0.25	<0.023	<0.023
	w4.26	>50	>50	3.67	1.36	0.32	0.46	0.78	0.30	0.67	0.05	<0.023
	w4.10	>50	20.51	1.02	0.24	0.20	0.10	0.10	<0.023	0.15	<0.023	>50
WEEK 14	w14.21	>50	>50	>50	38.08	0.79	0.38	0.96	0.14	0.58	0.04	0.13
	w14.3	>50	>50	6.28	1.40	0.79	0.49	0.75	0.40	1.05	0.09	<0.023
	w14.4	>50	>50	3.60	1.00	0.72	0.27	0.88	0.40	0.60	0.08	<0.023
	w14.6	>50	>50	5.73	1.64	0.92	0.31	0.63	0.43	0.73	0.17	<0.023
	w14.29	>50	>50	5.34	1.02	0.86	0.75	1.05	0.61	0.88	0.17	0.02
	w14.34	>50	>50	4.84	0.94	0.84	0.52	1.09	0.78	0.89	0.12	<0.023
	w14.12	>50	>50	34.99	2.22	0.85	0.42	0.53	0.41	0.93	0.09	<0.023
WEEK 20	w20.14	>50	>50	10.80	1.99	0.91	0.63	0.61	0.48	0.96	0.09	<0.023
	w20.7	>50	>50	>50	31.29	0.85	0.43	1.30	0.28	0.85	0.06	0.14
	w20.27	>50	>50	10.28	2.06	0.98	0.39	0.46	0.27	1.13	0.10	<0.023
	w20.4	>50	>50	>50	47.61	0.94	0.65	1.81	0.18	1.00	0.06	0.12
	w20.19	>50	>50	8.99	2.12	1.99	1.16	1.24	1.11	1.63	0.27	0.02
	w20.25	>50	>50	8.54	1.69	1.85	1.08	0.85	0.75	1.41	0.18	<0.023
WEEK 30	w30.28	>50	>50	>50	>50	5.28	2.16	9.14	2.07	5.28	0.40	>50
	w30.13	>50	>50	>50	>50	4.73	1.15	4.39	1.49	5.11	2.96	>50
	w30.24	>50	>50	29.77	27.95	4.62	2.06	3.69	1.54	4.12	0.49	0.35
	w30.5	>50	>50	>50	7.72	1.83	0.80	0.58	0.67	2.08	1.17	0.04
	w30.34	>50	>50	>50	4.98	5.18	3.23	2.27	3.02	5.61	3.68	0.15
	w30.37	>50	>50	>50	6.45	6.92	4.25	2.60	2.79	7.57	3.99	0.17
WEEK 53	w53.31	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	w53.13	>50	>50	>50	>50	>50	>50	>50	33.78	>50	>50	11.58
	w53.28	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	12.64
	w53.22	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	34.28
	w53.6	>50	>50	>50	>50	>50	>50	>50	19.95	>50	>50	0.93
	w53.11	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	21.96
WEEK 78	w78.15	>50	>50	>50	>50	>50	46.43	>50	>50	>50	>50	22.63
	w78.1	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	w78.33	>50	>50	>50	>50	>50	>50	>50	>50	>50	33.95	32.10
	w78.6	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	w78.9	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	35.39
	w78.5	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	20.20
WEEK 100	w100.B4	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	49.40
	w100.A3	>50	>50	>50	>50	>50	>50	>50	>50	>50	45.37	45.65
	w100.A5	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	46.55
	w100.B6	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
	w100.A10	>50	>50	>50	>50	>50	>50	>50	48.62	>50	41.17	>50
	w100.B8	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50

VALUES ARE THE CONCENTRATIONS (μg/ml) OF ANTIBODIES REQUIRED FOR THE 50% INHIBITION (IC_{50}).

FIG. 16

VIRUS	MUTATION	UCA	IA4	IA3	IA2	IA1	CH235	CH236	CH239	CH240	CH241
T/F	NONE	>50	>50	5.22	0.97	0.91	0.63	0.61	0.48	0.94	0.14
M5	N279K	>50	27.69	1.21	0.69	0.20	0.18	0.26	0.06	0.22	<0.023
M6	V281A	>50	>50	21.93	>50	0.98	0.41	0.80	0.26	1.06	0.06
M10	V281G	>50	>50	>50	>50	0.47	0.47	1.75	0.19	1.57	<0.023
M19	V281D	>50	>50	>50	8.90	6.10	1.80	7.53	2.25	7.76	0.30
M11	N279D + V281G	>50	>50	>50	9.93	3.78	16.19	>50	5.78	14.32	0.96
M8	N280S + V281A	>50	>50	>50	>50	>50	48.20	>50	27.79	>50	14.97
M21	N280T + V281A	>50	>50	>50	>50	>50	>50	>50	>50	>50	12.79
M20	N280S + V281G	>50	>50	>50	>50	>50	>50	>50	>50	>50	33.35
M7	E275K + N279D + V281S	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50
M9	E275K + N279D + V281G	>50	>50	>50	>50	>50	>50	>50	>50	>50	>50

VALUES ARE THE CONCENTRATIONS (μg/ml) OF ANTIBODIES REQUIRED FOR THE 50% INHIBITION (IC_{50}).

FIG. 17

>703010505.TF
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCAATAGCAGTATAATAGAGGGA
ATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAAT
GCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTA
ATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTC
ACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCA
GTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGA
TCTGAAAATATAACAAACAATGTCAAAACAATAATAGTACATCTCAATGAATCTGTAAAG
ATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTGTAACATTAAT
GAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCT
CATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGC
TTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATAT
ATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAACCATCACA
ATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTAT
GCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACA
AGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGAC
AATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCA
CCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTG
ACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAG
GCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAG
GCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGC
TGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAAT
TATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAA
CAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAT
TGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATA
ATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGT
GGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGG
GACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATT
GCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGG
GAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTA
GAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGC
TTTGAAACAGCTTTGCTATAA

>703010505.W4.03
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCAATAGCAGTATAATAGAGGGA

FIG. 18

ATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAAT
GCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTA
ATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTC
ACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACGCATGGAATTAAGCCA
GTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGA
TCTGAAAATATAACAAACAATGTCAAAACAATAATAGTACATCTCAATGAATCTGTAAAG
ATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTGTAACATTAAT
GAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCT
CATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGC
TTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATAT
ATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAACCATCACA
ATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTAT
GCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACA
AGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGAC
AATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCA
CCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTG
ACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAG
GCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAG
GCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGC
TGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAAT
TATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAA
CAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAT
TGGCTGGGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATA
ATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGT
GGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGG
GACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATT
GCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGG
GAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTA
GAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGC
TTTGAAACAGCTTTGCTATAA

>703010505.W4.26
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCAATAGCAGTATAATAGAGGGA
ATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAAT
GCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTA
ATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTC
ACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCA
GTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGA
TCTGAAAATATAACAAACAATGTCAAAACAATAATAGTACATCTCAATGAATCTGTAAAG

FIG. 18
CONTINUED

ATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTGTAACATTAAT
GAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCT
CATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGC
TTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATAT
ATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAACCATCACA
ATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTAT
GCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACA
AGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGAC
AATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCA
CCCACTAATGTAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTG
ACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAG
GCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAG
GCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGC
TGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAAT
TATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAA
CAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAT
TGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATA
ATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGT
GGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGG
GACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATT
GCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGG
GAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTA
GAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGC
TTTGAAACAGCTTTGCTATAA

>703010505.W14.21
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCAATAGCAGTATAATAGAGGGA
ATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAAT
GCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTA
ATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTC
ACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCA
GTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGA
TCTGAAAATATAACAAACAATGGCAAAACAATAATAGTACATCTCAATGAATCTGTAAAG
ATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTGTAACATTAAT
GAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCT
CATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGC
TTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATAT

FIG. 18
CONTINUED

ATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAATCATCACA
ATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTAT
GCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACA
AGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGAC
AATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCA
CCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTG
ACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAG
GCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAG
GCAAAAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGC
TGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAAT
TATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAA
CAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAT
TGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATA
ATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGACGGT
GGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGG
GACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATT
GCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGG
GAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTA
GAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGC
TTTGAAACAGCTTTGCTATAA

>703010505.W20.14
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCAATAACAGTATAATAGAGGGA
ATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAAT
GCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTA
ATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTC
ACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCA
GTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGA
TCTGAAAATATAACAAACAATGCCAAAACAATAATAGTACATCTCAATGAATCTGTAAAG
ATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAAAAGCATATTGTAACATTAGT
GAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCT
CATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGC
TTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATAT
ATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAACCATCACA
CTCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTAT
GCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACA
AGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGAC
AATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCA
CCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTG

FIG. 18
CONTINUED

ACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAG
GCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAG
GCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGC
TGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAAT
TATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAA
CAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAT
TGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATA
ATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGT
GGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGG
GACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATT
GCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGG
GAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTA
GAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGC
TTTGAAACAGCTTTGCTATAA

>703010505.W30.28
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGATGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCATCAATAGCAGTATAATAGAGGGA
ATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAAT
GCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTA
ATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTC
ACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCA
GTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGA
TCTGAAAATATAACAAACAATGACAAAACAATAATAGTACATCTCAATGAATCTGTAAAG
ATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCACATTGTAACATTAGT
GAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCT
CATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGC
TTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATAT
ATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAACCATCACA
ATCCGCTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTAT
GCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACA
AGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGAC
AATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCA
CCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTG
ACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAG
GCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAG
GCAAGAGTCCTGGCCTTAGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGC
TGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
AGTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAAT
TATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAA
CAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAT

FIG. 18
CONTINUED

TGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATA
ATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGT
GGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGG
GACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATT
GCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGG
GAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTA
GAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGC
TTTGAAACAGCTTTGCTATAA

>703010505.W30.13
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGATGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCATCAATAGCAGTATAATAGAGGGA
ATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAAT
GCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTA
ATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTC
ACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCA
GTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGA
TCTGAAAATATAACAAACAATGACAAAACAATAATAGTACATCTCAATGAATCTGTAAAG
ATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTGTAACATTAGT
GAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCT
CATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGC
TTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATAT
ATGGCTAATAGTACAGATATGGCTAATAGTACGGAAACTAACAATACACGACCCATCACA
ATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTAT
GCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACA
AGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGAC
AATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAATAGCA
CCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTG
ACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAG
GCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAG
GCAAGAGTCCTGGCCTTAGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGC
TGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAAT
TATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAA
CAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAT
TGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATA
ATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGT
GGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGG
GACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATT
GCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGG
GAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT

FIG. 18
CONTINUED

GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTA
GAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGC
TTTGAAACAGCTTTGCTATAA

>703010505.W53.31
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTAGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCGATGCTACTGCCAGCAATGCTACTGCCAGCAATGCT
ACTGCCAGCAATAGCAGTATAATAGAGGGAATGAAAAATTGCTCTTTCAATATAACCACA
GAATTAAGAGATAAGAGAGAGAAAAAGAATGCACTTTTTTATAAACTTGATATAGTACAA
CTAGATGGCAACTCTAGTCAGTATAGATTAATAAATTGTAATACCTCAGTCATAACACAA
GCCTGTCCAAAGGTCTCTTTTGACCCAATTCCTATACATTATTGTGCTCCAGCTGGTTAT
GCGATTCTAAAGTGTAATAATAAGACATTCAATGGAACAGGACCGTGTAATAATGTCAGC
ACAGTACAATGTACACATGGAATTAAGCCAGTGGTTTCAACTCAACTATTGTTAAATGGT
AGCCTAGCAGAAGGAGAGATAATAATTAGATCTGAAAATATAACAGACAATGGCAAAACA
ATAATAGTACATCTCAATGAATCTGTAAAGATTGAGTGTACGAGACCCAGTAATAACACA
AGAACAAGTATAAGAATAGGACCAGGACAAGCATTTTATGCAACAGGACAAGTAATAGGA
GACATAAGAGAAGCACATTGTAACATTAGTGAAAGTAAATGGAATGAAACTTTACAAAGG
GTAAGTAAAAAATTAAAAGAATACTTCCCTCATAAGAATATAACATTTCAACCATCCTCA
GGAGGGGACCTAGAAATTACAACACATAGTTTTAATTGTGGAGGAGAATTTTTCTATTGC
AATACATCAAGCCTGTTTAATAGGACATATATGGCTAATAGTACAGAAACTAACAGTACA
CGAATCATCACAATCCGCTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGA
AGAGCAATGTATGCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGA
CTACTATTGACAAGGGATGGAGGAAATAACAATACGGAGACATTCAGACCTGGAGGAGGA
AATATGAAGGACAATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCA
TTAGGAGTAGCACCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTG
GGAATGGGAGCTGTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCA
TCAATAACGCTGACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGC
AATTTGCTGAAGGCTATAGGGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATT
AAACAGCTCCAGGCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTA
GGGATGTGGGGCTGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGT
TGGAGTAATAAAACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGA
GAAATTAGCAATTATACAGAAATGATATATGAATTGCTTGAAGAATCACAAAACCAGCAG
GAAAAGAATGAACAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTT
AACATAACAAATTGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATA
GGTTTAAGAATAATTTTTGCTGTGCTCTCTTTAGTAAATAGAGTTAGGCAGGGATACTCA
CCTCTGTCATTGCAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATC
GAAGAAGAAGGTGGAGAGCAAGACAGAAAGAGATCAACGCGATTAGTGAGCGGATTCTTA
GCGCTTGTCTGGGACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGAC
TTCATATTAATTGCAGCGAGAGCGGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTA
CGGAGAGGATGGGAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAA
CTAAAAAGGAGTGCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACA
GATAGGATTCTAGAATTTGCATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGA
ATAAGACAGGGCTTTGAAACAGCTTTGCTATAA

FIG. 18
CONTINUED

>703010505.W78.15
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAGCTGTACCAATGCTACTAATGCTACTGCCAGCAATAGCAGTATA
TTAGAGGGAATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAG
AAAAAGAATGCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAG
TATAGATTAATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTT
GACCCAATTCCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAAT
AAGACATTCAATGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGA
ATTAAGCCAGTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATA
ATAATTAGATCTAAAAATATAACAGACAATGGCAAAACAATAATAGTACATCTCAATGAA
TCTGTAAAGATTGAGTGTACGAGACCCAGTAATAACACAAGAACAAGTATAAGAATAGGA
CCAGGACAAGCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCACATTGT
AACATTAGTGAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTGAAAAATTAAAAGAA
TACTTCCCTCATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACA
ACACATAGCTTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAAT
AGGACATATATGGCTACTAGTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGA
ATCATCACAATCCGCTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGA
GCAATGTATGCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTA
CTATTGACAAGGGATGGAGGAAAAAACGATACGGATACATTCAGACCTGAAGGAGGAAAT
ATGAAGGACAATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTA
GGAGTAGCACCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGA
ATGGGAGCTGTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCA
ATAACGCTGACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAAT
TTGCTGAAGGCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAA
CAGCTCCAGGCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGG
ATGTGGGGCTGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGG
AGTAATAAAACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAA
ATTAGCAATTATACAGAACTAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAA
AAGAATGAACAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAAC
ATAACAAATTGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGT
TTAAGAATAATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCT
CTGTCATTGCAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAA
GAAGAAGGTGGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCG
CTTGCCTGGGACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTC
ATATTAATTGCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGG
AGAGGGTGGGAAGCCCTTAAGTATCTGGGAAATCTTGTGCAGTATTGGGGCCTGGAACTA
AAAAGGAGTGCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGAT
AGGATTCTAGAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATA
AGACAGGGCTTTGAAACAGCTTTGCTATAA

>703010505.W100.B4
ATGAGAGTGATGGGGAGGCAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
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TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGGAAAATGACATGGTAGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCGATGCTAATGCTACTGCCAGCAATACCAATGCTACT

FIG. 18
CONTINUED

GCCAGCAATATCAATGCTACTGCCAGCAAGAACAGTATAATAGAGGAAATGAAAAATTGC
TCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAGAAAAAGTATGCACTTTTTTAT
AAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTAATAAATTGTAAT
ACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATTCCTATACATTAT
TGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTCAATGGAACAGGA
CCGTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCAGTGGTTTCAACT
CAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGATCTAAAAATATA
ACAGACAATGGCAAAACAATAATAGTACATCTCAATGAATCTGTAAAGATTGAATGTACG
AGACCCAGTAATAACACAAGAACAAGTATAAGAATAGGACCAGGACAAGCATTTTATGCA
ACAGGACAAGTAATAGGAGACATAAGAGAAGCACATTGTAACATTAGTGAAAGTAAATGG
AATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCTGATAAGAATATA
ACATTTCAATCATCCTCAGGAGGGGACCCAGAAATTACAACACATAGCTTTAATTGTGGA
GGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATATATGGCTAATAGT
ACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAATCATCACAATCCGCTGCAGA
ATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTATGCCCCTCCCATT
GCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACAAGGGATGGAGGA
AACAGCAGTACGGAGACATTCAGACCTGAAGGAGGAAATATGAAGGACAATTGGAGAAGT
GAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCACCCACTAATGCA
AGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCTGTGTTCCTTGGG
TTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTGACGGTACAGGCC
AGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAGGCTATAGAGGCT
CAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAGGCAAGAGTCCTG
GCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGCTGCTCTGGAAAA
CTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAAACTTATGATGAT
ATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAATTATACAGAAATG
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GCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAATGGCTGTGGTAT
ATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATAATTTTTGCTGTA
CTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTGCAGACCCTTATC
CCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGTGGAGAGCAAGAC
AGAAAGAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGGGACGACCTGCGG
AGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATTGCAGCGAGAGCG
GGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGGTGGGAAGCCCTTAAG
TATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGTGCTATTAGTTTA
TTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTAGAATTTGTATTA
GGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGCTTTGAAACAGCT
TTGCTATAA

FIG. 18
CONTINUED

>703010505.TF
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNVKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
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MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
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LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
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VVSTQLLLNGSLAEGEIIIRSENITNNVKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLGYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>703010505.W4.26
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNVKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
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AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
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FETALL
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MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
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LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNGKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ

FIG. 19

AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRIITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQAKVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEDG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>703010505.W20.14
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LCVTLNCTNATASNNSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNAKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIRKAYCNISESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITLHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>703010505.W30.28
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LCVTLNCTNATAINSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNDKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAHCNISESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIRCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
SYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>703010505.W30.13
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LCVTLNCTNATAINSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNDKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNISESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNNTRPITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGIA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK

FIG. 19
CONTINUED

TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
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LCVTLNCTDATASNATASNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQ
LDGNSSQYRLINCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFNGTGPCNNVS
TVQCTHGIKPVVSTQLLLNGSLAEGEIIIRSENITDNGKTIIVHLNESVKIECTRPSNNT
RTSIRIGPGQAFYATGQVIGDIREAHCNISESKWNETLQRVSKKLKEYFPHKNITFQPSS
GGDLEITTHSFNCGGEFFYCNTSSLFNRTYMANSTETNSTRIITIRCRIKQIINMWQEVG
RAMYAPPIAGNITCISNITGLLLTRDGGNNNTETFRPGGGNMKDNWRSELYKYKVVEVKP
LGVAPTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQS
NLLKAIGAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSS
WSNKTYGDIWDNMTWMQWEREISNYTEMIYELLEESQNQQEKNEQDLLALDRWNSLWNWF
NITNWLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGI
EEEGGEQDRKRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGL
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IRQGFETALL
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LCVTLSCTNATNATASNSSILEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQ
YRLINCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFNGTGPCNNVSTVQCTHG
IKPVVSTQLLLNGSLAEGEIIIRSKNITDNGKTIIVHLNESVKIECTRPSNNTRTSIRIG
PGQAFYATGQVIGDIREAHCNISESKWNETLQRVSEKLKEYFPHKNITFQPSSGGDLEIT
THSFNCGGEFFYCNTSSLFNRTYMATSTDMANSTETNSTRIITIRCRIKQIINMWQEVGR
AMYAPPIAGNITCISNITGLLLTRDGGKNDTDTFRPEGGNMKDNWRSELYKYKVVEVKPL
GVAPTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSN
LLKAIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSW
SNKTYGDIWDNMTWMQWEREISNYTELIYELLEESQNQQEKNEQDLLALDRWNSLWNWFN
ITNWLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIE
EEGGEQDRNRSTRLVSGFLALAWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLR
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RQGFETALL
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LCVTLNCTDANATASNTNATASNINATASKNSIIEEMKNCSFNITTELRDKREKKYALFY
KLDIVQLDGNSSQYRLINCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFNGTG
PCNNVSTVQCTHGIKPVVSTQLLLNGSLAEGEIIIRSKNITDNGKTIIVHLNESVKIECT
RPSNNTRTSIRIGPGQAFYATGQVIGDIREAHCNISESKWNETLQRVSKKLKEYFPDKNI
TFQSSSGGDPEITTHSFNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRIITIRCR
IKQIINMWQEVGRAMYAPPIAGNITCISNITGLLLTRDGGNSSTETFRPEGGNMKDNWRS
ELYKYKVVEVKPLGVAPTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQA
RQLLSGIVQQQSNLLKAIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGK
LICTTNVYWNSSWSNKTYDDIWDNMTWMQWEREISNYTEMIYDLLEESQNQQEKNEQDLL
ALDRWNSLWNWFNITKWLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLI
PSPRGPDRPGGIEEEGGEQDRKRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARA
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GICRAIRNIPTRIRQGFETALL

FIG. 19
CONTINUED

>703010505.W14.3
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GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGACGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCAATAGCAGTATAATAGAGGGA
ATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAAT
GCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTA
ATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGTGATTCTAAAGTGTAATAATAAGACATTC
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GTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGA
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ATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTGTAACATTAAT
GAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCT
CATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGC
TTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATAT
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ATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTAT
GCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACA
AGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGAC
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CCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTG
ACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAG
GCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAG
GCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGC
TGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAAT
TATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAA
CAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAT
TGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATA
ATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGT
GGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGG
GACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATT
GCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGG
GAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTA
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TTTGAAACAGCTTTGCTATAA

>703010505.W14.8
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GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
TTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCAATAGCAGTATAATAGAGAGA

FIG. 20

ATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAAT
GCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTA
ATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTC
ACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCA
GTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGA
TCTGAAAATATAACAAACAATGTCAAAACAATAATAGTACATCTCAATGAATCTGTAAAG
ATTGAGTGTACGAGACCCAATAATAAAACAAGAGCAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTGTAACATTAAT
GAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCT
CATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGC
TTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATAT
ATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAACCATCACA
ATCCGCTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTAT
GCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACA
AGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGAC
AATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCA
CCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTG
ACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAG
GCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAG
GCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGC
TGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAAT
TATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAA
CAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAT
TGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATA
ATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGT
GGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGG
GACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATT
GCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGCCTCAAGGGACTACGGAGAGGATGG
GAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTA
GAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGC
TTTGAAACAGCTTTGCTATAA

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ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTAATGCCAGCAATAACAGTATAATAGAGGGA
ATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAAT
GCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTA
ATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTC
ACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCA
GTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGA
TCTGAAAATATAACAAACAATGGCAAAACAATAATAGTACATCTCAATGAATCTGTAAAG
ATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA

FIG. 20
CONTINUED

GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTGTAACATTAGT
GAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCT
CATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGC
TTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATAT
ATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAATCATCACA
ATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTAT
GCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACA
AGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGAC
AATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCA
CCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTG
ACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAG
GCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAG
GCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGC
TGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAAT
TATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAA
CAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAT
TGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATA
ATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGT
GGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGG
GACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCACATTAATT
GCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGG
GAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTA
GAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGC
TTTGAAACAGCTTTGCTATAA

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ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCAATATCAGTATAATAGAGGGA
ATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAAT
GCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTA
ATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTC
ACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCA
GTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGA
TCTGAAAATATAACAAACAATGGCAAAACAATAATAGTACATCTCAATGAATCTGTAAAG
ATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGATATAAGAGAAGCATATTGTAACATTAGT
GAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCT
CATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGC
TTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATAT
ATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAATCATCACA
ATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTAT
GCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACA

FIG. 20
CONTINUED

AGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGAC
AATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCA
CCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTG
ACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAG
GCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAG
GCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGC
TGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAAT
TATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAA
CAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAAT
TGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATA
ATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGT
GGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGG
GACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATT
GCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGG
GAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTA
GAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGC
TTTGAAACAGCTTTGCTATAA

>703010505.W20.9
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTGCCAGCAATAGCAGTATAATAGAGGGAATG
AAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAATGCA
CTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTAATA
AATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATTCCT
ATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTCACT
GGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCAGTG
GTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGATCT
GAAAATATAACAAACAATGCCAAAACAATAATAGTACATCTCAATGAATCTGTAAAGATT
GAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAAGCA
TTTTATGCAACAGGACAAGTAATAGGAGACATAAGAAAAGCATATTGTAACATTAATGAA
AGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCTCAT
AAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGCTTT
AATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATATATG
GCTAATAGTACAGATATGGCTAATAGTACAGAAACTAACAATACACGAACCATCACAATC
CACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTATGCC
CCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACAAGG
GATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGACAAT
TGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCACCC
ACTAATGCAAGAAGGAGAGTGGTGGAAAGAGAAAAAAGAGCAGTGGGAATGGGAGCTGTG
TTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCTGACG
GTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAGGCT
ATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAGGCA
AGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGCTGC

FIG. 20
CONTINUED

TCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAAACT
TATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAATTAT
ACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAACAA
GATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAATTGG
CTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATAATT
TTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTGCAG
ACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGTGGA
GAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGCCTGGGAC
GACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATTGCA
GCGAGAGCGGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGGGAA
GCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGTGCT
ATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTAGAA
TTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGCTTT
GAAACAGCTTTGCTATAA

>703010505.W30.12
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTAATGCTACTGCCAGCAATAGCAGTATA
ATAGAGGGAATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAG
AAAAAGAATGCACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAG
TATAGATTAATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTT
GACCCAATTCCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAAT
AAGACATTCACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGA
ATTAAGCCAGTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATA
ATAATTAGATCTGAAAATATAACAAACAATGACAAAACAATAATAGTACATCTCAATGAA
TCTGTAAAGATTGAGTGTACGAGACCCAGTAATAAAACAAGAACAAGTATAAGAATAGGA
CCAGGACAAGCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTGT
AACATTAGTGAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAA
TACTTCCCTCATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACA
ACACATAGCTTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAAT
AGGACATATATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGA
AACATCACAATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGA
GCAATGTATGCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTA
CTATTGACAAGGGATGGAGGAAAAAACGATACGGAGACATTCAGACCTGGAGGAGGAAAT
ATGAAGGATAATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTA
GGAGTAGCACCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGA
ATGGGAGCTGTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCA
ATAACGCTGACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAAT
TTGCTGAAGGCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAA
CAGCTCCAGGCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGG
ATGTGGGGCTGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGG
AGTAATAAAACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAA
ATTAGCAATTATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAA
AAGAATGAACAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAAC
ATAACAAATTGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGT
TTAAGAATAATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCT
CTGTCGTTGCAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAA

FIG. 20
CONTINUED

GAAGAAGGTGGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCG
CTTGTCTGGGACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTC
ATATTAATTGCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGG
AGAGGATGGGAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTA
AAAAGGAGTGCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGAT
AGGATTCTAGAATTTATATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGAATA
AGACAGGGCTTTGAAACAGCTTTGCTATAA

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ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGAAACTGTACCAATGCTACTGCC
AGCAATAGCAGTATAATAGAGGGAATGAAAAATTGCTCTTTCAATATAACCACAGAATTA
AGAGATAAGAGAGAGAAAAAGAATGCACTTTTTTTATAAACTTGATATAGTACAACTAGAT
GGCAACTCTAGTCAGTATAGATTAATAAATTGTAATACCTCAGTCATAACACAAGCCTGT
CCAAAGGTCTCTTTTGACCCAATTCCTATACATTATTGTGCTCCAGCTGGTTATGCGATT
CTAAAGTGTAATAATAAGACATTCACTGGAACAGGACCGTGTAATAATGTCAGCACAGTA
CAATGTACACATGGAATTAAGCCAGTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTA
GCAGAAGGAGAGATAATAATTAGATCTGAAAATATAACAAACAGTGGCAAAACAATAATA
GTACATCTCAATGAATCTGTAAAGATTGAGTGTACGAGACCCAATAATAAAACAAGAACA
AGTATAAGAATAGGACCAGGACAAGCATTTTATGCAACAGGACAAGTAATAGGAGACATA
AGAGAAGCATATTGTAACATTAGTGAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGT
AAAAAATTAAAAGAATACTTCCCTCATAAGAATATAACATTTCAACCATCATCAGGAGGG
GACCTAGAAATTACAACACATAGCTTTAATTGTGGAGGAGAATTTTTCTATTGCAATACA
TCAAGCCTGTTTAATAGGACATATATGGCTAATAGTACAGATATGGCTAATAGTACAGAA
ACTAACAGTACACGAATCATCACAATCCACTGCAGAATAAAACAAATTATAAACATGTGG
CAGGAGGTGGGACGAGCAATGTATGCCCCTCCCATTGCAGGAAACATAACATGTATATCA
AGTATCACAGGACTACTATTGACAAGGGATGGAGGAGAAAACAATACGGAGACATTCAGA
CCTGGAGGAGGAAATATGAAGGACAATTGGAGAAGTGAATTATATAAATATAAAGTGGTA
GAAGTTAAGCCATTAGGAGTAGCACCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAA
AAAAGAGCAGTGGGAATGGGAGCTGTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACT
ATGGGCGCAGCATCAATAACGCTGACGGTACAGGCCAGACAATTATTGTCTGGTATAGTG
CAACAGCAAAGCAATTTGCTGAAGGCTATAGAGGCTCAACAGCATATGTTGAAACTCACG
GTCTGGGGCATTAAACAGCTCCAGGCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGAT
CAACAGCTCCTAGGGATGTGGGGCTGCTCTGGAAAACTCATCTGCACCACTAATGTATAT
TGGAACTCTAGTTGGAGTAATAAAACTTATGGTGATATTTGGGATAACATGACCTGGATG
CAGTGGGAGAGAGAAATTAGCAATTATACAGAAATAATATATGAATTGCTTGAAGAATCA
CAAAACCAGCAGGAAAAGAATGAACAAGATTTACTAGCATTGGACAGATGGAACAGTCTG
TGGAATTGGTTTAACATAACAAATTGGCTGTGGTATATAAAAATATTCATAATGATAGTA
GGAGGCTTGATAGGTTTAAGAATAATTTTTGCTGTGTTTTCTTTAGTAAATAGAGTTAGG
CAGGGATACTCACCTCTATCGTTGCAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGG
CCCGGAGGAATCGAAGAAGAAGGTGGAGAGCAAGACAGAAACAGATCAACGCGATTAGTG
AGCGGATTCTTAGCGCTTGTCTGGGACGACCTGCGGAGCCTGTGCCTTTTCATCTACCAC
CGATTGAGAGACTTCATATTAATTGCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGT
CTCAAGGGACTACGGAGAGGATGGGAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTAT
TGGGGCCTGGAACTAAAAAGGAGTGCTATTAGTCTATTGGATACCCTAGCAATAGCAGTA
GGTGAAGGAACAGATAGGATTCTAGAATTTGTATTAGGAATTTGTAGAGCTATCCGCAAC
ATACCTACAAGAATAAGACAGGGCTTTGAAACAGCTTTGCTATAA

FIG. 20
CONTINUED

>703010505.W53.19
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTAGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCGATGCTACTGCCAGCAATGCTACTGCCAGCAATGCT
ACTGCCAGCAATAGCAGTATAATAGAGGAAATGAAAAATTGCTCTTTCAATATAACCACA
GAATTAAGAGATAAGAGAGAGAAAAAGAATGCACTTTTTTATAAACTTGATATAGTACAA
CTAGATGGCAACTCTAGTCAGTATAGATTAATAAATTGTAATACCTCAGCCATAACACAA
GCCTGTCCAAAGGTCTCTTTTGACCCAATTCCTATACATTATTGTGCTCCAGCTGGTTAT
GCGATTCTAAAGTGTAATAATAAGACATTCAATGGAACAGGACCGTGTAATAATGTCAGC
ACAGTACAATGTACACATGGAATTAAGCCAGTGGTTTCAACTCAACTATTGTTAAATGGT
AGCCTAGCAGAAGGAGAGATAATAATTAGATCTGAAAATATAACAGACAATGGCAAAACA
ATAATAGTACATCTCAATGAATCTGTAAAGATTGAGTGTACGAGACCCAGTAATAACACA
AGAACAAGTATAAGAATAGGACCAGGACAAGCATTTTATGCAACAGGACAAGTAATAGGA
GACATAAGAGAAGCACATTGTAACATTAGTGAAAGTAAATGGAATGAAACTTTACAAAGG
GTAAGTAAAAAATTAAAAGAATACTTCCCTCATAAGAATATAACATTTCAACCATCCTCA
GGAGGGGACCTAGAAATTACAACACATAGCTTTAATTGTGGAGGAGAATTTTTCTATTGC
AATACATCAAGCCTGTTTAATAGGACATATATGGCTAATAGTACAGAAACTAACAGTACA
CGAATCATCACAATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGA
CGAGCAATGTATGCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGA
CTACTATTGACAAGGGATGGAGGAAATAACAATACGGAGACATTCAGACCTGGAGGAGGA
AATATGAAGGACAATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCA
TTAGGAGTAGCACCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTG
GGAATGGGAGCTGTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCA
TCAATAACGCTGACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGC
AATTTGCTGAAGGCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATT
AAACAGCTCCAGGCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTA
GGGATGTGGGGCTGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAACTCTAGT
TGGAGTAATAAAACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGA
GAAATTAGCAATTATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAG
GAAAAGAATGAACAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTT
AACATAACAAACTGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATA
GGTTTAAGAATAATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCA
CCTCTGTCTTTGCAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATC
GAAGAAGAAGGTGGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTA
GCGCTTGCCTGGGACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGAC
TTCATATTAATTGCAGCGACGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTA
CGGAGAGGGTGGGAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAA
CTAAAAGGGAGTGCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACA
GATAGGATTCTAGAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACAAGA
ATAAGACAGGGCTTTGAAACAGCTTTGCTATAA

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ATGAGAGTGATGGGGAGACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGGC
TTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTG
TGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAA
GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCA
CTCTGTGTCACTCTAAACTGTACCGATGCTACTGCCAGCAATGCTACTGCCAGCAATAGC

FIG. 20
CONTINUED

AGTATAATAGAGGGAATGAATAGTAGTATAATAGAGGGAATGAAAAATTGCTCTTTCAAT
ATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAATGCACTTTTTTATAAACTTGAT
ATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTAATAAATTGTAATACCTCAGTC
ATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATTCCTATACATTATTGTGCTCCA
GCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATTCAATGGAACAGGACCGTGTAAT
AATGTCAGCACAGTACAATGTACACATGGAATTAAGCCAGTGGTTTCAACTCAACTATTG
TTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGATCTGAAAACATAACAGACAAT
GGCAAAACAATAATAGTACATCTCAATGAATCTGTAAAGATTGAGTGTACGAGACCCAGT
AATAACACAAGAACAAGTATAAGAATAGGACCAGGACAAGCATTTTATGCAACAGGACAA
GTAATAGGAGACATAAGAGAAGCACATTGTAACATTAGTGAAAGTAAATGGAATGAAACT
TTACAAAGGGTAAGTGAAAAATTAAAAGAATACTTCCCTCATAAGAATATAACATTTCAA
CCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGCTTTAATTGTGGAGGAGAATTT
TTCTATTGCAATACATCAAGCCTGTTTAACAGGACATATATGGCTACTAGTACAGATATG
GCTAATAGTACAGAAACTAACAGTACACGAATCATCACAATCCGCTGCAGAATAAAACAA
ATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTATGCCCCTCCCATTGCAGGAAAC
ATAACATGTATATCAAATATCACAGGACTACTATTGACAAGGGATGGAGGAAAAAACAAT
ACGGAGACATTCGAGACATTCAGACCTGGAGGAGGAAATATGAAGGACAATTGGAGAAGT
GAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCACCCACTAATGCA
AGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCTGTGTTCCTTGGG
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AGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAGGCTATAGAGGCT
CAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAGGCAAGAGTCCTG
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CTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAAACTTATGGTGAT
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ATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATAATTTTTGCTGTG
CTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTACAGACCCTTATC
CCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGTGGAGAGCAAGAC
AGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGCCTGGGACGACCTGCGG
AGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATTGCAGCGAGAGCG
GGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGGGAAGCCCTTAAG
TATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGTGCTATTAGTCTA
TTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTAGAATTTGTATTA
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TTGCTATAA

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GTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATG
GTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAGGTTGACCCCA
CTCTGTGTCACTCTAAACTGTATCAATGCTACTAATGCTACTGCCAGCAATAACAGTATA
TTAGAGGGAATGAAAAATTGCTCTTTCAATATAGCCACAGAATTAAGAGATAAGAGAGAG
AAAAAGAATGCACTTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAG
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GACCCAATTCCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAAT
AAGACATTCAATGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATGGA
ATTAAGCCAGTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATA
ATAATTAGATCTAAAAATATAACAGACAATGGCAAAACAATAATAGTACATCTCAATGAA

FIG. 20
CONTINUED

TCTGTAAAGATTGAGTGTACGAGACCCAGTAATAACACAAGAACAAGTATAAGAATAGGA
CCAGGACAAGCATTTTATGCAACAGGACAAGTAATAGGAAATATAAGAGAAGCACATTGT
AACATTAGTGAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAA
TACTTCCCTGATAAGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACA
ACACATAGCTTTAGTTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAAT
AGGACATATATGGCTACTAATACAGATATGGCTAATAGTACAGAAACTAACAGTACACGA
ATCATCACAATCCGCTGCAGAATAAGACAAATTATAAACATGTGGCAGGAGGTGGGACGA
GCAATGTATGCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGACTA
CTATTGACAAGGGATGGAGGAGAAAACAATACGGAGACATTCGAGACATTCAGACCTGGA
GGAGGAAATATGAAGGACAATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTT
AAGCCATTAGGAGTAGCACCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGA
GCAGTGGGAATGGGAGCTGTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGC
GCAGCATCAATAACGCTGACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAG
CAAAGCAATTTGCTGAAGGCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGG
GGCATTAAACAGCTCCAGGCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAG
CTCCTAGGGATGTGGGGCTGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAAC
TCTAGTTGGAGTAATAAAACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGG
GAGAGAGAAATTAGCAATTATACAGAACTAATATATGAATTGCTTGAAGAATCACAAAAC
CAGCAGGAAAAGAATGAACAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAAT
TGGTTTAACATAACAAATTGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGC
TTGATAGGTTTAAGAATAATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGA
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GGAATCGAAGAAGAAGGTGGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGA
TTCTTAGCGCTTGCCTGGGACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTG
AGAGACTTCATATTAATTGCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAG
GGACTACGGAGAGGGTGGGAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGC
CTGGAACTAAAAAGGAGTGCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAA
GGAACAGATAGGATTCTAGAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCT
ACAAGAATAAGACAGGGCTTTGAAACAGCTTTGCTATAA

FIG. 20
CONTINUED

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MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYVILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNVKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTIKIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILKFVLGICRAIRNIPTRIRQG
FETALL
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LCVTLNCTNATASNSSIIERMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNVKTIIVHLNESVKIECTRPNNKTRASIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIRCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
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MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
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LCVTLNCTNANASNNSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNGKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNISESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRIITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
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AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFTLIAARAGELLGRSSLKGLRRGW
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LCVTLNCTNATASNISIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNGKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ

FIG. 21

AFYATGQVIGDIREAYCNISESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRIITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
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MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
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LCVTLNCTNAASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRLI
NCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKPV
VSTQLLLNGSLAEGEIIIRSENITNNAKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQA
FYATGQVIGDIRKAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHSF
NCGGEFFYCNTSSLFNRTYMANSTDMANSTETNNTRTITIHCRIKQIINMWQEVGRAMYA
PPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVAP
TNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLKA
IEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNKT
YGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITNW
LWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEGG
EQDRNRSTRLVSGFLALAWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGWE
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ETALL
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LCVTLNCTNATNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQ
YRLINCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHG
IKPVVSTQLLLNGSLAEGEIIIRSENITNNDKTIIVHLNESVKIECTRPSNKTRTSIRIG
PGQAFYATGQVIGDIREAYCNISESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEIT
THSFNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRNITIHCRIKQIINMWQEVGR
AMYAPPIAGNITCISNITGLLLTRDGGKNDTETFRPGGGNMKDNWRSELYKYKVVEVKPL
GVAPTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSN
LLKAIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSW
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ITNWLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIE
EEGGEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLR
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RQGFETALL
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GNSSQYRLINCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTV
QCTHGIKPVVSTQLLLNGSLAEGEIIIRSENITNSGKTIIVHLNESVKIECTRPNNKTRT
SIRIGPGQAFYATGQVIGDIREAYCNISESKWNETLQRVSKKLKEYFPHKNITFQPSSGG
DLEITTHSFNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRIITIHCRIKQIINMW
QEVGRAMYAPPIAGNITCISSITGLLLTRDGGENNTETFRPGGGNMKDNWRSELYKYKVV
EVKPLGVAPTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIV
QQQSNLLKAIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVY

FIG. 21
CONTINUED

WNSSWSNKTYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSL
WNWFNITNWLWYIKIFIMIVGGLIGLRIIFAVFSLVNRVRQGYSPLSLQTLIPSPRGPDR
PGGIEEEGGEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSS
LKGLRRGWEALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRN
IPTRIRQGFETALL
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MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
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LCVTLNCTDATASNATASNATASNSSIIEEMKNCSFNITTELRDKREKKNALFYKLDIVQ
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TVQCTHGIKPVVSTQLLLNGSLAEGEIIIRSENITDNGKTIIVHLNESVKIECTRPSNNT
RTSIRIGPGQAFYATGQVIGDIREAHCNISESKWNETLQRVSKKLKEYFPHKNITFQPSS
GGDLEITTHSFNCGGEFFYCNTSSLFNRTYMANSTETNSTRIITIHCRIKQIINMWQEVG
RAMYAPPIAGNITCISNITGLLLTRDGGNNNTETFRPGGGNMKDNWRSELYKYKVVEVKP
LGVAPTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQS
NLLKAIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSS
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NITNWLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGI
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LCVTLNCTDATASNATASNSSIIEGMNSSIIEGMKNCSFNITTELRDKREKKNALFYKLD
IVQLDGNSSQYRLINCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFNGTGPCN
NVSTVQCTHGIKPVVSTQLLLNGSLAEGEIIIRSENITDNGKTIIVHLNESVKIECTRPS
NNTRTSIRIGPGQAFYATGQVIGDIREAHCNISESKWNETLQRVSEKLKEYFPHKNITFQ
PSSGGDLEITTHSFNCGGEFFYCNTSSLFNRTYMATSTDMANSTETNSTRIITIRCRIKQ
IINMWQEVGRAMYAPPIAGNITCISNITGLLLTRDGGKNNTETFETFRPGGGNMKDNWRS
ELYKYKVVEVKPLGVAPTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQA
RQLLSGIVQQQSNLLKAIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGK
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ALDRWNSLWNWFNITNWLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLI
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IKPVVSTQLLLNGSLAEGEIIIRSKNITDNGKTIIVHLNESVKIECTRPSNNTRTSIRIG
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THSFSCGGEFFYCNTSSLFNRTYMATNTDMANSTETNSTRIITIRCRIRQIINMWQEVGR
AMYAPPIAGNITCISNITGLLLTRDGGENNTETFETFRPGGGNMKDNWRSELYKYKVVEV
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SSWSNKTYGDIWDNMTWMQWEREISNYTELIYELLEESQNQQEKNEQDLLALDRWNSLWN
WFNITNWLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPG
GIEEEGGEQDRNRSTRLVSGFLALAWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLK
GLRRGWEALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIP
TRIRQGFETALL

FIG. 21
CONTINUED

```
703010505.TF        MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAK
703010505.W4.03     ------------------------------------------------------
703010505.W4.26     ------------------------------------------------------
703010505.W14.21    ------------------------------------------------------
703010505.W20.14    ------------------------------------------------------
703010505.W30.28    ------------------------------------------------------
703010505.W30.13    ------------------------------------------------------
703010505.W53.31    ------------------------------------------------------
703010505.W78.15    ------------------------------------------------------
703010505.W100.B4   -----R-------------L-----------------------------------

703010505.W14.3     ------------------------------------------------------
703010505.W14.8     ------------------------------------------------------
703010505.W20.7     ------------------------------------------------------
703010505.W20.26    ------------------------------------------------------
703010505.W20.9     ------------------------------------------------------
703010505.W30.12    ------------------------------------------------------
703010505.W30.19    ------------------------------------------------------
703010505.W53.19    ------------------------------------------------------
703010505.W53.13    -----R------------------------------------------------
703010505.W78.1     ------------------------------------------------------

703010505.TF        LNCT.........NATASNS........SIIEGMKNCSFNITTELRDKREKKNA
703010505.W4.03     ----.........------........------------------------
703010505.W4.26     ----.........------........------------------------
703010505.W14.21    ----.........------........------------------------
703010505.W20.14    ----.........-----N........------------------------
703010505.W30.28    ----.........----I--........------------------------
703010505.W30.13    ----.........----I--........------------------------
703010505.W53.31    ----DATASNATAS------........------------------------
703010505.W78.15    -S--NAT.......------........--L---------------------
703010505.W100.B4   ----DANATASNT.------INATASKN.----E-----------------Y-
```

FIG. 22

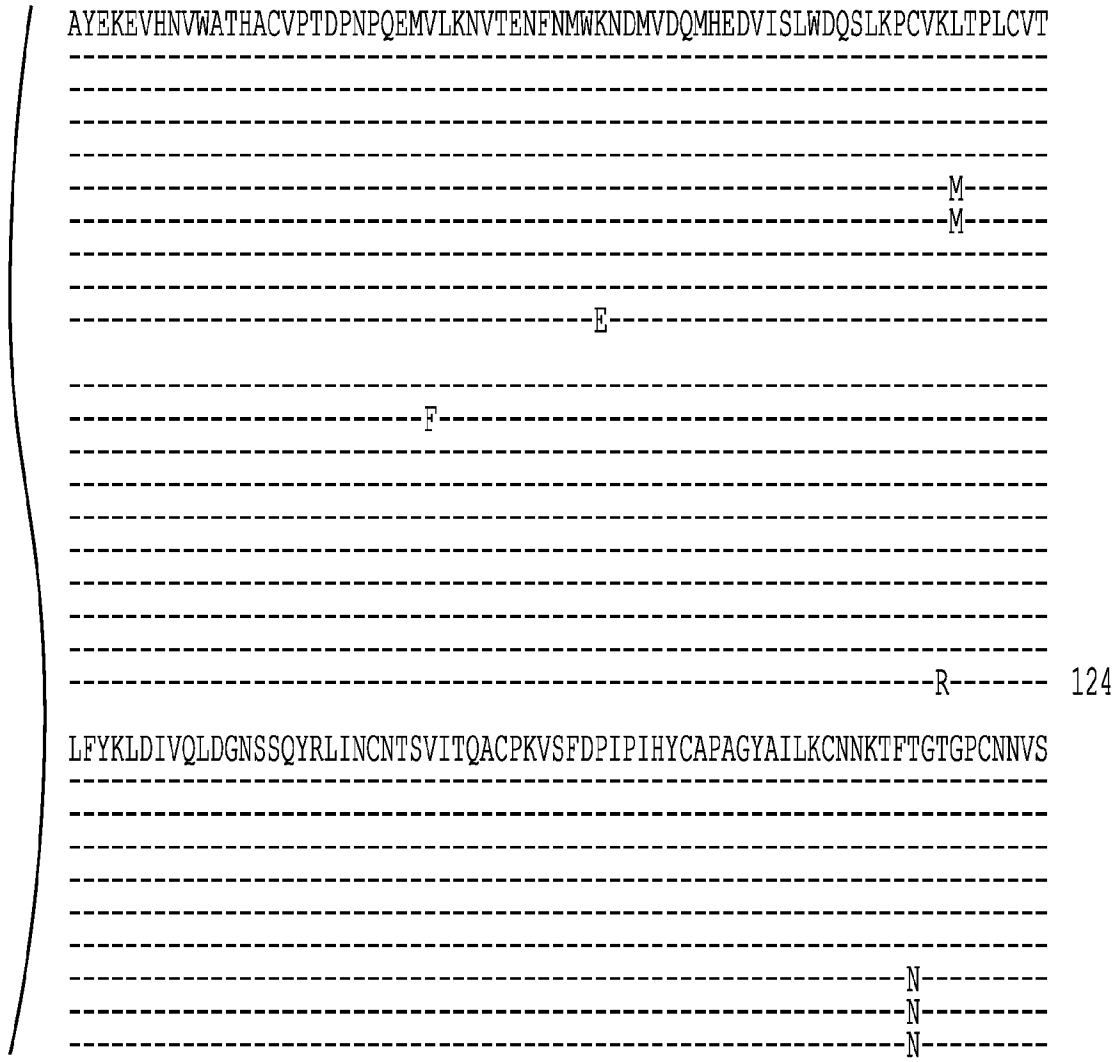

FIG. 22
CONTINUED

```
703010505.W14.3     ----.........------.......------------------------
703010505.W14.8     ----.........------.......----R-------------------
703010505.W20.7     ----.........--N---N.......------------------------
703010505.W20.26    ----.........-----I.......------------------------
703010505.W20.9     ----.........--.---.......------------------------
703010505.W30.12    ----NAT.....------.......------------------------
703010505.W30.19    ----NATARNCT..------.....------------------------
703010505.W53.19    ----DATASNATAS------.....----E-------------------
703010505.W53.13    ----DATAS.....-------SIIEGMNS----------------------
703010505.W78.1     ---INAT.....------N.....--L---------A-----------

703010505.TF        TVQCTHGIKPVVSTQLLLNGSLAEGEIIIRSENITNNVKTIIVHLNESVKIECTR
703010505.W4.03     ------------------------------------------------------
703010505.W4.26     ------------------------------------------------------
703010505.W14.21    ----------------------------------G-----------------
703010505.W20.14    ----------------------------------A-----------------
703010505.W30.28    ----------------------------------D-----------------
703010505.W30.13    ----------------------------------D-----------------
703010505.W53.31    --------------------------------D-G-----------------
703010505.W78.15    ------------------------------K---D-G-----------------
703010505.W100.B4   ------------------------------K---D-G-----------------

703010505.W14.3     ------------------------------------------------------
703010505.W14.8     ------------------------------------------------------
703010505.W20.7     ----------------------------------G-----------------
703010505.W20.26    ----------------------------------G-----------------
703010505.W20.9     ----------------------------------A-----------------
703010505.W30.12    ----------------------------------D-----------------
703010505.W30.19    ----------------------------------SG----------------
703010505.W53.19    --------------------------------D-G-----------------
703010505.W53.13    --------------------------------D-G-----------------
703010505.W78.1     ------------------------------K---D-G-----------------
```

FIG. 22
CONTINUED

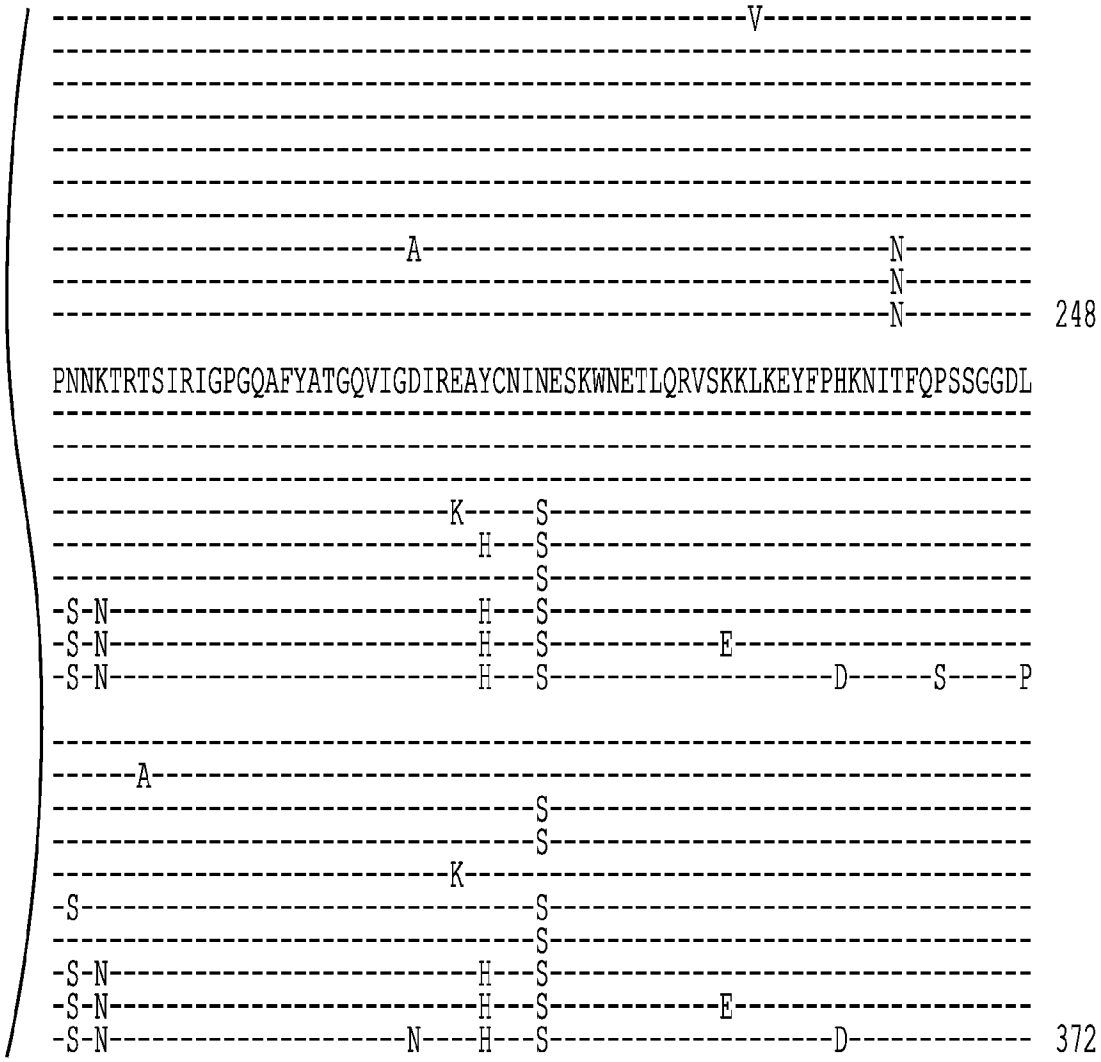

FIG. 22
CONTINUED

```
703010505.TF          EITTHSFNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQII
703010505.W4.03       ------------------------------------------------------
703010505.W4.26       ------------------------------------------------------
703010505.W14.21      ---------------------------------------I----------
703010505.W20.14      ----------------------------------------L-------
703010505.W30.28      ----------------------------------------R-------
703010505.W30.13      -------------------------------------N--P----------
703010505.W53.31      -------------------------.....----------I---R-------
703010505.W78.15      ----------------------------T---------I---R-------
703010505.W100.B4     ---------------------------------------I---R-------

703010505.W14.3       ----------------------------------------K---------
703010505.W14.8       ----------------------------------------R-------
703010505.W20.7       ---------------------------------------I----------
703010505.W20.26      ---------------------------------------I----------
703010505.W20.9       -------------------------------------N------------
703010505.W30.12      ----------------------------------------N----------
703010505.W30.19      ---------------------------------------I----------
703010505.W53.19      -------------------------.....----------I----------
703010505.W53.13      ----------------------------T---------I---R-------
703010505.W78.1       -------S-------------------TN----------I---R---R---

703010505.TF          PLGVAPTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSG
703010505.W4.03       ------------------------------------------------------
703010505.W4.26       --------V-----------------------------------------------
703010505.W14.21      ------------------------------------------------------
703010505.W20.14      ------------------------------------------------------
703010505.W30.28      ------------------------------------------------------
703010505.W30.13      ---I--------------------------------------------------
703010505.W53.31      ------------------------------------------------------
703010505.W78.15      ------------------------------------------------------
703010505.W100.B4     ------------------------------------------------------
```

FIG. 22
CONTINUED

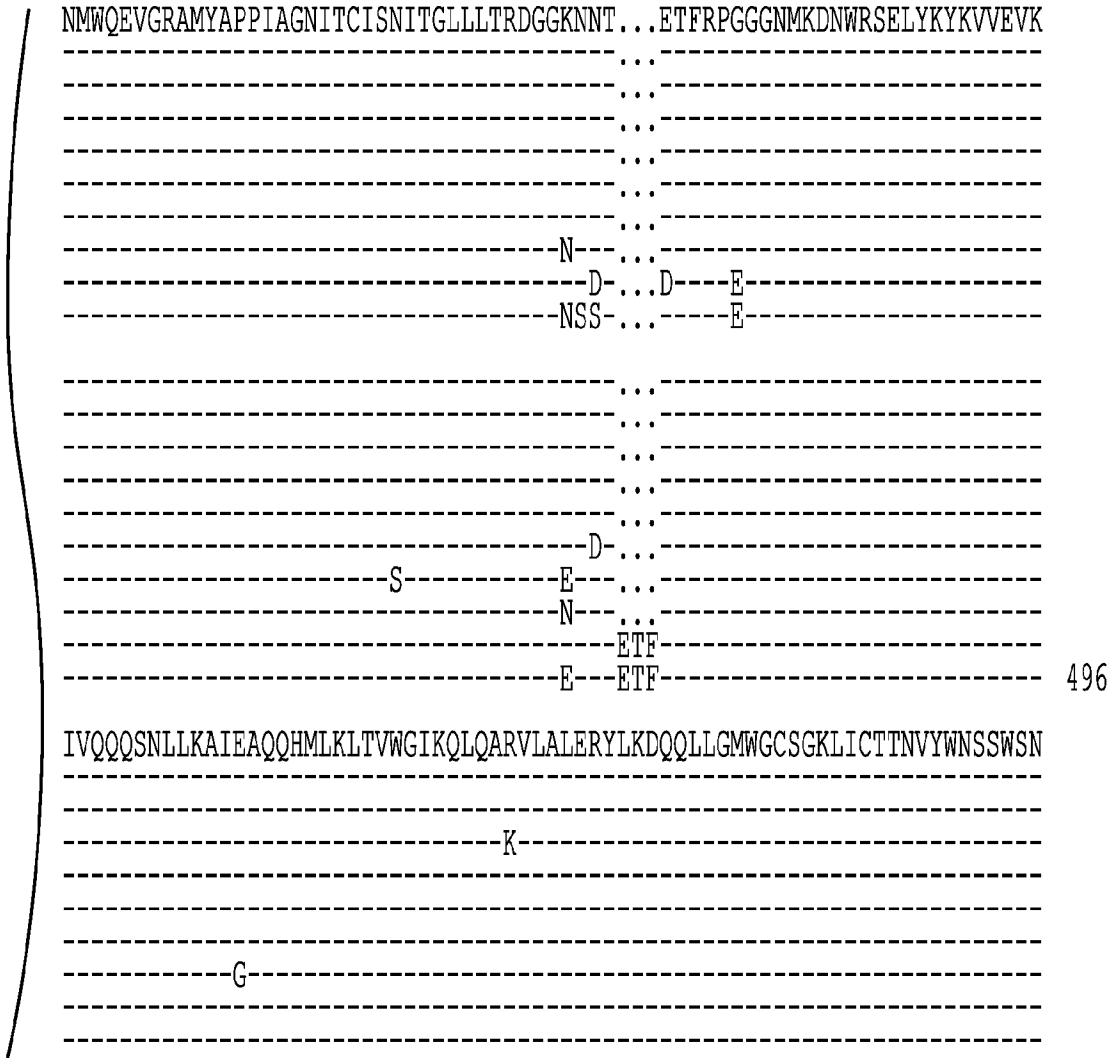

FIG. 22
CONTINUED

```
703010505.W14.3     --------------------------------------------------
703010505.W14.8     --------------------------------------------------
703010505.W20.7     --------------------------------------------------
703010505.W20.26    --------------------------------------------------
703010505.W20.9     --------------------------------------------------
703010505.W30.12    --------------------------------------------------
703010505.W30.19    --------------------------------------------------
703010505.W53.19    --------------------------------------------------
703010505.W53.13    --------------------------------------------------
703010505.W78.1     --------------------------------------------------

703010505.TF        KTYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWN
703010505.W4.03     --------------------------------------------------
703010505.W4.26     --------------------------------------------------
703010505.W14.21    --------------------------------------------------
703010505.W20.14    --------------------------------------------------
703010505.W30.28    -S------------------------------------------------
703010505.W30.13    --------------------------------------------------
703010505.W53.31    ----------------------M---------------------------
703010505.W78.15    ----------------------L---------------------------
703010505.W100.B4   ---D------------------M--D-----------------------

703010505.W14.3     --------------------------------------------------
703010505.W14.8     --------------------------------------------------
703010505.W20.7     --------------------------------------------------
703010505.W20.26    --------------------------------------------------
703010505.W20.9     --------------------------------------------------
703010505.W30.12    --------------------------------------------------
703010505.W30.19    --------------------------------------------------
703010505.W53.19    --------------------------------------------------
703010505.W53.13    ------------------D-------------------------------
703010505.W78.1     ----------------------L---------------------------
```

FIG. 22
CONTINUED

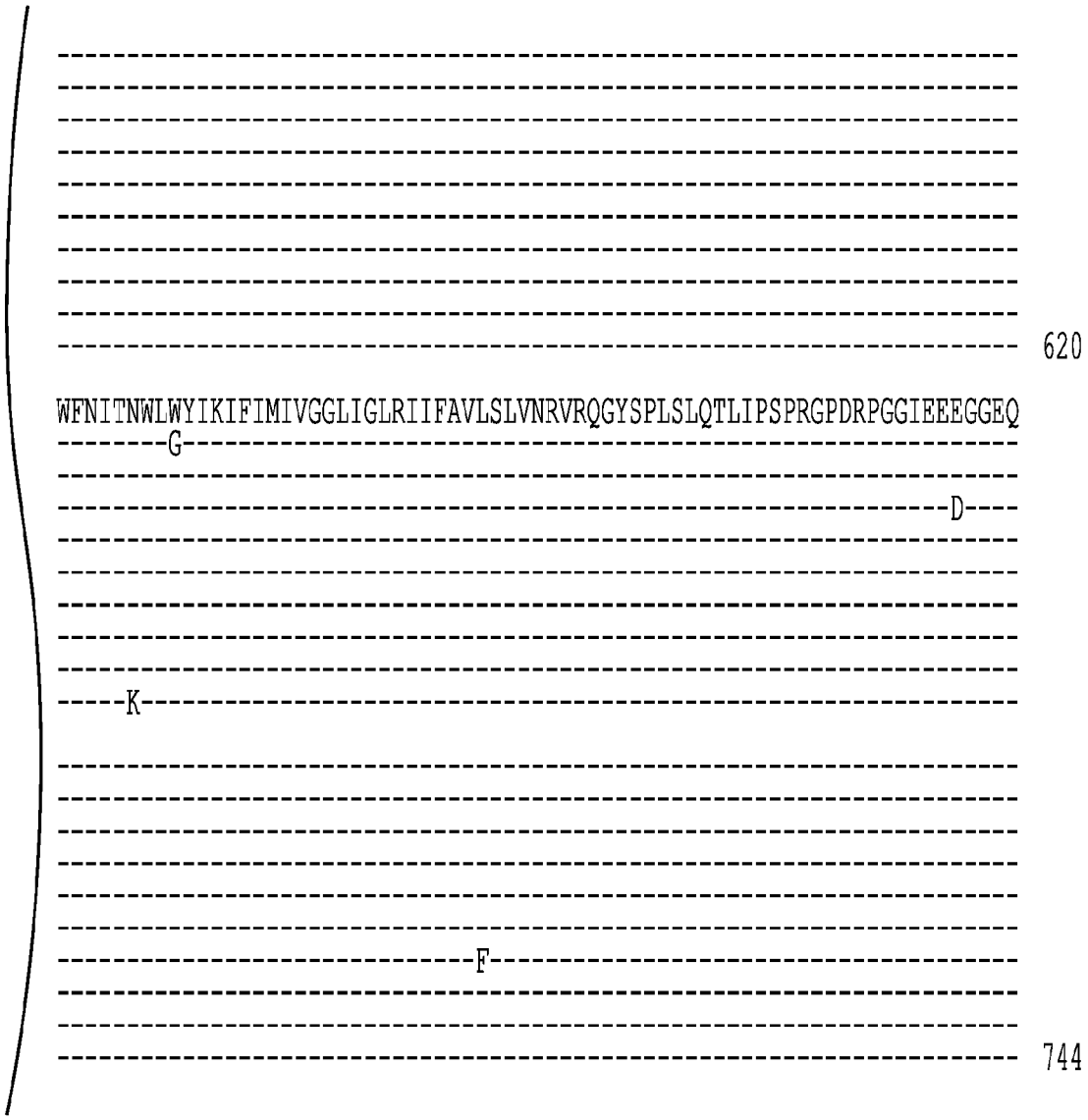

FIG. 22
CONTINUED

```
703010505.TF        DRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRR
703010505.W4.03     ------------------------------------------------------
703010505.W4.26     ------------------------------------------------------
703010505.W14.21    ------------------------------------------------------
703010505.W20.14    ------------------------------------------------------
703010505.W30.28    ------------------------------------------------------
703010505.W30.13    ------------------------------------------------------
703010505.W53.31    --K---------------------------------------------------
703010505.W78.15    ----------A-------------------------------------------
703010505.W100.B4   --K---------------------------------------------------

703010505.W14.3     ------------------------------------------------------
703010505.W14.8     ------------------------------------------------------
703010505.W20.7     ---------------------------------T--------------------
703010505.W20.26    ------------------------------------------------------
703010505.W20.9     ----------A-------------------------------------------
703010505.W30.12    ------------------------------------------------------
703010505.W30.19    ------------------------------------------------------
703010505.W53.19    ----------A-------------------------------------------
703010505.W53.13    ----------A-------------------------------------------
703010505.W78.1     ----------A-------------------------------------------
```

FIG. 22
CONTINUED

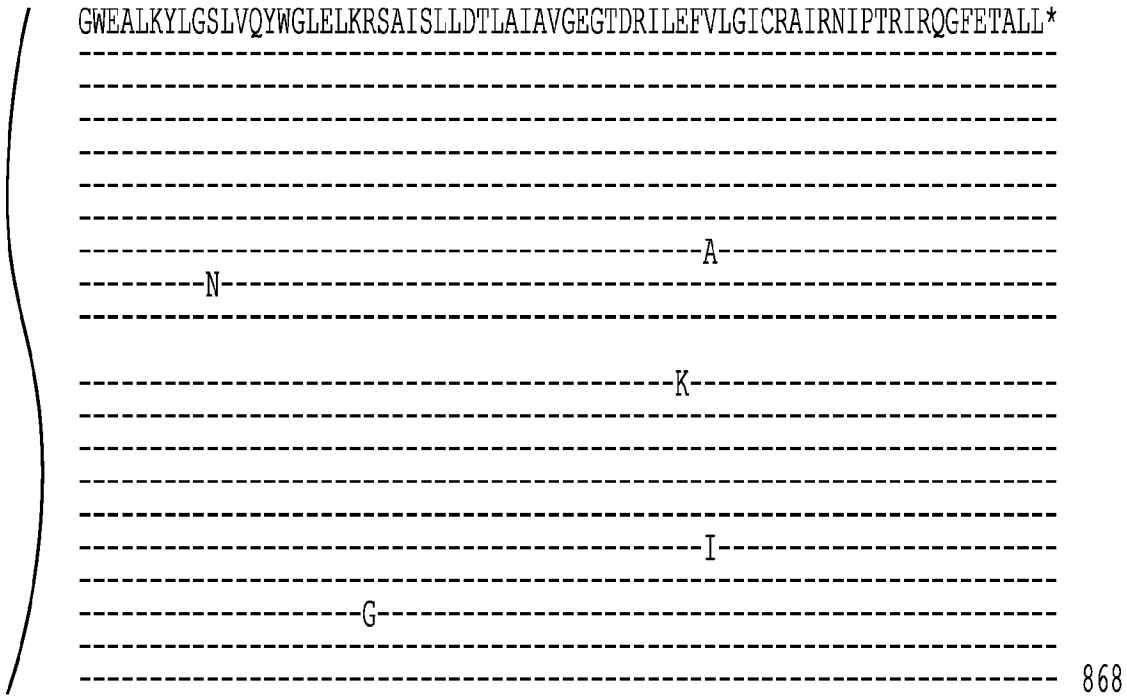

FIG. 22
CONTINUED

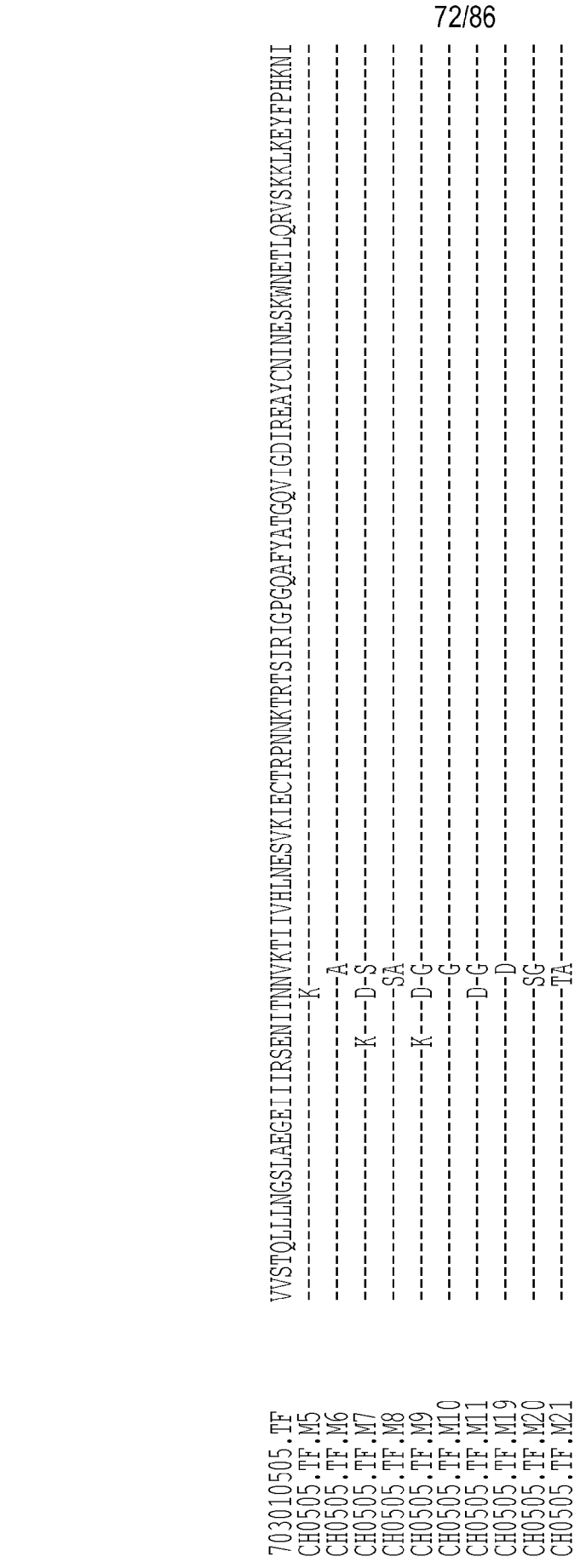
703010505.TF VVSTQLLINGSLAEGEIIRSENITNNVKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQAFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNI
CH0505.TF.M5 ----------K----------
CH0505.TF.M6 ----------A----------
CH0505.TF.M7 ----------K--D-S------
CH0505.TF.M8 ----------SA---------
CH0505.TF.M9 ----------K--D-G------
CH0505.TF.M10 ----------G----------
CH0505.TF.M11 ----------D-G--------
CH0505.TF.M19 ----------D----------
CH0505.TF.M20 ----------SG---------
CH0505.TF.M21 ----------TA---------

FIG. 23

>703010505.TF
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNVKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>CH0505.TF.M5
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITKNVKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>CH0505.TF.M6
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNAKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>CH0505.TF.M7
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSKNITDNSKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ

FIG. 24A

AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>CH0505.TF.M8
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNSAKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>CH0505.TF.M9
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSKNITDNGKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>CH0505.TF.M10
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNGKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN

FIG. 24A
CONTINUED

WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>CH0505.TF.M11
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITDNGKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>CH0505.TF.M19
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNNDKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL
>CH0505.TF.M20
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNSGKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL

FIG. 24A
CONTINUED

>CH0505.TF.M21
MRVMGIQRNYPQWWIWSMLGFWMLMICNGMWVTVYYGVPVWKEAKTTLFCASDAKAYEKE
VHNVWATHACVPTDPNPQEMVLKNVTENFNMWKNDMVDQMHEDVISLWDQSLKPCVKLTP
LCVTLNCTNATASNSSIIEGMKNCSFNITTELRDKREKKNALFYKLDIVQLDGNSSQYRL
INCNTSVITQACPKVSFDPIPIHYCAPAGYAILKCNNKTFTGTGPCNNVSTVQCTHGIKP
VVSTQLLLNGSLAEGEIIIRSENITNTAKTIIVHLNESVKIECTRPNNKTRTSIRIGPGQ
AFYATGQVIGDIREAYCNINESKWNETLQRVSKKLKEYFPHKNITFQPSSGGDLEITTHS
FNCGGEFFYCNTSSLFNRTYMANSTDMANSTETNSTRTITIHCRIKQIINMWQEVGRAMY
APPIAGNITCISNITGLLLTRDGGKNNTETFRPGGGNMKDNWRSELYKYKVVEVKPLGVA
PTNARRVVEREKRAVGMGAVFLGFLGAAGSTMGAASITLTVQARQLLSGIVQQQSNLLK
AIEAQQHMLKLTVWGIKQLQARVLALERYLKDQQLLGMWGCSGKLICTTNVYWNSSWSNK
TYGDIWDNMTWMQWEREISNYTEIIYELLEESQNQQEKNEQDLLALDRWNSLWNWFNITN
WLWYIKIFIMIVGGLIGLRIIFAVLSLVNRVRQGYSPLSLQTLIPSPRGPDRPGGIEEEG
GEQDRNRSTRLVSGFLALVWDDLRSLCLFIYHRLRDFILIAARAGELLGRSSLKGLRRGW
EALKYLGSLVQYWGLELKRSAISLLDTLAIAVGEGTDRILEFVLGICRAIRNIPTRIRQG
FETALL

FIG. 24A
CONTINUED

>CH0505.TF.M6
ATGAGAGTGATGGGGATACAGAGGAAT
TATCCACAATGGTGGATATGGAGCATGTTAGGCTTTTGGATGCTAATGAT
TTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTGTGGAAAG
AAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAA
GAAGTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAA
TCCACAAGAAATGGTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGA
AAAATGACATGGTGGATCAGATGCATGAAGATGTAATTAGTTTATGGGAT
CAAAGCCTCAAGCCATGTGTAAAGTTGACCCCACTCTGTGTCACTCTAAA
CTGTACCAATGCTACTGCCAGCAATAGCAGTATAATAGAGGGAATGAAAA
ATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAG
AATGCACTTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAG
TCAGTATAGATTAATAAATTGTAATACCTCAGTCATAACACAAGCCTGTC
CAAAGGTCTCTTTTGACCCAATTCCTATACATTATTGTGCTCCAGCTGGT
TATGCGATTCTAAAGTGTAATAATAAGACATTCACTGGAACAGGACCGTG
TAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCAGTGGTTT
CAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATT
AGATCTGAAAATATAACAAACAATGCCAAAACAATAATAGTACATCTCAA
TGAATCTGTAAAGATTGAGTGTACGAGACCCAATAATAAAACAAGAACAA
GTATAAGAATAGGACCAGGACAAGCATTTTATGCAACAGGACAAGTAATA
GGAGACATAAGAGAAGCATATTGTAACATTAATGAAAGTAAATGGAATGA
AACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCTCATAAGA
ATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACAT
AGCTTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTT
TAATAGGACATATATGGCTAATAGTACAGATATGGCTAATAGTACAGAAA
CTAACAGTACACGAACCATCACAATCCACTGCAGAATAAAACAAATTATA
AACATGTGGCAGGAGGTGGGACGAGCAATGTATGCCCCTCCCATTGCAGG
AAACATAACATGTATATCAAATATCACAGGACTACTATTGACAAGGGATG
GAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAG
GACAATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCC
ATTAGGAGTAGCACCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAA
AAAGAGCAGTGGGAATGGGAGCTGTGTTCCTTGGGTTCTTGGGAGCGGCA
GGAAGCACTATGGGCGCAGCATCAATAACGCTGACGGTACAGGCCAGACA
ATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAGGCTATAG
AGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTC
CAGGCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCT
AGGGATGTGGGGCTGCTCTGGAAAACTCATCTGCACCACTAATGTATATT
GGAACTCTAGTTGGAGTAATAAAACTTATGGTGATATTTGGGATAACATG
ACCTGGATGCAGTGGGAGAGAGAAATTAGCAATTATACAGAAATAATATA
TGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAACAAGATT
TACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACA
AATTGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGAT
AGGTTTAAGAATAATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGC
AGGGATACTCACCTCTGTCGTTGCAGACCCTTATCCCAAGCCCGAGGGGA
CCAGACAGGCCCGGAGGAATCGAAGAAGAAGGTGGAGAGCAAGACAGAAA
CAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGGGACGACC
TGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTA
ATTGCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACT
ACGGAGAGGATGGGAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATT
GGGGCCTGGAACTAAAAAGGAGTGCTATTAGTCTATTGGATACCCTAGCA
ATAGCAGTAGGTGAAGGAACAGATAGGATTCTAGAATTTGTATTAGGAAT
TTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGCTTTGAAA
CAGCTTTGCTATAA

FIG. 24B

>CH0505.TF.M8
ATGAGAGTGATGGGGATACAGAGG
AATTATCCACAATGGTGGATATGGAGCATGTTAGGCTTTTGGATGCTAAT
GATTTGTAATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTGTGGA
AAGAAGCAAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAG
AAAGAAGTGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCC
CAATCCACAAGAAATGGTTTTAAAAAATGTAACAGAAAATTTCAACATGT
GGAAAAATGACATGGTGGATCAGATGCATGAAGATGTAATTAGTTTATGG
GATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCCACTCTGTGTCACTCT
AAACTGTACCAATGCTACTGCCAGCAATAGCAGTATAATAGAGGGAATGA
AAAATTGCTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAA
AAGAATGCACTTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTC
TAGTCAGTATAGATTAATAAATTGTAATACCTCAGTCATAACACAAGCCT
GTCCAAAGGTCTCTTTTGACCCAATTCCTATACATTATTGTGCTCCAGCT
GGTTATGCGATTCTAAAGTGTAATAATAAGACATTCACTGGAACAGGACC
GTGTAATAATGTCAGCACAGTACAATGTACACATGGAATTAAGCCAGTGG
TTTCAACTCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATA
ATTAGATCTGAAAATATAACAAACAGTGCCAAAACAATAATAGTACATCT
CAATGAATCTGTAAAGATTGAGTGTACGAGACCCAATAATAAAACAAGAA
CAAGTATAAGAATAGGACCAGGACAAGCATTTTATGCAACAGGACAAGTA
ATAGGAGACATAAGAGAAGCATATTGTAACATTAATGAAAGTAAATGGAA
TGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCTCATA
AGAATATAACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACA
CATAGCTTTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCT
GTTTAATAGGACATATATGGCTAATAGTACAGATATGGCTAATAGTACAG
AAACTAACAGTACACGAACCATCACAATCCACTGCAGAATAAAACAAATT
ATAAACATGTGGCAGGAGGTGGGACGAGCAATGTATGCCCCTCCCATTGC
AGGAAACATAACATGTATATCAAATATCACAGGACTACTATTGACAAGGG
ATGGAGGAAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATG
AAGGACAATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAA
GCCATTAGGAGTAGCACCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAG
AAAAAAGAGCAGTGGGAATGGGAGCTGTGTTCCTTGGGTTCTTGGGAGCG
GCAGGAAGCACTATGGGCGCAGCATCAATAACGCTGACGGTACAGGCCAG
ACAATTATTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAGGCTA
TAGAGGCTCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAG
CTCCAGGCAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCT
CCTAGGGATGTGGGGCTGCTCTGGAAAACTCATCTGCACCACTAATGTAT
ATTGGAACTCTAGTTGGAGTAATAAAACTTATGGTGATATTTGGGATAAC
ATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAATTATACAGAAATAAT
ATATGAATTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAACAAG
ATTTACTAGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATA
ACAAATTGGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTT
GATAGGTTTAAGAATAATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTA
GGCAGGGATACTCACCTCTGTCGTTGCAGACCCTTATCCCAAGCCCGAGG
GGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGGTGGAGAGCAAGACAG
AAACAGATCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGGGACG
ACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATA
TTAATTGCAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGG
ACTACGGAGAGGATGGGAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGT
ATTGGGGCCTGGAACTAAAAAGGAGTGCTATTAGTCTATTGGATACCCTA
GCAATAGCAGTAGGTGAAGGAACAGATAGGATTCTAGAATTTGTATTAGG
AATTTGTAGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGCTTTG
AAACAGCTTTGCTATAA

FIG. 24B
CONTINUED

>CH0505.TF.M10
ATGAGAGTG
ATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGTTAGG
CTTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTACTATG
GGGTACCTGTGTGGAAAGAAGCAAAAACTACTCTATTTTGTGCATCAGAT
GCTAAAGCATATGAGAAAGAAGTGCATAATGTCTGGGCTACACATGCCTG
TGTACCCACAGACCCCAATCCACAAGAAATGGTTTTAAAAAATGTAACAG
AAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATGCATGAAGAT
GTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGACCCC
ACTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCAATAGCAGTA
TAATAGAGGGAATGAAAAATTGCTCTTTCAATATAACCACAGAATTAAGA
GATAAGAGAGAGAAAAAGAATGCACTTTTTTATAAACTTGATATAGTACA
ACTAGATGGCAACTCTAGTCAGTATAGATTAATAAATTGTAATACCTCAG
TCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATTCCTATACAT
TATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGACATT
CACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACACATG
GAATTAAGCCAGTGGTTTCAACTCAACTATTGTTAAATGGTAGCCTAGCA
GAAGGAGAGATAATAATTAGATCTGAAAATATAACAAACAATGGCAAAAC
AATAATAGTACATCTCAATGAATCTGTAAAGATTGAGTGTACGAGACCCA
ATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAAGCATTTTAT
GCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTGTAACATTAA
TGAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTAAAAG
AATACTTCCCTCATAAGAATATAACATTTCAACCATCCTCAGGAGGGGAC
CTAGAAATTACAACACATAGCTTTAATTGTGGAGGAGAATTTTTCTATTG
CAATACATCAAGCCTGTTTAATAGGACATATATGGCTAATAGTACAGATA
TGGCTAATAGTACAGAAACTAACAGTACACGAACCATCACAATCCACTGC
AGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAATGTA
TGCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACAGGAC
TACTATTGACAAGGGATGGAGGAAAAAACAATACGGAGACATTCAGACCT
GGAGGAGGAAATATGAAGGACAATTGGAGAAGTGAATTATATAAATATAA
AGTGGTAGAAGTTAAGCCATTAGGAGTAGCACCCACTAATGCAAGAAGGA
GAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCTGTGTTCCTT
GGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAACGCT
GACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAAAGCA
ATTTGCTGAAGGCTATAGAGGCTCAACAGCATATGTTGAAACTCACGGTC
TGGGGCATTAAACAGCTCCAGGCAAGAGTCCTGGCCTTGGAAAGATACCT
AAAGGATCAACAGCTCCTAGGGATGTGGGGCTGCTCTGGAAAACTCATCT
GCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAAACTTATGGT
GATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTAGCAA
TTATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAGCAGG
AAAAGAATGAACAAGATTTACTAGCATTGGACAGATGGAACAGTCTGTGG
AATTGGTTTAACATAACAAATTGGCTGTGGTATATAAAAATATTCATAAT
GATAGTAGGAGGCTTGATAGGTTTAAGAATAATTTTTGCTGTGCTTTCTT
TAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTGCAGACCCTT
ATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAGAAGG
TGGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTCTTAG
CGCTTGTCTGGGACGACCTGCGGAGCCTGTGCCTTTTCATCTACCACCGA
TTGAGAGACTTCATATTAATTGCAGCGAGAGCGGGGGAACTTCTGGGACG
CAGCAGTCTCAAGGGACTACGGAGAGGATGGGAAGCCCTTAAGTATCTGG
GAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGTGCTATTAGT
CTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGATTCT
AGAATTTGTATTACGAATTTGTAGAGCTATCCGCAACATACCTACAAGAA
TAAGACAGGGCTTTGAAACAGCTTTGCTATAA

FIG. 24B
CONTINUED

>CH0505.TF.M11
ATGAG
AGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAGCATGT
TAGGCTTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAGTCTAC
TATGGGGTACCTGTGTGGAAAGAAGCAAAAACTACTCTATTTTGTGCATC
AGATGCTAAAGCATATGAGAAAGAAGTGCATAATGTCTGGGCTACACATG
CCTGTGTACCCACAGACCCCAATCCACAAGAAATGGTTTTAAAAAATGTA
ACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATGCATGA
AGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAAGTTGA
CCCCACTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCAATAGC
AGTATAATAGAGGGAATGAAAAATTGCTCTTTCAATATAACCACAGAATT
AAGAGATAAGAGAGAGAAAAAGAATGCACTTTTTTATAAACTTGATATAG
TACAACTAGATGGCAACTCTAGTCAGTATAGATTAATAAATTGTAATACC
TCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATTCCTAT
ACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAATAAGA
CATTCACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAATGTACA
CATGGAATTAAGCCAGTGGTTTCAACTCAACTATTGTTAAATGGTAGCCT
AGCAGAAGGAGAGATAATAATTAGATCTGAAAATATAACAGACAATGGCA
AAACAATAATAGTACATCTCAATGAATCTGTAAAGATTGAGTGTACGAGA
CCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAAGCATT
TTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTGTAACA
TTAATGAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAAAATTA
AAAGAATACTTCCCTCATAAGAATATAACATTTCAACCATCCTCAGGAGG
GGACCTAGAAATTACAACACATAGCTTTAATTGTGGAGGAGAATTTTTCT
ATTGCAATACATCAAGCCTGTTTAATAGGACATATATGGCTAATAGTACA
GATATGGCTAATAGTACAGAAACTAACAGTACACGAACCATCACAATCCA
CTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACGAGCAA
TGTATGCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATATCACA
GGACTACTATTGACAAGGGATGGAGGAAAAAACAATACGGAGACATTCAG
ACCTGGAGGAGGAAATATGAAGGACAATTGGAGAAGTGAATTATATAAAT
ATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCACCCACTAATGCAAGA
AGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCTGTGTT
CCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATCAATAA
CGCTGACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAACAGCAA
AGCAATTTGCTGAAGGCTATAGAGGCTCAACAGCATATGTTGAAACTCAC
GGTCTGGGGCATTAAACAGCTCCAGGCAAGAGTCCTGGCCTTGGAAAGAT
ACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGCTGCTCTGGAAAACTC
ATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAAACTTA
TGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGAAATTA
GCAATTATACAGAAATAATATATGAATTGCTTGAAGAATCACAAAACCAG
CAGGAAAAGAATGAACAAGATTTACTAGCATTGGACAGATGGAACAGTCT
GTGGAATTGGTTTAACATAACAAATTGGCTGTGGTATATAAAAATATTCA
TAATGATAGTAGGAGGCTTGATAGGTTTAAGAATAATTTTTGCTGTGCTT
TCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTGCAGAC
CCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGAAGAAG
AAGGTGGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCGGATTC
TTAGCGCTTGTCTGGGACGACCTGCGGAGCCTGTGCCTTTTCATCTACCA
CCGATTGAGAGACTTCATATTAATTGCAGCGAGAGCGGGGGAACTTCTGG
GACGCAGCAGTCTCAAGGGACTACGGAGAGGATGGGAAGCCCTTAAGTAT
CTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGTGCTAT
TAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGATAGGA
TTCTAGAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATACCTACA
AGAATAAGACAGGGCTTTGAAACAGCTTTGCTATAA

FIG. 24B
CONTINUED

>CH0505.TF.M5
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAG
CATGTTAGGCTTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAG
TCTACTATGGGGTACCTGTGTGGAAAGAAGCAAAAACTACTCTATTTTGT
GCATCAGATGCTAAAGCATATGAGAAAGAAGTGCATAATGTCTGGGCTAC
ACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATGGTTTTAAAAA
ATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAA
GTTGACCCCACTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCA
ATAGCAGTATAATAGAGGGAATGAAAAATTGCTCTTTCAATATAACCACA
GAATTAAGAGATAAGAGAGAGAAAAAGAATGCACTTTTTTATAAACTTGA
TATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTAATAAATTGTA
ATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAA
TAAGACATTCACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAAT
GTACACATGGAATTAAGCCAGTGGTTTCAACTCAACTATTGTTAAATGGT
AGCCTAGCAGAAGGAGAGATAATAATTAGATCTGAAAATATAACAAAAAA
TGTCAAAACAATAATAGTACATCTCAATGAATCTGTAAAGATTGAGTGTA
CGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTG
TAACATTAATGAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAA
AATTAAAAGAATACTTCCCTCATAAGAATATAACATTTCAACCATCCTCA
GGAGGGGACCTAGAAATTACAACACATAGCTTTAATTGTGGAGGAGAATT
TTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATATATGGCTAATA
GTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAACCATCACA
ATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACG
AGCAATGTATGCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATA
TCACAGGACTACTATTGACAAGGGATGGAGGAAAAAACAATACGGAGACA
TTCAGACCTGGAGGAGGAAATATGAAGGACAATTGGAGAAGTGAATTATA
TAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCACCCACTAATG
CAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATC
AATAACGCTGACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAAC
AGCAAAGCAATTTGCTGAAGGCTATAGAGGCTCAACAGCATATGTTGAAA
CTCACGGTCTGGGGCATTAAACAGCTCCAGGCAAGAGTCCTGGCCTTGGA
AAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGCTGCTCTGGAA
AACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGA
AATTAGCAATTATACAGAAATAATATATGAATTGCTTGAAGAATCACAAA
ACCAGCAGGAAAAGAATGAACAAGATTTACTAGCATTGGACAGATGGAAC
AGTCTGTGGAATTGGTTTAACATAACAAATTGGCTGTGGTATATAAAAAT
ATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATAATTTTTGCTG
TGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGA
AGAAGAAGGTGGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCG
GATTCTTAGCGCTTGTCTGGGACGACCTGCGGAGCCTGTGCCTTTTCATC
TACCACCGATTGAGAGACTTCATATTAATTGCAGCGAGAGCGGGGGAACT
TCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGGGAAGCCCTTA
AGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGA
TAGGATTCTAGAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATAC
CTACAAGAATAAGACAGGGCTTTGAAACAGCTTTGCTATAA

FIG. 24B
CONTINUED

>CH0505.TF.M7
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAG
CATGTTAGGCTTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAG
TCTACTATGGGGTACCTGTGTGGAAAGAAGCAAAAACTACTCTATTTTGT
GCATCAGATGCTAAAGCATATGAGAAAGAAGTGCATAATGTCTGGGCTAC
ACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATGGTTTTAAAAA
ATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAA
GTTGACCCCACTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCA
ATAGCAGTATAATAGAGGGAATGAAAAATTGCTCTTTCAATATAACCACA
GAATTAAGAGATAAGAGAGAGAAAAAGAATGCACTTTTTTATAAACTTGA
TATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTAATAAATTGTA
ATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAA
TAAGACATTCACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAAT
GTACACATGGAATTAAGCCAGTGGTTTCAACTCAACTATTGTTAAATGGT
AGCCTAGCAGAAGGAGAGATAATAATTAGATCTAAAAATATAACAGACAA
TAGCAAAACAATAATAGTACATCTCAATGAATCTGTAAAGATTGAGTGTA
CGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTG
TAACATTAATGAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAA
AATTAAAAGAATACTTCCCTCATAAGAATATAACATTTCAACCATCCTCA
GGAGGGGACCTAGAAATTACAACACATAGCTTTAATTGTGGAGGAGAATT
TTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATATATGGCTAATA
GTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAACCATCACA
ATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACG
AGCAATGTATGCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATA
TCACAGGACTACTATTGACAAGGGATGGAGGAAAAAACAATACGGAGACA
TTCAGACCTGGAGGAGGAAATATGAAGGACAATTGGAGAAGTGAATTATA
TAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCACCCACTAATG
CAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATC
AATAACGCTGACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAAC
AGCAAAGCAATTTGCTGAAGGCTATAGAGGCTCAACAGCATATGTTGAAA
CTCACGGTCTGGGGCATTAAACAGCTCCAGGCAAGAGTCCTGGCCTTGGA
AAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGCTGCTCTGGAA
AACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGA
AATTAGCAATTATACAGAAATAATATATGAATTGCTTGAAGAATCACAAA
ACCAGCAGGAAAAGAATGAACAAGATTTACTAGCATTGGACAGATGGAAC
AGTCTGTGGAATTGGTTTAACATAACAAATTGGCTGTGGTATATAAAAAT
ATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATAATTTTTGCTG
TGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGA
AGAAGAAGGTGGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCG
GATTCTTAGCGCTTGTCTGGGACGACCTGCGGAGCCTGTGCCTTTTCATC
TACCACCGATTGAGAGACTTCATATTAATTGCAGCGAGAGCGGGGGAACT
TCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGGGAAGCCCTTA
AGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGA
TAGGATTCTAGAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATAC
CTACAAGAATAAGACAGGGCTTTGAAACAGCTTTGCTATAA

FIG. 24B
CONTINUED

>CH0505.TF.M9
ATGAGAGTGATGGGGATACAGAGGAATTATCCACAATGGTGGATATGGAG
CATGTTAGGCTTTTGGATGCTAATGATTTGTAATGGGATGTGGGTCACAG
TCTACTATGGGGTACCTGTGTGGAAAGAAGCAAAAACTACTCTATTTTGT
GCATCAGATGCTAAAGCATATGAGAAAGAAGTGCATAATGTCTGGGCTAC
ACATGCCTGTGTACCCACAGACCCCAATCCACAAGAAATGGTTTTAAAAA
ATGTAACAGAAAATTTCAACATGTGGAAAAATGACATGGTGGATCAGATG
CATGAAGATGTAATTAGTTTATGGGATCAAAGCCTCAAGCCATGTGTAAA
GTTGACCCCACTCTGTGTCACTCTAAACTGTACCAATGCTACTGCCAGCA
ATAGCAGTATAATAGAGGGAATGAAAAATTGCTCTTTCAATATAACCACA
GAATTAAGAGATAAGAGAGAGAAAAAGAATGCACTTTTTTATAAACTTGA
TATAGTACAACTAGATGGCAACTCTAGTCAGTATAGATTAATAAATTGTA
ATACCTCAGTCATAACACAAGCCTGTCCAAAGGTCTCTTTTGACCCAATT
CCTATACATTATTGTGCTCCAGCTGGTTATGCGATTCTAAAGTGTAATAA
TAAGACATTCACTGGAACAGGACCGTGTAATAATGTCAGCACAGTACAAT
GTACACATGGAATTAAGCCAGTGGTTTCAACTCAACTATTGTTAAATGGT
AGCCTAGCAGAAGGAGAGATAATAATTAGATCTAAAAATATAACAGACAA
TGGCAAAACAATAATAGTACATCTCAATGAATCTGTAAAGATTGAGTGTA
CGAGACCCAATAATAAAACAAGAACAAGTATAAGAATAGGACCAGGACAA
GCATTTTATGCAACAGGACAAGTAATAGGAGACATAAGAGAAGCATATTG
TAACATTAATGAAAGTAAATGGAATGAAACTTTACAAAGGGTAAGTAAAA
AATTAAAAGAATACTTCCCTCATAAGAATATAACATTTCAACCATCCTCA
GGAGGGGACCTAGAAATTACAACACATAGCTTTAATTGTGGAGGAGAATT
TTTCTATTGCAATACATCAAGCCTGTTTAATAGGACATATATGGCTAATA
GTACAGATATGGCTAATAGTACAGAAACTAACAGTACACGAACCATCACA
ATCCACTGCAGAATAAAACAAATTATAAACATGTGGCAGGAGGTGGGACG
AGCAATGTATGCCCCTCCCATTGCAGGAAACATAACATGTATATCAAATA
TCACAGGACTACTATTGACAAGGGATGGAGGAAAAAACAATACGGAGACA
TTCAGACCTGGAGGAGGAAATATGAAGGACAATTGGAGAAGTGAATTATA
TAAATATAAAGTGGTAGAAGTTAAGCCATTAGGAGTAGCACCCACTAATG
CAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGAGCAGTGGGAATGGGAGCT
GTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAGCACTATGGGCGCAGCATC
AATAACGCTGACGGTACAGGCCAGACAATTATTGTCTGGTATAGTGCAAC
AGCAAAGCAATTTGCTGAAGGCTATAGAGGCTCAACAGCATATGTTGAAA
CTCACGGTCTGGGGCATTAAACAGCTCCAGGCAAGAGTCCTGGCCTTGGA
AAGATACCTAAAGGATCAACAGCTCCTAGGGATGTGGGGCTGCTCTGGAA
AACTCATCTGCACCACTAATGTATATTGGAACTCTAGTTGGAGTAATAAA
ACTTATGGTGATATTTGGGATAACATGACCTGGATGCAGTGGGAGAGAGA
AATTAGCAATTATACAGAAATAATATATGAATTGCTTGAAGAATCACAAA
ACCAGCAGGAAAAGAATGAACAAGATTTACTAGCATTGGACAGATGGAAC
AGTCTGTGGAATTGGTTTAACATAACAAATTGGCTGTGGTATATAAAAAT
ATTCATAATGATAGTAGGAGGCTTGATAGGTTTAAGAATAATTTTTGCTG
TGCTTTCTTTAGTAAATAGAGTTAGGCAGGGATACTCACCTCTGTCGTTG
CAGACCCTTATCCCAAGCCCGAGGGGACCAGACAGGCCCGGAGGAATCGA
AGAAGAAGGTGGAGAGCAAGACAGAAACAGATCAACGCGATTAGTGAGCG
GATTCTTAGCGCTTGTCTGGGACGACCTGCGGAGCCTGTGCCTTTTCATC
TACCACCGATTGAGAGACTTCATATTAATTGCAGCGAGAGCGGGGGAACT
TCTGGGACGCAGCAGTCTCAAGGGACTACGGAGAGGATGGGAAGCCCTTA
AGTATCTGGGAAGTCTTGTGCAGTATTGGGGCCTGGAACTAAAAAGGAGT
GCTATTAGTCTATTGGATACCCTAGCAATAGCAGTAGGTGAAGGAACAGA
TAGGATTCTAGAATTTGTATTAGGAATTTGTAGAGCTATCCGCAACATAC
CTACAAGAATAAGACAGGGCTTTGAAACAGCTTTGCTATAA

FIG. 24B
CONTINUED

>CH0505.TF.M21
ATGAGAGTGATGGGGATACAGAGGAATTATCC
ACAATGGTGGATATGGAGCATGTTAGGCTTTTGGATGCTAATGATTTGTA
ATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTGTGGAAAGAAGCA
AAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAAGT
GCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCAC
AAGAAATGGTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAAT
GACATGGTGGATCAGATGCATGAAGATGTAATTAGTTTATGGGATCAAAG
CCTCAAGCCATGTGTAAAGTTGACCCCACTCTGTGTCACTCTAAACTGTA
CCAATGCTACTGCCAGCAATAGCAGTATAATAGAGGGAATGAAAAATTGC
TCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAATGC
ACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGT
ATAGATTAATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAG
GTCTCTTTTGACCCAATTCCTATACATTATTGTGCTCCAGCTGGTTATGC
GATTCTAAAGTGTAATAATAAGACATTCACTGGAACAGGACCGTGTAATA
ATGTCAGCACAGTACAATGTACACATGGAATTAAGCCAGTGGTTTCAACT
CAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGATC
TGAAAATATAACAAACACTGCCAAAACAATAATAGTACATCTCAATGAAT
CTGTAAAGATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATA
AGAATAGGACCAGGACAAGCATTTTATGCAACAGGACAAGTAATAGGAGA
CATAAGAGAAGCATATTGTAACATTAATGAAAGTAAATGGAATGAAACTT
TACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCTCATAAGAATATA
ACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGCTT
TAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATA
GGACATATATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAAC
AGTACACGAACCATCACAATCCACTGCAGAATAAAACAAATTATAAACAT
GTGGCAGGAGGTGGGACGAGCAATGTATGCCCCTCCCATTGCAGGAAACA
TAACATGTATATCAAATATCACAGGACTACTATTGACAAGGGATGGAGGA
AAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGACAA
TTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAG
GAGTAGCACCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGA
GCAGTGGGAATGGGAGCTGTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAG
CACTATGGGCGCAGCATCAATAACGCTGACGGTACAGGCCAGACAATTAT
TGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAGGCTATAGAGGCT
CAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAGGC
AAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGA
TGTGGGGCTGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAAC
TCTAGTTGGAGTAATAAAACTTATGGTGATATTTGGGATAACATGACCTG
GATGCAGTGGGAGAGAGAAATTAGCAATTATACAGAAATAATATATGAAT
TGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAACAAGATTTACTA
GCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAATTG
GCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTT
TAAGAATAATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGA
TACTCACCTCTGTCGTTGCAGACCCTTATCCCAAGCCCGAGGGGACCAGA
CAGGCCCGGAGGAATCGAAGAAGAAGGTGGAGAGCAAGACAGAAACAGAT
CAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGGGACGACCTGCGG
AGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATTGC
AGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGA
GAGGATGGGAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGC
CTGGAACTAAAAAGGAGTGCTATTAGTCTATTGGATACCCTAGCAATAGC
AGTAGGTGAAGGAACAGATAGGATTCTAGAATTTGTATTAGGAATTTGTA
GAGCTATCCGCAACATACCTACAAGAATAAGACAGGGCTTTGAAACAGCT
TTGCTATAA

FIG. 24B
CONTINUED

>CH0505.TF.M19
ATGAGAGTGATGGGGATACAGAGGAATTATCC
ACAATGGTGGATATGGAGCATGTTAGGCTTTTGGATGCTAATGATTTGTA
ATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTGTGGAAAGAAGCA
AAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAAGT
GCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCAC
AAGAAATGGTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAAT
GACATGGTGGATCAGATGCATGAAGATGTAATTAGTTTATGGGATCAAAG
CCTCAAGCCATGTGTAAAGTTGACCCCACTCTGTGTCACTCTAAACTGTA
CCAATGCTACTGCCAGCAATAGCAGTATAATAGAGGGAATGAAAAATTGC
TCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAATGC
ACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAGT
ATAGATTAATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAAG
GTCTCTTTTGACCCAATTCCTATACATTATTGTGCTCCAGCTGGTTATGC
GATTCTAAAGTGTAATAATAAGACATTCACTGGAACAGGACCGTGTAATA
ATGTCAGCACAGTACAATGTACACATGGAATTAAGCCAGTGGTTTCAACT
CAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGATC
TGAAAATATAACAAACAATGACAAAACAATAATAGTACATCTCAATGAAT
CTGTAAAGATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTATA
AGAATAGGACCAGGACAAGCATTTTATGCAACAGGACAAGTAATAGGAGA
CATAAGAGAAGCATATTGTAACATTAATGAAAGTAAATGGAATGAAACTT
TACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCTCATAAGAATATA
ACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGCTT
TAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAATA
GGACATATATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAAC
AGTACACGAACCATCACAATCCACTGCAGAATAAAACAAATTATAAACAT
GTGGCAGGAGGTGGGACGAGCAATGTATGCCCCTCCCATTGCAGGAAACA
TAACATGTATATCAAATATCACAGGACTACTATTGACAAGGGATGGAGGA
AAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGACAA
TTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTAG
GAGTAGCACCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAGA
GCAGTGGGAATGGGAGCTGTGTTCCTTGGGTTCTTGGGAGCGGCAGGAAG
CACTATGGGCGCAGCATCAATAACGCTGACGGTACAGGCCAGACAATTAT
TGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAGGCTATAGAGGCT
CAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAGGC
AAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGGA
TGTGGGGCTGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAAC
TCTAGTTGGAGTAATAAAACTTATGGTGATATTTGGGATAACATGACCTG
GATGCAGTGGGAGAGAGAAATTAGCAATTATACAGAAATAATATATGAAT
TGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAACAAGATTTACTA
GCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAATTG
GCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGTT
TAAGAATAATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGGA
TACTCACCTCTGTCGTTGCAGACCCTTATCCCAAGCCCGAGGGGACCAGA
CAGGCCCGGAGGAATCGAAGAAGAAGGTGGAGAGCAAGACAGAAACAGAT
CAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGGGACGACCTGCGG
AGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATTGC
AGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGGA
GAGGATGGGAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGGC
CTGGAACTAAAAAGGAGTGCTATTAGTCTATTGGATACCCTAGCAATAGC
AGTAGGTGAAGGAACAGATAGGATTCTAGAATTTGTATTAGGAATTTGTA
GAGCTATCCGCAACATACCTACAAGAATAAGACAGGGCTTTGAAACAGCT
TTGCTATAA

FIG. 24B
CONTINUED

>CH0505.TF.M20
ATGAGAGTGATGGGGATACAGAGGAATTATC
CACAATGGTGGATATGGAGCATGTTAGGCTTTTGGATGCTAATGATTTGT
AATGGGATGTGGGTCACAGTCTACTATGGGGTACCTGTGTGGAAAGAAGC
AAAAACTACTCTATTTTGTGCATCAGATGCTAAAGCATATGAGAAAGAAG
TGCATAATGTCTGGGCTACACATGCCTGTGTACCCACAGACCCCAATCCA
CAAGAAATGGTTTTAAAAAATGTAACAGAAAATTTCAACATGTGGAAAAA
TGACATGGTGGATCAGATGCATGAAGATGTAATTAGTTTATGGGATCAAA
GCCTCAAGCCATGTGTAAAGTTGACCCCACTCTGTGTCACTCTAAACTGT
ACCAATGCTACTGCCAGCAATAGCAGTATAATAGAGGGAATGAAAAATTG
CTCTTTCAATATAACCACAGAATTAAGAGATAAGAGAGAGAAAAAGAATG
CACTTTTTTATAAACTTGATATAGTACAACTAGATGGCAACTCTAGTCAG
TATAGATTAATAAATTGTAATACCTCAGTCATAACACAAGCCTGTCCAAA
GGTCTCTTTTGACCCAATTCCTATACATTATTGTGCTCCAGCTGGTTATG
CGATTCTAAAGTGTAATAATAAGACATTCACTGGAACAGGACCGTGTAAT
AATGTCAGCACAGTACAATGTACACATGGAATTAAGCCAGTGGTTTCAAC
TCAACTATTGTTAAATGGTAGCCTAGCAGAAGGAGAGATAATAATTAGAT
CTGAAAATATAACAAACAGTGGCAAAACAATAATAGTACATCTCAATGAA
TCTGTAAAGATTGAGTGTACGAGACCCAATAATAAAACAAGAACAAGTAT
AAGAATAGGACCAGGACAAGCATTTTATGCAACAGGACAAGTAATAGGAG
ACATAAGAGAAGCATATTGTAACATTAATGAAAGTAAATGGAATGAAACT
TTACAAAGGGTAAGTAAAAAATTAAAAGAATACTTCCCTCATAAGAATAT
AACATTTCAACCATCCTCAGGAGGGGACCTAGAAATTACAACACATAGCT
TTAATTGTGGAGGAGAATTTTTCTATTGCAATACATCAAGCCTGTTTAAT
AGGACATATATGGCTAATAGTACAGATATGGCTAATAGTACAGAAACTAA
CAGTACACGAACCATCACAATCCACTGCAGAATAAAACAAATTATAAACA
TGTGGCAGGAGGTGGGACGAGCAATGTATGCCCCTCCCATTGCAGGAAAC
ATAACATGTATATCAAATATCACAGGACTACTATTGACAAGGGATGGAGG
AAAAAACAATACGGAGACATTCAGACCTGGAGGAGGAAATATGAAGGACA
ATTGGAGAAGTGAATTATATAAATATAAAGTGGTAGAAGTTAAGCCATTA
GGAGTAGCACCCACTAATGCAAGAAGGAGAGTGGTGGAGAGAGAAAAAAG
AGCAGTGGGAATGGGAGCTGTGTTCCTTGGGTTCTTGGGAGCGGCAGGAA
GCACTATGGGCGCAGCATCAATAACGCTGACGGTACAGGCCAGACAATTA
TTGTCTGGTATAGTGCAACAGCAAAGCAATTTGCTGAAGGCTATAGAGGC
TCAACAGCATATGTTGAAACTCACGGTCTGGGGCATTAAACAGCTCCAGG
CAAGAGTCCTGGCCTTGGAAAGATACCTAAAGGATCAACAGCTCCTAGGG
ATGTGGGGCTGCTCTGGAAAACTCATCTGCACCACTAATGTATATTGGAA
CTCTAGTTGGAGTAATAAAACTTATGGTGATATTTGGGATAACATGACCT
GGATGCAGTGGGAGAGAGAAATTAGCAATTATACAGAAATAATATATGAA
TTGCTTGAAGAATCACAAAACCAGCAGGAAAAGAATGAACAAGATTTACT
AGCATTGGACAGATGGAACAGTCTGTGGAATTGGTTTAACATAACAAATT
GGCTGTGGTATATAAAAATATTCATAATGATAGTAGGAGGCTTGATAGGT
TTAAGAATAATTTTTGCTGTGCTTTCTTTAGTAAATAGAGTTAGGCAGGG
ATACTCACCTCTGTCGTTGCAGACCCTTATCCCAAGCCCGAGGGGACCAG
ACAGGCCCGGAGGAATCGAAGAAGAAGGTGGAGAGCAAGACAGAAACAGA
TCAACGCGATTAGTGAGCGGATTCTTAGCGCTTGTCTGGGACGACCTGCG
GAGCCTGTGCCTTTTCATCTACCACCGATTGAGAGACTTCATATTAATTG
CAGCGAGAGCGGGGGAACTTCTGGGACGCAGCAGTCTCAAGGGACTACGG
AGAGGATGGGAAGCCCTTAAGTATCTGGGAAGTCTTGTGCAGTATTGGGG
CCTGGAACTAAAAAGGAGTGCTATTAGTCTATTGGATACCCTAGCAATAG
CAGTAGGTGAAGGAACAGATAGGATTCTAGAATTTGTATTAGGAATTTGT
AGAGCTATCCGCAACATACCTACAAGAATAAGACAGGGCTTTGAAACAGC
TTTGCTATAA

FIG. 24B
CONTINUED

PATENT COOPERATION TREATY

PCT

DECLARATION OF NON-ESTABLISHMENT OF INTERNATIONAL SEARCH REPORT
(PCT Article 17(2)(a), Rules 13*ter*.1(c) and (d) and 39)

Applicant's or agent's file reference 1234300.00152WO1	**IMPORTANT DECLARATION**	Date of mailing *(day/month/year)* 28 DEC 2015
International application No. PCT/US15/41619	International filing date *(day/month/year)* 22 July 2015	(Earliest) Priority Date *(day/month/year)* 22 July 2014
International Patent Classification (IPC) or both national classification and IPC IPC: C12Q 1/68; CPC: C12Q 2600/158		
Applicant DUKE UNIVERSITY		

This International Searching Authority hereby declares, according to Article 17(2)(a), that **no international search report will be established** on the international application for the reasons indicated below.

1. ☐ The subject matter of the international application relates to:
   - a. ☐ scientific theories
   - b. ☐ mathematical theories
   - c. ☐ plant varieties
   - d. ☐ animal varieties
   - e. ☐ essentially biological processes for the production of plants and animals, other than microbiological processes and the products of such processes
   - f. ☐ schemes, rules or methods of doing business
   - g. ☐ schemes, rules or methods of performing purely mental acts
   - h. ☐ schemes, rules or methods of playing games
   - i. ☐ methods for treatment of the human body by surgery or therapy
   - j. ☐ methods for treatment of the animal body by surgery or therapy
   - k. ☐ diagnostic methods practised on the human or animal body
   - l. ☐ mere presentations of information
   - m. ☐ computer programs for which this International Searching Authority is not equipped to search prior art
2. ☐ The failure of the following parts of the international application to comply with prescribed requirements prevents a meaningful search from being carried out:
   ☐ the description ☐ the claims ☐ the drawings
3. ☒ A meaningful search could not be carried out without the sequence listing; the applicant did not, within the prescribed time limit:
   - ☒ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in a form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
   - ☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
   - ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a) or (b).
4. Further comments:
   Applicant failed to submit a valid electronic seq. listing in respone to the ISA/225.

Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Blaine Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774