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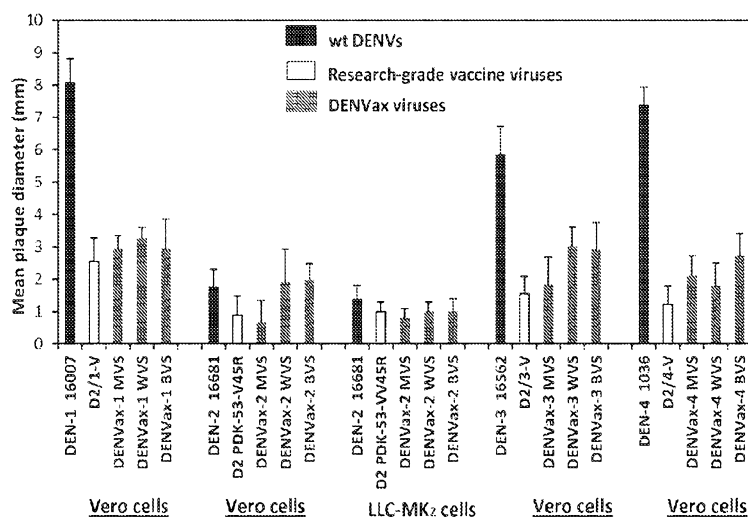
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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR DENGUE VIRUS CHIMERIC CONSTRUCTS IN VACCINES

Fig. 6



(57) Abstract: Embodiments herein report compositions, uses and manufacturing of dengue virus constructs and live attenuated dengue viruses. Some embodiments concern a composition that includes, but is not limited to, a tetravalent dengue virus composition. In certain embodiments, compositions can include constructs of one or more serotypes of dengue virus, such as dengue-1 (DEN-1) virus, dengue-2 (DEN-2) virus, dengue-3 (DEN-3) or dengue-4 (DEN-4) virus constructs. In other embodiments, constructs disclosed herein can be combined in a composition to generate a vaccine against more one or more dengue virus constructs that may or may not be subsequently passaged in mammalian cells.



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COMPOSITIONS AND METHODS FOR DENGUE VIRUS CHIMERIC CONSTRUCTS IN VACCINES

PRIORITY

[0001] This PCT Application claims priority to U.S. Provisional Application No. 61/800,204 filed March 15, 2013. This application is incorporated herein in its entirety by reference for all purposes.

FEDERALLY FUNDED RESEARCH

[0002] Some embodiments disclosed herein were supported in part by grant number R43 AI084291-01 from the National Institutes of Health. The U.S. Government may have certain rights to practice the subject invention.

FIELD

[0003] Embodiments herein report compositions, methods, uses and manufacturing procedures for dengue virus constructs and vaccine compositions thereof. Some embodiments concern a composition that includes, but is not limited to, chimeric flavivirus virus constructs that alone or in combination with other constructs can be used in a vaccine composition. In certain embodiments, compositions can include constructs of more than one serotypes of dengue virus, such as dengue-1 (DEN-1) virus, dengue-2 (DEN-2) virus, dengue-3 (DEN-3) virus and/or dengue-4 (DEN-4) virus. In other embodiments, manufacturing strategy that can improve the safety and genetic stability of recombinant live-attenuated chimeric dengue vaccine (DENVax) viruses. Certain embodiments include at least one live, attenuated dengue virus in combination with dengue virus chimeric constructs identified to be both safe and effective in vaccine compositions where the constructs have undergone additional passages in cell cultures. **BACKGROUND**

[0004] Infection with dengue virus can lead to a painful fever of varying severity. To date, four serotypes of dengue virus have been identified: dengue-1 (DEN-1), dengue-2 (DEN-2), or dengue-3 (DEN-3) in combination with dengue-4 (DEN-4). Dengue fever is caused by infection of a dengue virus. Other subtypes may be discovered in the future (e.g. DEN-5). Dengue virus serotypes 1-4 can also cause dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS). The most severe consequences of infection, DHF and DSS, can be life threatening. Dengue viruses cause 50-100 million cases of debilitating dengue fever, 500,000 cases of DHF/DSS, and more than 20,000 deaths each year. To date, there is no

effective vaccine to protect against dengue fever and no drug treatment for the disease. Mosquito control efforts have been ineffective in preventing dengue outbreaks in endemic areas or in preventing further geographic spread of the disease. It is estimated that 3.5 billion people are threatened by infection with dengue virus. In addition, dengue virus is a leading cause of fever in travelers to endemic areas, such as Asia, Central and South America, and the Caribbean.

[0005] All four dengue virus serotypes are endemic throughout the tropical regions of the world and constitute the most significant mosquito-borne viral threat to humans in tropical regions, worldwide. Dengue viruses are transmitted to humans primarily by *Aedes aegypti* mosquitoes. Infection with one dengue virus serotype results in life-long protection from re-infection by that serotype, but does not prevent secondary infection by one of the other three dengue virus serotypes. In fact, previous infection with one dengue virus serotype leads to an increased risk of severe disease (DHF/DSS) upon secondary infection with a different serotype. The development of an effective vaccine represents an important approach to the prevention and control of this global emerging disease. Multiple immunizations make complete vaccine coverage difficult both for public health efforts in dengue virus endemic countries as well as travelers.

SUMMARY

[0006] Embodiments herein concern compositions, methods and uses of chimeric dengue virus constructs. In some embodiments, a composition can include chimeric dengue virus constructs having an attenuated dengue virus backbone with structural genes from at least one other dengue virus serotype. Other embodiments concern at least one live, attenuated virus in combination with one or more chimeric dengue viruses. Other embodiments can include a composition of chimeric dengue viruses having a modified DEN-2 backbone (e.g. PDK-53 as a starting backbone in P1 (passage-1) and passage variability (after passage and growth *in vitro* on a permissive cell line) as indicated for P2, P3,...P8..P10 etc.) and one or more structural components of DEN-1, DEN-2, DEN-3 or DEN-4. In other embodiments, an immunogenic composition is generated where when introduced to a subject, the composition produces an immune response to one or more dengue viruses in the subject. Therefore, constructs contemplated herein can be generated and passaged *in vitro*, and each of the passages provides an attenuated dengue virus contemplated of use in a pharmaceutically acceptable vaccine composition. In certain embodiments a live, attenuated virus can be a live, attenuated dengue-2 virus alone or in combination with one or more chimeric dengue viruses.

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[0007] In certain examples, chimeric dengue virus constructs of dengue virus serotypes can include passage 7 (P7) live, attenuated viruses or chimeric viruses having nucleic acid sequences identified by SEQ ID NOS: 1, 9, 17 and 25 or polypeptide sequences indicated by SEQ ID NOS: 2, 10, 18 and 26. It is contemplated herein that any of the passages for any of the live, attenuated viruses described herein can be used in an immunogenic composition to induce immune responses to the represented dengue viruses (e.g. serotypes 1-4). In accordance with these embodiments, an immunogenic composition that includes a P-8 isolated live, attenuated virus can be administered to a subject to induce an immunogenic response against one or more dengue virus serotypes depending on the construct selected. In addition, a live, attenuated virus can be combined with one or more of these chimeric viruses. This is contemplated for each of the live, attenuated viruses isolated/produced in each subsequent cell passages (e.g. African Green Monkey Vero cell production, hereinafter: Vero cells). It is contemplated herein that any cell line (e.g. GMP-produced cell bank, FDA or EMA-approved) capable of producing dengue viruses is of use to passage any of the viral constructs at a manufacturing scale or as appropriate contemplated herein for subsequent use in a vaccine or immunogenic composition against Dengue virus.

[0008] In other embodiments, compositions contemplated herein can be combined with other immunogenic compositions against other Flaviviruses such as West Nile virus, Japanese encephalitis or any other flavivirus chimeric construct and/or live, attenuated virus. In certain embodiments, a single composition can be used against multiple flaviviruses.

[0009] In certain embodiments, an immunogenic composition of the present invention can include chimeric dengue viruses against one or more of DEN-1, DEN-2, DEN-3 and/or DEN-4, alone or in combination with a live, attenuated dengue virus composition.

[0010] In other embodiments, a construct can include a construct having adaptive mutations in the structural or non-structural regions of the virus that increase growth or production without affecting attenuation or safety of the virus when introduced to a subject. In certain embodiments, any of the contemplated chimeric dengue virus constructs can include a live, attenuated DEN-2 virus having specific mutations used as a backbone where the live attenuated DEN-2 PDK virus further includes structural proteins of one or more of prM (premembrane) and E (envelope) structural proteins of the other dengue virus serotypes. In addition, a DEN-2 backbone can include additional mutations in order to increase production of or enhance the immune response to a predetermine composition in a subject upon administration (e.g. chimeric Dengue virus 2/1, 2/3 or 2/4).

[00011] In some embodiments, structural protein genes can include prM and E genes of DEN-1, DEN-2, DEN-3 or DEN-4 on a DEN-2 backbone having one or two mutations that are part of a live, attenuated dengue virus. For example, a dengue construct, in certain embodiments can include those constructs termed DENVax-1-A, DENVax-2-F, DENVax-3-F, and DENVax-4-F (see Example section) where the DEN-2 backbone has one or more mutations (e.g. not found in the P1 or other previous passaged virus or PDK-53) from the DEN-2 live, attenuated virus previously demonstrated to be safe and effective to induce an immune response. The DEN-2 live, attenuated virus of the instant application is an improved version of the originally used DEN-2 live, attenuated virus. A chimeric construct of the instant invention can include a modified attenuated DEN-2 PDK-53 backbone, having one or more structural proteins of the second dengue virus serotype wherein the structural proteins can include additional mutations to increase an immunogenic response to the chimeric construct. In some embodiments, certain mutations acquired by attenuated DEN-2 PDK-53 can produce a conservative amino acid change or not in a constructs different from the P1 construct which can result in desirable traits for production etc.

[00012] In other embodiments, a live, attenuated DEN-2 genome can be used to generate constructs of dengue virus serotype 1 (DEN-1) and dengue virus serotype 3 (DEN-3), dengue virus serotype 4 (DEN-4) where one or more structural protein genes of the DEN-2 viral genome can be replaced by one or more structural protein genes of DEN-1, DEN-3 or DEN-4, respectively. In some embodiments, a structural protein can be the C, prM or E protein of a second dengue virus. In certain embodiments, structural protein genes include the prM and E genes of DEN-1, DEN-3 or DEN-4. These hybrid viruses express the surface antigens of DEN-1, DEN-3 or DEN-4 while retaining the attenuation phenotypes of the parent attenuated DEN-2.

[00013] Constructs disclosed herein can include chimeric constructs of DEN-4, DEN-2, DEN-1, and DEN-3 expressing surface antigens of DEN-1, DEN-3 and DEN-4 using attenuated DEN-2 virus as a backbone.

[00014] In certain embodiments, compositions of the instant invention can include a composition that comprises a single chimeric dengue virus construct disclosed herein and a pharmaceutically acceptable carrier or excipient. Alternatively, compositions of the instant invention can include a composition that comprises two or more, or three or more chimeric dengue virus constructs disclosed herein, and a pharmaceutically acceptable carrier or excipient. In accordance with these embodiments, a one or more dengue virus chimeric constructs contemplated herein can be combined with one or more, live attenuated dengue

viruses. In certain embodiments, a live, attenuated virus can be a live, attenuated DEN-2 virus wherein additional mutations in the NCR, NS1 regions or other regions increase the immune response, increase viral growth or other improvement for an improved live, attenuated dengue virus.

[00015] In certain embodiments, the attenuation loci, nucleotide 5'NCR-57-T, NS1-53-Asp, and NS3-250-Val, of the DENV-2 vaccine have been previously determined, and all of these changes are shared by the common PDK-53 virus-specific genetic background of the four DENVax viruses. The genetic sequence of the three attenuation loci as well as the previously established *in vitro* and *in vivo* attenuation phenotypes of these vaccine candidates were carefully monitored for the cGMP-manufactured DENVax seeds. This report describes strategies used to generate master virus seeds (MVS) as well as their genetic and phenotypic characterization of use in the manufacture of dengue virus vaccine compositions. These MVS can be used for manufacture of clinical materials and ultimately commercial vaccine supplies.

Brief Description of the Drawings

[00016] The following drawings form part of the present specification and are included to further demonstrate certain embodiments. Some embodiments may be better understood by reference to one or more of these drawings alone or in combination with the detailed description of specific embodiments presented.

[00017] **Fig. 1** represents an exemplary chart reflecting an exemplary chimeric construct of the instant invention, DEN-2/DEN-4 compared to previously generated constructs and wild type dengue viruses.

[00018] **Fig. 2** represents an exemplary histogram plot comparing various responses using a live, attenuated DEN-2 backbone (with additional mutations) and a second dengue virus serotype as structural components substituted for the dengue-2 structural components (e.g. DENVax-1 MVS). This plot illustrates plaque sizes of the DENVax MVS. Wild-type Dengue viruses and previously published research-grade vaccine candidate viruses were included for control and comparison. This plot illustrates improved production of the dengue virus constructs compared to control dengue virus chimeric constructs.

[00019] **Fig. 3** represents an exemplary histogram plot that represents temperature sensitivities of DENVax MVS (Master Virus Seed). Wild type dengue viruses and previously published research-grade vaccine candidate viruses were included for comparison with the MVS grade.

[00020] Fig. 4 represents an exemplary histogram plot that represents viral growth of DENVax MVS in C6/36 cells compared to controls. Wild-type dengue viruses and research-grade vaccine candidate viruses were included for comparison with the DENVax MVS.

[00021] Figs. 5A-5C represent exemplary plots of neurovirulence in newborn mice. Pooled results of several experiments summarizing the neurovirulence of wt DENV-2 16681 virus in CDC-ICR ($n=72$) and Taconic-ICR ($n=32$) newborn mice challenged ic with 10^4 pfu of the virus (A). Neurovirulence of DENVax MVS tested in Taconic-ICR mice with a dose of 10^4 pfu (B) or 10^3 pfu (C). The numbers of animals tested per group in one experiment ($n=16$) or two pooled experiments ($n=31$ or 32) are indicated.

[00022] Fig. 6 represents an exemplary histogram illustrating plaque size of the DENVax MVS, WVS, and BVS. Mean plaque diameters $\pm$ SD (error bars) of the virus plaques in Vero or LLC-MK₂ cells under agarose overlay measured on day 9 pi. Wild type DENVs and previously published research-grade vaccine candidate viruses were included for control and comparison.

[00023] Fig. 7 represents an exemplary histogram plot illustrating growth of DENVax MSV, WVS, and BVS in C6/36 cells at two incubation temperatures to verify their retention of this *in vitro* attenuation marker after large scale manufacturing.

[00024] Fig. 8 represents an exemplary histogram plotting restricted growth of DENVax MVS, WVS, and BVS in C6/36 cells. Mean titers $\pm$ SD (error bars) of the viruses replicated in C6/36 cells 7 days pi. The wt Dengue viruses and previously published research-grade vaccine candidate viruses were included for comparison.

[00025] Figs. 9A-9B represent exemplary graphs of data of neurovirulence of DENVax MVS in newborn ICR mice. (A) IC inoculations of the virus at dose of 10^4 PFU. (B) IC inoculation of the virus at dose of 10^3 PFU.

[00026] Fig. 10 represents an exemplary chart comparing new live, attenuated viruses to previously generated live, attenuated dengue viruses.

Definitions

[00027] As used herein, "a" or "an" may mean one or more than one of an item.

[00028] As used herein the specification, "subject" or "subjects" may include, but are not limited to, mammals such as humans or mammals, domesticated or wild, for example dogs, cats, other household pets (e.g. hamster, guinea pig, mouse, rat), ferrets, rabbits, pigs, horses, cattle, prairie dogs, wild rodents, or zoo animals.

[00029] As used herein, the terms "virus chimera," "chimeric virus," "flavivirus

chimera" and "chimeric flavivirus" can mean a construct comprising a portion of the nucleotide sequence of a dengue-2 virus and further nucleotide sequence that is not from dengue-2 virus or is from a different flavivirus. A "dengue chimera" comprises at least two different dengue virus serotypes but not a different flavivirus. Thus, examples of other dengue viruses or flaviviruses include, but are not limited to, sequences from dengue-1 virus, dengue-3 virus, dengue-4 virus, West Nile virus, Japanese encephalitis virus, St. Louis encephalitis virus, tick-borne encephalitis virus, yellow fever virus and any combination thereof.

[00030] As used herein, "nucleic acid chimera" can mean a construct of the invention comprising nucleic acid comprising a portion of the nucleotide sequence of a dengue-2 virus and further nucleotide sequence that is not of the same origin as the nucleotide sequence of the dengue-2 virus. Correspondingly, any chimeric flavivirus or flavivirus chimera disclosed herein can be recognized as an example of a nucleic acid chimera.

[00031] As used herein, "a live, attenuated virus" can mean a wild-type virus, mutated or selected for traits of use in vaccine or other immunogenic compositions wherein some traits can include reduced virulence, safety, efficacy or improved growth etc.

DESCRIPTION

[00032] In the following sections, various exemplary compositions and methods are described in order to detail various embodiments. It will be obvious to one skilled in the art that practicing the various embodiments does not require the employment of all or even some of the specific details outlined herein, but rather that concentrations, times and other specific details may be modified through routine experimentation. In some cases, well-known methods or components have not been included in the description.

[00033] In accordance with embodiments of the present invention, there may be employed conventional molecular biology, protein chemistry, microbiology, and recombinant DNA techniques within the skill of the art. Such techniques are explained fully in the literature. See, *e.g.*, Sambrook, Fritsch & Maniatis, *Molecular Cloning: A Laboratory Manual*, Second Edition 1989, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.; *Animal Cell Culture*, R. I. Freshney, ed., 1986).

[00034] Embodiments herein concern compositions, methods and uses for inducing immune responses against one or more dengue virus serotypes in a subject, individually or simultaneously. In accordance with these embodiments, attenuated dengue viruses and nucleic acid chimeras are generated and used in vaccine compositions disclosed herein. Some embodiments concern modified or mutated dengue constructs or chimeras. Other

embodiments concern introducing mutations to modify the amino acid sequences of structural proteins of dengue viruses wherein the mutation increase immunogenicity to the virus.

[00035] Live, attenuated dengue viruses of all four serotypes have been developed by passaging wild-type viruses in cell culture. These are some of the most promising live, attenuated vaccine candidates for immunization against flavivirus and in particular dengue virus infection and/or disease. These vaccine candidates have been designated by a combination of their dengue serotype, the cell line through which they were passaged and the number of times they were passaged. Thus, a dengue serotype 1 wild-type virus passaged in PDK cells 13 times is designated as DEN-1 PDK-13 virus. Other vaccine candidates are DEN-2 PDK-53, DEN-3 PGMK-30/FRhL-3 (e.g. thirty passages in primary green monkey kidney cells, followed by three passages in fetal rhesus lung cells and DEN-4 PDK-48). These four candidate vaccine viruses were derived by tissue culture passage of wild-type parental DEN-1 16007, DEN-2 16681, DEN-3 16562 and DEN-4 1036 viruses, respectively.

[00036] In certain embodiments, live, attenuated dengue-2 PDK-53 vaccine virus contained a mixture of viruses, with the population containing varying nucleotide differences. After genetic characterization of the attenuating mutations, certain attenuating characteristics were outlined and engineered into a cDNA infectious clone. RNA was transcribed from this infectious clone and introduced into Vero cells as a passage 1 of the newly characterized and derived PDK-53-Vero-DEN-2-P 1 virus (see for example, Table 1). This attenuated virus was created for each DEN serotype, but for DEN-1, DEN-3 and DEN-4, the prM and E genes were engineered into 3 separate cDNA infectious clones, thus generating four separate PDK-53-Vero viruses (termed herein as: PDK-53-Vero-DEN-2-P 1, PDK-53-Vero-DEN-1-P 1, PDK-53-Vero-DEN-3-P 1, and PDK-53-Vero-DEN-4-P 1). These attenuated vaccine virus strains were passaged in Vero cells 10 times (Table 1), and each separate lineage acquired mutations upon their adaptation to grow in Vero cells (Table 3). Certain embodiments here are directed to derivation and uses for these live, attenuated dengue viruses.

[00037] Previous human clinical trials with these attenuated viruses have indicated that DEN-2 PDK-53 has the lowest infectious dose (50% minimal infectious dose of 5 plaque forming units or PFU) in humans, is strongly immunogenic, and produces no apparent safety concerns. The DEN-1 PDK-13, DEN-3 PGMK-30/FRhL-3 and DEN-4 PDK-48 vaccine virus candidates have higher 50% minimal infectious doses of 10,000,

3500, and 150 PFU, respectively, in humans. Although only one immunization with monovalent DEN-2 PDK-53 virus or DEN-4 PDK-48 virus was required to achieve 100% seroconversion in human subjects, a booster was needed to achieve the same seroconversion rate for DEN-1 PDK-13 and DEN-3 PGMK-30/FRhL-3 viruses, which have the two highest infectious doses for humans.

[00038] DEN-2 PDK-53 virus vaccine candidate, also abbreviated PDK-53, has several measurable biological markers associated with attenuation, including temperature sensitivity, small plaque size, decreased replication in mosquito C6136 cell culture, decreased replication in intact mosquitoes, loss of neurovirulence for suckling mice and decreased incidence of viremia in monkeys. Clinical trials of the candidate PDK-53 vaccine have demonstrated its safety and immunogenicity in humans. Furthermore, the PDK-53 vaccine induces dengue virus-specific T-cell memory responses in human vaccine recipients. Some embodiments herein describe an improvement on the DEN-2 PDK-53 used in chimeric constructs disclosed herein.

[00039] Immunogenic flavivirus chimeras having a dengue-2 virus backbone and at least one structural protein of another dengue virus serotype can be used for preparing the dengue virus chimeras and methods for producing the dengue virus chimeras are described. The immunogenic dengue virus chimeras are provided, alone or in combination, in a pharmaceutically acceptable carrier as immunogenic compositions to minimize, inhibit, or immunize individuals against infection by one or more serotypes, such as dengue virus serotypes DEN-1, DEN-2, DEN-3 and DEN-4, alone or in combination. When combined, the immunogenic dengue virus chimeras may be used as multivalent vaccines (e.g. bi-, tri- and tetravalent) to confer simultaneous protection against infection by more than one species or strain of flavivirus. In certain embodiments, the dengue virus chimeras are combined in an immunogenic composition useful as a bivalent, trivalent or tetravalent vaccine against the known dengue virus serotypes or confer immunity to other pathogenic flaviviruses by including nucleic acids encoding one or more proteins from a different flavivirus.

[00040] In some embodiments, avirulent, immunogenic dengue virus chimeras provided herein contain the nonstructural protein genes of the attenuated dengue-2 virus (e.g. PDK-53), or the equivalent thereof, and one or more of the structural protein genes or immunogenic portions thereof of the flavivirus against which immunogenicity is to be induced in a subject. For example, some embodiments concern a chimera having attenuated dengue-2 virus PDK-53 genome as the viral backbone, and one or more structural protein

genes encoding capsid, premembrane/membrane, or envelope of the PDK-53 genome, or combinations thereof, replaced with one or more corresponding structural protein genes from DEN-1, DEN-3 or DEN-4 or other flavivirus to be protected against, such as a different flavivirus or a different dengue virus serotype. In accordance with these embodiments, a nucleic acid chimera disclosed herein can have functional properties of the attenuated dengue-2 virus and is avirulent, but expresses antigenic epitopes of the structural gene products of DEN-1, DEN-3 or DEN-4 in addition to other flaviviruses and is immunogenic (e.g. induces an immune response to the gene products in a subject). Then, these DNA constructs are used to transcribe RNA from an infectious clone, this RNA is introduced into Vero cells again producing a new progeny virus at P1. These new progeny viruses are distinguishable from PDK-53. (See *e.g.* P1-P10).

[00041] In another embodiment, a nucleic acid chimera can be a nucleic acid chimera having, but not limited to, a first nucleotide sequence encoding nonstructural proteins from an attenuated dengue-2 virus, and a second nucleotide sequence encoding a structural protein from dengue-4 virus alone or in combination with another flavivirus. In other embodiments, the attenuated dengue-2 virus can be vaccine strain PDK-53 having one or more mutated amino acids (see Examples). These additional mutations confer desirable traits of use as live, attenuated dengue-2 or as chimeric constructs described herein. Some embodiments include structural proteins of one or more of C, prM or E protein of a second dengue virus.

[00042] Other aspects include that chimeric viruses can include nucleotide and amino acid substitutions, deletions or insertions for example, in the control PDK-53 dengue-2 genome to reduce interference with immunogenicity responses to a targeted dengue virus serotype. These modifications can be made in structural and nonstructural proteins alone or in combination with the example modifications disclosed herein and can be generated by passaging the attenuated virus and obtaining an improved composition for inducing an immune response against one or more dengue virus serotypes.

[00043] Certain embodiments disclosed herein provide for method for making the chimeric viruses of this invention using recombinant techniques, by inserting the required substitutions into the appropriate backbone genome. Other embodiments herein concern passaging a confirmed (e.g. safe and effective) live, attenuated chimeric virus for additional improvements. In certain embodiments, a dengue-2 backbone used herein can include one or more mutations presented in Table 3. In other embodiments, a dengue-dengue chimera of the instant application can include one or more mutations as presented in Table 3. In yet

other embodiments, a dengue-dengue chimera can include all of the mutations for each chimera as represented in Table 3 for Den-2/Den-1, Den-2/Den-3 or Den-2/Den-4.

Pharmaceutical compositions that include a live, attenuated virus represented by the constructs of Table 3 are contemplated. For example, mono-, di-, tri- or tetravalent compositions are contemplated of use herein using chimeras and live, attenuated dengue-2 viruses as presented in Table 3.

[00044] In certain embodiments, a live, attenuated DEN-2 variant contemplated herein can be formulated into a pharmaceutical composition wherein the pharmaceutical composition can be administered alone or in combination with dengue-dengue chimeras or dengue-flavivirus chimeras. In certain embodiments, a bi-, tri or tetravalent compositions can be administered in a single application or in multiple applications to a subject.

Flavivirus Chimeras

[00045] Dengue virus types 1-4 (DEN-1 to DEN-4) are mosquito-borne flavivirus pathogens. The flavivirus genome contains a 5'-noncoding region (5'-NC), followed by a capsid protein (C) encoding region, followed by a premembrane/membrane protein (prM) encoding region, followed by an envelope protein (E) encoding region, followed by the region encoding the nonstructural proteins (NS1-NS2A-NS2B-NS3-NS4A-NS4B-NS5) and finally a 3' noncoding region (3'NC). The viral structural proteins are C, prM and E, and the nonstructural proteins are NS1-NS5. The structural and nonstructural proteins are translated as a single polyprotein and processed by cellular and viral proteases.

[00046] Flavivirus chimeras can be constructs formed by fusing non-structural protein genes from one type, or serotype, of dengue virus or virus species of the flaviviridae, with protein genes, for example, structural protein genes, from a different type, or serotype, of dengue virus or virus species of the flaviviridae. Alternatively, a flavivirus chimera of the invention is a construct formed by fusing non-structural protein genes from one type, or serotype, of dengue virus or virus species of the flaviviridae, with further nucleotide sequences that direct the synthesis of polypeptides or proteins selected from other dengue virus serotypes or other viruses of the flaviviridae.

[00047] In other embodiments, avirulent, immunogenic flavivirus chimeras provided herein contain the nonstructural protein genes of the attenuated dengue-2 virus, or the equivalent thereof, and one or more of the structural protein genes, or antigenic portions thereof, of the flavivirus against which immunogenicity is to be conferred. Suitable flaviviruses include, but are not limited to those listed in Table 1.

[00048] Other suitable dengue viruses for use in constructing the chimeras can be

wild-type, virulent DEN-1 16007, DEN-2 16681, DEN-3 16562 and DEN-4 1036 and attenuated, vaccine-strain DEN-1 PDK-13, DEN-2 PDK-53, DEN-3 PMK-30/FRhL-3 and DEN-4 PDK-48. Genetic differences between the DEN-1, DEN-2, DEN-3 and DEN-4 wild type/attenuated virus pairs are contemplated along with changes in the amino acid sequences encoded by the viral genomes.

[00049] Sequence listings for DEN-2 PDK-53 correspond to the DEN-2 PDK-53-V variant, wherein genome nucleotide position 5270 is mutated from an A to a T and amino acid position 1725 of the polyprotein or amino acid position 250 of the NS3 protein contains a valine residue. The DEN-2 PDK-53 variant without this nucleotide mutation, DEN-2 PDK-53-E, differs from PDK-53-V only in this one position. DEN-2 PDK-53-E has an A at nucleotide position 5270 and a glutamate at polyprotein amino acid position 1725, NS3 protein amino acid position 250. It is understood that embodiments herein include modified PDK 53 that include one or more passages in a separate host cell (e.g. Vero cells, see Table 1) where desirable traits of use in vaccine compositions contemplated herein are generated.

[00050] In certain embodiments, designations of the chimeras can be based on the DEN-2 virus-specific infectious clone modified backbones and structural genes (prM-E or C-prM-E) insert of other dengue viruses or other flaviviruses. DEN-2 for the dengue-2 backbone, followed by the strain from which the structural genes are inserted. One DEN-2 backbone variant is reflected in the next letter after the number designation. One particular DEN-2 backbone variant from which the chimera was constructed is indicated by the following letter placed after a hyphen, parent 16681 (P), PDK-53-E (E), or PDK-53-V (V); the last letter indicates the C-prM-E structural genes from the parental (P) strain or its vaccine derivative (V) or the prM-E structural genes from the parental (P) or its vaccine derivative (V1). For example; DEN-2/1-VP denotes the chimera comprising the attenuated DEN-2 PDK-53V backbone comprising a valine at NS3-250 and the C-prM-E genes from wild-type DEN-1 16007; DEN-2/1-VV denotes the DEN-2 PDK-53V backbone with the vaccine strain of dengue-1, DEN-1 PDK-13; DEN-2/1-VP1 denotes the DEN-2 PDK-53V backbone and the prM-E genes from wild-type DEN-1 16007; DEN-2/3-VP1 denotes the DEN-2 PDK-53V backbone and the prM-E genes from wild-type DEN-3 16562; DEN-2/4VP1 denotes the DEN-2 PDK-53V backbone and the prM-E genes from wild-type DEN-4 1036. Other chimeras disclosed herein are indicated by the same manner.

[00051] In one embodiment, chimeras disclosed herein contain attenuated dengue-2 virus PDK-53 genome as the viral backbone, in which the structural protein genes encoding

C, prM and E proteins of the PDK-53 genome, or combinations thereof, can be replaced with the corresponding structural protein genes from dengue-1, dengue-3 or dengue-4 virus and optionally, another flavivirus to be protected against, such as a different flavivirus or a different dengue virus strain.

[00052] In the nonstructural protein regions, a Gly-to-Asp (wild type-to-PDK-53) mutation was discovered at nonstructural protein NS1-53 (genome nucleotide position 2579); a Leu-to-Phe (wild type-to-PDK-53) mutation was discovered at nonstructural protein NS2A-181 (genome nucleotide position 4018); a Glu-to-Val (wild type-to-PDK-53) mutation was discovered at nonstructural protein NS3-250 (genome nucleotide position 5270); and a Gly-to-Ala mutation (wild type-to-PDK-53) was discovered at nonstructural protein NS4A-75 (genome nucleotide position 6599). The live, attenuated DEN-2 virus of the instant invention further includes mutations as presented in any chimera or live, attenuated dengue-2 virus of Table 3.

[00053] PDK-53 virus strain has a mixed genotype at genome nucleotide 5270. A significant portion (approximately 29%) of the virus population encodes the non-mutated NS3-250-Glu that is present in the wild type DEN-2 16681 virus rather than the NS3-250-Val mutation. As both genetic variants are avirulent, this mutation may not be necessary in an avirulent chimera.

[00054] Previously, it was discovered that avirulence of the attenuated PDK-53 virus strain can be attributed to mutations in the nucleotide sequence encoding nonstructural proteins and in the 5' noncoding region. For example, a single mutation at NS1-53, a double mutation at NS1-53 and at 5'NC-57, a double mutation at NS1-53 and at NS3-250 and a triple mutation at NS1-53, at 5'NC-57 and at NS3-250, result in attenuation of the DEN-2 virus. Therefore, the genome of any dengue-2 virus containing such non-conservative amino acid substitutions or nucleotide substitutions at these loci can be used as a base sequence for deriving the modified PDK-53 viruses disclosed herein. Another mutation in the stem of the stem/loop structure in the 5' noncoding region will provide additional avirulent phenotype stability, if desired. Mutations to this region disrupt potential secondary structures important for viral replication. A single mutation in this short (only 6 nucleotide residues in length) stem structure in both DEN and Venezuelan equine encephalitis viruses disrupts the formation of the hairpin structure. Further mutations in this stem structure decrease the possibility of reversion at this locus, while maintaining virus viability.

[00055] Mutations disclosed herein can be achieved by any method known in the art including, but not limited to, naturally-occurring or selected clones having additional

features once passaged in a cell line of interest (*e.g.* Vero cells). It is understood by those skilled in the art that the virulence screening assays, as described herein and as are well known in the art, can be used to distinguish between virulent and avirulent backbone structures.

Construction of Flavivirus Chimeras

[00056] Flavivirus chimeras described herein can be produced by splicing one or more of the structural protein genes of the flavivirus against which immunity is desired into a PDK-53 dengue virus genome backbone, or other methods known in the art, using recombinant engineering to remove the corresponding PDK-53 gene and replace it with a dengue-1, dengue-3 or dengue-4 virus gene or other gene known in the art.

[00057] Alternatively, using the sequences provided in the sequence listing, the nucleic acid molecules encoding the flavivirus proteins may be synthesized using known nucleic acid synthesis techniques and inserted into an appropriate vector. Avirulent, immunogenic virus is therefore produced using recombinant engineering techniques known to those skilled in the art.

[00058] A target gene can be inserted into the backbone that encodes a flavivirus structural protein of interest for DEN-1, DEN-3, DEN-4 or other flavivirus. A flavivirus gene to be inserted can be a gene encoding a C protein, a PrM protein and/or an E protein. The sequence inserted into the dengue-2 backbone can encode both PrM and E structural proteins. The sequence inserted into the dengue-2 backbone can encode all or one of C, prM and E structural proteins.

[00059] Suitable chimeric viruses or nucleic acid chimeras containing nucleotide sequences encoding structural proteins of other flaviviruses or dengue virus serotypes can be evaluated for usefulness as vaccines by screening them for the foregoing phenotypic markers of attenuation that indicate avirulence and by screening them for immunogenicity. Antigenicity and immunogenicity can be evaluated using *in vitro* or *in vivo* reactivity with flavivirus antibodies or immunoreactive serum using routine screening procedures known to those skilled in the art.

Dengue Virus Vaccines

[00060] In certain embodiments, chimeric viruses and nucleic acid chimeras can provide live, attenuated viruses useful as immunogens or vaccines. Some embodiments include chimeras that exhibit high immunogenicity to dengue-4 virus while producing no dangerous pathogenic or lethal effects.

[00061] To reduce occurrence of DHF/DSS in subjects, a tetravalent vaccine is

needed to provide simultaneous immunity for all four serotypes of the virus. A tetravalent vaccine is produced by combining a live, attenuated dengue-2 virus of the instant application with dengue-2/1, dengue-2/3, and dengue-2/4 chimeras described above in a suitable pharmaceutical carrier for administration as a multivalent vaccine.

[00062] The chimeric viruses or nucleic acid chimeras of this invention can include structural genes of either wild-type or live, attenuated virus in a virulent or an attenuated DEN-2 virus backbone. For example, the chimera may express the structural protein genes of wild-type DEN-4 1036 virus, its candidate vaccine derivative in either DEN-2 backgrounds.

[00063] Viruses used in the chimeras described herein can be grown using techniques known in the art. Virus plaque titrations are then performed and plaques counted in order to assess the viability and phenotypic characteristics of the growing cultures. Wild type viruses can be passaged through cultured cell lines to derive attenuated candidate starting materials.

[00064] Chimeric infectious clones can be constructed from the various dengue serotype clones available. The cloning of virus-specific cDNA fragments can also be accomplished, if desired. The cDNA fragments containing the structural protein or nonstructural protein genes are amplified by reverse transcriptase-polymerase chain reaction (RT-PCR) from dengue virus RNA with various primers. Amplified fragments are cloned into the cleavage sites of other intermediate clones. Intermediate, chimeric dengue virus clones are then sequenced to verify the accuracy of the inserted dengue virus-specific cDNA.

[00065] Full genome-length chimeric plasmids constructed by inserting the structural protein and/or nonstructural protein gene region of dengue serotype viruses into vectors are obtainable using recombinant techniques well known to those skilled in the art.

Nucleotide and Amino Acid Analysis

[00066] The NS1-53 mutation in the DEN-2 PDK-53 vaccine virus is significant for the attenuated phenotype of this virus, because the NS1-53-Gly of the DEN-2 16681 virus is conserved in nearly all flaviviruses, including the tick-borne viruses, sequenced to date. DEN-4 vaccine virus can also contain an amino acid mutation in the NS1 protein at position 253. This locus, which is a Gln-to-His mutation in DEN-4 PDK-48 vaccine virus, is Gln in all four wild serotypes of dengue virus. This Gln residue is unique to the dengue viruses within the flavivirus genus. The NS1 protein is a glycoprotein that is secreted from flavivirus-infected cells. It is present on the surface of the infected cell and NS1-specific antibodies are present in the serum of virus-infected individuals. Protection of animals immunized with NS1 protein or passively with NS1-specific antibody has been reported.

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The NS1 protein appears to participate in early viral RNA replication.

[0067] The mutations that occurred in the NS2A, NS2B, NS4A, and NS4B proteins of the DEN-1, -2, -3 and -4 attenuated strains are conservative in nature. The NS4A-75 and NS4A-95 mutations of DEN-2 and DEN-4 vaccine viruses, respectively, occurred at sites of amino acid conservation among dengue viruses, but not among flaviviruses in general.

[0068] The flaviviral NS3 protein possesses at least two recognized functions: the viral proteinase and RNA helicase/NTPase. The 698-aa long (DEN-2 virus) NS3 protein contains an amino-terminal serine protease domain (NS3-5 I-His, -75-Asp, -135-Sercatalytic triad) that is followed by sequence motifs for RNA helicase/NTPase functions (NS3-196-GAGKT, -284-DEAH, -459-GRIGR). None of the mutations in the NS3 proteins of DEN-1, DEN-2, or DEN-3 virus occurred within a recognized motif. The NS3-510 Tyr-to-Phe mutation in DEN-1 PDK-13 virus was conservative. Since the wild-type DEN-2, -3 and -4 viruses contain Phe at this position, it is unlikely that the Tyr-to-Phe mutation plays a role in the attenuation of DEN-1 virus. The NS3-182 Glu-to-Lys mutation in DEN-1 PDK-13 virus occurred at a position that is conserved as Asp or Glu in most mosquito-borne flaviviruses and it may play some role in attenuation. This mutation was located 15 amino acid residues upstream of the GAGKT helicase motif. As noted in previous reports, the NS3-250-Glu in DEN-2 16681 virus is conserved in all mosquito borne flaviviruses except for yellow fever virus.

[0069] Nucleic acid probes selectively hybridize with nucleic acid molecules encoding the DEN-1, DEN-3 and DEN-4 viruses or complementary sequences thereof. By "selective" or "selectively" is meant a sequence which does not hybridize with other nucleic acids to prevent adequate detection of the dengue virus. Therefore, in the design of hybridizing nucleic acids, selectivity will depend upon the other components present in a sample. The hybridizing nucleic acid should have at least 70% complementarity with the segment of the nucleic acid to which it hybridizes. As used herein to describe nucleic acids, the term "selectively hybridizes" excludes the occasional randomly hybridizing nucleic acids, and thus, has the same meaning as "specifically hybridizing." The selectively hybridizing nucleic acid of this invention can have at least 70%, 80%, 85%, 90%, 95%, 97%, 98%, and 99% complementarity with the segment of the sequence to which it hybridizes, preferably 85% or more.

[0070] Sequences, probes and primers which selectively hybridize to the encoding nucleic acid or the complementary, or opposite, strand of the nucleic acid are contemplated. Specific hybridization with nucleic acid can occur with minor modifications or substitutions

in the nucleic acid, so long as functional species-specific hybridization capability is maintained. By "probe" is meant nucleic acid sequences that can be used as probes or primers for selective hybridization with complementary nucleic acid sequences for their detection or amplification, which probes can vary in length from about 5 to 100 nucleotides, or preferably from about 10 to 50 nucleotides, or most preferably about 18-24 nucleotides.

[00071] If used as primers, the composition preferably includes at least two nucleic acid molecules which hybridize to different regions of the target molecule so as to amplify a desired region. Depending on the length of the probe or primer, the target region can range between 70% complementary bases and full complementarity and still hybridize under stringent conditions. For example, for the purpose of detecting the presence of the dengue virus, the degree of complementarity between the hybridizing nucleic acid (probe or primer) and the sequence to which it hybridizes is at least enough to distinguish hybridization with a nucleic acid from other organisms.

[00072] Nucleic acid sequences encoding the DEN-4, DEN-3 or DEN-1 virus (e.g. structural elements) can be inserted into a vector, such as a plasmid, and recombinantly expressed in a living organism (e.g. into a dengue-2 backbone) to produce recombinant dengue virus peptides and/or polypeptides and/or viruses.

Nucleic Acid Detection Methods

[00073] A rapid genetic test that is diagnostic for each of the vaccine viruses described herein is provided by the current invention. This embodiment of the invention enhances analyses of viruses isolated from the serum of vaccinated humans who developed a viremia, as well as enhancing characterization of viremia in nonhuman primates immunized with the candidate vaccine viruses.

[00074] These sequences include a diagnostic TaqMan probe that serves to report the detection of the cDNA amplicon amplified from the viral genomic RNA template by using a reverse-transcriptase/polymerase chain reaction (RT/PCR), as well as the forward and reverse amplimers that are designed to amplify the cDNA amplicon, as described below. In certain instances, one of the amplimers has been designed to contain a vaccine virus-specific mutation at the 3'-terminal end of the amplimer, which effectively makes the test even more specific for the vaccine strain because extension of the primer at the target site, and consequently amplification, will occur only if the viral RNA template contains that specific mutation.

[00075] Automated PCR-based nucleic acid sequence detection system can be used, or other known technology for nucleic acid detection. The TaqMan assay is a highly

specific and sensitive assay that permits automated, real time visualization and quantitation of PCR-generated amplicons from a sample nucleic acid template. TaqMan can determine the presence or absence of a specific sequence. In this assay, a forward and a reverse primer are designed to anneal upstream and downstream of the target mutation site, respectively. A specific detector probe, which is designed to have a melting temperature of about 10.degree. C. higher than either of the amplimers and containing the vaccine virus-specific nucleotide mutation or its complement (depending on the strand of RT/PCR amplicon that is being detected), constitutes the third primer component of this assay.

[00076] A probe designed to specifically detect a mutated locus in one of the vaccine viral genomes will contain the vaccine-specific nucleotide in the middle of the probe. This probe will result in detectable fluorescence in the TaqMan assay if the viral RNA template is vaccine virus-specific. However, genomic RNA templates from wild-type DEN viruses will have decreased efficiency of probe hybridization because of the single nucleotide mismatch (in the case of the parental viruses DEN viruses) or possibly more than one mismatch (as may occur in other wild-type DEN viruses) and will not result in significant fluorescence. The DNA polymerase is more likely to displace a mismatched probe from the RT/PCR amplicon template than to cleave the mismatched probe to release the reporter dye (TaqMan Allelic Discrimination assay, Applied Biosystems).

[00077] One strategy for diagnostic genetic testing makes use of molecular beacons. The molecular beacon strategy also utilizes primers for RT/PCR amplification of amplicons, and detection of a specific sequence within the amplicon by a probe containing reporter and quencher dyes at the probe termini. In this assay, the probe forms a stem-loop structure. The molecular beacons assay employs quencher and reporter dyes that differ from those used in the TaqMan assay.

Pharmaceutical Compositions

[00078] Embodiments herein provide for administration of compositions to subjects in a biologically compatible form suitable for pharmaceutical administration *in vivo*. By "biologically compatible form suitable for administration in vivo" is meant a form of the active agent (e.g. pharmaceutical chemical, protein, gene, of the embodiments) to be administered in which any toxic effects are outweighed by the therapeutic effects of the active agent. Administration of a therapeutically active amount of the therapeutic compositions is defined as an amount effective, at dosages and for periods of time necessary to achieve the desired result. For example, a therapeutically active amount of a compound may vary according to factors such as the disease state, age, sex, and weight of the

individual, and the ability of antibody to elicit a desired response in the individual. Dosage regimens may be adjusted to provide the optimum therapeutic response.

[00079] In one embodiment, the compound (e.g. pharmaceutical chemical, protein, peptide etc. of the embodiments) may be administered in a convenient manner, for example, subcutaneous, intravenous, by oral administration, inhalation, intradermal, transdermal application, intravaginal application, topical application, intranasal or rectal administration. Depending on the route of administration, the active compound may be contained in a protective buffer (e.g. FTA, F127/trehalose/albumin). In one embodiment, a composition may be orally administered. In another embodiment, the composition may be administered intravenously. In one embodiment, the composition may be administered intranasally, such as inhalation. In yet another embodiment, the composition may be administered intradermally using a needle-free system (e.g. Pharmajet®) or other intradermal administration system.

[00080] A composition may be administered to a subject in an appropriate carrier or diluent, co-administered with enzyme inhibitors or in an appropriate carrier such as liposomes. The term "pharmaceutically acceptable carrier" as used herein is intended to include diluents such as saline and aqueous buffer solutions. It may be necessary to coat the compound with, or co-administer the compound with, a material to prevent its inactivation. The active agent may also be administered parenterally, or intraperitoneally. Dispersions can also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations may contain a preservative to prevent the growth of microorganisms or other stabilizing formulation (e.g. FTA).

[00081] Pharmaceutical compositions suitable for injectable use may be administered by means known in the art. For example, sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion may be used. In all cases, the composition can be sterile and can be fluid to the extent that easy syringability exists. It might be stable under the conditions of manufacture and storage and may be preserved against the contaminating action of microorganisms such as bacteria and fungi. The pharmaceutically acceptable carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of

dispersion and by the use of surfactants. Prevention of microorganisms can be achieved by heating, exposing the agent to detergent, irradiation or adding various antibacterial or antifungal agents.

[00082] Sterile injectable solutions can be prepared by incorporating active compound (e.g. a compound that induces an immune response to one or more dengue virus serotypes) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization.

[00083] Upon formulation, solutions will be administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective. The formulations are easily administered in a variety of dosage forms, such as the type of injectable solutions described above. It is contemplated that compositions are especially suitable for intramuscular, subcutaneous, intradermal, intranasal and intraperitoneal administration. A particular ratio may be sought such as a 1:1, 1:2 or other ratio (e.g. PFUs of a given dengue virus serotype)

[00084] The active therapeutic agents may be formulated within a mixture predetermined ratios. Single dose or multiple doses can also be administered on an appropriate schedule for a given situation (e.g. prior to travel, outbreak of dengue fever).

[00085] In another embodiment, nasal solutions or sprays, aerosols or inhalants may be used to deliver the compound of interest. Additional formulations that are suitable for other modes of administration include suppositories and pessaries.

[00086] Certain formulations can include excipients, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate and the like.

[00087] A pharmaceutical composition may be prepared with carriers that protect active ingredients against rapid elimination from the body, such as time-release formulations or coatings. Such carriers include controlled release formulations, such as, but not limited to, microencapsulated delivery systems, and biodegradable, biocompatible polymers, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, polyorthoesters, polylactic acid and others are known.

[00088] Pharmaceutical compositions are administered in an amount, and with a frequency, that is effective to inhibit or alleviate side effects of a transplant and/or to reduce or prevent rejection. The precise dosage and duration of treatment may be determined empirically using known testing protocols or by testing the compositions in model systems known in the art and extrapolating therefrom. Dosages may also vary with the severity of

the condition. A pharmaceutical composition is generally formulated and administered to exert a therapeutically useful effect while minimizing undesirable side effects. In general, dose ranges from about 10^2 to 10^6 PFU can be administered initially and optionally, followed by a second administration within 30 days or up to 180 days later, as needed. In certain embodiments, a subject can receive dual administration of a mono, bi-, tri or tetravalent composition disclosed herein wherein the composition is a single composition mixture or has predetermined compositions of different dengue virus serotypes. In some embodiments, a DEN2/4 chimera can be present in higher concentrations than other dengue virus serotypes such as a live, attenuated dengue-1.

[00089] It will be apparent that, for any particular subject, specific dosage regimens may be adjusted over time according to the individual need.

[00090] In one embodiment, a composition disclosed herein can be administered to a subject subcutaneously or intradermally.

[00091] The pharmaceutical compositions containing live, attenuated dengue viruses may be administered to individuals, particularly humans, for example by subcutaneously, intramuscularly, intranasally, orally, topically, transdermally, parenterally, gastrointestinally, transbronchially and transalveolarly. Topical administration is accomplished via a topically applied cream, gel, rinse, etc. containing therapeutically effective amounts of inhibitors of serine proteases. Transdermal administration is accomplished by application of a cream, rinse, gel, etc. capable of allowing the inhibitors of serine proteases to penetrate the skin and enter the blood stream. In addition, osmotic pumps may be used for administration. The necessary dosage will vary with the particular condition being treated, method of administration and rate of clearance of the molecule from the body.

[00092] In certain embodiments of the methods of the present invention, the subject may be a mammal such as a human or a veterinary and/or a domesticated animal or livestock or wild animal.

Therapeutic Methods

[00093] In one embodiment of the present invention, methods provide for inducing an immune response to dengue virus serotype(s) using a mono, bi-, tri or tetravalent formulation of live, attenuated and/or chimeric viral constructs contemplated herein.

[00094] Embodiments of the present invention is further illustrated by the following non-limiting examples, which are not to be construed in any way as imposing limitations upon the scope thereof. On the contrary, it is to be clearly understood that resort may be had to various other embodiments, modifications, and equivalents thereof which, after reading

the description herein, may suggest themselves to those skilled in the art without departing from the spirit of the present invention or the scope of the appended claims.

EXAMPLES

[00095] The following examples are included to demonstrate certain embodiments presented herein. It should be appreciated by those of skill in the art that the techniques disclosed in the Examples which follow represent techniques discovered to function well in the practices disclosed herein, and thus can be considered to constitute preferred modes for its practice. However, those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in particular embodiments which are disclosed and still obtain a like or similar result without departing from the spirit and scope herein.

Example 1

[00096] In some exemplary methods, compositions used to generate as referred to herein as “master virus seeds (MVS)” are disclosed. These compositions may be derived from one or more live, attenuated dengue viruses, such as DEN-1, DEN-2, DEN-3, and DEN-4. In certain methods, compositions may be derived from one or more live attenuated Dengue viruses that include but are not limited to, specific constructs disclosed herein referred to as DENVax-1, DENVax-2, DENVax-3, and DENVax-4. In other exemplary methods, strategies used to generate and characterize these compositions are provided. In yet other embodiments, tetravalent dengue virus formulations and genetic and phenotypic characterization of these formulations are provided.

Production and analysis of pre-master DENVax viruses

[00097] Certain procedures were performed to generate pre-master dengue virus seeds, such as serial amplification and purification of dengue viruses (e.g. DENVax). First, DENVax viruses were re-derived by transfection of viral RNA transcribed from the full-length recombinant DENVax cDNA into production-certified cells (e.g. Vero cells), resulting in P1 (passage 1) virus seed. The four P1 viruses from each of dengue-1 to dengue-4 were then amplified and plaque purified to obtain the candidate pre-master vaccine P7 seeds (see Table 1). Certain tests were performed to analyze passages of dengue viruses. For example, full-length genome sequencing demonstrated that all four of the P2 (passage 2) seed viruses were genetically identical to their homologous progenitor, research-derived, research-grade candidate vaccine virus. The original plaque phenotypes were also retained in the P2 viruses. Six plaque purified viruses (P3 A-F) were isolated for each serotype of dengue virus (e.g. DENVax1-4) from the P2 seeds, and each isolated plaque was directly plaque purified two more times. The third plaque purification (P5) of

each virus was amplified twice (P6 A-F and P7 A-F) in Vero cells to produce the potential pre-master P7 DENVax seeds (Table 1).

Table 1 Example of a cGMP Rederivation of DENVax Viruses in WCB-Vero Cells

Passage	Seed Production/Purification	Characterizations
P1	Transfect WCB-Vero with transcribed viral RNAs	Plaque titrate
P2	Amplify P1 virus	Full genome sequence
P3	Pick 6 plaques (A-F)/serotype from P2 plaque assay	Plaque purification
P4	Pick plaques A-F from P3 plaque assay	Plaque purification
P5	Pick plaques A-F from P4 plaque assay	Plaque purification
P6	Amplify P5 A-F plaques	Plaque titrate
P7	Pre-master seeds: Amplify P6 A-F	Full genome sequence, TaqMAMA, Plaque phenotypes
P8*	MVS: Amplify selected P7 virus seed	Full genetic and phenotypic characterization
P9	WVS: Amplify P8 Master Seed viruses	Full genome sequence, TaqMAMA
P10	BVS: Amplify P9 Working Seed viruses	Full genome sequence, TaqMAMA
* One optimal P7 seed (A, B, C, D, E, or F) was selected based on the genetic and plaque analysis to make P8 MVS		

[00098] Some tests were further performed to characterize P7 DENVax seeds, such as analysis of genome sequences and plaque phenotypes of the P7 seeds, and comparison with P2 seeds (Table 2). Plaque phenotypes of the P7 viruses were generally similar to those of the P2 seeds. In some exemplary experiments, virus titers were monitored. Virus titers reached over 6.0 log pfu/ml for most of the P7 seeds, except for 5 viruses. Genome sequencing of more than 60 candidate vaccine virus seeds after 10 or more serial passages in Vero cells identified no reversion event at NS1-53 and NS3-250 of the three major attenuation determinants of the DENV-2 PDK-53 genetic vector, suggesting that these 2 loci are quite stable in candidate vaccine virus seeds. All sequence chromatograms of the 24 candidate strains generated from both forward and reverse sequencing for these two sites were homogenous without any minor nucleotide populations evident at the NS1-53 and NS3-250 genetic loci. In contrast to the NS1 and NS3 sites, different levels of reversions at the 5'NCR-57 attenuation locus were identified from multiple serially passaged research grade vaccine viruses, suggesting this locus might not be as stable as NS1 and NS3 after multiple passages in cell culture. Therefore, a sensitive mismatch amplification assay

(TaqMAMA) was developed to accurately measure the reversion rate at the 5'NCR-57 locus by real-time RT-PCR. In some studies, the 5'NCR-57 reversion rates of all 24 of the P7 seeds were measured by the TaqMAMA. Depending on the concentration of the input viral RNA for each virus in the assay, the sensitivity limit of the TaqMAMA ranged between 0.01% and 0.07% reversion, which is much more sensitive than the 10-30% reversion sensitivity limit detectable by consensus genome sequence analysis. The resulting data illustrates that 15 of the 24 P7 viruses had minimal or undetectable reversion (< 0.07%), one virus (DENVax-3-D) had almost 100% reversion, and 8 viruses (1 DENVax-1, 1 DENVax-2, 2 DENVax-3, and 4 DENVax-4) had partial reversion ranging from 0.08% to 12.85% (Table 2). Full-length genome sequencing was conducted for 16 of the 24 P7 viruses with low levels of 5'NCR57 reversion as measured by TaqMAMA. All the sequenced viruses maintained the other two DENVax attenuation determinants (NS1-53, NS3-250), and all had acquired additional mutations that were not present in the original, engineered recombinant cDNA clones (Table 2). In one exemplary target vaccine composition, DENVax-1-A, DENVax-2-F, DENVax-3-F, and DENVax-4-F were selected as target pre-master seed for each serotype because their genotypes and plaque phenotypes most closely resembled those of the originally designed vaccine recombinants. The DENVax-1-A, DENVax-2-F, and DENVax-4-F had two non-synonymous mutations, and the DENVax-3-F had one. The evidence suggests these additional mutations observed in these 4 pre-master seeds do not cause safety concerns or immunogenicity alterations for the viruses. These pre-master seeds were further amplified to generate the MVS (master seed, designated as P7, Table 1).

[00099] Exemplary methods provided herein used purified in-vitro transcribed viral RNA from cloned cDNA plasmid as the pure source to transfect vaccine-certified Vero cells to generate vaccine virus. Serial plaque purifications and full-genome sequence analyses were incorporated into the manufacturing procedures to ensure manufactured vaccine seeds with optimal purity and genetic stability. Six cloned viruses were prepared as potential pre-master seeds for each serotype of DENVax. Through genomic analysis, including TaqMAMA and complete genomic sequencing, as well as characterization of viral plaque phenotypes, pre-master seeds were chosen to advance to master virus seeds production for each serotype (serotypes 1-4). The selected pre-master seeds had undetectable reversions (<0.01% or <0.07%) at the 5'NCR-57 locus, with 1 or 2 amino acid substitutions in their genomes, and retained the small plaque phenotypes previously observed.

Table 2. Characterizations of pre-master (P7) seeds

Virus	Clone ^a	TaqMAMA ^b	Log ₁₀ pfu/ml	Plaque ^c	Mutations identified in genome ^d
DENVax-1	A	**	6.85	P2	NS2A-116 I-L, NS2B-92 E-D, one silent
	B	*	6.93	P2	nd ^e
	C	*	6.93	D	nd
	D	**	7.02	D	C-67 K-A; one silent
	E	0.57%	7.28	P2	nd
	F	**	7.18	P2	E473 T-M; one silent
DENVax-2	A	0.03%	6.33	P2	NS1-341 K-N
	B	*	6.33	P2	E-305 K-T, two silent
	C	*	5.84	L	NS4A-18 T-A, four silent
	D	0.08%	6.20	P2	NS2B-99 I-L, one 3'NCR
	E	0.03%	6.31	P2	prM-52 K-E, NS5-412 I-V, two silent
	F	**	6.15	P2	prM-52 K-E, NS5-412 I-V
DENVax-3	A	*	6.00	P2	NS5-200 K-N, one silent, one 3'NCR
	B	0.05%	6.27	P2	NS2A-33 I-T, NS2A-59 M-T
	C	0.30%	6.25	P2	nd
	D	100.00%	6.27	P2	nd
	E	0.31%	6.00	P2	nd
	F	**	6.30	P2	E-223 T-S, one silent
DENVax-4	A	0.47%	5.60	P2	E323 K-R/K, NS2B-21 L-F/L, NS2B-39 T-S, one silent
	B	*	5.65	D	NS2A-126 A-V; NS4A-5 N-D; NS5-383 K-R, one silent
	C	4.50%	5.90	P2	nd
	D	12.85%	5.97	D	nd
	E	0.52%	6.85	S	prM-85 E-D, NS2B-45 T-A, NS5-320 M-T, NS5-551 E-G, two silent
	F	0.02%	6.93	S	NS2A-66 D-G, NS4A-21 A-V, four silent

^a Cloned viruses (by serial plaque purifications) selected for further development of MVS are designated bold.

^b *: Reversion rate < 0.07% (detection limit). **: Reversion rate < 0.01% (detection limit)

^c Plaque phenotypes: P2: similar to P2 virus; L = larger than P2 virus, D = similar size, but appear somewhat different in clearness of the plaques; S = smaller than P2.

^d Substitutions differing from the engineered DENVax cDNA clones. Amino acid mutations are listed with residue position of the virus protein and the changes (wt-mutation). Total number of silent mutations in structural and non-structural genes of each seed is listed. Mutations at non-coding region (NCR) are also noted.

^e nd = Not done. These clones had higher 5'NCR-57 reversion rates (by TaqMAMA) than other clones, so were excluded from further sequence analysis.

Example 2

[000100] In some exemplary methods, compositions of master virus seeds, working virus seeds and bulk virus seeds as well as their genetic and phenotypic characterization are described. These compositions are provided for manufacture of clinical materials and ultimately commercial vaccine supplies. Serial plaque purifications and full-genome sequence analyses were incorporated into the manufacturing process to ensure compositions of vaccine seeds with optimal safety and genetic stability for manufacture of clinical trial materials.

Production and manufacturing quality controls for MVS, WVS, and BVS

[000101] In some studies, MVS of the 4 DENVax were produced by amplifying the pre-master P7 seed in certified Vero cells. In other studies, MVS were used to make large amount of WVS in cell factories. Further, the BVS stocks of DENVax were amplified from the WVS and were formulated into tetravalent drug product mixtures to be used for human clinic trials. Quality controls for product release were performed in some exemplary methods, including, but not limited to, testing all of the MVS, WVS, and BVS for identity, infectious titer, sterility, mycoplasma, and in vitro and in vivo adventitious agents. All seeds passed the virus identity test using serotype-specific RT-PCR assays, which showed positive amplification corresponding to its serotype and negative for heterologous serotypes (data not shown). No detectable mycoplasma or adventitious agents were detected in the MVS, WVS, or BVS stocks.

Genetic analysis of the MVS, WVS, and BVS

[000102] In certain exemplary methods, after generation of MVS from the selected pre-MVS (P7) strains selected above were produced and the respective viral RNA was sequenced again. Full-length genome sequencing revealed that the MVS for DENVax-1 was identical to its pre-master seed, while the WVS and subsequent BVS acquired 2 additional substitutions at E-483 and NS4B-108 (see Tables 2 and 3). The Ala substitution at E-483 represented part of the genotype in the MVS, but became the dominant genotype in BVS. DENVax-2 and DENVax-3 were identical to their respective pre-master seeds (Table 2 and 3). The DENVax-2 MVS was identical to its pre-master seed, and the WVS and BVS had 2 additional mutations at NS4A-36 and NS4B-111. Both mutations were partial in WVS and were the major genotype in the BVS. The MVS of DENVax-3 was again identical to the pre-master seed, but the WVS and BVS contained an additional aa substitution at NS4A-23. The DENVax-4 MVS acquired an additional amino acid mutation, at locus NS2A-99 (from Lys to Lys/Arg mixed genotype) during production of the MVS (Table 3). Its WVS and BVS retained the NS2A-99 Lys/Arg mixed genotype, and the BVS

had an extra NS4B-238 Ser/Phe mixed genotype. Consensus sequence results also confirmed that MVS, WVS as well as BV retained the three genetic determinants of attenuation at the 5'NCR-57, NS1-53, and NS3-250 loci. Analysis of the least stable attenuating locus by TaqMAMA demonstrated that the 5'NCR-57 reversion rate between <0.7% to and 0.13% among MVS, ≤0.07% among WVS, and between <0.07 and 0.21% among BVS. A 3% reversion at the 5'NCR-57 locus was considered the maximum permissible rate for acceptance of a vaccine lot (**Table 3**).

Table 3. Nucleotide and amino acid substitutions in DENVax seeds

DENVax	Nucleotides	Amino Acids	Pre-master	MVS ^a	WVS ^a	BVS ^a
DENVax-1	2384 G-C	E-483 Gly-Ala	-	-	Gly/Ala	Ala
	3823 A-C	NS2A-116 Ile-Leu	Leu	Leu	Leu	Leu
	4407 A-T	NS2B-92 Glu-Asp	Asp	Asp	Asp	Asp
	7148 C-T	NS4B-108 Thr-Ile	-	-	Ile	Ile
	7311 A-G	silent	G	G	G	G
	TaqMAMA 5'NCR-57 reversion % ^b		--	-	-	-
DENVax-2	592 A-G	prM-52 Lys-Glu	Glu	Glu	Glu	Glu
	6481 G-C	NS4A-36 Ala-Pro	-	-	Ala/Pro	Pro
	7156 C-T	NS4B-111 Leu-Phe	-	-	Leu/Phe	Phe
	8803 A-G	NS5-412 Ile-Val	Val	Val	Val	Val
	TaqMAMA 5'NCR-57 reversion % ^b		--	-	0.07%	0.21%
DENVax-3	1603 A-T	E-223 Thr-Ser	Ser	Ser	Ser	Ser
	6436 G-A	NS4A-23 Asp-Asn	-	-	Asn	Asn
	7620 A-G	silent	G	G	G	G
	TaqMAMA 5'NCR-57 reversion % ^b		--	-	-	-
DENVax-4	225 A-T	silent	T	T	T	T
	3674 A-G	NS2A-66 Asp-Gly	Gly	Gly	Gly	Gly
	3773 A-A/G	NS2A-99 Lys-Lys/Arg	-	Lys/Arg	Lys/Arg	Lys/Arg
	5391 C-T	silent	T	T	T	T
	6437 C-T	NS4A-21 Ala-Val	Val	Val	Val	Val
	7026 T-C	silent	T/C	T/C	T/C	T/C
	7538 C-C/T	NS4B-238 Ser-Ser/Phe	-	-	Ser/Phe	Ser/Phe
	9750 A-C	silent	C	C	C	C
	TaqMAMA 5'NCR-57 reversion % ^b		-	0.13%	-	-
^a Bold: Changes started at MVS stocks.						
^b "--" indicates reversion rate < 0.01% (detection limit), "-" indicates reversion rate < 0.07% (detection limit)						

[000103] Full-genome sequence analysis revealed that an additional amino acid mutation developed in the DENVax-4 MVS, while the other three DENVax MVS lots retained the consensus genome sequence of their pre-master seeds. Overall, from deriving of the P1 seeds to the pre-master (P7) seeds, only 1 or 2 non-synonymous mutations occurred in a given seed. From P1 to MVS (P8) seeds, 2 to 7 nucleotide substitutions were identified in any given DENVax seed and only 2 to 3 of these substitutions resulted in amino acid changes. Thus, minor changes occurred. RNA viruses are error-prone in their

genome replication, so genetic substitutions in flavivirus genome during cell passages are not unexpected. None of the silent mutations in the MVS were within the 5' or 3'NCR that may affect virus replication. Only the change in prM-52 Lys-Glu of the DENVax-2, and the substitution in NS2A-66 Asp-Gly of DENVax-4 are not conservative changes. The NS2A-66 mutation of the DENVax-4 is in the nonstructural backbone part of the DENV-2 PDK-53. Although NS2A-66 locus is usually Asp among various strains of DENV-2, it is usually Gly for DENV-4. It is possible that the Asp to Gly change in the DENVax-4 is relevant for fitness of the DENVax-4 in Vero cells. The DENVax-2 prM-52 mutation resides in the C-terminal portion of the prM that is cleaved out from the mature virus particles. In some exemplary methods, phenotypic characterization was performed to confirm that none of the mutations in the MVS seeds significantly altered the attenuation phenotypes of the vaccine.

[000104] The DENVax viruses demonstrated high genetic stability during the manufacturing process. The three defined DENV-2 PDK-53 attenuation loci located in 5'NCR, NS1-53, and NS3-250 remained stable in the consensus genome sequence upon serial passage of the DENVax from pre-Master strains to bulk vaccine preparations. The highly sensitive TaqMAMA of the 5'NCR-57 locus demonstrated minimal or undetectable reversion in the MVS, WVS (P9/Working), and BVS (Bulk Virus Seed for vaccines) of dengue virus serotypes. The 5'NCR-57 reversion rates of the DENVax BVS preparations (P10-equivalent) were significantly lower than the 5'NCR-57 reversion rates that evolved in research-grade vaccine candidates after 10-serial passages in Vero cells (4-74% reversion). The strategy for large-scale manufacturing of the DENVax seeds provided herein resulted in a genetically stable vaccine seed which retained the attenuation markers in the candidate vaccine viruses.

Plaque phenotype of DENVax MVS

[000105] In one exemplary method, plaque phenotypes of the DENVax MVS were compared with wild type Dengue viruses and their homologous research-grade chimeric viruses in Vero cells (Fig. 2). All of the MVS of DENVax-1, -2, and -3 produced plaques that were significantly smaller than their wild type homologs and very similar (within 0.4-mm differences) to their homologous research-grade viruses in Vero cells. DENVax-4 MVS was also significantly smaller than the wild type DENV-4, but was slightly larger (0.9 mm difference) than the original lab derived D2/4-V chimera.

[000106] Fig. 2 represents an exemplary histogram illustrating plaque sizes of the DENVax MVS in contrast with control wild type viruses and research-grade vaccine

candidate viruses. Mean plaque diameters (mm) $\pm$ SD (error bars) of the virus plaques in Vero cells under agarose overlay measured on day 9 pi. The wild type DEN viruses, represented by black bars, and previously published research-grade vaccine candidate viruses, represented by white bars, were included for control and comparison to the DENVax master vaccine seeds represented by grey bars.

Temperature sensitivity of DENVax MVS

[000107] In another exemplary method, temperature sensitivity was tested in Vero cells for the DENVax MVS and compared with their homologous wild type and the original research-grade chimeric vaccine virus. The wild type (wt) DENV-3 16562 was not temperature sensitive. The wt dengue virus serotype 1 and dengue virus serotype-4 were moderately temperature sensitive at 39°C (titers were approximately 1.0 log₁₀ pfu/ml lower at 39°C than at 37°C, Fig. 3). Wt Dengue virus serotype-2 16681 was the most temperature sensitive of the wt Dengue viruses tested, and resulted in a 100-fold titer drop at 39°C. DENVax-1, -2, and -3 were as temperature sensitive as their original homologous research-grade chimeric vaccine viruses (Fig. 2). Titers at 39°C dropped between 2.0 and 3.0 log₁₀ pfu/ml for these DENVax strains. DENVax-4 also was temperature sensitive, demonstrating a 5-fold reduction in titer. However, the original research-grade D2/4-V demonstrated about a 10-fold reduction in titer. The final stabilized DENVax-4 MVS contained F127 (and other agents known to stabilize these formulations (FTA)), which was shown to enhance thermal stability of the Dengue viruses. The presence of the F127 in DENVax-4 MVS likely contributed to the less pronounced temperature sensitivity of the virus in the Vero culture assay. In a separate experiment, temperature sensitivity of an MSV-derived DENVax-4 strain in the absence of F127 was further evaluated. To remove the F127 from the strain, viral RNA was isolated from a DENVax-4 bulk virus preparation and was transfected into Vero cells. This DENVax-4 virus appeared to be as temperature sensitive as the D2/4 V research strain (titer reduced 1.5 log₁₀ pfu/ml) on day 3 pi in the absence of F127 (Fig. 3).

[000108] Fig. 3 illustrates an exemplary histogram illustrating temperature sensitivities of DENVax MVS. The wild type Dengue viruses and previously published research-grade vaccine candidate viruses were included for comparison. The DENVax-4 MVS contains additional F-127 that can mask the temperature sensitivity results of the virus in this assay. A separate experiment analyzing a surrogate DENVax-4 in the absence of F127 was also included. Mean titers $\pm$ SD (error bars) of the viruses replicated in Vero cells at 37°C or

39°C.

DENVax MVS replication in mosquito C6/36 cells

[000109] In some exemplary methods, the DENVax MVS were grown in C6/36 cells to verify their retention of the *in vitro* attenuation phenotype, with the knowledge that the research-grade chimeric vaccine viruses retained the attenuation phenotype of the backbone DENV-2 PDK53 virus in these mosquito cells. Compared to the wt Dengue viruses, DENVax-1, DENVax-2 and DENVax-4 MVS showed significant growth reduction (at least 3 log₁₀ pfu/ml reduction) in C6/36 cells on day 6 pi (Fig. 4). The DENVax-3 MSV also exhibited reduced growth compared to the wt DENV-3 16562, but the reduction was not as marked (1-2 log₁₀ pfu/ml reduction). However, the C6/36 titers of the DENVax-3 seed lots were similar (within 1 log₁₀ pfu/ml difference) to the C6/36 titer of the original research-grade chimeric D2/3-V vaccine virus.

[000110] Fig. 4 illustrates an exemplary histogram plotting restricted growth of DENVax MVS (grey bars) in C6/36 cells in comparison with wt Dengue viruses (black bars) and research-grade vaccine viruses (white bars). Mean titers ± SD (error bars) of the viruses replicated in C6/36 cells 6 days pi.

Virus infection, dissemination, and transmission rates in whole mosquitoes

[000111] In some exemplary methods, the infection and dissemination rates of the DENVax were compared with their parental wt Dengue viruses. In certain exemplary experiments, oral infection experiments were conducted in *Ae. aegypti* mosquitoes. Infectious blood meals were back-titrated to measure the virus titers and only the experiments with similar virus titers in the blood meal (less than 1 log₁₀ pfu/ml differences) between parental Dengue viruses and DENVax for each serotype were included for comparisons in Table 4. DENVax-1, DENVax-2, and research-grade D2 PDK-53-VV45R did not infect mosquitoes through oral feeding, which is significantly different ($p < 0.0001$) from their parental viruses, DENV-1 16007 (44% infection) and DENV-2 16681 (43.3% infection). Because no mosquito was infected by DENVax-1 and -2, there was little to no dissemination concern for these two vaccine viruses. While DENVax-4 did infect some mosquitoes through oral feeding (2 out of 55), the infection rate was significantly lower ($p < 0.05$) than its parental wt virus, DENV-4 1036 (8 out of 50). DENVax-3 did not infect any mosquitoes in two experiments with blood meal viral titers of 5.2±0.02 log₁₀ pfu/ml (Table 4), and in a separate experiment with blood meal viral titer of 6.0 log₁₀ pfu/ml, only 1 out of 30 mosquitoes became infected (data not shown). However, wt Dengue virus-3 16562 also

had a very low infection rate (8%) at 5.2 log₁₀ pfu/ml, and the rate did not increase in a separate experiment with a higher blood meal viral titer at 6.2 log₁₀ pfu/ml (3%, 1 positive out of 30 mosquitoes, data not shown). Although the wild type (wt) Dengue virus-3 and Dengue virus-4 had significantly lower infection rates than the wt Dengue virus-1 and Dengue virus-2, the mean virus titers in the infected mosquitoes were similar (3.1 to 3.9 log₁₀ pfu/mosquito). In contrast, the DENVax-4 titers from the two infected mosquitoes were both minimal (0.7 log₁₀ pfu/mosquito), which was 1,000-fold lower than the titer from the mosquitoes infected by wt Dengue virus serotype-4 1036 (3.9 ± 1.5 pfu/mosquito).

[000112] For those mosquitoes that were infected, dissemination out of the midgut could be assessed by determining whether virus was present in the legs. The four parental DENVs resulted in dissemination rates ranging between 36.3% and 62.5%, and their mean virus titers (in log₁₀ pfu) from the legs were between 0.9±0.3 and 2.2±0.7 (excluding negative samples). Neither of the two DENVax-4 infected mosquitoes resulted in virus dissemination to the legs (Table 4). While disseminated virus was detectable in the legs, none of the four wt Dengue viruses was detectable in saliva of orally infected mosquitoes, suggesting that oral feeding conditions may not be sufficiently sensitive to measure the transmission rate of these DENVs. Therefore, in other exemplary methods, highly stringent artificial mosquito infections by direct IT inoculation were subsequently performed (Table 4). Except for DENVax-4, all viruses (wt and DENVax) achieved 100% infection of the IT inoculated *Ae. aegypti*. The DENVax-4 inoculum had a slightly lower viral titer than the other three viral inocula, but it still successfully infected 70% of the inoculated mosquitoes. Despite the high body infection rates achieved by IT inoculation, all four DENVax viruses exhibited significantly lower ($p < 0.005$) or non-detectable transmission rates (0-10%) compared to the wt Dengue viruses (43-87%, Table 4). The DENVax viruses demonstrated little to no infection and dissemination after oral feeding, and the highly stringent IT results affirmed the minimal transmission capacity of these DENVax viruses in *Ae. aegypti*.

Table 4: Virus infection, dissemination, and transmission rates in whole mosquitoes

Virus	Oral Feed					IT inoculation				
	Blood Meal ^a	Infection ^b	Body Titer ^c		Dissemination ^e	Inoculum	Infection ^b	Body Titer ^c	Saliva ^f	
	Mean±SD	% (P/N)	Mean±SD	P^d	% (P/N) ^f	pfu/dose	% (P/N)	Mean±SD	% (P/N)	P^d

DENV-1 16007	6.6	44.0% (11/25)	3.6 ± 1.5		36.3% (4/11)	53.9	100% (30/30)	4.7 ± 0.48	43% (13/30)	
DENVax-1	6.9	0% (0/30)	NA	<0.0 001	NA	67.8	100% (30/30)	3.4 ± 0.39	10% (3/30)	<0.00 5
DENV-2 16681	6.6	43.3% (13/30)	3.1 ± 1.5		38.5% (5/13)	67.8	100% (30/30)	5.2 ± 0.34	87% (26/30)	
D2 PDK53- VV45R	6.4	0% (0/30)	NA	<0.0 001	NA	56.4	100% (30/30)	4.0 ± 0.20	0% (0/30)	<0.00 01
DENVax-2	6.4	0% (0/30)	NA	<0.0 001	NA	52.7	100% (30/30)	3.5 ± 0.27	7% (2/30)	<0.00 01
DENV-3 16562	5.2	8% (2/25)	3.8 ± 0.2		50% (1/23)	34.0	100% (30/30)	4.2 ± 0.50	67% (20/30)	
DENVax-3	5.2 ± 0.02	0% (0/50)	NA	0.10 8	NA	37.3	100% (30/30)	3.3 ± 0.36	3% (1/30)	<0.00 01
DENV-4 1036	5.8 ± 0.5	16% (8/50)	3.9 ± 1.5		62.5% (5/8)	69.4	100% (30/30)	5.2 ± 0.45	70% (21/30)	
DENVax-4	5.4 ± 0.4	3.6% (2/55)	0.7 ± 0.0	0.03 3	0% (0/2)	11.8	70% (21/30)	1.1 ± 0.46	0% (0/21)	<0.00 01
^a Virus titers or Mean±standard deviation if from more than 1 experiment in blood meal (log ₁₀ pfu/ml) by back titration ^b Rate of virus detected in mosquito bodies. <i>P/N</i> = positive/total mosquitoes ^c Mean virus titers ± standard deviation (log ₁₀ pfu/mosquito) in mosquito body, only positive sample are included for calculation ^d Statistic analysis of the differences between wt DENV and DENVax by Fisher Exact probability ^e Rate of virus detected in legs of the positively infected mosquitoes ^f Rate of virus detected in saliva of the positively infected mosquitoes. Used to measure transmission efficiency										

[000113] Vector competence is an important safety component for live-attenuated flavivirus vaccine viruses. Previously, the research-grade DENV-2 PDK-53-VV45R virus and wt derivatives were tested in *Ae. aegypti*, and found that the NS1-53-Asp attenuating mutation was the dominant determinant for impaired mosquito replication. The other two major attenuation loci of the DENV-2 PDK-53 vaccine, nucleotide 5'NCR-57-T and NS3-250-Val, also exhibited some inhibiting effect on replication in mosquitoes, thus providing additional, redundant restrictions for mosquito vector competence. Some exemplary methods described herein were used to test the mosquito oral and IT infection and replication for all four DENVax strains. DENVax-1, -2, and -3 did not infect any *Ae. aegypti* mosquitoes through oral infection (Table 4). The DENVax-4 infected only 3.6% of orally exposed mosquitoes, a level significantly lower than that of the wt DENV-4 with a replicative mean titer in the mosquito bodies lower than that of wt DENV-4 infected mosquitoes. Surprisingly, DENVax-4 was detected in the legs of the infected mosquitoes, suggesting that DENVax-4 was not able to disseminate from the mosquito midgut following oral infection. The infection rates for the DENVax-1, -2, and -4 were all significantly less than their wt counterparts, but the difference was not significant between DENVax-3 and wt DENV-3 16562 due to the very low infection rates for both viruses. Compared to other wt strains of DENV assessed in *Ae. aegypti* collected from the same Mae Sot Province, Thailand, the parental wt Dengue virus strains used for engineering DENVax appeared to have lower infectious and dissemination rates by oral infection. The wt DENV-1 PUO359,

DENV-2 PUO218, DENV-3 PaH881/88, and DENV-4 1288 used for engineering the Yellow Fever (YF) 17D vaccine-based ChimeriVax-DEN vaccines had infection rates ranging 47-77%. In contrast, the YF 17D vaccine cannot infect *Ae. aegypti*. Although the ChimeriVax strains contained the prM-E from these highly infectious wt DENV, the ChimeriVax retain the mosquito attenuation phenotype of their YF 17D replicative backbone. Results provided herein also indicated that the mosquito attenuation of DENV-2 PDK-53 backbone was maintained in the DENVax strains. In addition, using the wt Dengue virus strains with lower mosquito-infectivity in constructs included in compositions described herein provides an additional safety feature.

[000114] The oral infection results illustrate that the DENVax had minimum mosquito infectivity and dissemination capacity. In addition, the more sensitive and stringent IT infection experiments were performed to further analyze the potential of DENVax to be transmitted by *Ae. aegypti*. The IT results demonstrated that all four DENVax viruses had non-detectable or minimal mosquito transmission potential compared to their wt counterparts. DENVax transmission could only theoretically occur if (1) vector feeds on a vaccinee with a sufficient viremia titer to infect mosquito midgut, (2) the virus is capable of replicating in the midgut epithelium and able to subsequently disseminate out of the midgut, and (3) the disseminated virus can replicate in salivary gland and expectorate sufficient virus in saliva for transmission. The threshold of human viremia required to infect mosquitoes has not been established adequately, but human viremia can be 10^6 - 10^8 mosquito infectious dose₅₀ (MID₅₀)/ml after natural wt DENV infection. This MID₅₀ was based on direct IT inoculation of mosquitoes with diluted human plasma. Analysis of DENVax in nonhuman primates indicated that viremia titers following DENVax immunization were very low (less than 2.4 log₁₀ pfu/ml) and lasted for 2-7 days. Given the low viremia levels and the low mosquito infection, dissemination, and transmission capacity of DENVax, it is unlikely that these vaccine viruses could be transmitted by mosquitoes in nature or cause viremia.

[000115] Therefore, it is proposed that any of the passages of any of the serotypes (P1-P10) could be used in a composition to generate a safe and effective vaccine against one, two, three or all four dengue virus serotypes.

Neurovirulence in suckling mice

[000116] The original research-grade vaccine viruses were highly attenuated for neurovirulence in newborn ICR mice maintained in-house at DVBD/CDC. All of these mice survived ic (intracerebral) challenge with 10^4 pfu of each vaccine virus. The wt

Dengue virus serotype-2 16681 virus, on the other hand, resulted in 62.5% - 100% mortality in these CDC-ICR mice in various experiments. In some experiments, commercial ICR mice obtained from Taconic Labs (Taconic-ICR) were used to study neurovirulence in newborn mice. It was observed that newborn Taconic-ICR mice were significantly more susceptible to Dengue virus serotype-2 infection than the previous CDC-ICR mice. Fig. 5A summarizes the neurovirulence of wt Dengue virus serotype-2 16681 in CDC-ICR colony and Taconic-ICR newborn mice challenged ic with 10^4 pfu of the virus. The Taconic-ICR mice (100% mortality in 32 mice, average survival time of 8.3 ± 0.5 days) were more susceptible to ic Dengue virus serotype-2 16681 challenge than the previous CDC-ICR mice (91% fatalities in 72 mice, average survival time of 14.6 ± 2.3 days).

[000117] In other exemplary methods, in order to evaluate neurovirulence of the DENVax MVS, the Taconic-ICR mice initially were challenged ic (intracerebrally) with a dose of approximately 10^4 pfu of wt Dengue virus serotype-2 16681, D2 PDK-53 VV45R, D2/3-V, or DENVax 1-4 virus in one (n=16) or two (n=31-32) experiments (Fig. 5B). At this dose, D2/3-V research grade virus, as well as DENVax-1, and DENVax-3 MVS exhibited fully attenuated neurovirulence phenotypes (no illness or mortality). As expected, wt Dengue virus serotype-2 was found to be “fatal”, with average mouse survival time (AST) of 8.3 ± 0.8 days. In these Dengue virus serotype-2-sensitive Taconic-ICR mice, the D2 PDK-53-VV45R research grade virus resulted in 81.3% mortality. The DENVax-2 MVS and DENVax-4 MVS were uniformly fatal in the Taconic-ICR, showing AST values of 9.8 ± 1.7 , 10.2 ± 1.4 , and 11.3 ± 0.4 days, respectively.

[000118] In some exemplary methods, the neurovirulence of wt Dengue virus serotype-2 16681 virus was compared with that of D2 PDK-53 VV45R, DENVax-2 MVS and DENVax-4 MVS, as well as D2/4-V research grade virus, at a 10-fold lower dose (10^3 pfu, Fig. 5C). The wt Dengue virus serotype-2 retained a uniformly fatal neurovirulent phenotype, with AST of 9.0 ± 1.4 days, at this lower challenge dose. The other 4 viruses exhibited intermediate neurovirulence phenotypes, and the degree of neurovirulence was serotype-specific. The D2 PDK-53-VV45R virus and its DENVax-2 MVS cognate showed significant attenuation (32.3% survival with AST of 13.1 ± 3.8 days and 31.2% survival with AST of 10.5 ± 3.4 days, respectively). Both the DENVax-4 MVS and the research grade D2/4-V virus were highly attenuated for neurovirulence (81.3% survival with AST of 18.8 ± 5.8 days and 100% survival, respectively). The results suggested that MVS of DENVax-1 and -3 exhibited complete attenuation of neurovirulence, while DENVax-2 and -4 MVS lots retained attenuation phenotypes that closely resembled their homologous

research-grade virus vaccine candidates.

[000119] Figs. 5A-5C represent exemplary graphs illustrating neurovirulence in newborn mice tested with various compositions including wt Dengue virus serotype-2 and different attenuated Dengue viruses. Pooled results of numerous experiments summarizing the neurovirulence of wt Dengue virus serotype-2 16681 virus in CDC-ICR ($n=72$) and Taconic-ICR ($n=32$) newborn mice challenged ic with 10^4 pfu of the virus (A). Neurovirulence of DENVax MVS tested in Taconic-ICR mice with a dose of 10^4 pfu (B) or 10^3 pfu (C). The numbers of animals tested per group in one experiment ($n=16$) or two pooled experiments ($n=31$ or 32) are indicated.

Plaque phenotype of WVS, and BVS

[000120] Certain studies were performed to compare plaque phenotypes of WVS and BVS with MVS, wt Dengue viruses and their homologous lab derived, research-grade chimeras in Vero cells (Fig. 6). Mean plaque sizes were calculated from 10 plaques for each vaccine virus, but from reduced numbers of wt DENV-1, -3, and -4. All of the MVS viruses of DENVax-1, -2, and -3 produced plaques that were significantly smaller than their wt homologs and very similar (within 0.4-mm differences) to their homologous research-grade viruses in Vero cells. DENVax-4 MVS was also significantly smaller than the wt DENV-4, but was slightly (0.9 mm) larger than the original lab derived D2/4-V chimera. With the exception of the DENVax-2, all of the WVS and BVS of the DENVax-1, -3, -4 retained significantly smaller plaque sizes than those produced from their wt homologs. The DENVax-2 WVS and BVS produced plaques that were similar to the plaques of wt DENV-2 virus in Vero cells, but when tested in LLC-MK₂ cells all of the DENVax-2 manufactured seeds produced plaques that were somewhat smaller than those of the wt DENV-2 (1.4 ± 0.4) and similar to the lab derived D2 PDK-53-VV45R (1.0 ± 0.3) (Fig. 6).

[000121] Evaluation of the phenotypic markers of viral attenuation, including small plaque phenotype, temperature sensitivity, reduced replication in mosquito cells, reduced infection/dissemination/transmission by mosquitoes, and reduced neurovirulence in newborn ICR mice, were assessed for the compositions of MVS stocks. Results indicated that all of the DENVax retained the expected attenuation phenotypes similar to the original research-grade vaccine viruses. Given the mutations responsible for attenuation are conserved in all MVS, WVS and BV, it can be expected the attenuated phenotypes to be retained in the material manufactured for human clinical testing.

[000122] Fig. 6 represents an exemplary histogram illustrating plaque size of the DENVax MVS, WVS, and BVS. Mean plaque diameters $\pm$ SD (error bars) of the virus

plaques in Vero or LLC-MK₂ cells under agarose overlay measured on day 9 pi. The wt DENVs and previously published research-grade vaccine candidate viruses were included for control and comparison.

Virus replication in mosquito C6/36 cells

[000123] Previous studies demonstrated that the research-grade PDK-53-based chimeric vaccine viruses retained the attenuation phenotype of the backbone DENV-2 PDK53 virus in C6/36 cells. In some exemplary methods, the DENVax MSV, WVS, and BVS were grown in C6/36 cells to verify their retention of this in vitro attenuation marker after large scale manufacturing. Compared to the wt Dengue viruses, except for DENVax-3, the manufactured seeds showed marked growth reduction (at least 3 log₁₀ PFU/ml reduction) in C6/36 cells on day 6 pi (Fig. 7). The DENVax-3 seeds also exhibited reduced growth compared to the wt DENV-3 16562, but the reduction was not as marked (1-2 log₁₀ PFU/ml reduction). However, the titers of the DENVax-3 seed lots were similar (within 1 log₁₀ PFU/ml difference) to the original research-grade chimeric D2/3-V vaccine virus.

[000124] Fig. 8 represents an exemplary histogram plotting restricted growth of DENVax MVS, WVS, and BVS in C6/36 cells. Mean titers ± SD (error bars) of the viruses replicated in C6/36 cells 7 days pi. The wt Dengue viruses and previously published research-grade vaccine candidate viruses were included for comparison.

Neurovirulence in suckling mice

[000125] Additional experiments were performed to analyze neurovirulence in newborn ICR mice. At an intracranial dose of 10⁴ PFU, the survival rates for wt DENV-2 16681 and the D2 PDK-53-VV45R were 0% and 18.8%, respectively (Fig. 9A) in the ICR mice, but were about 20% for wt DENV-2 16681 and 100% for the D2 PDK-53-VV45R in the CDC ICR mice. In this study, DENVax-1 and DENVax-3 MVS were attenuated (100% survival) for the mice at a dose of 10⁴ PFU, but the MVS of DENVax-2 and DENVax-4 caused 100% mortality at the dose of over 10⁴ PFU (Fig. 5A). However, when tested at a dose of 10³ PFU of virus, the DENVax-2 (31.3% survival) and DENVax-4 (81.3% survival) showed reduced neurovirulence relative to wt Dengue virus serotype-2 16681 (0% survival), and their survival rates were similar to those of the research-grade vaccine candidates D2 PKD-53-VV45R (32.3%) and D2/4-V (100%), respectively (Fig. 9B). Although, wt DENV-1, -3, or -4 were not included for comparison in this study, previous work demonstrated that wt DENV-1 16007 was attenuated in the CDC-ICR mice by the ic route, while both wt DENV-3 16562 and DENV-4 1036 were highly virulent (0% survival) for the CDC-ICR mice. It is likely that these 3 wt DENV would exhibit similar or greater virulence in the

more susceptible Taconic ICR mice. Therefore, inclusion of these wt Dengue viruses for comparison with their homologous DENVax MVSs was considered to be uninformative. This study indicated that all 4 DENVax MVSs and original laboratory derived candidate vaccine viruses exhibit comparable mouse attenuation phenotypes relative to the wt DENV-2 16681.

[000126] Figs. 9A-9B represent exemplary graphs of data of neurovirulence of DENVax MVS in newborn ICR mice. (A) IC inoculations of the virus at dose of 10^4 PFU. (B) IC inoculation of the virus at dose of 10^3 PFU

[000127] All seed lots of the DENVax were tested for the identity, sterility, and freedom from undesirable agents. Full-genome sequence analysis revealed that one extra amino acid mutation evolved in the DENVax-4 MVS, while the other 3 DENVax MVSs retained the consensus genome sequence of their pre-master seeds. In WVS lots, the DENVax-3 acquired an extra amino acid mutation and the other 3 serotypes accumulated 2 extra amino acid substitutions, relative to their pre-master seeds. Genome sequences of all the 4 BVS lots were identical to their WVS lots. Overall from the P2 seeds to the pre-master (P7) seeds, only 1 or 2 non-silent mutations occurred in a given seed. Between pre-master and BCS (P10) seeds, only 1 to 2 nucleotide substitutions were observed, all of which occurred in NS2A, 4A, or 4B, with the exception of single nucleotide change resulting in a conserved glycine and alanine at residue E-483. From P2 to BVS (P10) seeds, total 3 to 8 nucleotide substitutions were identified in any given DENVax seed, and only 2 to 4 of these substitutions resulted in amino acid changes. None of the silent mutations in the BVS were within the 5'- or 3'-NCR region which may affects virus replication. These results suggest that the DENVax viruses were genetically highly stable during manufacture. The three defined DENV-2 PDK-53 attenuation loci located in 5'NCR, NS1-53, and NS3-250 remained unchanged in the consensus genome sequence upon serial passage of the DENVax to generate BVS stocks. The highly sensitive TaqMAMA of the 5'-NCR-57 locus showed minimal or undetectable reversion in the MVS, WVS, and BVS of DENVax. The highest reversion rate of 0.21% was identified in the DENVax-2 BVS. The reversion rates of the P10-equivalent BVS (<0.07% to 0.21%) were significantly lower than the reversion rates that evolved in other vaccine candidates after serial passages in Vero cells (4-74% reversion by P10). This suggests that this strategy for large scale manufacturing of the DENVax seeds is successful, regarding maintaining genetic stability and retention of attenuation markers in the candidate vaccine viruses.

[000128] Since MVS stocks disclosed herein will be used for future manufacturing of

WVS and BVS lots, full panels of virus attenuation phenotype evaluations, including small plaque phenotype, temperature sensitivity, reduced replication in mosquito cells, reduced infection/dissemination/transmission in whole mosquitoes, and reduced neurovirulence in newborn ICR mice, were conducted for all MVS or their equivalent surrogate stocks. For the WVS and BVS stocks, plaque size, infectivity in mosquito cells, were also performed to confirm their attenuations. Results indicated that all the MVS stocks of the 4 serotypes of DENVax retained the expected attenuation phenotypes, such as small plaques, reduced replication in C6/36 cells, and reduced mouse neurovirulence, similar to the original lab-derived vaccine viruses (Figs. 6, 8, and 9). Except for the DENVax-4, all other 3 MVS stocks of DENVax were TS at 39°C as shown in Figs 3 and 7.

[000129] For the WVS and BVS stocks, two attenuation phenotypes, small plaques and restricted replication in C6/36 cells, were analyzed and confirmed. Since there are very little genetic changes between the MVS and BVS, it was expected that they would retain the attenuation phenotypes as MVS. In addition to the experiments described in this report, safety and immunogenicity of the manufactured DENVax in Ag129 mice and nonhuman primate have been tested.

[000130] Exemplary methods are provided herein to demonstrate manufacture of DENVax MVS, WVS, and BVS stocks under cGMP. The BVS stocks were used to formulate the tetravalent DENVax currently in human clinical trial evaluations. A unique manufacture strategy to optimize the genetic stability and safety of the manufactured MVS was provided in some exemplary methods. Since the main attenuation loci of the DENVax have been well characterized previously and a highly sensitive and quantifiable SNP assay, TaqMAMA was developed to integrate genome sequence and the TaqMAMA to identify optimal pre-master seeds for making the MVS. The genetic and phenotypic characterizations of the MVS were fully analyzed to confirm that these viruses retained desirable attenuations for safety of the vaccine. This may be the only live, attenuated viral vaccine that can be efficiently analyzed for all the major attenuation genetic loci during manufacturing from pre-master all the way to BVS stocks. Results provided herein exemplified the advantage of strategically designed live-attenuated vaccines in vaccine safety.

[000131] **Fig. 10** represents an exemplary table comparing new live, attenuated viruses to previously generated live, attenuated dengue viruses. Mutations are indicated where different from a control virus (e.g. 16681), or other live, attenuated dengue-2 viruses.

Materials and methods

Viruses and cells

[000132] DENV-1 16007, DENV-2 16681, DENV-3 16562, and DENV-4 1034 served as wild-type (wt) DENV controls, and they were the parental genotype viruses for the four recombinant DENVax vaccine candidates. DENVax progenitor research-grade viruses, designated as D2/1-V, D2 PDK-53-VV45R, D2/3-V, and D2/4-V, were prepared and characterized previously. Vero (African green monkey kidney) cells used for making the master and working cell banks for vaccine production were originated from the American Type Culture Collection (ATCC) CCL81 cell line that has been characterized by the World Health Organization (WHO) for vaccine manufacture (WCB-Vero cells).

Derivation of live recombinant DENVax viruses from cDNA clones

[000133] To re-derive the candidate vaccine viruses under cGMP manufacturing conditions, the previously engineered DENV infectious cDNA clones, pD2-PDK-53-VV45R, pD2/1-V, pD2/4-V, and *in vitro*-ligated pD2/3-V containing the full genome-length viral cDNAs were used to make fresh viral RNA transcripts by *in vitro* transcription as described previously. Briefly, XbaI-linearized DENV genomic cDNAs were treated with proteinase K, extracted with phenol/chloroform and precipitated in ethanol to remove any residual proteins, and then suspended in RNase-free Tris-EDTA buffer prior to transcription. The *in vitro* transcription was conducted using the AmpliScribe T7 High Yield Transcription kit (Epicentre Technologies) following the manufacturer's recommended protocol. The RNA A-cap analog, m7G(5')ppp(5')A (New England BioLabs), was incorporated during the 2-hr transcription reaction to add the 5'-terminal A-cap to the RNA transcript. The samples were then treated with DNase I to digest the template cDNA, followed by low pH phenol/chloroform extraction and ethanol precipitation to remove residual DNA and proteins. The purified RNA transcripts, suspended in RNase-free water, were distributed in 20- μ l aliquots and stored at -80°C until ready for transfection of cells. The integrity and concentration of the RNA transcripts were analyzed by agarose gel electrophoresis. Each 20- μ l aliquot was estimated to contain sufficient genome-length viral RNA to permit transfection of $0.4-1 \times 10^7$ production-certified Vero cells by electroporation.

[000134] Transfection of each RNA transcript into WCB-Vero cells was performed in the cGMP facility at Shantha Biotechnics. DENVax RNA transcripts were thawed, mixed with 400 μ l of the Vero cell suspension (1×10^7 cells/ml), and transferred to a pre-chilled sterile electroporation cuvette (4-mm gap) for electroporation by a Gene Pulser Xcell total system (BioRad Laboratories). Each sample was pulsed once at 250V/ ∞ Ohms/500 μ F,

incubated for 10-15 min at room temperature, transferred to a 75-cm² flask containing 30 ml of cell growth medium (MEM with 10% FBS), and incubated at 36°C ± 1°C, 5% CO₂ for 6 to 11 days. The culture medium was harvested, clarified by centrifugation, stabilized, and stored in small aliquots below -60°C. The viral titers of candidate vaccine stocks (termed P1 for passage level 1) resulting from transfection were determined by plaque titration assay in Vero cells and used for further propagation of the DENVax seeds.

Manufacture of DENVax virus seeds

[000135] P1 virus seeds were used to propagate DENVax pre-master, master, working, and bulk virus seed lots through a strategy designed to ensure the optimal genetic stability and safety of the manufactured lots. This strategy included three serial plaque purifications, as well as genetic analyses of viruses at various passage levels to select the optimal clonal virus population for continued seed production (Table 1). Briefly, the P1 seeds harvested from transfected cells were amplified once by infection of Vero cells at a MOI of 0.001 to generate the P2 seeds. Aliquots of the P2 seed stocks were evaluated by plaque morphology and complete viral genomic sequencing. The genetically confirmed P2 stocks were plated on Vero cell monolayers with overlay medium as described in the plaque titration section below to generate well-isolated plaques. After visualization with neutral red, six individual plaques from each of the 4 serotypes of vaccine viruses were isolated (plaque clones A to F) and mixed into 0.5 ml of culture medium (passage P3). Each of the six plaque suspensions was subjected to two additional rounds of plaque purification, resulting in twice- and thrice-plaque purified virus seeds at passages P4 and P5, respectively. The P5 viruses were amplified through two sequential Vero passages to produce P7 seed stocks.

[000136] Genetic analysis of the three major DENVax attenuation loci using spot sequencing and/or Taqman-based mismatched amplification mutation assay (TaqMAMA) as previously disclosed, and plaque phenotype analysis were conducted to screen all 24 P7 seeds. Seeds possessing appropriate initial characteristics were then further characterized by full genomic sequencing. As a result of these analyses, one of the 6 (clone A-F) P7 seeds of each DENVax serotype was selected to be the pre-master seed, based on the presence of the DENV-2 PDK-53 attenuating mutations, minimal genomic sequence alterations, and expected plaque phenotype. Each selected pre-master seed was expanded to master virus seed (MVS or P8) by a one-time passage of the virus at MOI of 0.001 in multiple 175 cm² flasks of Vero cells. Except for the DENVax-4 MVS, the master virus seeds were harvested at 8-10 days post infection (pi). The MVS stocks were harvested at 6-10 days post infection (pi), clarified by centrifugation, stabilized by the addition of sucrose/phosphate/glutamate

solution (final concentration 7.5 % sucrose, 3.4 mM potassium dihydrogen phosphate, 7.2 mM dipotassium hydrogen phosphate, 5.4 mM monosodium glutamate, respectively) and 0.95 to 1.90% FBS (final concentration). DENVax-4 MVS was prepared differently to optimize its yield. Briefly, multiple flasks of cells were infected with DENVax-4 pre-master seed at a MOI of 0.001 in the presence of 0.1% F-127TM, poloxamer 407, (other EO-PO block copolymers have been assessed and may substitute here, see issued patent) that have been demonstrated to enhance DENV virus thermal stability. Infectious media was harvested days 6-10 pi, and stabilized with 17% FBS (final concentration), pooled, and frozen. All four DENVax MVS stocks were stored as 1-ml aliquots below -60°C.

[000137] The DENVax working virus seeds (WVS) were prepared by one-time passage in Vero cell culture of the MVS at a MOI of 0.001. The procedures were similar to the production of MVS, except they were cultured in multiple-layer cell factories (6360 cm²). The WVS stocks were filtered through 10 µM and 0.45µM filters, stabilized with the same stabilizers used for the MVS, aliquoted into 30ml PETG bottles or 2.0 ml cryovials, and stored below -60°C.

[000138] In certain methods, bulk virus seeds (BVS) were produced by infecting multiple cell factories (6360 cm² each) of confluent Vero cells with 90 mL of diluted WVS to attain a MOI of 0.001. A media used for dilution of the WVS inocula contained 0.1% F-127TM without serum. After 1.5 hr adsorption, cells were washed 3 times with PBS, and 800 ml of serum-free DMEM medium was added to each cell factory, and the factories were incubated at 36(±1)°C in 5(±0.5)% CO₂. After incubation for four days, small aliquots of medium were collected for sterility testing. Viruses were harvested between day 5 and day 10 pi, and immediately clarified by filtration through a 0.45 µm pore size filter, and 1L of each clarified virus pool was stabilized by addition of 500 ml of 3x FTA buffer (final concentrations of 15% trehalose, 1.0% Pluronic[®] F-127TM poloxamer 407, 0.1% human albumin USP in PBS, pH 7.4). The stabilized virus was distributed into 1-L PETG bottles and stored frozen below -60°C for subsequent pooling and quality control testing. All stabilized virus harvests with a virus titer above 10⁵ PFU/ml and an acceptable level of residual DNA were rapidly thawed in a water bath at 32°C, then aseptically pooled and mixed. Each pooled monovalent BVS was distributed into labeled PETG containers and stored at below -60°C until further use.

Manufacture product quality controls

[000139] The MVS, WVS, and BVS seeds were tested for identity, sterility, and

detectable adventitious agents. The identity of each vaccine stock was confirmed by RT-PCR with DENVax serotype-specific primers. The amplified cDNA fragments contained the E/NS1 chimeric junction site to permit identification of each of the four DENVax serotypes. Each seed was tested in all 4 serotype-specific RT-PCR reactions to confirm viral identity and freedom from cross contamination with heterologous DENVax serotypes. Sterility testing was performed in accordance with USP 71 (United States Pharmacopeia, section 71). Mycoplasma testing was performed.

[000140] The following *in vitro* and *in vivo* tests for viral contamination were all performed using unclarified, unstabilized DENVax harvests collected during manufacture of the seeds. Harvested infectious media were first neutralized with DENV rabbit polyclonal antiserum (Inviragen) at $36 \pm 1^\circ\text{C}$ for 1 hr to inactivate the DENV. For *in vitro* test, the neutralized seeds were inoculated into three indicator cells lines, MRC5, VERO and MA104, in 25 cm^2 flasks. Echo virus (CPE control) or mumps virus (hemadsorption control) were used as positive CPE or hemadsorption control, respectively. All cells were monitored daily for CPE for a total of 14 days. At the end of 14 days, the culture supernatant was removed and replaced with 10 mL of a guinea pig red blood cell (RBC) solution (3 mL of 0.5% guinea pig RBC in phosphate buffered saline, made up to 10 mL with cell growth medium). The flasks were then incubated at $5 \pm 3^\circ\text{C}$ for 30 minutes followed by incubation at room temperature for 30 minutes. The monolayers were washed with PBS and observed under 10 X magnification for the presence of any star-shaped clumps of RBCs for hemadsorption.

[000141] *In vivo* tests for adventitious agents were performed in suckling mice, post-weaning mice and guinea pigs. Suckling mice were inoculated with 0.1ml or 0.01 ml (10 mice in each dose group) of the DENV-antiserum neutralized seed sample through intraperitoneal (ip) injection. Similarly, 10 post-weaning mice were each inoculated ip with 0.5 ml or 0.03 ml of the sample. Guinea pigs (5/group) were each inoculated ip with 5.0 mL. Suckling mice were observed daily for morbidity and mortality for a total of 14 days following inoculation. Post-weaning mice were observed for a total of 28 days, and guinea pigs were observed for a total of 42 days following inoculation. The test articles met the acceptance criterion if $\geq 80\%$ of the inoculated animals remained healthy throughout the observation period.

[000142] The *in vivo* testing for contaminants was also performed in embryonated chicken eggs and was conducted. For every sample, 10 embryonated hen eggs (9 days old) were each inoculated with 0.5 mL of the DENV antiserum-neutralized sample into the

allantoic fluid and incubated at 35°C for 3 days. The allantoic fluids from these 10 eggs were harvested, pooled and passaged into the allantoic fluid of 10 fresh embryonated eggs (10-11 days old; 0.5mL/egg) and incubated at 35°C for a further 3 days. Similarly, for each sample, 10 embryonated eggs (6-7 days old) were each inoculated with 0.5 mL per egg (DENVax-2 monovalent BVS) or 0.25 mL per egg (DENVax-1, DENVax-3 and DENVax-4 BVS) by injection into the yolk sac and incubated at 35°C for 9 days. The yolk sacs from these 10 eggs were harvested and pooled, and a 10% suspension was passaged into the yolk sacs of 10 fresh embryonated eggs (6-7 days old; 0.5 mL/egg) and incubated at 35°C for a further 9 days. Eggs inoculated into the allantoic fluid (both initial and passage inoculations) were observed for viability after 3 days incubation. Both pools of allantoic fluid were tested for hemagglutination activity using chicken, guinea pig and human type O erythrocytes at 4°C and 25°C. Eggs inoculated into the yolk sack (both initial and passage inoculations) were observed for viability after 9 days of incubation.

Virus plaque assay and immunofocus assay

[000143] Virus titers were measured by plaque assay or immunofocus assay using Vero cells. Plaque assays were performed in double agarose overlays in six-well plates of confluent Vero cells as previously described, and they were also used to evaluate the plaque phenotypes of the DENVax seeds. For accurate comparison, plaque sizes of all viruses were measured and compared in the same experiment. After visualization with neutral red on day 9 pi, up to 10 well isolated plaques for each virus were measured for mean plaque size calculation. Fewer plaques were measured for wt DENV-1, -3, and -4, whose larger plaque sizes often did not permit measurement of 10 well-separated plaques.

[000144] Because tetravalent DENVax contains all four DENV serotypes, a DENV serotype-specific immunofocus assay was developed to quantitate each DENVax component in the tetravalent formulations. Immunofocus assays of each individual DENVax MVS were compared with the plaque assays to ensure virus titration results were comparable between the two assays. The immunofocus assay was conducted in 6-well plates of confluent Vero cells infected with serially diluted viruses. Cells were overlaid with a balanced salt medium (BSS/YE-LAH medium) containing 0.7% high viscosity carboxymethyl cellulose (Sigma) and incubated for 7 days at 37°C with 5% CO₂. After removal of overlays, cell sheets were washed 3 times with PBS, fixed with cold 80% acetone for 30min at -20°C, washed once with PBS, and blocked with a blocking buffer containing 2.5% (w/v) nonfat dry milk, 0.5% Triton X-100, 0.05% Tween-20 in PBS at 37°C for 30 min. Blocked cells were incubated with diluted DENV serotype-specific MAbs,

1F1 (DENV-1), 3H5 (DENV-2), 8A-1 (DENV-3), or 1H10 (DENV-4) in blocking buffer at 37°C for 1 hour or 4°C overnight, washed 3 times with washing buffer (0.05% Tween-20 in PBS), and incubated with alkaline phosphatase- or horse radish peroxidase (HRP)-conjugated affinity-pure goat anti-mouse IgG (Jackson Immuno Research Laboratories) at 37°C for 45-60 min. Plates were washed 3 times before the appropriate substrate, 1-Step NBT/BCIP plus suppressor (Pierce) for alkaline phosphatase or Vector-VIP kit (Vector Labs) for HRP, was added for color development. Color development was stopped by rinsing with water when the foci were fully developed. Stained immunofoci were directly visualized and counted on a light box.

Genetic sequence

[000145] Full length genomes of the MVS and WVS were sequenced (see below). Briefly, viral RNA was extracted from DENVax seeds by using the QIAamp viral RNA kit (Qiagen), and overlapping cDNA fragments covering the entire genome were amplified using the Titan One Tube RT-PCR kit (Roche Applied Science, Inc.). The amplified cDNA fragments were gel purified before sequencing with both forward and reverse primers using the BigDye Terminator v3.1 cycle sequencing kit (Applied Biosystems). Sequence reactions were cleaned using the BigDye XTerminator Purification kit (Applied Biosystems), and run on the 3130xl Genetic analyzer (Applied Biosystems) at DVBD/CDC. The Lasergene SeqMan software (DNASTar, Inc) was used for genome analysis and comparison.

Taqman-based mismatch amplification mutation assay (TaqMAMA)

[000146] TaqMAMA is a sensitive, quantitative single nucleotide polymorphism assay developed to permit finer assessment of the level of reversion at the 5'NC-57 locus of attenuation, and was further optimized for this study. Extracted viral RNA from MVS and WVS were analyzed by the TaqMAMA with both sets of primers/Taqman probe that are specific to wt or the vaccine 5'NC-57 region. The forward primers used to detect DENV-2 wt and vaccine sequences were D2-41-GC and D2-40-TT, respectively. The 3'-terminal nucleotide of each forward primer matched the specific 5'NCR-57 nucleotide for each virus, while the nucleotide adjacent to the 3'-terminal nucleotide in each primer differed from the DENV-2 viral genomic sequence to enhance the mismatch effect. The reverse primer, CD-207, and the Taqman probe, CD-169F, for both wt and vaccine sets were identical. Sequences of the primers and probe as well as cycling conditions were described previously. The real time RT-PCR was performed with the iQ5 or CFX-95 system (BioRad), using a BioRad iScript RT-PCR (for probes) kit, in a 25- μ l reaction containing 5 μ l of viral RNA

template, 0.4 uM of each primer, and 0.2 uM of the probe. Triplicate reactions for each wt- and vaccine-specific assay were conducted for each sample. Genome copy numbers were determined relative to a standard curve prepared for each viral genotype, where the RNA standards were transcripts derived from plasmids containing nt 1-2670 of each genotype-specific cDNA. In addition, the specificity of the assay was confirmed by testing each RNA standard with the heterologous genotype primer/probe sets to ensure minimum cross-reactivity in every experiment. The results were reported as the percentage of viral genomes showing reversion. Previously, due to higher cross-reactive backgrounds that limited the input RNA levels for this assay, the original detection sensitivity was about 0.1% reversion (discrimination power). Since then, the assay has been further optimized using improved real-time PCR equipment and reaction kits, and the cross-reactive background was decreased considerably at much high levels (7-8 log₁₀ copies) of RNA template input. This optimization resulted in significant improvement of the detection sensitivity, down to 0.01-0.07% reversion.

Virus replication in mosquito C6/36 cells and temperature sensitivity in mammalian Vero cells

[000147] The replication phenotypes of the four DENVax MVS stocks and wt DENV-1, -2, -3, and -4 viruses were evaluated in C6/36 mosquito cells (*Aedes albopictus*). C6/36 cells grown in 6-well plates were infected in duplicate with each virus at a MOI of 0.001 and incubated with 4 ml/well of DMEM medium containing 2% FBS in a 5% CO₂ incubator at 28°C. Small aliquots of the culture supernatant were collected for each virus on day 6 pi, mixed with an equal volume of medium containing 40% FBS, and stored at -80°C until ready for virus plaque titration.

[000148] Temperature sensitivity was conducted by comparing viral growth at 39°C versus growth at 37°C at five days pi of Vero cells in 6-well plates. Cells were infected in quadruplicate with each virus at a MOI of 0.001 at 37°C. Following adsorption of virus, the infected cultures were incubated with 4 ml/well of DMEM medium containing 2% FBS in 2 separate 5% CO₂ incubators, one set (duplicate plates) at 37°C and the other at 39°C. Aliquots (50-μl) of the culture supernatant were collected on day 5 pi, mixed with an equal volume of DMEM containing 40% of FBS, and stored at -80°C until ready for virus plaque titration. Incubator temperatures were calibrated with NIST-traceable factory-calibrated thermometers (-1 to 51 °C; ERTCO).

Mosquito infection, dissemination, and transmission

[000149] *Aedes aegypti* mosquitoes used for the study were from a colony established in 2002 from a village near Mae Sot (16° N, 33° E), Thailand. After emerging from larvae, adult mosquitoes were maintained at 28°C at a 16:8 (light:dark) photoperiod with 10% sucrose solution provided *ad libitum*. Five-to-seven day old female mosquitoes were used for infectious blood meal feeding or intrathoracic (IT) inoculations. Aliquots of freshly cultured DENVax and wt DENV were used immediately upon harvest (without any freeze-thaw cycle) to make virus blood meals as indicated below for oral infection. Remaining virus supernatants were supplemented with FBS to a final concentration of 20%, and aliquots were stored at -80°C for future virus plaque titration and IT inoculation experiments. The freshly prepared DENVax seeds for these experiments were amplified from the pre-master seeds in Vero cells, and were considered DENVax MVS equivalents.

[000150] Infectious blood meals were prepared by mixing fresh virus at a ratio of 1:1 with defibrinated chicken blood (Colorado Serum Company) on the day of oral infection. Mosquitoes were sugar-starved overnight and then offered the virus:blood mixture for 1 hour using a Hemotek membrane feeding system (Discovery Workshops). A 50-μl aliquot of the blood meal was retained at -80°C for back-titration of virus doses. Fully-engorged females were sorted under cold anesthesia and placed into cartons with 10% sucrose solution provided *ad libitum*. Cartons were placed at 28°C with a photoperiod of 16:8 h (light:dark). After 14 days, 25-30 mosquitoes from each virus group were anesthetized via exposure to triethylamine (Flynap®, Carolina Biological Supply Company) and one hind leg was removed and placed in 0.5 ml of DMEM with 10% FBS and 5% penicillin/streptomycin (100U/ml and 100μg/ml respectively). Saliva was collected by inserting the proboscis of the anesthetized mosquito into a capillary tube containing 2.5% FBS and 25% sucrose solution. Mosquitoes were allowed to salivate for at least 15 minutes and then capillary tubes and bodies were placed into separate tubes containing DMEM. Mosquito bodies, legs and saliva were stored at -80°C until they were triturated and assayed for infectious virus. For IT inoculation, mosquitoes were cold-anesthetized and inoculated with approximately 50 pfu of virus in 0.34 μl inoculum. Inoculated mosquitoes were kept for 7 days in the same conditions as described above. Mosquitoes were then anesthetized, and their saliva and bodies were collected as described above. Samples were stored at -80°C until further processing.

[000151] To process the samples for virus titration, body and leg samples were homogenized with copper coated BBs (Crossman Corporation, NY) at 24 cycles/second for 4 min using a mixer mill, and then clarified by centrifuging at 3,000 x g for 3 min. Saliva

samples were centrifuged at 3,000 x g for 3 minutes to expel fluid from capillary tubes. Ten-fold dilutions of the body and leg homogenates and saliva samples were tested for presence of infectious virus by plaque assay. Results from bodies, legs, and saliva were used for determining the infection, dissemination, and transmission rates, respectively.

Mouse neurovirulence

[000152] Timed pregnant female ICR mice were obtained from Taconic Labs, and monitored several times each day to determine approximate birth times of pup litters. In a given experiment, approximately 12-24 hours after birth, two litters of eight pups per virus (n=16), was challenged with 10^3 to 10^4 pfu of virus in 20 μ l of diluent by intracranial (ic) inoculation using a 30-gauge needle. Animals were monitored at least 3 times daily for at least 32 days following challenge. At the first sign of illness (rough fur, hunched back, weight loss, abnormal movement, paralysis, or lethargy) animals were euthanized by lethal anesthetization with isoflurane gas, followed by cervical dislocation. The post-infection day of euthanasia represented the “time to illness/morbidity” or “survival time” for the animal. The animal experiments were conducted following a DVBD/CDC IACUC-approved animal protocol.

Derivation of Master Seed Viruses

DENVax-1 Master Virus Seed (MVS)

[000153] Nucleotide sequence of the chimeric viral genome and deduced amino acid sequence of the translated protein are provided herein. Most of the prM-E gene (nt 457 to -2379, underlined) is wild-type (wt) DEN-1 16007 virus specific; the remaining genome is DEN-2 PDK-53 virus specific. All engineered substitutions differ from wt virus (D1 16007 or D2 16681), as well as extra mutations (changes from engineered cDNA clone) detected in the MVS are marked.

Substitutions Included in the Genome and Protein:

- [000154]** Junction sites between D1 (prM-E) and D2 backbone:
- MluI** (nt 451-456): engineered silent mutation, nt-453 A-to-G
 - NgoMIV** (nt 2380-2385): engineered mutations, nt-2381/2382 TG-to-CC (resulted in E-482 Val-to-Ala change)
- [000155]** D2 PDK-53 virus backbone (change from wt D2 16681): all in bold
- 5'-noncoding region(NCR)-57 (nt-57 C-to-T): major attenuation locus (in red)**
 - NS1-53 Gly-to-Asp (nt-2579 G-to-A): major attenuation locus (in red)**
 - NS2A-181 Leu-to-Phe (nt-4018 C-to-T)**
 - NS3-250 Glu-to-Val (nt-5270 A-to-T): major attenuation locus (in red)**
 - nt-5547 (NS3 gene) T-to-C silent mutation**

f. NS4A-75 Gly-to-Ala (nt-6599 G-to-C)

* nt-8571 C-to-T silent mutation of PDK-53 is not engineered in the vaccine virus

[000156] DEN-1 prM-E (change from wt D1 16007)

a. Engineered nt-1575 T-to-C silent mutation to remove native XbaI site

[000157] Additional substitutions found in vaccine seed (0.03% nt different from original clone)

a. NS2A-116 Ile-to-Leu (nt-3823 A-to-C, in bold)

b. NS2B-92 Glu-to-Asp (nt-4407 A-to-T, in bold)

c. nt-7311 A-to-G silent mutation (in bold)

NCP-57-T, D2 PDK-53 attenuation locus (wt D2 16681: C)

>5'-Noncoding Region | >C

10 20 30 40 50 60 70 80 90 100

AGTTGTTAGTCTACGTGGACCGACAAAGACAGATTCTTTGAGGGAGCTAAGCTCAATGTAGTTCTAACAGTTTTTAATTAGAGAGCAGATCTCTGATGA
M N

110 120 130 140 150 160 170 180 190 200

ATAACCAACGGAAAAAGGCGAAAAACACGCCTTTCAATATGCTGAAACGCGAGAGAAACCGCGTGTGCGACTGTGCAACAGCTGACAAAGAGATTCTCACT
N Q R K K A K N T P F N M L K R E R N R V S T V Q Q L T K R F S L

210 220 230 240 250 260 270 280 290 300

TGGAATGCTGCAGGGACGAGGACCATTAATACTGTTTCATGGCCCTGGTGGCGTTCCTTCGTTTCTTAACAATCCCAACAGCAGGGATATTGAAGAGA
G M L Q G R G P L K L F M A L V A F L R F L T I P P T A G I L K R

310 320 330 340 350 360 370 380 390 400

TGGGAACAATTAATAAATCAAAAGCTATTAATGTTTGGAGAGGTTTCAGGAAAGAGATTGGAAGGATGCTGAACATCTTGAATAGGAGACGCAGATCTG
W G T I K K S K A I N V L R G F R K E I G R M L N I L N R R R R S A

>prM Beginning of D1 16007 sequence

410 420 430 440 450 460 470 480 490 500

CAGGCATGATCATTATGCTGATTCCAACAGTGATGGCGTTCCATTTAACCACGGTGGGGAGAGCCGCATATGATAGTTAGCAAGCAGGAAAGAGGAAA
G M I I M L I P T V M A F H L T T R G G E P H M I V S K Q E R G K

Engineered MluI splicing site (nt-453 A-to-G silent)

510 520 530 540 550 560 570 580 590 600

GTCACCTTTTGTTCAGACCTCTGCAAGTGTCAACATGTGCAACCTCATTTGCGATGGATTTGGGAGAGTTGTGTGAGGACACCGATGACCTACAAATGCCCC
S L L F K T S A G V N M C T L I A M D L G E L C E D T M T Y K C P

610 620 630 640 650 660 670 680 690 700

CGGATCACTGAGGCGGAACAGATGACGTTGACTGTTGGTGAATGCCACGGACACATGGGTGACCTATGGAACGTGCTCTCAAAGTGGCGAACACCGAC
R I T E A E P D D V D C W C N A T D T W V T Y G T C S Q T G E H R R

>M

710 720 730 740 750 760 770 780 790 800

GAGACAAACGTTCCGTCGATTGGCCCCACACGTGGGGCTTGGCCTAGAAACAAGACCCGAAACGTGGATGTCTCTGAAGGTGCTTGGAAACAGATACA
D K R S V A L A P H V G L G L E T R A E T W M S S E G A W K Q I Q

810 820 830 840 850 860 870 880 890 900

AAAAGTAGAGACTTGGGCTCTGAGACATCCAGGATTCACGGTGATAGCCCTTTTCTAGCATGCCATAGGAACATCCATCACCAGAAAGGGATCATT
K V E T W A L R H P G F T V I A L F L A H A I G T S I T Q K G I I

>E

910 920 930 940 950 960 970 980 990 1000

TTCATTTTGCTGATGCTGGTAACACCATCTATGGCCATGCGTGGGAATAGGCAACAGAGACTTCGTGGAAGGACTGTCAGGAGCAACATGGGTGG
F I L L M L V T P S M A M R C V G I G N R D F V E G L S G A T W V D

1010 1020 1030 1040 1050 1060 1070 1080 1090 1100

ATGTGGTACTGGAGCATGGAAGTTGCGTCACCAACCATGGCAAAAAACAAACCAACACTGGACATGAACTCTTGAAGACGGAGGTACAAACCTGCACT
V V L E H G S C V T T M A K N K P T L D I E L L K T E V T N P A V

1110 1120 1130 1140 1150 1160 1170 1180 1190 1200

TCTGCGTAAATTTGTGATTGAAGCTAAATATCAAAACACCAACCGATTTCGAGATGTCCAACACAAGGAGAAGCCACACTGGTGAAGAAACAGACCGC
L R K L C I E A K I S N T T T D S R C P T Q G E A T L V E E Q D A

1210 1220 1230 1240 1250 1260 1270 1280 1290 1300

AACTTTGTGTGCCGACGACGTTCTGTGACAGAGGCTGGGGCAATGGCTGTGGCTATTTCGAAAAGGTAGTCTAATAACGTGTGCCAAGTTTAAGTGTG

N F V C R R T F V D R G W G N G C G L F G K G S L I T C A K F K C V

1310 1320 1330 1340 1350 1360 1370 1380 1390 1400

TGACAAACTAGAAAGGAAGATAGTTCAATATGAAAACCTAAATATTTCAGTGATAGTCACCGTCCACACTGGAGATCAGCACCAGGTGGGAAATGAGAC

T K L E G K I V Q Y E N L K Y S V I V T V H T G D Q H Q V G N E T

1410 1420 1430 1440 1450 1460 1470 1480 1490 1500

TACAGAACATGGAACAACCTGCAACCATACACCTCAAGCTCCTACGTCGGAATACAGCTGACCGACTACGGAACCCCTTACATTAGATTGTTACCTAGG

T E H G T T A T I T P Q A P T S E I Q L T D Y G T L T L D C S P R

1510 1520 1530 1540 1550 1560 1570 1580 1590 1600

ACAGGGCTAGATTTTAAACGAGATGGTGTGCTGACAATGAAAGAAAGATCATGGCTTGTCCACAAACAATGGTTCCTAGACTTACCACTGCCTTGGACCT

T G L D F N E M V L L T M K E R S W L V H K Q W F L D L P L P W T S

Engineered silent mutation (nt-1575 T-to-C): remove the native DEN-1 virus-specific xbaI site

1610 1620 1630 1640 1650 1660 1670 1680 1690 1700

CTGGGGCTTCAACATCCCAAGAGACTTGAACAGACAAGATTTACTGGTCACATTTAAGACAGCTCATGCAAGAAGCAGGAAGTAGTCGTACTAGGATC

G A S T S Q E T W N R Q D L L V T F K T A H A K K Q E V V V L G S

1710 1720 1730 1740 1750 1760 1770 1780 1790 1800

ACAAGAAGGAGCAATGCACACTGCGCTGACTGGAGCGACAGAAATCCAAACGTCAGGAACGACACAATTTTCGAGGACACCTAAATGCAGACTAAAA

Q E G A M H T A L T G A T E I Q T S G T T T I F A G H L K C R L K

1810 1820 1830 1840 1850 1860 1870 1880 1890 1900

ATGGACAACTAACTTTAAAGGGATGTCATATGTGATGTGCACAGGCTCATTCAAGTTAGAGAAAAGTGGCTGAGACCCAGCATGGAACCTGTTCTGG

M D K L T L K G M S Y V M C T G S F K L E K E V A E T Q H G T V L V

1910 1920 1930 1940 1950 1960 1970 1980 1990 2000

TGCAGGTAAATATGAAGGAACAGACGACCATGCAAGATTCCTTTTCGACCCAAGATGAGAAAGGAGCAACCCAGAATGGGAGATTAAATACAGCCAA

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

2010 2020 2030 2040 2050 2060 2070 2080 2090 2100

CCCCATAGTCACTGACAAAGAAAAACCAGTCAATATTGAGGCAGAACCCCTTTGGTGAGAGCTACATCGTGGTAGAGCAGGTGAAAAAGCTTTGAAA

P I V T D K E K P V N I E A E P P F G E S Y I V V G A G E K A L K

2110 2120 2130 2140 2150 2160 2170 2180 2190 2200

CTAAGCTGGTTCAAGAAAGGAAGCAGCATAGGGAAAATGTTTGAAGCAACTGCCCCAGGAGCAGCAAGGATGGCCATTCTGGGAGACACCGCATGGGACT

L S W F K K G S S I G K M F E A T A R G A R R M A I L G D T A W D F

2210 2220 2230 2240 2250 2260 2270 2280 2290 2300

TCGGTTCTATAGGAGGAGTGTTCACGTCTATGGGAAAACCTGGTACACCAAGTTTTGGAACTGCATATGGAGTTTGTGTTAGCGGAGTTTCTTGGACCAT

G S I G G V F T S M G K L V H Q V F G T A Y G V L F S G V S W T M

End of D1 16007 sequence

2310 2320 2330 2340 2350 2360 2370 2380 2390 2400

GAAAAATAGGAATAGGAGATTCTGCTGACATGGCTAGGATTAAATTCAAGGAACACGTCCTTTTCGATGATGTGCATCGCAGCCGGCATTGTGACACTGTAT

K I G I G I L L T W L G L N S R N T S L S M M C I A A G I V T L Y

Engineered NgoMIV splicing site, E-482 Val-to-Ala (nt-2381/2382 TG-to-CC)

>NS1

2410 2420 2430 2440 2450 2460 2470 2480 2490 2500

TTGGGAGTCATGGTGCAGGCCGATAGTGGTTGCGTTGTGAGCTGGAAAAACAAAGAACTGAAATGTGGCAGTGGGATTTTCATCAGACAAACGTGCACA

L G V M V Q A D S G C V V S W K N K E L K C G S G I F I T D N V H T

2510 2520 2530 2540 2550 2560 2570 2580 2590 2600

CATGGACAGAACAAATACAAGTTCCAACAGAAATCCCTTCAAACCTAGCTTCAGCTATCCAGAAAGCCCATGAAGAGGACATTTGTGGAATCCGCTCAGT

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

D2 PDX-53 NS1-53-Asp attenuation locus (wt D2 16531: Gly, nt-2573-3)

2610 2620 2630 2640 2650 2660 2670 2680 2690 2700

AACAAGACTGGAGAATCTGATGTGGAACAAATAACACCAGAATTGAATCACATTTATCAGAAAAATGAGGTGAAGTTAACTATTATGACAGGAGACATC

T R L E N L M W K Q I T P E L N H I L S E N E V K L T I M T G D I

2710 2720 2730 2740 2750 2760 2770 2780 2790 2800

AAAGGAATCATGCAGGCAGGAAACGATCTCTGCGGCCTCAGCCCACTGAGCTGAAGTATTCATGGAACATGGGGCAAAGCAAAATGCTCTCTACAG

K G I M Q A G K R S L R P Q P T E L K Y S W K T W G K A K M L S T E

2810 2820 2830 2840 2850 2860 2870 2880 2890 2900

AGTCTCATAACAGACCTTTCTCATTGATGGCCCCGAAACAGCAGAATGCCCAACACAAATAGAGCTTGAATTCGTTGGAAGTTGAAGACTATGGCTT

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

2910 2920 2930 2940 2950 2960 2970 2980 2990 3000

TGGAGTATTCACCACCAATATATGGCTAAAATTGAAAGAAAAACAGGATGTATTCTGCGACTCAAAACTCATGTGACGGCCATAAAGACAACAGAGCC

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

3010 3020 3030 3040 3050 3060 3070 3080 3090 3100
GTCCATGCCGATATGGGTTATTGGATAGAAAAGTGCACCTCAATGACACATGGAAGATAGAGAAAGCCTCTTTTCATTGAAGTTAAAACTGCCACTGGCCAA
V H A D M G Y W I E S A L N D T W K I E K A S F I E V K N C H W P K

3110 3120 3130 3140 3150 3160 3170 3180 3190 3200
AATCACACACCTCTGGAGCAATGGAGTGCTAGAAAAGTGAGATGATAATTCCAAAGAATCTCGCTGGACCAGTGTCTCAACACAATATAGACCAGGCTA
S H T L W S N G V L E S E M I I P K N L A G P V S Q H N Y R P G Y

3210 3220 3230 3240 3250 3260 3270 3280 3290 3300
CCATACACAAATAACAGGACCATTGGCATCTAGGTAAGCTTGAGATGGACTTTGATTCTGTGATGGAACAACAGTGGTAGTACTGAGGACTGCGGAAAT
H T Q I T G P W H L G K L E M D F D F C D G T T V V V T E D C G N

3310 3320 3330 3340 3350 3360 3370 3380 3390 3400
AGAGGACCTCTTTGAGAACAACTGCCTCTGGAAAACCTATAACAGAATGGTGTGCCGATCTTGACATTACCACCGCTAAGATACAGAGGTGAGG
R G P S L R T T T A S G K L I T E W C C R S C T L P P L R Y R G E D

>NS2A

3410 3420 3430 3440 3450 3460 3470 3480 3490 3500
ATGGGTGCTGGTACGGGATGGAATCAGACCATTGAAGGAGAAAGAAGAGAATTTGGTCAACTCCTTGGTCACAGCTGGACATGGGCAGGTGCGAACCTT
G C W Y G M E I R P L K E K E E N L V N S L V T A G H G Q V D N F

3510 3520 3530 3540 3550 3560 3570 3580 3590 3600
TTCAGTAGGAGTCTTGGGAATGGCATTGTTCTGGAGGAAATGCTTAGGACCCGAGTAGGAACGAAACATGCAATACTACTAGTTGCAGTTTCTTTTGTG
S L G V L G M A L F L E E M L R T R V G T K H A I L L V A V S F V

3610 3620 3630 3640 3650 3660 3670 3680 3690 3700
ACATTGATCACAGGGAACATGTCTTTAGAGACCTGGGAAGAGTGATGGTTATGGTAGGCCCACTATGACGGATGACATAGGTATGGGCGTGACTTATC
T L I T G N M S F R D L G R V M V M V G A T M T D D I G M G V T Y L

3710 3720 3730 3740 3750 3760 3770 3780 3790 3800
TTGCCCTACTAGCAGCTTCAAAGTCAGACCAACTTTGCAGCTGGACTACTCTTGAGAAAGCTGACCTCCAAGGAATTGATGATGACTACTATAGGAAT
A L L A A F K V R P T F A A G L L L R K L T S K E L M M T T I G I

3810 3820 3830 3840 3850 3860 3870 3880 3890 3900
TGTAATCTCTCCAGAGCACCTACCAGAGACCATCTTGAGTTGACTGATGCGTTAGCCTTAGGCATGATGGTCTCAAATGGTGAGAAATATGGAA
V L L S Q S T L P E T I L E L T D A L A L G M M V L K M V R N M E

|
Additional NS2A-116 Ile-to-Leu (nt3823 A-to-C) mutation in master and pre-master seed

3910 3920 3930 3940 3950 3960 3970 3980 3990 4000
AAGTATCAATTGGCAGTGACTATCATGGCTATCTTGTGCGTCCCAAACGCAGTGATATTACAAAACGCATGGAAAGTGAGTTGCACAATATTGGCAGTG
K Y Q L A V T I M A I L C V P N A V I L Q N A W K V S C T I L A V V

4010 4020 4030 4040 4050 4060 4070 4080 4090 4100
TGTCGGTTTCCCACTGTTCTTAACATCCTCAGCAAAAACAGATTGGATACCATTAGCATTGACGATCAAAGGTCTCAATCCAACAGCTATTTTCT
S V S P L F L T S S Q Q K T D W I P L A L T I K G L N P T A I F L

|
D2 PDK-53 specific NS2A-181-Phe (wt D2 16681: Leu, nt-4018-C)

>NS2B

4110 4120 4130 4140 4150 4160 4170 4180 4190 4200
AACAACCTCTCAAGAACCAGCAAGAAAAGGAGCTGGCCATTAAATGAGGCTATCATGGCAGTCGGGATGGTGAGCATTTTAGCCAGTTCTCTCTAAAA
T T L S R T S K K R S W P L N E A I M A V G M V S I L A S S L L K

4210 4220 4230 4240 4250 4260 4270 4280 4290 4300
AATGATATTCATGACAGGACCATAGTGGCTGGAGGGCTCCTCACTGTGTGCTACGTGCTCACTGGACGATCGGCCGATTGGAACTGGAGAGAGCAG
N D I P M T G P L V A G G L L T V C Y V L T G R S A D L E L E R A A

4310 4320 4330 4340 4350 4360 4370 4380 4390 4400
CCGATGTCAAATGGGAAGACCAGGCAGAGATATCAGGAAGCAGTCCAATCCTGTCAATAACAATATCAGAAGATGGTAGCATGTGATAAAAAATGAAGA
D V K W E D Q A E I S G S S P I L S I T I S E D G S M S I K N E E

4410 4420 4430 4440 4450 4460 4470 4480 4490 4500
GGAAGATCAAACTGACCATCTAGTAACAGGATTGCTGGTGATCTCAGGACTTTTCTGTATCAATACCAATCAGGCAGCAGCATGGTACCTG
E D Q T L T I L I R T G L L V I S G L F P V S I P I T A A A W Y L

|
Additional NS2B-92 Glu-to-Asp (nt-4407 A-to-T) mutation (in master and pre-master seed)

>NS3

4510 4520 4530 4540 4550 4560 4570 4580 4590 4600
TGGGAAGTGAAGAAACAACGGCCGGAGTATTGTGGGATGTTCTCTACCCCCACCCATGGGAAGGCTGAAGTGAAGATGGAGCCTATAGAATTAAGC

W E V K K Q R A G V L W D V P S P P P M G K A E L E D G A Y R I K Q

4610 4620 4630 4640 4650 4660 4670 4680 4690 4700
 AAAAAGGGATTCTTGGATATTCACAGATCGGAGCCGGAGTTTACAAAGGAACATTCCATACAAATGTGGCATGTACACGTGGCGCTGTTCTAATGCA
 K G I L G Y S Q I G A G V Y K E G T F H T M W H V T R G A V L M H

4710 4720 4730 4740 4750 4760 4770 4780 4790 4800
 TAAAGGAAAGAGGATTGAACCATCATGGGCGGACGTCAAGAAAGACCTAATATCATATGGAGGAGGCTGGAAGTTAGAAGGAGAATGGAAGGAAGGAGAA
 K G K R I E P S W A D V K K D L I S Y G G G W K L E G E W K E G E

4810 4820 4830 4840 4850 4860 4870 4880 4890 4900
 GAAGTCCAGGTATTGGCACTGGAGCCTGGAAAAAATCCAAGAGCCGTCCAAACGAAACCTGGTCTTTTCAAAACCAACCCGGAACAATAGGTGCTGTAT
 E V Q V L A L E P G K N P R A V Q T K P G L F K T N A G T I G A V S

4910 4920 4930 4940 4950 4960 4970 4980 4990 5000
 CTCTGGACTTTTCTCCTGGAACGTGAGGATCTCCAATTATCGACAAAAAGGAAAAAGTTGTGGGTCTTTATGGTAATGGTGTGTGTACAAGGAGTGGAGC
 L D F S P G T S G S P I I D K K G K V V G L Y G N G V V T R S G A

5010 5020 5030 5040 5050 5060 5070 5080 5090 5100
 ATATGTGAGTGCTATAGCCAGACTGAAAAAGCATTGAAGACAACCCAGAGATCGAAGATGACATTTTCCGAAAGAGAAGACTGACCATCATGGACCTC
 Y V S A I A Q T E K S I E D N P E I E D D I F R K R R L T I M D L

5110 5120 5130 5140 5150 5160 5170 5180 5190 5200
 CACCCAGGAGCGGAAAGACGAAGAGATACCTTCCGGCCATAGTCAGAGAAGCTATAAAACGGGGTTTGAGAACATTAATCTTGGCCCCACTAGAGTTG
 H P G A G K T K R Y L P A I V R E A I K R G L R T L I L A P T R V V

5210 5220 5230 5240 5250 5260 5270 5280 5290 5300
 TGGCAGCTGAAATGGAGGAAGCCCTTAGAGGACTTCCAATAAGATACCAGACCCAGCCATCAGAGCTG^XGCACACCGGGCGGGAGATTGTGGACCTAAT
 A A E M E E A L R G L P I R Y Q T P A I R A V H T G R E I V D L M

|

D2 PDK-53 NS3-250-Val attenuation locus (wt D2 16681: Glu, nt-5270-A)

5310 5320 5330 5340 5350 5360 5370 5380 5390 5400
 GTGTCATGCCACATTTACCATGAGGCTGCTATCACCAGTTAGAGTGCCAACTACAACCTGATTATCATGGACGAAGCCCATTTACAGACCCAGCAAGT
 C H A T F T M R L L S P V R V P N Y N L I I M D E A H F T D P A S

5410 5420 5430 5440 5450 5460 5470 5480 5490 5500
 ATAGCAGCTAGAGGATACATCTCAACTCGAGTGGAGATGGGTGAGGACAGTGGGATTTTATGACAGCCACTCCCCGGGAGCAGAGACCCATTTCTCTC
 I A A R G Y I S T R V E M G E A A G I F M T A T P P G S R D P F P Q

5510 5520 5530 5540 5550 5560 5570 5580 5590 5600
 AGAGCAATGCACCAATCATAGATGAAGAAAGAGAAATCCCTGAACGCTCGTGGAAATTCGAGACATGAATGGGTACCGGATTTTAAAGGGGAGACTGTTTG
 S N A P I I D E E R E I P E R S W N S G H E W V T D F K G K T V W

|

D2 PDK-53 silent mutation nt-5547-C (wt D2 16681: T)

5610 5620 5630 5640 5650 5660 5670 5680 5690 5700
 GTTCGTCCAAGTATAAAAGCAGGAAATGATATAGCAGCTTGCCTGAGGAAAAATGGAAGAAAGTGATACAACCTCAGTAGGAAGACCTTTGATCTCTGAG
 F V P S I K A G N D I A A C L R K N G K K V I Q L S R K T F D S E

5710 5720 5730 5740 5750 5760 5770 5780 5790 5800
 TATGTCAGACTAGAACCAATGATTGGGACTTCGTGGTTACAACCTGACATTTTCAAGAAATGGGTGCCAATTTCAAGGCTGAGAGGGTTATAGACCCAGAC
 Y V K T R T N D W D F V V T T D I S E M G A N F K A E R V I D P R R

5810 5820 5830 5840 5850 5860 5870 5880 5890 5900
 GCTGCATGAAACCACTCATACTAACAGATGGTGAAGAGCGGGTGATTCTGGCAGGACCTATGCCAGTGACCCACTCTAGTGACGACAAAGAAGAGGGAG
 C M K P V I L T D G E E R V I L A G P M P V T H S S A A Q R R G R

5910 5920 5930 5940 5950 5960 5970 5980 5990 6000
 AATAGGAAGAAATCCAAAAATGAGAATGACCAGTACATATACATGGGGGAACCTCTGGAAAATGATGAAGACTGTGCACACTGGAAAGAAGCTAAATG
 I G R N P K N E N D Q Y I Y M G E P L E N D E D C A H W K E A K M

6010 6020 6030 6040 6050 6060 6070 6080 6090 6100
 CTCCTAGATAACATCAACACGCCAGAAGGAATCATTCCTAGCATGTTTGAACACAGAGCGTGAAAAGGTGGATGCCATTGATGGCGAATACCGCTTGAGAG
 L L D N I N T P E G I I P S M F E P E R E K V D A I D G E Y R L R G

6110 6120 6130 6140 6150 6160 6170 6180 6190 6200
 GAGAAGCAAGGAAAACCTTTGTAGACTTAATGAGAAGAGGAGACCTACCAGTCTGGTTGGCCTACAGAGTGGCAGCTGAAGGCATCAACTACGCAGACAG
 E A R K T F V D L M R R G D L P V W L A Y R V A A E G I N Y A D R

6210 6220 6230 6240 6250 6260 6270 6280 6290 6300
 AAGGTGGTGTGTTTGTATGGAGTCAAGAACCAAAATCCTAGAAGAAAACGTGGAAGTTGAAATCTGGACAAAAGAAGGGAAGGAATGAAACCC
 R W C F D G V K N N Q I L E E N V E V E I W T K E G E R K K L K P

>NS4A

6310 6320 6330 6340 6350 6360 6370 6380 6390 6400
AGATGGTTGGATGCTAGGATCTATTCTGACCCACTGGCGTAAAGAAATTTAGGAATTTGCAGCCGGAAGAAAGTCTCTGACCCTGAAACCTAATCACAG
R W L D A R I Y S D P L A L K E F K E F A A G R K S L T L N L I T E

6410 6420 6430 6440 6450 6460 6470 6480 6490 6500
AAATGGGTAGGCTCCCAACCTTCATGACTCAGAAGGCAAGAGACGCACTGGACAACTTAGCAGTGTGCACACGGCTGAGGCAGGTGGAAGGGCGTACAA
M G R L P T F M T Q K A R D A L D N L A V L H T A E A G G R A Y N

6510 6520 6530 6540 6550 6560 6570 6580 6590 6600
CCATGCTCTCAGTGAAGTCCCGAGACCTGGAGACATTGCTTTTACTGACACTTCTGGCTACAGTCACGGGAGGGATCTTTTATTCTTGATGAGCGCA
H A L S E L P E T L E T L L L L T L L A T V T G G I F L F L M S A

|
D2 PDK-53 specific NS4A-75-Ala (wt D2 16681: Gly, nt-6599-G)

6610 6620 6630 6640 6650 6660 6670 6680 6690 6700
AGGGGCATAGGGAAGATGACCTGGGAATGTGCTGCATAATCACGGCTAGCATCCTCTATGGTACGCACAAATACAGCCCACTGGATAGCAGCTTCAA
R G I G K M T L G M C C I I T A S I L L W Y A Q I Q P H W I A A S I

6710 6720 6730 6740 6750 6760 6770 6780 6790 6800
TAATACTGGAGTTTTTCTCATAGTTTTTGCTTATTCAGAACCTGAAAAACAGAGAACACCCCAAGACAACCAACTGACCTACGTTGTATAGCCATCCT
I L E F F L I V L L I P E P E K Q R T P Q D N Q L T Y V V I A I L

>NS4B

6810 6820 6830 6840 6850 6860 6870 6880 6890 6900
CACAGTGGTGGCCGCAACCATGGCAAACGAGATGGGTTTCTAGAAAAACGAAGAAGATCTCGGATTGGGAAGCATTGCAACCCAGCAACCCGAGAGC
T V V A A T M A N E M G F L E K T K K D L G L G S I A T Q Q P E S

6910 6920 6930 6940 6950 6960 6970 6980 6990 7000
AACATCCTGGACATAGATCTACGTCCTGCATCAGCATGGACGCTGTATGCCGTGGCCACAACATTGTGTACACCAATGTTGAGACATAGCATTGAAAAAT
N I L D I D L R P A S A W T L Y A V A T T F V T P M L R H S I E N S

7010 7020 7030 7040 7050 7060 7070 7080 7090 7100
CCTCAGTGAATGTGTCCCTAACAGCTATAGCCAACCAAGCCACAGTGTAAATGGGTCTCGGAAAGGATGGCCATTGTCAAAGATGGACATCGGAGTTCC
S V N V S L T A I A N Q A T V L M G L G K G W P L S K M D I G V P

7110 7120 7130 7140 7150 7160 7170 7180 7190 7200
CCTTCTCGCCATTGGATGCTACTCACAAAGTCAACCCCATAACTCTCACAGCAGCTCTTTTCTATTGGTAGCACATTATGCCATCATAGGGCCAGGACTC
L L A I G C Y S Q V N P I T L T A A L F L L V A H Y A I I G P G L

7210 7220 7230 7240 7250 7260 7270 7280 7290 7300
CAAGCAAAAGCAACAGAGAAGCTCAGAAAAGAGCAGCGCGGCATCATGAAAAACCAACTGTGATGGAATAACAGTGATTGACCTAGATCCAATAC
Q A K A T R E A Q K R A A A G I M K N P T V D G I T V I D L D P I P

7310 7320 7330 7340 7350 7360 7370 7380 7390 7400
CTTATGATCCGAAGTTTGAAAAGCAGTTGGGACAAGTAATGCTCCTAGTCCTCTGCGTGACTCAAGTATTGATGATGAGGACTACATGGGCTCTGTGTGA
Y D P K F E K Q L G Q V M L L V L C V T Q V L M M R T T W A L C E

|
Additional silent mutation (nt-7311 A-to-G, in master and pre-master seed)

7410 7420 7430 7440 7450 7460 7470 7480 7490 7500
GGCTTTAAACCTTAGCTACCGGGCCCATCTCCACATTGTGGGAAGGAAATCCAGGGAGGTTTGGAACTACTACCATTCGCGTGTCAATGGCTAACATTTT
A L T L A T G P I S T L W E G N P G R F W N T T I A V S M A N I F

> NS5

7510 7520 7530 7540 7550 7560 7570 7580 7590 7600
AGAGGGAGTTACTTGGCCGAGCTGGACTTCTCTTTTCTATTATGAAGAACACAACCAACAAGAAGGGGAAGTGGCAACATAGGAGAGACGCTTGGAG
R G S Y L A G A G L L F S I M K N T T N T R R G T G N I G E T L G E

7610 7620 7630 7640 7650 7660 7670 7680 7690 7700
AGAAATGGAAGCCGATTGAACGCATTTGGGAAAAAGTGAATTCAGATCTACAAGAAAAGTGGAAATCCAGGAAGTGATAGAACCTTAGCAAAAGAGG
K W K S R L N A L G K S E F Q I Y K K S G I Q E V D R T L A K E G

7710 7720 7730 7740 7750 7760 7770 7780 7790 7800
CATTAAGAGGAGAAACGACCATCACGCTGTGTGCGAGGCTCAGCAAACTGAGATGGTTCGTTGAGAGAAACATGGTTCACACCAGAGGGAAGTA
I K R G E T D H H A V S R G S A K L R W F V E R N M V T P E G K V

7810 7820 7830 7840 7850 7860 7870 7880 7890 7900
GTGGACCTCGGTTGTGGCAGAGGAGGCTGGTCATACTATTGTGGAGGACTAAAGATGTAAGAGAAGTCAAAGGCCCTAACAAAAGGAGGACAGGACAG
V D L G C G R G G W S Y Y C G G L K N V R E V K G L T K G G P G H E

7910 7920 7930 7940 7950 7960 7970 7980 7990 8000
AAGAACCATCCCCATGTCAACATATGGGTGGAATCTAGTGCCTCTTCAAAGTGAGTTGACGTTTCTTCATCCGCCAGAAAAGTGTGACACATTATT
E P I P M S T Y G W N L V R L Q S G V D V F F I P P E K C D T L L

8010 8020 8030 8040 8050 8060 8070 8080 8090 8100
GTGTGACATAGGGGAGTCAACCAATCCCAAGTGAAGCAGGACGAACACTCAGAGTCCTTAACCTTAGTAGAAAATTGGTTGACCAACAACTCAA
C D I G E S S P N P T V E A G R T L R V L N L V E N W L N N N T Q

8110 8120 8130 8140 8150 8160 8170 8180 8190 8200
TTTTGCATAAAGGTTCTCAACCCATATATGCCCTCAGTCATAGAAAAAATGGAAGCACTACAAAGGAAATATGGAGGAGCCTTAGTGAGGAATCCACTCT
F C I K V L N P Y M P S V I E K M E A L Q R K Y G G A L V R N P L S

8210 8220 8230 8240 8250 8260 8270 8280 8290 8300
CACGAAACTCCACACATGAGATGTACTGGGTATCCAATGCTTCCGGGAACATAGTGTTCATCAGTGAACATGATTTCAGGATGTTGATCAACAGATTTAC
R N S T H E M Y W V S N A S G N I V S S V N M I S R M L I N R F T

8310 8320 8330 8340 8350 8360 8370 8380 8390 8400
AATGAGATACAAGAAGCCACTTACGAGCCGGATGTTGACCTCGGAAGCGGAACCCGTAACATCGGGATTGAAAGTGAGATACCAAAACCTAGATATAATT
M R Y K K A T Y E P D V D L G S G T R N I G I E S E I P N L D I I

8410 8420 8430 8440 8450 8460 8470 8480 8490 8500
GGGAAAGAATAGAAAAATAAAGCAAGAGCATGAAACATCATGGCACTATGACCAAGACCAACCATAACAAACGTGGGCATACCATGGTAGCTATGAAA
G K R I E K I K Q E H E T S W H Y D Q D H P Y K T W A Y H G S Y E T

8510 8520 8530 8540 8550 8560 8570 8580 8590 8600
CAAAACAGACTGGATCGACATCATCCATGGTCAACGAGTGGTCAGGCTGCTGACAAAACCTTGGGACGTCGTCCTCCATGGTGACACAGATGGCAATGAC
K Q T G S A S S M V N G V V R L L T K P W D V V P M V T Q M A M T

8610 8620 8630 8640 8650 8660 8670 8680 8690 8700
AGACACGACTCCATTGGACAACAGCGCGTTTTTAAAGAGAAAGTGGACACGAGAACCCAGAAGACCGAAAGAGGCAGAAAGAACTAATGAAAAATAACA
D T T P F G Q Q R V F K E K V D T R T Q E P K E G T K K L M K I T

8710 8720 8730 8740 8750 8760 8770 8780 8790 8800
GCAGAGTGGCTTTGGAAAGAATTAGGGAAGAAAAAGACACCCAGGATGTGCACCAGAGAAGAATTACAAAGAAAGGTGAGAAGCAATGCAGCCTTGGGGG
A E W L W K E L G K K K T P R M C T R E E F T R K V R S N A A L G A

8810 8820 8830 8840 8850 8860 8870 8880 8890 8900
CCATATTCAGTATGAGAACAAAGTGGAAAGTCGGCAGCTGAGGCTGTTGAAGATAGTAGGTTTGGGAGCTGGTTGACAAGGAAAGGAATCTCCATCTTGA
I F T D E N K W K S A R E A V E D S R F W E L V D K E R N L H L E

8910 8920 8930 8940 8950 8960 8970 8980 8990 9000
AGGAAAGTGTGAAACATGTGTGTACAACATGATGGGAAAAAGAGAGAAGAAGCTAGGGGAATTTCGGCAAGGCAAAAGGCAGCAGAGCCATATGGTACATG
G K C E T C V Y N M M G K R E K K L G E F G K A K G S R A I W Y M

9010 9020 9030 9040 9050 9060 9070 9080 9090 9100
TGGCTTGGAGCAGCCTTCTTAGAGTTTGAAGCCCTAGGATTCTTAAATGAAGATCACTGGTTCTCCAGAGAGAACTCCCTGAGTGGAGTGAAGGAGAAG
W L G A R F L E F E A L G F L N E D H W F S R E N S L S G V E G E G

9110 9120 9130 9140 9150 9160 9170 9180 9190 9200
GGCTGCACAAGCTAGGTTACATTCTAAGAGACGTGAGCAAGAAAGAGGAGGAGCAATGTATGCCGATGACACCGCAGGATGGGATACAAGAATCACACT
L H K L G Y I L R D V S K K E G G A M Y A D D T A G W D T R I T L

9210 9220 9230 9240 9250 9260 9270 9280 9290 9300
AGAAGACCTAAAAAATGAAGAAATGGTAACAAACCATGGAAGGAGAAACACAAGAACTAGCCGAGGCCATTTTCAAACCTAACGTACCAAAACAAGGTG
E D L K N E E M V T N H M E G E H K K L A E A I F K L T Y Q N K V

9310 9320 9330 9340 9350 9360 9370 9380 9390 9400
GTGCGTGTGCAAGACCAACACCAAGAGGCACAGTAATGGACATCATATCGAGAAGAGACCAAGAGGTAGTGGACAAGTTGGCACCTATGGACTCAATA
V R V Q R P T P R G T V M D I I S R R D Q R G S G Q V G T Y G L N T

9410 9420 9430 9440 9450 9460 9470 9480 9490 9500
CTTTCACCAATATGGAAGCCCACTAATCAGACAGATGGAGGGAGAAGGAGTCTTTAAAGCATTACGACCTAACCAATCACAGAAGAAATCGCTGTGCA
F T N M E A Q L I R Q M E G E G V F K S I Q H L T I T E E I A V Q

9510 9520 9530 9540 9550 9560 9570 9580 9590 9600
AAACTGGTTAGCAAGAGTGGGCGCGAAAGGTTATCAAGAAATGGCCATCAGTGAGATGATTGTGTTGTGAAACCTTTAGATGACAGGTTTCGCAAGCGCT
N W L A R V G R E R L S R M A I S G D D C V V K P L D D R F A S A

9610 9620 9630 9640 9650 9660 9670 9680 9690 9700
TTAACAGCTCTAAATGACATGGGAAAGATTAGGAAAGACATACAACATGGGAACCTTCAAGAGGATGGAATGATTGGACACAAGTGCCCTTCTGTTCAC
L T A L N D M G K I R K D I Q Q W E P S R G W N D W T Q V P F C S H

9710 9720 9730 9740 9750 9760 9770 9780 9790 9800
ACCATTTCCATGAGTTAATCATGAAAGACGGTCGCGTACTCGTTGTTCCATGTAGAAACCAAGATGAACTGATTGGCAGAGCCCGAATCTCCCAAGGAGC
H F H E L I M K D G R V L V V P C R N Q D E L I G R A R I S Q G A

9810 9820 9830 9840 9850 9860 9870 9880 9890 9900
AGGGTGGTCTTTGCGGGAGACGGCCTGTTGGGGAAGTCTTACGCCCAATATGGAGCTTGATGTACTTCCACAGACGCGACCTCAGGCTGGCGGCAAAAT
G W S L R E T A C L G K S Y A Q M W S L M Y F H R R D L R L A A N

9910 9920 9930 9940 9950 9960 9970 9980 9990 10000
GCTATTTCGTCGAGTACCATCATGTTGGGTTCCAAAGTCGAACACCTGGTCCATACATGCTAAACATGAATGATGACAAAGGAGACATGCTGA
A I C S A V P S H W V P T S R T T W S I H A K H E W M T T E D M L T

10010 10020 10030 10040 10050 10060 10070 10080 10090 10100

CAGTCTGGAACAGGGTGTGGATTCAAGAAAACCCATGGATGGAAGACAAAACCTCCAGTGGGAATCATGGGAGGAAATCCCATACTTGGGGAAAAGAGAAGA
 V W N R V W I Q E N P W M E D K T P V E S W E E I P Y L G K R E D
 10110 10120 10130 10140 10150 10160 10170 10180 10190 10200
 CCAATGGTGCGGCTCATTGATTGGGTAAACAAGCAGGGCCACCTGGGCAAAGAACATCCAAGCAGCAATAAATCAAGTTAGATCCCTTATAGGCAATGAA
 Q W C G S L I G L T S R A T W A K N I Q A A I N Q V R S L I G N E
 >3'-Noncoding Region
 10210 10220 10230 10240 10250 10260 10270 10280 10290 10300
 GAATACACAGATTACATGCCATCCATGAAAAGATTGAGAAGAGAAGGAAGAAGCAGGAGTTCTGTGGTAGAAAGCAAACCTAACATGAAACAAGGCTA
 E Y T D Y M P S M K R F R R E E E E A G V L W *
 10310 10320 10330 10340 10350 10360 10370 10380 10390 10400
 GAAGTCAGGTCGGATTAAGCCATAGTACGGAATAAATATGCTACCTGTGAGCCCCGTCCAAGGACGTTAAAGAAGTCAGGCCATCATAAATGCCATAG
 10410 10420 10430 10440 10450 10460 10470 10480 10490 10500
 CTTGAGTAAACTATGCAGCCTGTAGCTCCACCTGAGAAGGTGTAAAAAATCCGGGAGGCCACAAACCATGGAAGCTGTACGCATGGCGTAGTGGACTAGC
 10510 10520 10530 10540 10550 10560 10570 10580 10590 10600
 GGTTAGAGGAGACCCCTCCCTTACAAATCGCAGCAACAATGGGGGCCAAGGCGAGATGAAGCTGTAGTCTCGCTGGAAGGACTAGAGGTTAGAGGAGAC
 10610 10620 10630 10640 10650 10660 10670 10680 10690 10700
 CCCCCGAAACAAAAACAGCATATTGACGCTGGGAAAGACCAGAGATCCTGCTGTCTCTCAGCATCATTCCAGGCACAGAACGCCAGAAAATGGAATG
 10710 10720
 GTGCTGTTGAATCAACAGGTTCT

DENVax-2 Master Virus Seed (MVS)

[000158] Nucleotide sequence of the recombinant viral genome and deduced amino acid sequence of the translated protein are provided herein. The engineered virus is based on D2 PDK-53 virus. All engineered substitutions that are different from wild-type DEN-2 16681 virus (also the parental virus for PDK-53), as well as extra mutations (changes from engineered cDNA clone) detected in the MVS are marked.

Substitutions Included in the Genome and Protein:

- [000159]** D2 PDK-53 virus backbone (change from wt D2 16681): all in bold
- 5'-noncoding region (NCR)-57 (nt-57 C-to-T): major attenuation locus (in red)
 - prM-29 Asp-to-Val (nt-524 A-to-T)
 - nt-2055 C-to-T (E gene) silent mutation
 - NS1-53 Gly-to-Asp (nt-2579 G-to-A): major attenuation locus (in red)
 - NS2A-181 Leu-to-Phe (nt-4018 C-to-T)
 - NS3-250 Glu-to-Val (nt-5270 A-to-T): major attenuation locus (in red)
 - nt-5547 (NS3 gene) T-to-C silent mutation
 - NS4A-75 Gly-to-Ala (nt-6599 G-to-C)

* nt-8571 C-to-T silent mutation of PDK-53 is not engineered in the vaccine virus

[000160] Engineered clone marker (silent mutation):

- nt-900 T-to-C silent mutation: infectious clone marker

[000161] Additional substitutions found in vaccine seed (0.02% nt different from original clone)

- prM-52 Lys-to-Glu (nt-592 A-to-G), in bold
- NS5-412 Ile-to-Val (nt-8803 A-to-G), in bold

NCR-57-P, D2 PDK-53 attenuation locus (wt D2 16681: C)
 >5'-NC 10 20 30 40 50 60 70 80 90 100 110 120 >C
 AGTTGTTAGTCTACGTGGACCGACAAAGACAGATTCTTTGAGGGAGCTAAGCTCAAAGTAGTTCTAACAGTTTTTAATTAGAGAGCAGATCTCTGATGAATAACCAACGGAAAAAGGCG
 M N N Q R K K A

130 140 150 160 170 180 190 200 210 220 230 240
AAAAACACGCTTTCAATATGCTGAAAACGCGAGAGAAAACCGCGTGTGCACTGTGCAACAGCTGACAAAGAGATTCTCACTTGAATGCTGCAGGGACGAGGACCATTAATACTGTTCAATG
K N T P F N M L K R E R N R V S T V Q Q L T K R F S L G M L Q G R G P L K L F M

250 260 270 280 290 300 310 320 330 340 350 360
GCCCTGGTGGCGTTCCTTCCTTTCTTAACAAATCCCACCAACAGCAGGGATATTGAAGAGATGGGGAACAATTAATAAATCAAAAGCTATTAATGTTTTGAGAGGGTTCAGGAAAGAGATT
A L V A F L R F L T I P P T A G I L K R W G T I K K S K A I N V L R G F R K E I

370 380 390 400 410 420 430 440 450 460 470 480
GGAAGGATGCTGAACATCTTGAATAGGAGACGAGATCTGCAGGCATGATCATTATGCTGATTCCAACAGTGTGGCGTTCCTATTAAACACACGTAAACGAGAGAACACACATGATCGTC
G R M L N I L N R R R R S A G M I I M L I P T V M A F H L T T R N G E P H M I V

490 500 510 520 530 540 550 560 570 580 590 600
AGCAGACAAGAGAAAGGAAAGTCTTCTGTTTAAAAACAGAGTTGGCGTGAACATGTTACCCCTGAGCCATGGACCTTGGTGAATTGTGTGAAGACACAATCAGTACGAGTGTCCC
S R Q E K G K S L L F K T E V G V N M C T L M A M D L G E L C E D T I T Y E C P

D2 PDK-53 specific prM-29 Val (wt D2 16681 Asp, nt-524-A) Additional prM-52 Lys-to-Glu mutation (nt-592 A-to-G)

610 620 630 640 650 660 670 680 690 700 710 720
CTTCTCAGGCAGAAATGAGCCAGAGACATAGACTGTTGGTGCAACTCTACGTCCACGTGGGTAACCTATGGGACGTGTACCACCATGGGAGAACATAGAGAGAAAAAGATCAGTGGCA
L L R Q N E P E D I D C W C N S T S T W V T Y G T C T T M G E H R R E K R S V A

730 740 750 760 770 780 790 800 810 820 830 840
CTCGTTCCACATGTGGGAATGGGACTGGAGACACGAACCTGAAACATGGATGTCTATCAGAGGGGCGCTGGAAACATGTCCAGAGAAATTGAAACTTGGATCTTGAGACATCCAGGCTTCACC
L V P H V G M G L E T R T E T W M S S E G A W K H V Q R I E T W I L R H P G F T

850 860 870 880 890 900 910 920 930 940 950 960
ATGATGCGCAATCCTGGCATACACCATAGGAAGACACATTTCGAAGAGCCCTGATCTTCATCTTACTGACAGCTGTCACTCCTTCAATGACAATGCGCTTGCATAGGAATGTCAAAT
M M A A I L A Y T I G T T H F Q R A L I F I L L T A V T P S M T M R C I G M S N

Engineered silent clone marker: nt-900 T-to-C silent mutation

970 980 990 1000 1010 1020 1030 1040 1050 1060 1070 1080
AGAGACTTTGTGGAAGGGGTTTCAGGAGGAAGCTGGGTTGACATAGTCTTAGAACATGGAAGCTGTGTGACGACGATGGCAAAAAACAAACCAACATTTGATTTTGAACATGATAAAAACA
R D F V E G V S G Q S W V D I V L E H G S C V T T M A K N K P T L D F E L I K T

1090 1100 1110 1120 1130 1140 1150 1160 1170 1180 1190 1200
GAAGCCAAACAGCCTGCCACCCTAAGGAAGTACTGTATAGAGGCAAGCTAACCAACACAACAACAGAAATCTCGCTGCCCAACACAAGGGGAACCCAGCCTAAATGAAGAGCAGGACAAA
E A K Q P A T L R K Y C I E A K L T N T T T E S R C P T Q G E P S L N E E Q D K

1210 1220 1230 1240 1250 1260 1270 1280 1290 1300 1310 1320
AGGTTCTGTGCAACACTCCATGTGTAGCAGAGATGGGAAATGGATGTGGACTATTTGGAAGGAGGCAATGTGACCTGTGTATGTTGAGATGCAAAAAAGAACATGGAAGGAAAA
R F V C K H S M V D R G W G N G C G L F G K G G I V T C A M F R C K K N M E G K

1330 1340 1350 1360 1370 1380 1390 1400 1410 1420 1430 1440
GTTGTGCAACCAAGAACTTGGAAATACACCATTTGTATAACCTCACTCAGGGGAGAGCATGCACTCGGAAATGACACAGGAAACATGGCAAGGAAATCAAAATACACCCACAGAGT
V V Q P E N L E Y T I V I T P H S G E E H A V G N D T G K H G K E I K I T P Q S

1450 1460 1470 1480 1490 1500 1510 1520 1530 1540 1550 1560
TCCATCACAGAAGCAAGATTGACAGGTTATGGCATGTGCACAATGGAGTGTCTCCAAAGAACGGGCTCGAATTCATGAGATGGTGTGCTGCAGATGGAAAAATAAGCTTGGCTGGTG
S I T E A E L T G Y G T V T M E C S P R T G L D F N E M V L L Q M E N K A W L V

1570 1580 1590 1600 1610 1620 1630 1640 1650 1660 1670 1680
CACAGGCAATGGTTCTAGACCTGGCGTTACCATGGTTGCGCGAGCGGACACACAAGAGGTCAAATTTGATACAGAAAGAGACATTGGTCACTTTCAAAATCCCATGCGAAGAAACAG
H R Q W F L D L P L P W L P G A D T Q G S N W I Q K E T L V T F K N P H A K K Q

1690 1700 1710 1720 1730 1740 1750 1760 1770 1780 1790 1800
GATGTTCTGTTTGGATCCCAAGAGGGGCCATGCACACAGCACTTACAGGGGCCACAGAAATCCAAATGTCATCAGGAAACTTACTCTTCACAGGACATCTCAAGTGCAGGCTGAGA
D V V L G S V E Q G A M H T A L T G A T E I Q M S S G N L L F T G H L K C R L R

1810 1820 1830 1840 1850 1860 1870 1880 1890 1900 1910 1920
ATGACAAGCTACAGCTCAAAGGAATGTCATCTATGTGCACAGGAAAGTTTAAAGTTGTGAAGGAAATAGCAGAAACACAACATGGAACAATAGTTATCAGAGTGCAATATGAAGGG
M D K L Q L K G M S Y S M C T G K F K V V K E I A E T Q H G T I V I R V Q Y E G

1930 1940 1950 1960 1970 1980 1990 2000 2010 2020 2030 2040
GACGGCTCTCATGCAAGATCCCTTTTGAGATAATGGATTGGAATAAGACATGTCTTAGTGCCTGATTACAGTCAACCCAATTTGTGACAGAAAAAGATAGCCCATCAACATAGAA
D G S P C K I P F E I M D L E K R H V L G R L I T V N P I V T E K D S P V N I E

2050 2060 2070 2080 2090 2100 2110 2120 2130 2140 2150 2160
GCAGAACTCCATTGGAGACAGCTACATCATAGGAGTAGAGCCGGGCAACTGAAGCTCAACTGGTTTAAAGAAAGGAAGTTCTATCGGCAAAATGTTGAGACAACATGAGGGGG
A E P P F G D S Y I I I G V E P G Q L K L N W F K K G S S I G Q M F E T T M R G

D2 PDK-53 nt-2055-T silent mutation (D2 16681: C)

2170 2180 2190 2200 2210 2220 2230 2240 2250 2260 2270 2280
GCGAAGAAATGGCCATTTTGGTGAACAGCGCTGGGATTTGGATCTCTGGGAGGAGTGTTCATCTATAGGAAAGGCTCTCCACCAAGTCTTTGGAGCAATCTATGGAGCTGCCTTC
A K R M A I L G D T A W D F G S L G G V F T S I G K A L H Q V F G A I Y G A A F

2290 2300 2310 2320 2330 2340 2350 2360 2370 2380 2390 2400
AGTGGGTTTTCATGACTATGAAAATCCTCATAGGAGTCAATTATCACATGGATAGGAATTCACGAGCACCTCACTGTCTGTGACACTAGTATTGGTGGAAATTTGTGACACTGTAT
S G V S W T M K I L I G V I I T W I G M N S R S T S L S V T L V L V G I V T L

>NS1

2410 2420 2430 2440 2450 2460 2470 2480 2490 2500 2510 2520
TTGGAGTCATGGTCCAGGCGGATAGTGGTGGCTGGGAAACAAAGAACTGAAATGTGGCAGTGGGATTTTCATCACAGACAACTGACACATGGAACAACATACAAAG
L G V M V Q A D S G C V V S W K N K E L K C G S G I F I T D N V H T W T E Q Y K

2530 2540 2550 2560 2570 2580 2590 2600 2610 2620 2630 2640

TTCCAACCAGAAATCCCCTTCAAACTAGCTTTCAGCTATCCAGAAAGCCCATTGAAGAGGACATTTTGTGGAATCCGCTCAGTAACAAGACTGGAGAATCTGATGTGGAAACAAATAACACCA
F Q P E S P S K L A S A I Q K A H E E E I C G I R S V T R L E N L M W K Q I T P

D2 PDK-53 NS1-53-~~Dep~~ attenuation locus (wt D2 16681: Gly, nt-2579-G)

2650 2660 2670 2680 2690 2700 2710 2720 2730 2740 2750 2760
GAATTGAATCACATTCTATCAGAAAATGAGGTGAAGTTAACTATTATGACAGGAGACATCAAGGAATCATGCAGGCAGGAAAACGATCTCTGGGCTCAGCCCACTGAGCTGAAGTAT
E L N H I L S E N E V K L T I M T G D I K G I M Q A G K R S L R P Q P T E L K Y

2770 2780 2790 2800 2810 2820 2830 2840 2850 2860 2870 2880
TCATGGAAAACATGGGGCAAGCAAAATGCTCTCTACAGAGTCTCATAACCAGACCTTTCTCATTGATGGCCCCGAAACAGCAGAATGCCCAACACAAATAGAGCTTGAATTGCTTG
S W K T W G K A K M L S T E S H N Q T F L I D G P E T A E C P N T N R A W N S L

2890 2900 2910 2920 2930 2940 2950 2960 2970 2980 2990 3000
GAAGTTGAAGACTATGGCTTTGAGTATTCAACCAATATATGGCTAAAATTGAAAGAAAAACAGGATGTATTCTGCGACTCAAAACTCATGTGAGCGGCATAAAAGACAAAGAGGCC
E V E D Y G F G V E T T N I W L K L K E K Q D V F C D S K L M S A A I K D N R A

3010 3020 3030 3040 3050 3060 3070 3080 3090 3100 3110 3120
GTCCATGCGATATGGTTTATGGATAGAAAGTCACTCAATGACACATGGAAGATAGAGAAAGCCCTTTTCATTGAAGTTAAAACTGCCACTGGCCAAAATCACACACCTCTGGAGC
V H A D M G Y W I E S A L N D T W K I E K A S F I E V K N C H W P K S H T L W S

3130 3140 3150 3160 3170 3180 3190 3200 3210 3220 3230 3240
AATGGAGTCTAGAAAGTATGATAATTCCAAAGAATCTCGCTGGACCTGCTCTCAACACAACTATAGACCAGGCTACCATAACAAATACAGGACCATGGCATCTAGTAAAGCTT
N G V L E S E M I I P K N L A G P V S Q H N Y R P G Y H T Q I T G P W H L G K L

3250 3260 3270 3280 3290 3300 3310 3320 3330 3340 3350 3360
GAGATGGACTTTGATTTCTGTGATGGAACAAACAGTGGTAGTACTGAGGACTGCGGAAATAGAGGACCCCTTTTGAGAACCACTGCTCTGGAAAACTCATAACAGAATGGTCTGC
E M D F D F C D G T T V V V T E D C G N R G P S L R T T T A S G K L I T E W C T

>NS2A

3370 3380 3390 3400 3410 3420 3430 3440 3450 3460 3470 3480
CGATCTTGACATTACCAACGCTAAGATACAGAGGTGAGGTGCTGTGTAAGGAGTGAATTCAGACCATTGAAGGAGAAAGAGAATTTGGTCAACTCCTTGGTCACAGTGGGA
R S C T L P P L R Y R G E D G C W Y G M E I R P L K E K E E N L V N S L V T A G

3490 3500 3510 3520 3530 3540 3550 3560 3570 3580 3590 3600
CATGGGCGGTGCAACATTTTCACTAGGAGTCTTGGGAATGGCATTTGTTCTCTGGAGGAATGCTTAGGACCCGAGTAGGAACGAAACATGCAATCTACTAGTTCAGTTCTTTTGTG
H G Q V D N F S L C V L G M A L F L E E M L R T R V G T K H A I L L V A V S F V

3610 3620 3630 3640 3650 3660 3670 3680 3690 3700 3710 3720
ACATTGATCACAGGGAACATGTCCCTTAGAGACCTGGGAAGAGTGTGGTTATGGTAGGCGCCACTATGACGGATGACATAGGTATGGCGTGACTTATCTTCCCTACTAGCAGCCTTC
T L I T G N M S F R D L G R V M V M V G A T M T D D I G M Q V T Y L A L L A A F

3730 3740 3750 3760 3770 3780 3790 3800 3810 3820 3830 3840
AAAGTCAGACCAACTTTTGCAGCTGGACTCTTGGAGAAAGTGTGACCTTCAAGGAATGTGATGATGACTACTAGGAATGTACTCTCTCCAGAGCACTACAGAGACCATTTCTT
K V R P T F A A G L L L R K L T S K E L M M T T I G I V L L S Q S T I P E T I L

3850 3860 3870 3880 3890 3900 3910 3920 3930 3940 3950 3960
GAGTTGACTGATGCGTTAGCCTTAGGCATGATGTCCTCAAAATGGTGAGAAATGGAAGATCAATTGGCAGTGACTATCATGGCTATCTTGTGCGTCCCAACGCAAGTATATTA
E L T D A L A L G M M V L K M V R N M E K Y Q L A V T I M A I L C V P N A V I L

3970 3980 3990 4000 4010 4020 4030 4040 4050 4060 4070 4080
CAAAACGATGGAAGTGAATTCACAAATATGGCAGTGGTGCTCGTTTCCCCTGTTCTTAACTCCCTCACAGCAAAAAACAGATTGGATACCATTTAGCATTCAGATCAAAAGTCTC
Q N A W K V S C T I L A V V S V S P L F L T S S Q Q K T D W I P L A L T I K G L

D2 PDK-53 specific NS2A-181-Phe (wt D2 16681: Leu, nt-4018-C)

>NS2B

4090 4100 4110 4120 4130 4140 4150 4160 4170 4180 4190 4200
AATCCAACAGCTATTTTCTAACAACCTCTCAAGAACAGCAAGAAAGGAGCTGGCCATTAATGAGGCTATCATGGCAGTGGGATGGTGAGCATTTTAGCCAGTTCTCTCTCAAAA
N P T A I F L T T S R T S K K R S W P L N E A I M A V G M V S I L A S S L L K

4210 4220 4230 4240 4250 4260 4270 4280 4290 4300 4310 4320
AATGATATTTCCATGACAGACCATTAGTGGCTGGAGGCTCTCACTGTGTGTCTAGTGTCTCACTGGACGATCGGCCGATTGGAACCTGGAGAGAGCAGCCGATGCAATGGGAAGAC
N D I P M T G P L V A G G L L T V C Y V L T G R S A D L E L E R A A D V K W E D

4330 4340 4350 4360 4370 4380 4390 4400 4410 4420 4430 4440
CAGGACAGATATCAGGAAGCAGTCCAATCTGTCAATAACAATATCAGAAGATGGTAGCATGTGCAATAAAAAATGAAGAGGAAGAACAAACACTGACCATACTCATTAGAACAGGATTG
Q A E I S G S S P I L S I T I S E D G S M S I K N E E E E Q T L T I L I R T G L

>NS3

4450 4460 4470 4480 4490 4500 4510 4520 4530 4540 4550 4560
CTGGTGATCTCAGGACTTTTCTGTATCAATACCAATCACGGCAGCAGCATGGTACCTGTGGGAAGTGAAGAAACAAACGGGCCGAGTATTGTGGGATGTTCTTCAACCCCAACCCATG
L V I S G L F P V S I P I T A A A W Y L W E V K K Q R A G V L W D V P S P P P M

4570 4580 4590 4600 4610 4620 4630 4640 4650 4660 4670 4680
GGAAAGGCTGAAGTGAAGATGAGCCCTATAGAATTAAAGCAAAAGGGATTCTTGGATATTTCCAGATCGGAGCCGAGTTTACAAAGAAGGAACATTCATCAATGTGGCATGTCA
G K A E L E D G A Y R I K Q K G I L G Y S Q I G A G V Y K E G T F H T M W H V T

4690 4700 4710 4720 4730 4740 4750 4760 4770 4780 4790 4800
CGTGGCCTGTTCTAATGCATAAAGGAAGAGGATTGAACCATCATGGGCGGAGTCAAGAAAGACCTAATATCATATGGAGGAGCTGGAAAGTTAGAGGAGAATGGAAAGGAAGGAA
R G A V L M H K G K R I E P S W A D V K K D L I S Y G G G W K L E G E W K E G E

4810 4820 4830 4840 4850 4860 4870 4880 4890 4900 4910 4920
GAAGTCCAGGTATGGCACTGGAGCTGGAAAAATCCAGAGCCGTCCAAACGAAACCTGCTTTTCAAAACCAACGCGGGAACATAGGTGTGTATCTCTGCACTTTTCTCTCGGA
E V Q V L A L E P Q K N P R A V Q T K P G L F K T N A G T I G A V S L D F S P G

4930 4940 4950 4960 4970 4980 4990 5000 5010 5020 5030 5040
ACGTCAAGATCTCCAATTATCGACAAAAAGGAAAGTTGGGTCTTTATGGTAATGGTGTGTTTACAGGAGTGGAGCATATGTGAGTGCTATAGCCCACTGAAAAAGCATTGAA
T S G S P I I D K K G K V V G L Y G N G V V T R S G A Y V S A I A Q T E K S I E

5050 5060 5070 5080 5090 5100 5110 5120 5130 5140 5150 5160
GACAAACCCAGAGATCGAAGATGACATTTTCCGAAAGAGAAGACTGACCATCATGGACCTCCACCCAGGAGCGGGAAGACGAAGAGATACCTTCCGGCCATAGTCAGAGAAGCTATAAAA
D N P E I E D D I F R K R R L T I M D L H P G A G K T K R Y L P A I V R E A I K

DE PDK-53 MS3-250-Vat attenuation locus (DE 15581: Glu, nt-5270-A)

D2 PDK-53 silent mutation nt-5547-C (D2 16681: T)

>NS4A

D2 PDK-53 specific NS4A-75-Ala (wt D2 16681: Gly, nt-6599-G)

>NS4B

>NS5

58

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E Y T D Y M P S M K R F R R E E E E A G V L W
10330      10340      10350      10360      10370      10380      10390      10400      10410      10420      10430      10440
CATAGTACGGAATACTATGCTACCTGTGAGCCCGTCCAAGGACGTTAAAGAAAGTCAGGCCATCATAAATGCCATAGCTTGAGTAAACTATGCAGCCTGTAGCTCCACCTGAGAAGG
10450      10460      10470      10480      10490      10500      10510      10520      10530      10540      10550      10560
TGTAATAAATCCGGGAGGCCACAAACCATGGAAGCTGTACGCATGGCGTAGTGGACTAGCGGTAGAGGAGACCCCTCCCTTACAAATCGCAGCAACAATGGGGGCCAAGCGAGATGA
10570      10580      10590      10600      10610      10620      10630      10640      10650      10660      10670      10680
AGCTGTAGTCTCGCTGGAAGGACTAGAGGTTAGAGGAGACCCCCCGAAACAAAAACAGCATATTGACGCTGGGAAAGACCAGAGATCCTGCTGCTCCTCAGCATCATTCAGGCACA
10690      10700      10710      10720
GAACGCCAGAAATGGAATGGTGTGTTGAATCAACAGTTCT

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DENVax-3 Master Virus Seed (MVS)

[000162] Nucleotide sequence of the chimeric viral genome and deduced amino acid sequence of the translated protein are provided herein. Most of the prM-E gene (nt-457 to -2373, underlined) is wild-type (wt) DEN-3 16562 virus-specific; the remaining nucleotide sequence is DEN-2 PDK-53 virus-specific. The E protein of DEN-3 virus has two fewer amino acids than the E protein of DEN-2. Therefore, nt position starting from NgoMIV is 6 nt less than the original DEN-2 PDK-53 nt position. All engineered substitutions differ from wt virus (DEN-3 16562 or DEN-2 16681), as well as extra mutations (changes from engineered cDNA clone) are marked.

Substitutions Included in the Genome and Proein:

[000163] Junction sites:

- MluI** (nt 451-456): engineered silent mutation, nt-453 A-to-G
- NgoMIV** (nt 2374-2379): engineered mutations, nt-2375/2376 TG-to-CC (resulted in E-480 Val-to-Ala change)

[000164] D2 PDK-53 virus backbone (change from wt D2 16681): in bold

- 5'-noncoding region(NCR)-57 (nt-57 C-to-T): major attenuation locus (in red)
- NS1-53 Gly-to-Asp (nt-2573 G-to-A): major attenuation locus (in red)
- NS2A-181 Leu-to-Phe (nt-4012 C-to-T)
- NS3-250 Glu-to-Val (nt-5264 A-to-T): major attenuation locus (in red)
- nt-5541 (NS3 gene) T-to-C silent mutation
- NS4A-75 Gly-to-Ala (nt-6593 G-to-C)

* nt-8565 C-to-T silent mutation of PDK-53 is not engineered in the vaccine virus

[000165] Engineered mutation in DEN-3 prM-E (change from wt D3 16562)

- Engineered nt-552 C-to-T silent mutation: clone marker
- Engineered E-345 His-to-Leu (nt-1970 A-to-T) for efficient replication in cultures

[000166] Additional substitutions found in vaccine seed (0.02% nt different from original clone)

- E-223 Thr-to-Ser mutation (nt-1603 A-to-T, in bold)
- nt-7620 A-to-G silent mutation (in bold)

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NCR-57-T, D2 PDK-53 attenuation locus (wt D2 16681:C)
> 5'-Noncoding Region      10      20      30      40      50      60      70      80      90     100
AGTTGTTAGTCTACGTGGACCGACAAAGACAGATTCTTTGAGGGAGCTAAGCTCAATGTAGTTCTAACAGTTTTTTAATTAGAGAGCAGATCTCTGATGA
M N

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110 120 130 140 150 160 170 180 190 200
 ATAACCAACGAAAAAGGCGAAAAACACGCCTTTCAATATGCTGAAACGCGAGAGAAACCGCGTGTGCACTGTGCAACAGCTGACAAAGAGATTCTCACT
 N Q R K K A K N T P F N M L K R E R N R V S T V Q Q L T K R F S L

210 220 230 240 250 260 270 280 290 300
 TGGAATGCTGCAGGGACGAGGACCATTAAACTGTTTCATGGCCCTGGTGGCGTTCTTCGTTTCTTAACAATCCCACCAACAGCAGGGATATTGAAGAGA
 G M L Q G R G P L K L F M A L V A F L R F L T I P P T A G I L K R

310 320 330 340 350 360 370 380 390 400
 TGGGGAACAATTAATAAATCAAAAGCTATTAATGTTTGTAGAGGGTTTCAGGAAAGAGATTGGAAGGATGCTGAACATCTTGAATAGGAGACGCAGATCTG
 W G T I K K S K A I N V L R G F R K E I G R M L N I L N R R R R S A

> prM Beginning of D3 16562 sequence
 410 420 430 440 450 460 470 480 490 500
 CAGGCATGATCATTATGCTGATTCCAACAGTGATGGCGTTCCATTTAACCAACCGCTGATGGAGAGCCGCGCATGATTGTGGGAAGAATGAAGAGAGAAA
 G M I I M L I P T V M A F H L T T R D G E P R M I V G K N E R G K

Engineered MluI splicing site (nt-453 A-to-G silent mutation)
 510 520 530 540 550 560 570 580 590 600
 ATCCCTACTTTTCAAGACAGCCTCTGGAATCAACATGTGCACACTCATAGCTATGGATCTGGGAGAGATGTGTGATGACACGGTCACCTACAAATGCCCC
 S L L F K T A S G I N M C T L I A M D L G E M C D D T V T Y K C P

Silent C-to-T nt mutation as clone marker
 610 620 630 640 650 660 670 680 690 700
 CACATTACCGAAGTGGAGCCTGAAGACATTGACTGCTGGTGCAACCTTACATCGACATGGGTGACTTATGGAACATGCAATCAAGCTGGAGAGCATAGAC
 H I T E V E P E D I D C W C N L T S T W V T Y G T C N Q A G E H R R

> M
 710 720 730 740 750 760 770 780 790 800
 GCGATAAGAGATCAGTGGCGTTAGCTCCCCATGTTGGCATGGGACTGGACACACGCACTCAAACCTGGATGTCGGCTGAAGGAGCTTGGAGACAAGTCGA
 D K R S V A L A P H V G M G L D T R T Q T W M S A E G A W R Q V E

810 820 830 840 850 860 870 880 890 900
 GAAGGTAGAGACATGGGCCCTTAGGCACCCAGGTTTACCATACTAGCCCTATTCTTGGCCATTACATAGGCACCTTCCTTGACCCAGAAAGTGGTTATT
 K V E T W A L R H P G F T I L A L F L A H Y I G T S L T Q K V V I

> E
 910 920 930 940 950 960 970 980 990 1000
 TTTATACTATTAATGCTGGTTACCCCATCCATGACAATGAGATGTGTAGGAGTAGGAAACAGAGATTTTGTGGAAGGCCTATCGGGAGCTACGTGGGTTG
 F I L L M L V T P S M T M R C V G V G N R D F V E G L S G A T W V D

1010 1020 1030 1040 1050 1060 1070 1080 1090 1100
 ACGTGGTGTCTGAGCACGGTGGGTGTGTGACTACCATGGCTAAGAAACAGCCACGCTGGACATAGAGCTTCAGAAGACCGAGGCCACCCAACCTGGCGAC
 V V L E H G G C V T T M A K N K P T L D I E L Q K T E A T Q L A T

1110 1120 1130 1140 1150 1160 1170 1180 1190 1200
 CCTAAGGAAGCTATGCATTGAGGGAATAATACCAACATAAACAACCGACTCAAGATGTCCCAAGGGGAAGCGATTTTACCTGAGGAGCAGGACCAG
 L R K L C I E G K I T N I T T D S R C P T Q G E A I L P E E Q D Q

1210 1220 1230 1240 1250 1260 1270 1280 1290 1300
 AACTACGTGTGTAAGCATACATACGTGGACAGAGGCTGGGGAACCGTTGTGGTTTGTGTTGGCAAGGGAAGCTTGGTGACATGCGCGAAATTTCAATGTT
 N Y V C K H T Y V D R G W G N G C G L F G K G S L V T C A K F Q C L

1310 1320 1330 1340 1350 1360 1370 1380 1390 1400
 TAGAATCAATAGAGGGAAGTGGTGCAACATGAGAACCTCAAATACACCGTCATCATCACAGTGACACAGGAGACCAACACCAGGTGGGAAATGAAAC
 E S I E G K V V Q H E N L K Y T V I I T V H T G D Q H Q V G N E T

1410 1420 1430 1440 1450 1460 1470 1480 1490 1500
 GCAGGGAGTACGCGCTGAGATAACACCCAGGCATCAACCGCTGAAGCCATTTTACCTGAATATGGAACCCCTCGGGCTAGAATGCTCACCACGGACAGGT
 Q G V T A E I T P Q A S T A E A I L P E Y G T L G L E C S P R T G

1510 1520 1530 1540 1550 1560 1570 1580 1590 1600
 TTGGATTTCAATGAAATGATCTCATTGACAAATGAAGAACAAAGCATGGATGGTACATAGACAATGGTTCTTTGACTTACCCCTACCATGGACATCAGGAG
 L D F N E M I S L T M K N K A W M V H R Q W F F D L P L P W T S G A

1610 1620 1630 1640 1650 1660 1670 1680 1690 1700
 CTTACGAGAAACACCAACTTGGAAACAGGAAAGAGCTTCTTGTGACATTTAAAAATGCACATGCAAAAAAGCAAGAGTAGTTGTTCTTGGATCACAGA
 S A E T P T W N R K E L L V T F K N A H A K K Q E V V V L G S Q E

Additional E-233 Thr-to-Ser mutation (wt D3 16562: nt-1603 A) in master and pre-master seed
 1710 1720 1730 1740 1750 1760 1770 1780 1790 1800
 GGGAGCAATGCATACAGCACTGACAGGAGCTACAGAGATCCAAACCTCAGGAGGCACAAGTATCTTTGCGGGGCACTTAAATGTAGACTCAAGATGGAC

G A M H T A L T G A T E I Q T S G G T S I F A G H L K C R L K M D

1810 1820 1830 1840 1850 1860 1870 1880 1890 1900
AAATTGGAAC TCAAGGGGATGAGCTATGCAATGTGCTTGAGTAGCTTTGTGTTGAAGAAAAGAGTCTCCGAAACGCAGCATGGGACAATACTCATTAAAGG
K L E L K G M S Y A M C L S S F V L K K E V S E T Q H G T I L I K V

1910 1920 1930 1940 1950 1960 1970 1980 1990 2000
TTGAGTACAAAGGGGAAGATGCACCCTGCAAGATTCTTTCTCCACGGAGGATGGACAAGGAAAAGCTCTCAATGGCAGACTGATCAGACCCAATCCAGT
E Y K G E D A P C K I P F S T E D G Q G K A L N G R L I T A N P V

Engineered E-345 His-to-Leu (wt D3 16562: nt-1970-A) for efficient growth

2010 2020 2030 2040 2050 2060 2070 2080 2090 2100
GGTGACCAAGAAGGAGGAGCCTGTCAACATTGAGGCTGAACCTCCTTTTGGAGAAAGTAACATAGTAATTGGAATTGGAGACAAAGCCCTGAAAATCAAC
V T K K E E P V N I E A E P P F G E S N I V I G I G D K A L K I N

2110 2120 2130 2140 2150 2160 2170 2180 2190 2200
TGGTACAAGAAGGGAAGCTCGATTGGGAAGATGTTTCGAGGCCACTGCCAGAGGTGCAAGGCGCATGGCCATCTTGGGAGACACAGCCTGGGACTTTGGAT
W Y K K G S S I G K M F E A T A R G A R R M A I L G D T A W D F G S

2210 2220 2230 2240 2250 2260 2270 2280 2290 2300
CAGTGGGTGGTGTTTTGAATTCTTAGGGAATGGTCCACCAATATTTGGGAGTGCTTACACAGCCCTATTGGTGGAGTCTCTGGATGATGAAAT
V G G V L N S L G K M V H Q I F G S A Y T A L F G G V S W M M K I

End of D3 16562 sequence

2310 2320 2330 2340 2350 2360 2370 2380 2390 2400
TGGAATAGGTGTCTCTTAACCTGGATAGGGTTGAACTCAAAAAATACTTCTATGTCATTTTCATGCATCGCGGCCCGGATTGTGACACTGTATTGGGA
G I G V L L T W I G L N S K N T S M S F S C I A A G I V T L Y L G

Engineered NgoMIV splicing site, E-480 Val-to-Ala (nt-2375/2376 TG-to-CC)

> NS1

2410 2420 2430 2440 2450 2460 2470 2480 2490 2500
GTCATGGTGCAGGCCGATAGTGGTTGCGTTGTGAGCTGGAAAAACAAAGAACTGAAATGTGGCAGTGGGATTTTCATCACAGACAACGTGCACACATGGA
V M V Q A D S G C V V S W K N K E L K C G S G I F I T D N V H T W T

2510 2520 2530 2540 2550 2560 2570 2580 2590 2600
CAGAAACAATACAAGTTCCAACAGAAATCCCCTTCAAACTAGCTTCAGCTATCCAGAAAGCCCATGAAGAGGACATTTGTGGAATCCGCTCAGTAACAAG
E Q Y K F Q P E S P S K L A S A I Q K A H E E E I C G I R S V T R

D2 PDK-53 NS1-53-Asp attenuation locus (wt D2 16581: Gly, nt-2573-3)

2610 2620 2630 2640 2650 2660 2670 2680 2690 2700
ACTGGAGAATCTGATGTGGAACAAATAACACCAGAATTGAATCACATTCTATCAGAAATGAGGTGAAGTTAACTATTATGACAGGAGACATCAAGGA
L E N L M W K Q I T P E L N H I L S E N E V K L T I M T G D I K G

2710 2720 2730 2740 2750 2760 2770 2780 2790 2800
ATCATGCAGGCAGGAAAACGATCTCTGCGGCTCAGCCCACTGAGCTGAAGTATTCATGGAACATGGGGCAAAGCAAAATGCTCTCTACAGAGTCTC
I M Q A G K R S L R P Q P T E L K Y S W K T W G K A K M L S T E S H

2810 2820 2830 2840 2850 2860 2870 2880 2890 2900
ATAACAGACCTTTCTCATTGATGGCCCCGAAACAGCAGAATGCCCCAACACAAATAGAGCTTGAATTCGTTGGAAGTTGAAGACTATGGCTTTGGAGT
N Q T F L I D G P E T A E C P N T N R A W N S L E V E D Y G F G V

2910 2920 2930 2940 2950 2960 2970 2980 2990 3000
ATTACACCACCAATATATGGCTAAAATGAAAGAAAAACAGGATGTATTCTGCGACTCAAAACTCATGTGAGCGGCCATAAAGACAACAGAGCCGTCAT
F T T N I W L K L K E K Q D V F C D S K L M S A A I K D N R A V H

3010 3020 3030 3040 3050 3060 3070 3080 3090 3100
GCCGATATGGGTTTATGGATAGAAAGTGCACCTCAATGACACATGGAAGATAGAGAAAGCCTTTTCATTGAAGTTAAAACTGCCACTGGCCAAAATCAC
A D M G Y W I E S A L N D T W K I E K A S F I E V K N C H W P K S H

3110 3120 3130 3140 3150 3160 3170 3180 3190 3200
ACACCCTCTGGAGCAATGGAGTGCTAGAAAGTGAGATGATAATTCCAAGAATCTCGCTGGACCACTGTCTCAACACAATATAGACCAGGCTACCATAC
T L W S N G V L E S E M I I P K N L A G P V S Q H N Y R P G Y H T

3210 3220 3230 3240 3250 3260 3270 3280 3290 3300
ACAAATAACAGGACCATGGCATCTAGGTAAGCTTGAGATGGACTTTGATTTCTGTGATGGAACAACAGTGGTAGTGACTGAGGACTGCCGAAATAGAGGA
Q I T G P W H L G K L E M D F D F C D G T T V V V T E D C G N R G

3310 3320 3330 3340 3350 3360 3370 3380 3390 3400
CCCTCTTTGAGAACAACTGCCTCTGGAAAACTCATAACAGAATGGTGTGCCGATCTTGACATTACCACCGCTAAGATACAGAGGTGAGGATGGGT
P S L R T T T A S G K L I T E W C C R S C T L P P L R Y R G E D G C

> NS2A

3410 3420 3430 3440 3450 3460 3470 3480 3490 3500

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

3510 3520 3530 3540 3550 3560 3570 3580 3590 3600
AGGAGTCTTGGGAATGGCATTGTTCTCTGGAGGAATGCTTAGGACCCGAGTAGGAACGAAACATGCAATACTACTAGTTGCAGTTTCTTTGTGACATTG
G V L G M A L F L E E M L R T R V G T K H A I L L V A V S F V T L

3610 3620 3630 3640 3650 3660 3670 3680 3690 3700
ATCACAGGGAACATGTCTTTAGAGACCTGGGAAGAGTGATGGTTATGGTAGGCGCCACTATGACGGATGACATAGGTATGGGCGTGACTTATCTTGCCCC
I T G N M S F R D L G R V M V M V G A T M T D D I G M G V T Y L A L

3710 3720 3730 3740 3750 3760 3770 3780 3790 3800
TACTAGCAGCCTTCAAAGTCAGACCAACTTTTGCAGCTGGACTACTCTTGAGAAAGCTGACCTCCAAGGAATTGATGATGACTACTATAGGAATTGTACT
L A A F K V R P T F A A G L L L R K L T S K E L M M T T I G I V L

3810 3820 3830 3840 3850 3860 3870 3880 3890 3900
CCTCTCCAGAGCACCATAACCAGAGACCATTCTTGAGTTGACTGATGCGTTAGCCTTAGGCATGATGGTCTCTCAAAATGGTGAGAAATATGGAAGATAT
L S Q S T I P E T I L E L T D A L A L G M M V L K M V R N M E K Y

3910 3920 3930 3940 3950 3960 3970 3980 3990 4000
CAATTGGCAGTGACTATCATGGCTATCTTGTCGTCCCAAACGCAGTGATATTACAAAACGCATGGAAAGTGAGTTGCACAATATTGGCAGTGGTGTCCG
Q L A V T I M A I L C V P N A V I L Q N A W K V S C T I L A V V S V

4010 4020 4030 4040 4050 4060 4070 4080 4090 4100
TTTCCCCACTGTTCTTAACATCCTCAGCAAAAAACAGATTGGATACCATTAGCATTGACGATCAAAGGTCTCAATCCAACAGCTATTTTCTAACAAC
S P L F L T S S Q Q K T D W I P L A L T I K G L N P T A I F L T T

|
D2 PDK-53 specific NS2A-181-Phe (wt D2 16681: Leu, nt-4012-C)

> NS2B

4110 4120 4130 4140 4150 4160 4170 4180 4190 4200
CCTCTCAAGAACCAGCAAGAAAAGGAGCTGGCCATTAAATGAGGCTATCATGGCAGTCGGGATGGTGAGCATTCTCTCTCAAAAAATGAT
L S R T S K K R S W P L N E A I M A V G M V S I L A S S L L K N D

4210 4220 4230 4240 4250 4260 4270 4280 4290 4300
ATTCCCATGACAGGACCATAGTGGCTGGAGGCTCCTCACTGTGTCTACGTGCTCACTGGACGATCGGCCGATTTGGAAGTGGAGAGAGCAGCCGATG
I P M T G P L V A G G L L T V C Y V L T G R S A D L E L E R A A D V

4310 4320 4330 4340 4350 4360 4370 4380 4390 4400
TCAAATGGGAAGACCAGGCAGAGATATCAGGAAGCAGTCCAATCCTGTCAATAACAATATCAGAAGATGGTAGCATGTCCGATAAAAAATGAAGAGGAAGA
K W E D Q A E I S G S S P I L S I T I S E D G S M S I K N E E E E

4410 4420 4430 4440 4450 4460 4470 4480 4490 4500
ACAAACACTGACCATACTCATTAGAACAGGATTGCTGGTGATCTCAGGACTTTTTCTGTATCAATACCAATCACGGCAGCAGCATGGTACCTGTGGGAA
Q T L T I L I R T G L L V I S G L F P V S I P I T A A A W Y L W E

> NS3

4510 4520 4530 4540 4550 4560 4570 4580 4590 4600
GTGAAGAAACAACGGGCGGAGTATGTGGGATGTTCTTCAACCCCAACCCATGGGAAAGGCTGAACCTGGAAGATGGAGCCTATAGAATTAAGCAAAAAG
V K K Q R A G V L W D V P S P P P M G K A E L E D G A Y R I K Q K G

4610 4620 4630 4640 4650 4660 4670 4680 4690 4700
GGATTCTTGATATTTCCAGATCGGAGCCGGAGTTTACAAAGAAGGAACATTCCATACAATGTGGCATGTACACGTGGCGCTGTTCTAATGCATAAAGG
I L G Y S Q I G A G V Y K E G T F H T M W H V T R G A V L M H K G

4710 4720 4730 4740 4750 4760 4770 4780 4790 4800
AAAGAGGATTGAACCATCATGGGCGGACGTCAAGAAAGACCTAATATCATATGGAGGAGGCTGGAAGTTAGAAGGAGAATGGAAGGAAGGAGAAGAAGTC
K R I E P S W A D V K K D L I S Y G G G W K L E G E W K E G E E V

4810 4820 4830 4840 4850 4860 4870 4880 4890 4900
CAGGTATTGGCACTGGAGCCTGGAAAAAATCCAAGAGCCGTCCAACGAAACCTGGTCTTTTCAAAACCAACGCCGGAACAATAGGTGCTGTATCTCTGG
Q V L A L E P G K N P R A V Q T K P G L F K T N A G T I G A V S L D

4910 4920 4930 4940 4950 4960 4970 4980 4990 5000
ACTTTTCTCTGGAACGTGAGGATCTCCAATTATCGACAAAAAGGAAGTTGTGGTCTTTATGGTAATGGTGTGTTACAAGGAGTGGAGCATATGT
F S P G T S G S P I I D K K G K V V G L Y G N G V V T R S G A Y V

5010 5020 5030 5040 5050 5060 5070 5080 5090 5100
GAGTGTATAGCCCAGACTGAAAAAAGCATTGAAGACAACCCAGAGATCGAAGATGACATTTTCCGAAAGAGAAGACTGACCATCATGGACCTCCACCCA
S A I A Q T E K S I E D N P E I E D D I F R K R R L T I M D L H P

5110 5120 5130 5140 5150 5160 5170 5180 5190 5200
GGAGCGGGAAGACGAAGAGATACCTTCCGGCCATAGTCAGAGAAGCTATAAAACGGGGTTTGAGAACATTAACTTGGCCCCCACTAGAGTTGTGGCAG
G A G K T K R Y L P A I V R E A I K R G L R T L I L A P T R V V A A

5210 5220 5230 5240 5250 5260 5270 5280 5290 5300
 CTGAAATGGAGGAAGCCCTTAGAGGACTTCCAATAAGATACCAGACCCAGCCATCAGAGCTGTCACACCGGGCGGGAGATTGTGGACCTAATGTGTCA
 E M E E A L R G L P I R Y Q T P A I R A V H T G R E I V D L M C H
 |
 D2 PDK-53 NS3-250-Val attenuation locus (D2 16681: Glu, nt-5270-A)

5310 5320 5330 5340 5350 5360 5370 5380 5390 5400
 TGCCACATTTACCATGAGGCTGCTATCACCAGTTAGAGTGCCAACTACAACCTGATTATCATGGACGAAGCCCATTTTCACAGACCCAGCAAGTATAGCA
 A T F T M R L L S P V R V P N Y N L I I M D E A H F T D P A S I A

5410 5420 5430 5440 5450 5460 5470 5480 5490 5500
 GCTAGAGGATACATCTCAACTCGAGTGGAGATGGGTGAGGCAGCTGGGATTTTATGACAGCCACTCCCCCGGAAGCAGAGACCCATTTCCTCAGAGCA
 A R G Y I S T R V E M G E A A G I F M T A T P P G S R D P F P Q S N

5510 5520 5530 5540 5550 5560 5570 5580 5590 5600
 ATGCACCAATCATAGATGAAGAAAGAGAAATCCCTGAACGCTCGTGGAAATCCCGACATGAATGGGTACGGATTTTAAAGGGAAGACTGTTTGGTTTCGT
 A P I I D E E R E I P E R S W N S G H E W V T D F K G K T V W F V
 |
 D2 PDK-53 silent mutation nt-5541-C (D2 16681: T)

5610 5620 5630 5640 5650 5660 5670 5680 5690 5700
 TCCAAGTATAAAGCAGGAAATGATATAGCAGCTTGCCTGAGGAAAAATGGAAGAAAGTGATACAACCTCAGTAGGAAGACCTTTGATTCTGAGTATGTC
 P S I K A G N D I A A C L R K N G K K V I Q L S R K T F D S E Y V

5710 5720 5730 5740 5750 5760 5770 5780 5790 5800
 AAGACTAGAACCAATGATTGGGACTTCTGTGTTTACAACCTGACATTTTCAAGAAATGGGTGCCAATTTCAAGGCTGAGAGGGTTATAGACCCAGACGCTGCA
 K T R T N D W D F V V T T D I S E M G A N F K A E R V I D P R R C M

5810 5820 5830 5840 5850 5860 5870 5880 5890 5900
 TGAAACCAAGTCACTAATAACAGATGGTGAAGAGCGGGTGATTCTGGCAGGACCTATGCCAGTGACCCACTCTAGTGACGACAAAGAAAGGGGAGAATAGG
 K P V I L T D G E E R V I L A G P M P V T H S S A A Q R R G R I G

5910 5920 5930 5940 5950 5960 5970 5980 5990 6000
 AAGAAATCCAAAAATGAGAATGACCAAGTACATATACATGGGGGAACCTCTGAAAAATGATGAAGACTGTGCACACTGGAAGAAAGCTAAAAATGCTCCTA
 R N P K N E N D Q Y I Y M G E P L E N D E D C A H W K E A K M L L

6010 6020 6030 6040 6050 6060 6070 6080 6090 6100
 GATAACATCAACACGCCAGAAGGAATCATTCTAGCATGTTTCAACACAGAGCGTGAAAGGTGGATGCCATTGATGGCGAATACCGCTTGAGAGGAGAAG
 D N I N T P E G I I P S M F E P E R E K V D A I D G E Y R L R G E A

6110 6120 6130 6140 6150 6160 6170 6180 6190 6200
 CAAGGAAAACCTTTGTAGACTTAATGAGAAGAGGAGACCTACCAAGTCTGGTTGGCTACAGAGTGGCAGCTGAAGGCATCAACTACGCGACAGAAAGGTG
 R K T F V D L M R R G D L P V W L A Y R V A A E G I N Y A D R R W

6210 6220 6230 6240 6250 6260 6270 6280 6290 6300
 GTGTTTGTGAGTCAAGAACAACCAATCCTAGAAGAAAACGTGGAAGTTGAAATCTGGACAAAAGAGGGGAAAGGAAGAAATTGAAACCCAGATGG
 C F D G V K N N Q I L E E N V E V E I W T K E G E R K K L K P R W

> NS4A

6310 6320 6330 6340 6350 6360 6370 6380 6390 6400
 TTGGATGCTAGGATCTATTCTGACCCACTGGCGCTAAAAGAATTTAAGGAATTTGAGCCGGAAGAAAGTCTCTGACCCCTGAACCTAATCACAGAAATGG
 L D A R I Y S D P L A L K E F K E F A A G R K S L T L N L I T E M G

6410 6420 6430 6440 6450 6460 6470 6480 6490 6500
 GTAGGCTCCCAACCTTCATGACTCAGAAGGCAAGAGACGCACTGGACAACCTAGCAGTGTGCACACGGCTGAGGCAGGTGGAAGGGCGTACAAACATGC
 R L P T F M T Q K A R D A L D N L A V L H T A E A G G R A Y N H A

6510 6520 6530 6540 6550 6560 6570 6580 6590 6600
 TCTCAGTGAACCTGCCGAGACCTGGAGACATTGCTTTTACTGACACTTCTGGCTACAGTCACGGGAGGGATCTTTTATCTTCTGATGAGCGCAAGGGGC
 L S E L P E T L E T L L L L T L L A T V T G G I F L F L M S A R G
 |
 D2 PDK-53 specific NS4A-75-Ala (wt D2 16681: Gly, nt-6599-G)

6610 6620 6630 6640 6650 6660 6670 6680 6690 6700
 ATAGGGAAGATGACCTGGGAATGTGCTGCATAATCAGCGCTAGCATCTCTATGGTACGCACAAATACAGCCACACTGGATAGCAGCTTCAATAATAC
 I G K M T L G M C C I I T A S I L L W Y A Q I Q P H W I A A S I I L

6710 6720 6730 6740 6750 6760 6770 6780 6790 6800
 TGGAGTTTTTCTCATAGTTTTGCTTATTCCAGAACCTGAAAAACAGAGAACACCCCAAGACAACTGACCTACGTTGTATAGCCATCTCAGAGT
 E F F L I V L L I P E P E K Q R T P Q D N Q L T Y V V I A I L T V

> NS4B

6810 6820 6830 6840 6850 6860 6870 6880 6890 6900
 GGTGGCCGCAACCATGGCAACGAGATGGGTTTCTAGAAAAACGAGAAAGATCTCGGATTGGGAAGCATTGCAACCCAGCAACCCGAGAGCAACATC
 V A A T M A N E M G F L E K T K K D L G L G S I A T Q Q P E S N I

6910 6920 6930 6940 6950 6960 6970 6980 6990 7000

CTGGACATAGATCTACGTCTGCATCAGCATGGACGCTGTATGCCGTGGCCACAACATTGTGTACACCAATGTTGAGACATAGCATTGAAAAATTCCTCAG
L D I D L R P A S A W T L Y A V A T T F V T P M L R H S I E N S S V

7010 7020 7030 7040 7050 7060 7070 7080 7090 7100
TGAATGTGTCCCTAACAGCTATAGCCAACCAAGCCACAGTGTAAATGGGTCTCGGGAAGGATGGCCATTGTCAAAGATGGACATCGGAGTTCCCTTCT
N V S L T A I A N Q A T V L M G L G K G W P L S K M D I G V P L L

7110 7120 7130 7140 7150 7160 7170 7180 7190 7200
CGCCATTGGATGCTACTCACAAGTCAACCCATAACTCTCACAGCAGCTCTTTCTTATTGGTAGCACATTATGCCATCATAGGGCCAGGACTCCAAGCA
A I G C Y S Q V N P I T L T A A L F L L V A H Y A I I G P G L Q A

7210 7220 7230 7240 7250 7260 7270 7280 7290 7300
AAAGCAACCAGAGAAAGCTCAGAAAAGAGCAGCGCGGCATCATGAAAAACCAACTGTCGATGGAATAACAGTGATTGACCTAGATCCAATACCTTATG
K A T R E A Q K R A A A G I M K N P T V D G I T V I D L D P I P Y D

7310 7320 7330 7340 7350 7360 7370 7380 7390 7400
ATCCAAAGTTTGAAGCAGTTGGGACAAGTAATGCTCTAGTCTCTGCGTGACTCAAGTATTGATGATGAGGACTACATGGGCTCTGTGTGAGGCTTT
P K F E K Q L G Q V M L L V L C V T Q V L M M R T T W A L C E A L

7410 7420 7430 7440 7450 7460 7470 7480 7490 7500
AACCTTAGCTACCGGGCCCATCTCCACATTGTGGGAAGGAAATCCAGGGAGGTTTGGAAACACTACCATTCGCGGTGTCAATGGCTAACATTTTGTAGAGG
T L A T G P I S T L W E G N P G R F W N T T I A V S M A N I F R G

> NS5

7510 7520 7530 7540 7550 7560 7570 7580 7590 7600
AGTTACTTGGCCGAGCTGGAAGTCTCTTTTCTATTATGAAGAACACAACCAACCAAGAGGGAAGTGGCAACATAGGAGAGACGTTGGAGAGAAAT
S Y L A G A G L L F S I M K N T T N T R R G T G N I G E T L G E K W

7610 7620 7630 7640 7650 7660 7670 7680 7690 7700
GGAAAGCCGATTGAACGCGTTGGGAAAAAGTGAATTCAGATCTACAAGAAAAGTGAATCCAGGAAGTGGATAGAACCCTTAGCAAAAGAGGCAATTAA
K S R L N A L G K S E F Q I Y K K S G I Q E V D R T L A K E G I K

Additional nt-7260 A-to-G silent mutation in master and pre-master seeds

7710 7720 7730 7740 7750 7760 7770 7780 7790 7800
AAGAGGAGAAACGACCATCACGCTGTGTCGCGAGGCTCAGCAAACTGAGATGGTTCGTTGAGAGAAACATGGTCACACCAGAAGGAAAGTAGTGGAC
R G E T D H H A V S R G S A K L R W F V E R N M V T P E G K V V D

7810 7820 7830 7840 7850 7860 7870 7880 7890 7900
CTCGTTGTGGCAGAGGAGGCTGGTCATACTATTGTGGAGGACTAAAGAATGTAAGAGAAGTCAAAGGCCTAACAAAAGAGGAGGACGAGACAGAAGAAC
L G C G R G G W S Y Y C G G L K N V R E V K G L T K G G P G H E E P

7910 7920 7930 7940 7950 7960 7970 7980 7990 8000
CCATCCCCATGTCAACATATGGGTGGAATCTAGTGCCTCTCAAAGTGGAGTTGACGTTTCTTTCATCCCGCCAGAAAAGTGTGACACATTATTGTGTGA
I P M S T Y G W N L V R L Q S G V D V F F I P P E K C D T L L C D

8010 8020 8030 8040 8050 8060 8070 8080 8090 8100
CATAGGGGAGTCATACCAAATCCACAGTGAAGCAGGACGAACACTCAGAGTCTTAACTTAGTAGAAAATTGGTTGAACAACAACACTCAATTTTGC
I G E S S P N P T V E A G R T L R V L N L V E N W L N N N T Q F C

8110 8120 8130 8140 8150 8160 8170 8180 8190 8200
ATAAAGGTTCTCAACCCATATATGCCCTCAGTCATAGAAAAAATGGAAGCACTACAAAGGAAATATGGAGGAGCCTTAGTGAGGAATCCACTCTCAGGAA
I K V L N P Y M P S V I E K M E A L Q R K Y G G A L V R N P L S R N

8210 8220 8230 8240 8250 8260 8270 8280 8290 8300
ACTCCACACATGAGATGTACTGGGTATCCAATGCTTCCGGGAACATAGTGTATCAGTGAACATGATTTCAGGATGTTGATCAACAGATTTACAATGAG
S T H E M Y W V S N A S G N I V S S V N M I S R M L I N R F T M R

8310 8320 8330 8340 8350 8360 8370 8380 8390 8400
ATACAAGAAAGCCACTTACGAGCCGGATGTTGACCTCGGAAGCGGAACCCGTAACATCGGGATTGAAAGTGAGATACCAAACTAGATATAATTGGGAAA
Y K K A T Y E P D V D L G S G T R N I G I E S E I P N L D I I G K

8410 8420 8430 8440 8450 8460 8470 8480 8490 8500
AGAATAGAAAAAATAAGCAAGAGCATGAACATCATGGCACTATGACCAAGACCACCCATACAAAACGTGGGCATACCATGGTAGCTATGAAACAAAAC
R I E K I K Q E H E T S W H Y D Q D H P Y K T W A Y H G S Y E T K Q

8510 8520 8530 8540 8550 8560 8570 8580 8590 8600
AGACTGGATCAGCATCATCCATGGTCAACGGAGTGGTCAGGCTGCTGACAAAACCTTGGGACGTCGTCCTCCCATGGTGACACAGATGGCAATGACAGACAC
T G S A S S M V N G V V R L L T K P W D V V P M V T Q M A M T D T

8610 8620 8630 8640 8650 8660 8670 8680 8690 8700
GACTCCATTGGACAACAGCGCGTTTTTAAAGAGAAAGTGGACACGAGAACCCAGAACCGAAAGGCACGAAGAACTAATGAAAATAACAGCAGAG
T P F G Q Q R V F K E K V D T R T Q E P K E G T K K L M K I T A E

8710 8720 8730 8740 8750 8760 8770 8780 8790 8800
TGGCTTTGGAAAGAAATTAGGGAAGAAAAAGACACCAGATGTGCACCAGAGAAGAAATCACAAGAAAGGTGAGAAGCAATGCAGCCTTGGGGGCCATAT
W L W K E L G K K K T P R M C T R E E F T R K V R S N A A L G A I F

8810 8820 8830 8840 8850 8860 8870 8880 8890 8900
TCACTGATGAGAACAAAGTGAAGTCGGCAGCTGAGGCTGTTGAAGATAGTAGGTTTTGGGAGCTGGTTGACAAGGAAAGGAATCTCCATCTTGAAGGAAA
T D E N K W K S A R E A V E D S R F W E L V D K E R N L H L E G K

8910 8920 8930 8940 8950 8960 8970 8980 8990 9000
GTGTGAAACATGTGTGTACAACATGATGGGAAAAAGAGAGAAGAAGCTAGGGGAATTTCGGCAAGGCAAAAGGCAGCAGAGCCATATGGTACATGTGGCTT
C E T C V Y N M M G K R E K K L G E F G K A K G S R A I W Y M W L

9010 9020 9030 9040 9050 9060 9070 9080 9090 9100
GGAGCACGCTTCTTAGAGTTTGAAGCCCTAGGATTCTTAAATGAAGATCACTGGTTCTCCAGAGAGAACTCCCTGAGTGGAGTGAAGGAGAAGGGCTGC
G A R F L E F E A L G F L N E D H W F S R E N S L S G V E G E G L H

9110 9120 9130 9140 9150 9160 9170 9180 9190 9200
ACAAGCTAGGTTACATTCTAAGAGACGTGAGCAAGAAAGAGGGAGGAGCAATGTATGCCGATGACACCGCAGGATGGGATACAAGAATCACACTAGAAGA
K L G Y I L R D V S K K E G G A M Y A D D T A G W D T R I T L E D

9210 9220 9230 9240 9250 9260 9270 9280 9290 9300
CCTAAAAATGAAGAAATGGTAACAAACCATGGAAGGAGAACACAGAACTAGCCGAGGCCATTTTCAAACCTAACGTACCAAAACAGGTGGTGGCT
L K N E E M V T N H M E G E H K K L A E A I F K L T Y Q N K V V R

9310 9320 9330 9340 9350 9360 9370 9380 9390 9400
GTGCAAGAGCAACACCAAGAGGCACAGTAATGGACATCATATCGAGAAGAGACCAAGAGGTAGTGGACAAGTTGGCACCTATGGACTCAATACCTTTCA
V Q R P T P R G T V M D I I S R R D Q R G S G Q V G T Y G L N T F T

9410 9420 9430 9440 9450 9460 9470 9480 9490 9500
CCAATATGGAAGCCCACTAATCAGACAGATGGAGGGAGAAGGAGTCTTTAAAGCATTGAGCACCTAACATCAGAGAAGAAATCGCTGTGCAAAACTG
N M E A Q L I R Q M E G E G V F K S I Q H L T I T E E I A V Q N W

9510 9520 9530 9540 9550 9560 9570 9580 9590 9600
GTTAGCAAGAGTGGGGCGCGAAGGTTATCAAGAATGGCCATCAGTGGAGATGATTGTGTGTGTGAAACCTTTAGATGACAGGTTGCGAAGCGCTTTAACA
L A R V G R E R L S R M A I S G D D C V V K P L D D R F A S A L T

9610 9620 9630 9640 9650 9660 9670 9680 9690 9700
GCTCTAAATGACATGGGAAAGATTAGGAAAGACATACAACAATGGGAACCTTCAAGAGGATGGAATGATTGGACACAAGTGCCCTTCTGTTTACACCATT
A L N D M G K I R K D I Q Q W E P S R G W N D W T Q V P F C S H H F

9710 9720 9730 9740 9750 9760 9770 9780 9790 9800
TCCATGAGTTAATCATGAAAGACGGTCGCGTACTCGTTGTTCCATGTAGAAACCAAGATGAAGTATTGGCAGAGCCCGAATCTCCCAAGGAGCAGGGTG
H E L I M K D G R V L V V P C R N Q D E L I G R A R I S Q G A G W

9810 9820 9830 9840 9850 9860 9870 9880 9890 9900
GTCTTTGCGGAGACGGCCTGTTTGGGGAAGTCTTACGCCCAAATGTGGAGCTTGATGTACTTCCACAGACGCGACCTCAGGCTGGCGGCAAATGCTATT
S L R E T A C L G K S Y A Q M W S L M Y F H R R D L R L A A N A I

9910 9920 9930 9940 9950 9960 9970 9980 9990 10000
TGCTCGGCAGTACCATCATATTGGGTTCCAACAAGTCGAACAACCTGGTCCATACATGCTAAACATGAATGGATGACAACGGAAGACATGCTGACAGTCT
C S A V P S H W V P T S R T T W S I H A K H E W M T T E D M L T V W

10010 10020 10030 10040 10050 10060 10070 10080 10090 10100
GGAACAGGGTGTGGATTCAAGAAAACCCATGGATGGAAGACAAAACCTCCAGTGAATCATGGGAGGAAATCCCATACTTGGGGAAGAGAAAGACCAATG
N R V W I Q E N P W M E D K T P V E S W E E I P Y L G K R E D Q W

10110 10120 10130 10140 10150 10160 10170 10180 10190 10200
GTGCGGCTCATTTGATTGGGTTAACAAGCAGGGCCACCTGGGCAAAGAACATCCAAGCAGCAATAAATCAAGTTAGATCCCTTATAGGCAATGAAGAATAC
C G S L I G L T S R A T W A K N I Q A A I N Q V R S L I G N E E Y

> 3'-Noncoding Region

10210 10220 10230 10240 10250 10260 10270 10280 10290 10300
ACAGATTACATGCCATCCATGAAAAGATTCAAGAAGAGAAGAGGAAGAGCAGGAGTTCTGTGGTAGAAAGCAAACTAACATGAAACAAGGCTAGAAGTC
T D Y M P S M K R F R R E E E E A G V L W *

10310 10320 10330 10340 10350 10360 10370 10380 10390 10400
AGGTCGGATTAAGCCATAGTACGGAAAAAATATGCTACCTGTGAGCCCCGTCCAAGGACGTTAAAAGAAGTCAGGCCATCATAAATGCCATAGCTTGAG

10410 10420 10430 10440 10450 10460 10470 10480 10490 10500
TAAACTATGCAGCCTGTAGCTCCACCTGAGAAGGTGTAAAAAATCCGGGAGGCCACAAACCATGGAAGCTGTACGCATGGCGTAGTGGACTAGCGGTTAG

10510 10520 10530 10540 10550 10560 10570 10580 10590 10600
AGGAGACCCCTCCCTTACAAATCGCAGCAACAATGGGGGCCCAAGGCGAGATGAAGCTGTAGTCTCGCTGGAAGGACTAGAGGTTAGAGGAGACCCCCC

10610 10620 10630 10640 10650 10660 10670 10680 10690 10700
GAAACAAAAAACAGCATATTGACGCTGGGAAAGACCAGAGATCCTGTGTCTCTCAGCATCATTCAGGCACAGAACGCCAGAAAATGGAATGGTGCTG

10710

TTGAATCAACAGGTTCT

DENVax-4 Master Virus Seed (MVS)

[000167] Nucleotide sequence of the chimeric viral genome and deduced amino acid sequence of the translated protein. Most of the prM-E gene (nt-457 to -2379, underlined) is wild-type (wt) DEN-4 1036 virus-specific; the remaining nucleotide sequence is DEN-2 PDK-53 virus-specific. All engineered substitutions differ from wt virus (DEN-3 16562 or DEN-2 16681), as well as extra mutations (changes from engineered cDNA clone) are marked.

Substitutions Included in the Genome and Protein:

[000168] Junction sites:

- MluI (nt 451-456): engineered silent mutation, nt-453 A-to-G
- NgoMIV (nt 2380-2385): engineered mutations, nt-2381/2382 TG-to-CC (resulted in E-482 Val-to-Ala change)

[000169] D2 PDK-53 virus backbone (change from wt D2 16681)

- 5'-noncoding region(NCR)-57 (nt-57 C-to-T): major attenuation locus (in red)
- NS1-53 Gly-to-Asp (nt-2579 G-to-A): major attenuation locus (in red)
- NS2A-181 Leu-to-Phe (nt-4018 C-to-T, in bold)
- NS3-250 Glu-to-Val (nt-5270 A-to-T): major attenuation locus (in red)
- nt-5547 (NS3 gene) T-to-C silent mutation (in bold)
- NS4A-75 Gly-to-Ala (nt-6599 G-to-C, in bold)

* nt-8571 C-to-T silent mutation of PDK-53 is not engineered in the vaccine virus

[000170] Engineered substitutions in cDNA clone

- Engineered C-100 Arg-to-Ser (nt-396 A-to-C): may improve viral replication in culture
- Engineered nt-1401 A-to-G silent mutation
- Engineered E-364 Ala-to-Val (nt-2027 C-to-T): may improve viral replication in culture
- Engineered E-447 Met-to-Leu (nt-2275 A-to-C): may improve viral replication in culture

[000171] Additional substitutions found in vaccine seed (0.06% nt different from original clone)

- nt-225 (C gene) A-to-T silent mutation (in bold)
- NS2A-66 Asp-to-Gly (nt-3674 A-to-G) mutation (in bold)
- NS2A-99 Lys-to-Lys/Arg mix (nt-3773 A-to-A/G mix, in bold)
- nt-5391 C-to-T (NS3 gene) silent mutation (in bold)
- NS4A-21 Ala-to-Val (nt-6437 C-to-T, in bold)
- nt-7026 T-to-C/T mix silent mutation (in bold)
- nt-9750 A-to-C silent mutation (in bold)

NCR-57-T, D2 PDK-53 attenuation locus (wt D2 16681: C)

> 5'-Noncoding Region

10	20	30	40	50	60	70	80	90	100
AGTTGTTAGTCTACGTGGACCGACAAAGACAGATTCTTTGAGGGAGCTAAGCTCAATGTAGTTCTAACAGTTTTTTAATTAGAGAGCAGATCTCTGATGA									
									M N
110	120	130	140	150	160	170	180	190	200

ATAACCAACGGAAAAAGGCGAAAAACACGCCTTTCAATATGCTGAAACGCGAGAGAAACCGCGTGTGCAACAGCTGACAAAGAGATTCTCACT
N Q R K K A K N T P F N M L K R E R N R V S T V Q Q L T K R F S L

210 220 230 240 250 260 270 280 290 300
TGGAATGCTGCAGGGACGAGGACCTTTAAACTGTTTCATGGCCCTGGTGGCGTTCCTTCGTTTCTTAACAATCCACCAACAGCAGGATATTGAAGAGA
G M L Q G R G P L K L F M A L V A F L R F L T I P P T A G I L K R

Additional nt-225 A-to-T silent mutation in master and pre-master seeds

310 320 330 340 350 360 370 380 390 400
TGGGGAACAATTAATAAATCAAAAGCTATTATGTTTGGAGGGGTTCAAGGAAAGAGATTGGAAGGATGCTGAACATCTTGAATAGGAGACGCAGCTCTG
W G T I K K S K A I N V L R G F R K E I G R M L N I L N R R R S S A

Engineered C-100 Arg-to-Ser (nt 396 A-to-C)

> prM Beginning of D4 1036 sequence
410 420 430 440 450 460 470 480 490 500
CAGGCATGATCATTATGCTGATTCCAACAGTGATGGCGTTCCATTTAACCAACGCGTGATGGCGAACCCCTCATGATAGTGGCAAAACATGAAAGGGGGAG
G M I I M L I P T V M A F H L T T R D G E P L M I V A K H E R G R

Engineered MluI splicing site (nt-453 A-to-G silent)

510 520 530 540 550 560 570 580 590 600
ACCTCTCTTGTTTAAGACAACAGAGGGGATCAACAAATGCACTCTCATTTGCCATGGACTTGGGTGAAATGTGTGAGGACACTGTACGTATAAATGCCCC
P L L F K T T E G I N K C T L I A M D L G E M C E D T V T Y K C P

610 620 630 640 650 660 670 680 690 700
TTACTGGTCAATACCGAACCTGAAGACATTGATTGCTGGTGCAATCTCACGTCTACCTGGGTCAATGATGAGGACATGACCCAGAGCGGAGAACGGAGAC
L L V N T E P E D I D C W C N L T S T W V M Y G T C T Q S G E R R R

> M

710 720 730 740 750 760 770 780 790 800
GAGAGAAGCGCTCAGTAGCTTTAACCACCATTCAGGAATGGGATTGGAACAAGAGCTGAGACATGGATGTCATCGGAAGGGGCTTGGAGCATGCTCA
E K R S V A L T P H S G M G L E T R A E T W M S S E G A W K H A Q

810 820 830 840 850 860 870 880 890 900
GAGAGTAGAGAGCTGGATACTCAGAAACCCAGGATTTCGCGCTCTTGGCAGGATTATGGCTTATATGATTGGGCAACAGGAATCCAGCGAACTGTCTTC
R V E S W I L R N P G F A L L A G F M A Y M I G Q T G I Q R T V F

> E

910 920 930 940 950 960 970 980 990 1000
TTTGTCTCAATGATGCTGGTCGCCCCATCCTACGGAATGCGATGCGTAGGAGTAGGAAACAGAGACTTTGTGGAAGGAGTCTCAGGTGGAGCATGGGTCG
F V L M M L V A P S Y G M R C V G V G N R D F V E G V S G G A W V D

1010 1020 1030 1040 1050 1060 1070 1080 1090 1100
ATCTGGTGCTAGAACATGGAGGATGCGTCACAACCATGGCCCAGGAAAAACCAACCTTGGATTTTGAAGTGAAGCAACAGCCAAGGAAGTGGCTCT
L V L E H G G C V T T M A Q G K P T L D F E L T K T T A K E V A L

1110 1120 1130 1140 1150 1160 1170 1180 1190 1200
GTTAAGAACCTATTGCATTGAAGCCTCAATATCAAAACATAACCAAGGCAACCAAGATGTCCAACGCAAGGAGAGCCTTATCTAAAGAGGAGAACAGACCA
L R T Y C I E A S I S N I T T A T R C P T Q G E P Y L K E E Q D Q

1210 1220 1230 1240 1250 1260 1270 1280 1290 1300
CAGTACATTTGCCGGAGAGATGTGGTAGACAGAGGGTGGGGCAATGGCTGTGGCTTGTGTTGAAAAGGAGGAGTGTGACATGTGGCAAGTTTTCATGTT
Q Y I C R R D V V D R G W G N G C G L F G K G G V V T C A K F S C S

1310 1320 1330 1340 1350 1360 1370 1380 1390 1400
CGGGGAAGATAACAGGCAATTTGGTCCAAATTGAGAACCTTGAATACACAGTGGTTGTAACAGTCCACAATGGAGACACCCATGCAGTAGGAAATGACAC
G K I T G N L V Q I E N L E Y T V V V T V H N G D T H A V G N D T

1410 1420 1430 1440 1450 1460 1470 1480 1490 1500
GTCCAATCATGGAGTTACAGCCACGATAACTCCAGGTCAACATCGGTGGAAGTCAAATTGCCGACTATGGAGAACTAACACTCGATTGTGAACCCAGG
S N H G V T A T I T P R S P S V E V K L P D Y G E L T L D C E P R

Silent nt-1401 A-to-G mutation in engineered clone

1510 1520 1530 1540 1550 1560 1570 1580 1590 1600
TCTGGAATTGACTTTAATGAGATGATTCTGATGAAAAAGAAAAAGCAATGGCTTGTGCATAAGCAATGGTTTGTGGATCTACCTCTACCATTGGACAG
S G I D F N E M I L M K M K K K T W L V H K Q W F L D L P L P W T A

1610 1620 1630 1640 1650 1660 1670 1680 1690 1700
CAGGAGCAGACACATCAGAGGTTCACTGGAATTACAAAGAGAGAAATGGTGACATTTAAGGTTCTCATGCCAAGAGACAGGATGTGACAGTGCTGGGATC
G A D T S E V H W N Y K E R M V T F K V P H A K R Q D V T V L G S

1710 1720 1730 1740 1750 1760 1770 1780 1790 1800
TCAGGAAGGAGCCATGCATTCTGCCCCGCTGGAGCCACAGAAGTGGACTCCGGTGATGGAATCACATGTTTGCAGGACATCTCAAGTGCAAAGTCCCGT
Q E G A M H S A L A G A T E V D S G D G N H M F A G H L K C K V R

1810 1820 1830 1840 1850 1860 1870 1880 1890 1900
 ATGGAGAAATTGAGAATCAAGGGAATGTCATACACGATGTGTTTCAGGAAAGTTCTCAATTGACAAAGAGATGGCAGAAACACAGCATGGGACAAACAGTGG
 M E K L R I K G M S Y T M C S G K F S I D K E M A E T Q H G T T V V

1910 1920 1930 1940 1950 1960 1970 1980 1990 2000
 TGAAAGTCAAGTATGAAGGTGCTGGAGCTCCGTGTAAAGTCCCATAGAGATAAGAGATGTGAACAAGGAAAAAGTGGTTGGGCGTATCATCTCATCCAC
 K V K Y E G A G A P C K V P I E I R D V N K E K V V G R I I S S T

2010 2020 2030 2040 2050 2060 2070 2080 2090 2100
 CCCTTTGGCTGAGAATACCAACAGTGTAAACCAACATAGAGTTAGAACCCCTTTGGGGACAGCTACATAGTGATAGGTGTTGGAAACAGTGCATTAACA
 P L A E N T N S V T N I E L E P P F G D S Y I V I G V G N S A L T

Engineered E-364 Ala-to-Val (nt-2027 C-to-T) to improve viral growth in culture

2110 2120 2130 2140 2150 2160 2170 2180 2190 2200
 CTCCATTGGTTTCAGGAAAGGAGTTCCATTGGCAAGATGTTTGAGTCCACATACAGAGGTGCAAAACGAATGGCCATTCTAGGTGAAACAGCTTGGGATT
 L H W F R K G S S I G K M F E S T Y R G A K R M A I L G E T A W D F

2210 2220 2230 2240 2250 2260 2270 2280 2290 2300
 TTGGTTCGGTTGGTGGACTGTTACATCATTGGGAAAGGCTGTGCACCAAGGTTTGGAAAGTGTGTATACAACCTGTTGGAGGAGTCTCATGGATGAT
 G S V G G L F T S L G K A V H Q V F G S V Y T T L F G G V S W M I

Engineered E-447 Met-to-Leu (nt-2275 A-to-C) mutation

2310 2320 2330 2340 2350 2360 2370 2380 2390 2400
 TAGAATCCTAATTGGGTTCTAGTGTGTGGATTGGCAGCAACTCAAGGAACACTTCAATGGCTATGACGTGCATAGCTGCCGGCATTGTGACACTGTAT
 R I L I G F L V L W I G T N S R N T S M A M T C I A A G I V T L Y

Engineered NgomIV splicing site, E-482 Val-to-Ala (nt-2381/2382 TG-to-CC)

> NS1

2410 2420 2430 2440 2450 2460 2470 2480 2490 2500
 TTGGGGTGCATGGTGCAGGCCGATAGTGGTTGCGTTGTGAGCTGGAACAAAGAACTGAAATGTGGCAGTGGGATTTTCATCAGACAAACGTCACACA
 L G V M V Q A D S G C V V S W K N K E L K C G S G I F I T D N V H T

2510 2520 2530 2540 2550 2560 2570 2580 2590 2600
 CATGGACAGAAACAATACAAGTTCCAACCAAGATCCCTTCAAACCTAGCTTCAAGCTATCCAGAAAGCCCATGAAGAGGACATTGTGGAATCCGCTCAGT
 W T E Q Y K F Q P E S P S K L A S A I Q K A H E E I C G I R S V

D2 PDR-53 NS1-53-Asp attenuation locus (wt D2 15681: Gly, nt-2579-G)

2610 2620 2630 2640 2650 2660 2670 2680 2690 2700
 AACAAGACTGGAGAATCTGATGTGGAACAAATAACACCAGAATTGAATCACATTCTATCAGAAATGAGGTGAAGTTAACTATTATGACAGGAGACATC
 T R L E N L M W K Q I T P E L N H I L S E N E V K L T I M T G D I

2710 2720 2730 2740 2750 2760 2770 2780 2790 2800
 AAAGGAATCATGCAGGCAGGAAACGATCTCTGCGGCCTCAGCCCACTGAGCTGAAGTATTTCATGGAAAACATGGGGCAAAGCAAAATGCTCTCTACAG
 K G I M Q A G K R S L R P Q P T E L K Y S W K T W G K A K M L S T E

2810 2820 2830 2840 2850 2860 2870 2880 2890 2900
 AGTCTCATAACCAGACCTTTCTCATTGATGGCCCCGAAACAGCAGAATGCCCAACACAAATAGAGCTTGAATTCGTTGGAAGTTGAAGACTATGGCTT
 S H N Q T F L I D G P E T A E C P N T N R A W N S L E V E D Y G F

2910 2920 2930 2940 2950 2960 2970 2980 2990 3000
 TGGAGTATTCACCACCAATATATGGCTAAAAATTGAAAGAAAAACAGGATGTATTCTGCGACTCAAAACTCATGTGAGCGGCCATAAAAGACAACAGAGCC
 G V F T T N I W L K L K E K Q D V F C D S K L M S A A I K D N R A

3010 3020 3030 3040 3050 3060 3070 3080 3090 3100
 GTCCATGCCGATATGGGTTATTGGATAGAAAAGTGCATCAATGACACATGGAAGATAGAGAAAGCCTCTTTTCATTGAAGTTAAAACTGCCACTGGCCAA
 V H A D M G Y W I E S A L N D T W K I E K A S F I E V K N C H W P K

3110 3120 3130 3140 3150 3160 3170 3180 3190 3200
 AATCACACACCTCTGGAGCAATGGAGTGCTAGAAAGTGAGATGATAATTCCAAGAAATCTCGCTGGACCACTGTCTCAACACAACATATAGACCAGGCTA
 S H T L W S N G V L E S E M I I P K N L A G P V S Q H N Y R P G Y

3210 3220 3230 3240 3250 3260 3270 3280 3290 3300
 CCATACACAAATAACAGGACCATGGCATCTAGTAAGCTTGAGATGGACTTTGATTCTGTGATGGAACAACAGTGGTAGTGACTGAGGACTGCGGAAAT
 H T Q I T G P W H L G K L E M D F D F C D G T T V V V T E D C G N

3310 3320 3330 3340 3350 3360 3370 3380 3390 3400
 AGAGGACCTCTTTGAGAACCAACCACTGCCTCTGGAACCACTCATAACAGAATGGTGTGCCGATCTGACATTACCAACCGCTAAGATACAGAGGTGAGG
 R G P S L R T T T A S G K L I T E W C C R S C T L P P L R Y R G E D

> NS2A

3410 3420 3430 3440 3450 3460 3470 3480 3490 3500

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

3510 3520 3530 3540 3550 3560 3570 3580 3590 3600
TTCACTAGGAGTCTTGGGAATGGCATTGTTCTCTGGAGGAATGCTTAGGACCCGAGTAGGAACGAAACATGCAATACTACTAGTTGCAGTTCTTTTGTG
S L G V L G M A L F L E E M L R T R V G T K H A I L L V A V S F V

3610 3620 3630 3640 3650 3660 3670 3680 3690 3700
ACATTGATCACAGGGAACATGTCCTTTAGAGACCTGGGAAGAGTGATGGTTATGGTAGGCCCACTATGACGGGTGACATAGGTATGGGCGTGACTTATC
T L I T G N M S F R D L G R V M V M V G A T M T G D I G M G V T Y L

Additional NS2A-66 Asp-to-Gly (nt-3674 A-to-G mutation) in master and pre-master seeds

3710 3720 3730 3740 3750 3760 3770 3780 3790 3800
TTGCCCTACTAGCAGCCTTCAAAGTCAGACCAACTTTTGCAGCTGGACTACTCTTGAGAAAGCTGACCTCCAGGGAATTGATGATGACTACTATAGGAAT
A L L A A F K V R P T F A A G L L R K L T S K E L M M T T I G I

Additional NS2A-99 K to R/K (mix) (nt-3773 A-to-G/A) mutation in master seed

3810 3820 3830 3840 3850 3860 3870 3880 3890 3900
TGTACTCCTCTCCAGAGCACCATACCAGAGACCATTCTTGAGTTGACTGATGCGTTAGCCTTAGGCATGATGGTCCTCAAAATGGTGAGAAATATGGAA
V L L S Q S T I P E T I L E L T D A L A L G M M V L K M V R N M E

3910 3920 3930 3940 3950 3960 3970 3980 3990 4000
AAGTATCAATTGGCAGTGACTATCATGGCTATCTTGTGCGTCCCAACGCAGTGATATTACAAAACGCATGGAAAGTGAGTTGCACAATATTGGCAGTGG
K Y Q L A V T I M A I L C V P N A V I L Q N A W K V S C T I L A V V

4010 4020 4030 4040 4050 4060 4070 4080 4090 4100
TGTCCTGTTCCCACTGTTCTTAACATCCTCACAGCAAAAAACAGATTGGATACCATTAGCATTGACGATCAAAGGTCTCAATCCAACAGCTATTTTCT
S V S P L F L T S S Q Q K T D W I P L A L T I K G L N P T A I F L

D2 PDK-53 specific NS2A-181-Phe (wt D2 16681: Leu, nt-4018-C)

> NS2B

4110 4120 4130 4140 4150 4160 4170 4180 4190 4200
AACAAACCTCTCAAGAACCAGCAAGAAAAGGAGCTGGCCATTAAATGAGGCTATCATGGCAGTCGGGATGGTGAGCATTTTAGCCAGTTCTCTCTAAAA
T T L S R T S K K R S W P L N E A I M A V G M V S I L A S S L L K

4210 4220 4230 4240 4250 4260 4270 4280 4290 4300
AATGATATTCCCATGACAGACCATTAGTGGCTGGAGGGCTCCTCACTGTGTGCTACGTGCTCACTGGACGATCGGCCGATTGGAACTGGAGAGAGCAG
N D I P M T G P L V A G G L L T V C Y V L T G R S A D L E L E R A A

4310 4320 4330 4340 4350 4360 4370 4380 4390 4400
CCGATGTCAAATGGGAAGACCAGGCAGAGATATCAGGAAGCAGTCCAATCCTGTCAATAACAATATCAGAAGATGGTAGCATGTCGATAAAAAATGAAGA
D V K W E D Q A E I S G S S P I L S I T I S E D G S M S I K N E E

4410 4420 4430 4440 4450 4460 4470 4480 4490 4500
GGAAGAACAAACACTGACCATACTATTAGAACAGGATTGCTGGTGATCTCAGGACTTTTCTGTATCAATACCAATCACGGCAGCAGCATGGTACCTG
E E Q T L T I L I R T G L L V I S G L F P V S I P I T A A A W Y L

> NS3

4510 4520 4530 4540 4550 4560 4570 4580 4590 4600
TGGGAAGTGAAGAAACAACGGCCGAGTATTGTGGGATGTTCTTACCCCCACCATGGGAAAGGCTGAACCTGGAAGATGGAGCCTATAGAATTAAGC
W E V K K Q R A G V L W D V P S P P P M G K A E L E D G A Y R I K Q

4610 4620 4630 4640 4650 4660 4670 4680 4690 4700
AAAAAGGGATTCTTGATATTCCAGATCGGAGCCGAGTTTACAAAGAAGGAACATTCCATACAATGTGGCATGTACACGTGGCGCTGTTCTAATGCA
K G I L G Y S Q I G A G V Y K E G T F H T M W H V T R G A V L M H

4710 4720 4730 4740 4750 4760 4770 4780 4790 4800
TAAAGGAAAGAGGATTGAACCATCATGGGCGGACGTCAAGAAAGACCTAATATCATATGGAGGAGGCTGGAAGTTAGAAGGAGAATGGAAGGAAGGAGAA
K G K R I E P S W A D V K K D L I S Y G G G W K L E G E W K E G E

4810 4820 4830 4840 4850 4860 4870 4880 4890 4900
GAAGTCCAGTATTGGCACTGGAGCCTGGAAAAATCCAAGAGCCGTCCAACGAAACCTGGTCTTTTCAAACCAACCCGGAACAATAGGTGCTGTAT
E V Q V L A L E P G K N P R A V Q T K P G L F K T N A G T I G A V S

4910 4920 4930 4940 4950 4960 4970 4980 4990 5000
CTCTGGACTTTTCTCTGGAACGTGAGATCTCCAATTATCGACAAAAAGGAAAAAGTTGTGGGTCTTTATGGTAATGGTGTGTACAGGAGTGGAGC
L D F S P G T S G S P I I D K K G K V V G L Y G N G V V T R S G A

5010 5020 5030 5040 5050 5060 5070 5080 5090 5100
ATATGTGAGTGCTATAGCCAGACTGAAAAAGCATTGAAGACACCCAGAGATCGAAGATGACATTTTCCGAAAGAGAAGACTGACCATCATGGACCTC
Y V S A I A Q T E K S I E D N P E I E D D I F R K R R L T I M D L

5110 5120 5130 5140 5150 5160 5170 5180 5190 5200
CACCCAGGACGGGAAAGACGAAGAGATACCTTCCGGCCATAGTCAGAGAAGCTATAAAACGGGGTTTGAGAACATTAATCTTGCCCCCTAGAGTTG
H P G A G K T K R Y L P A I V R E A I K R G L R T L I L A P T R V V

5210 5220 5230 5240 5250 5260 5270 5280 5290 5300
TGGCAGCTGAAATGGAGGAAGCCCTTAGAGGACTTCCAATAAGATACCGAGACCCAGCCATCAGAGCTGTGCACACCGGGCGGGAGATTGTGGACCTAAT
A A E M E E A L R G L P I R Y Q T P A I R A V H T G R E I V D L M

D2 PDK-53 NS3-250-Val attenuation locus (D2 16681: Glu, nt-5270-A)

5310 5320 5330 5340 5350 5360 5370 5380 5390 5400
GTGTCATGCCACATTTACCATGAGGCTGCTATCACCAGTTAGAGTGCCAACTACAACCTGATTATCATGGACGAAGCCATTTACAGATCCAGCAAGT
C H A T F T M R L L S P V R V P N Y N L I I M D E A H F T D P A S

Additional nt-5391 C-to-T silent mutation in mater and pre-master seeds

5410 5420 5430 5440 5450 5460 5470 5480 5490 5500
ATAGCAGCTAGAGGATACATCTCAACTCGAGTGGAGATGGGTGAGGCAGCTGGGATTTTATGACAGCCACTCCCCGGGAAGCAGAGACCCATTTCTCTC
I A A R G Y I S T R V E M G E A A G I F M T A T P P G S R D P F P Q

5510 5520 5530 5540 5550 5560 5570 5580 5590 5600
AGAGCAATGCACCAATCATAGATGAAGAAAGAGAAATCCCTGAACGCTCGTGGAATTCGGACATGAATGGGTCACGGATTTTAAAGGGAAGACTGTTTG
S N A P I I D E E R E I P E R S W N S G H E W V T D F K G K T V W

D2 PDK-53 specific silent mutation nt-5547-C (D2 16681: T)

5610 5620 5630 5640 5650 5660 5670 5680 5690 5700
GTTTCGTTCCAAGTATAAAAGCAGGAAATGATATAGCAGCTTGCCTGAGGAAAAATGGAAGAAAGTGATACAACCTCAGTAGGAAGACCTTTGATTTCTGAG
F V P S I K A G N D I A A C L R K N G K K V I Q L S R K T F D S E

5710 5720 5730 5740 5750 5760 5770 5780 5790 5800
TATGTCAAGACTAGAACCAATGATTGGGACTTCGTGGTTACAACCTGACATTTCAGAAATGGGTGCCAATTTCAAGGCTGAGAGGGTTATAGACCCAGAC
Y V K T R T N D W D F V V T T D I S E M G A N F K A E R V I D P R R

5810 5820 5830 5840 5850 5860 5870 5880 5890 5900
GCTGCATGAAACCACTACTACTAACAGATGGTGAAGAGCGGTGATTCTGGCAGGACCTATGCCAGTGACCCACTCTAGTGCAGCACAAAGAAGAGGGAG
C M K P V I L T D G E E R V I L A G P M P V T H S S A A Q R R G R

5910 5920 5930 5940 5950 5960 5970 5980 5990 6000
AATAGGAAGAAATCCAAAAATGAGAATGACCAGTACATATACATGGGGGAACCTCTGGAATAATGATGAAGACTGTGCACACTGGAAGAAAGCTAAAAATG
I G R N P K N E N D Q Y I Y M G E P L E N D E D C A H W K E A K M

6010 6020 6030 6040 6050 6060 6070 6080 6090 6100
CTCCTAGATAACATCAACACGCCAGAAGGAATCATTCTAGCATGTTTCAAGACAGAGCGTGAAAGGTGGATGCCATTGATGGCAGTAACCGCTTGAGAG
L L D N I N T P E G I I P S M F E P E R E K V D A I D G E Y R L R G

6110 6120 6130 6140 6150 6160 6170 6180 6190 6200
GAGAAGCAAGGAAACCTTTGTAGACTTAATGAGAAGAGGAGACCTACCACTGCTGGTGGCCTACAGAGTGGCAGCTGAAGGCATCAACTACGCAGACAG
E A R K T F V D L M R R G D L P V W L A Y R V A A E G I N Y A D R

6210 6220 6230 6240 6250 6260 6270 6280 6290 6300
AAGGTGGTGGTTTGTATGGAGTCAAGAACAACCAATCCTAGAAGAAAACGTGGAAGTTGAAATCTGGACAAAAGAAGGGGAAAGGAATGAAACCC
R W C F D G V K N N Q I L E E N V E V E I W T K E G E R K K L K P

> NS4A

6310 6320 6330 6340 6350 6360 6370 6380 6390 6400
AGATGGTTGGATGCTAGGATCTATTCTGACCCACTGGCGCTAAAAGAATTTAAGGAATTTGCAGCCGGAAGAAAGTCTCTGACCCTGAACCTAATCACAG
R W L D A R I Y S D P L A L K E F K E F A A G R K S L T L N L I T E

6410 6420 6430 6440 6450 6460 6470 6480 6490 6500
AAATGGGTAGGCTCCCAACCTTCATGACTCAGAAGGTAAGAGACGCACCTGGACAACCTTAGCAGTGCTGCACACGGCTGAGGCAGGTGGAAGGGCGTACAA
M G R L P T F M T Q K V R D A L D N L A V L H T A E A G G R A Y N

Additional NS4A-21 Ala-to-Val (nt-6437 C-to-T) mutation in mater and pre-master seeds

6510 6520 6530 6540 6550 6560 6570 6580 6590 6600
CCATGCTCTCAGTGAAGTCCCGAGACCTGGAGACATTGCTTTTACTGACACTTCTGGCTACAGTCACGGGAGGGATCTTTTATTCTTGATGAGCGCA
H A L S E L P E T L E T L L L L T L L A T V T G G I F L F L M S A

D2 PDK-53 specific NS4A-75-Ala (wt D2 16681: Gly, nt-6599-G)

6610 6620 6630 6640 6650 6660 6670 6680 6690 6700
AGGGGCATAGGGAAGATGACCCCTGGGAATGTGCTGCATAATCACGGCTAGCATCCTCCTATGGTACGCACAAATACAGCCACACTGGATAGCAGCTTCAA
R G I G K M T L G M C C I I T A S I L L W Y A Q I Q P H W I A A S I

6710 6720 6730 6740 6750 6760 6770 6780 6790 6800
TAATACTGGAGTTTTTCTCATAGTTTTGCTTATTCCAGAACCTGAAAAACAGAGAACACCCCAAGACAACCAACTGACCTACGTTGTCATAGCCATCCT

I L E F F L I V L L I P E P E K Q R T P Q D N Q L T Y V V I A I L

> NS4B

6810 6820 6830 6840 6850 6860 6870 6880 6890 6900
CACAGTGGTGGCCGCAACCATGGCAAACGAGATGGGTTTCCTAGAAAAACGAAGAAAGATCTCGGATTGGGAAGCATTGCAACCCAGCAACCCGAGAGC
T V V A A T M A N E M G F L E K T K D L G L G S I A T Q Q P E S

6910 6920 6930 6940 6950 6960 6970 6980 6990 7000
AACATCCTGGACATAGATCTACGTCTGCATCAGCATGGACGCTGTATGCCGTGGCCACAACATTGTTACACCAATGTTGAGACATAGCATTGAAAATT
N I L D I D L R P A S A W T L Y A V A T T F V T P M L R H S I E N S

7010 7020 7030 7040 7050 7060 7070 7080 7090 7100
CCTCAGTGAATGTGTCCCTAACAGCCATAGCCAACCAAGCCACAGTGTTAATGGGTCTCGGGAAAGGATGGCCATTGTCAAAGATGGACATCGGAGATTCC
S V N V S L T A I A N Q A T V L M G L G K G W P L S K M D I G V P

Additional nt-7026 T-to-C/T mix silent mutation in master and pre-master seeds

7110 7120 7130 7140 7150 7160 7170 7180 7190 7200
CCTTCTCGCCATTGGATGCTACTCACAAGTCAACCCATAACTCTCACAGCAGCTCTTTTCTTATTGGTAGCACATTATGCCATCATAGGCCAGGACTC
L L A I G C Y S Q V N P I T L T A A L F L L V A H Y A I I G P G L

7210 7220 7230 7240 7250 7260 7270 7280 7290 7300
CAAGCAAAAGCAACCGAGAGAGCTCAGAAAAGAGCAGCGGCGGCATCATGAAAAACCAACTGTCGATGGAATAACAGTGATTGACCTAGATCCAATAC
Q A K A T R E A Q K R A A A G I M K N P T V D G I T V I D L D P I P

7310 7320 7330 7340 7350 7360 7370 7380 7390 7400
CTTATGATCCAAAGTTTGAAGCAGTTGGGACAAGTAATGCTCTAGTCTCTGCGTGACTCAAGTATTGATGATGAGGACTACATGGGCTCTGTGTGA
Y D P K F E K Q L G Q V M L L V L C V T Q V L M M R T T W A L C E

7410 7420 7430 7440 7450 7460 7470 7480 7490 7500
GGCTTTAACCTTAGCTACCGGGCCCATCTCCACATTGTGGGAAGGAAATCCAGGGAGGTTTTGGAACTACTACCATTCGCGGTGTCATGGCTAACATTTTT
A L T L A T G P I S T L W E G N P G R F W N T T I A V S M A N I F

> NS5

7510 7520 7530 7540 7550 7560 7570 7580 7590 7600
AGAGGGAGTTACTTGGCCGAGCTGGACTTCTCTTTTCTATTATGAAGAACAACCAACACAAGAAGGGGAAGTGGCAACATAGGAGAGACGCTTGGAG
R G S Y L A G A G L L F S I M K N T T N T R R G T G N I G E T L G E

7610 7620 7630 7640 7650 7660 7670 7680 7690 7700
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|

Additional nt-9750 A-to-C silent mutation in master and pre-master seeds

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> 3'-Noncoding Region

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10310 10320 10330 10340 10350 10360 10370 10380 10390 10400
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10710 10720
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[000172] Throughout this specification and the claims which follow, unless the context requires otherwise, the word “comprise”, and variations such as “comprises” and “comprising”, will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

[000173] The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A pharmaceutical composition comprising at least one nucleic acid chimera comprising a nucleic acid sequence encoding a polypeptide comprising a dengue-1/dengue-2 chimera comprising a nucleic acid sequence represented by SEQ ID NO: 1 (Pre-master), SEQ ID NO: 3 (MVS), SEQ ID NO: 5 (WVS), SEQ ID NO: 7 (BVS) or a combination thereof, and a pharmaceutically acceptable excipient.
2. Use of the composition according to claim 1 in the manufacture of a vaccine for inducing an immune response to dengue virus in a subject.
3. A pharmaceutical composition comprising at least one nucleic acid sequence comprising a nucleic acid sequence encoding a modified live, attenuated dengue-2 virus comprising a nucleic acid sequence represented by SEQ ID NO: 9 (Pre-master), SEQ ID NO: 11 (MVS), SEQ ID NO: 13 (WVS), SEQ ID NO: 15 (BVS) or a combination thereof, and a pharmaceutically acceptable excipient.
4. A pharmaceutical composition comprising at least one polypeptide molecule encoded by a nucleic acid sequence encoding a live, attenuated dengue-2 virus comprising the polypeptide molecule represented by SEQ ID NO: 10 (Pre-master), SEQ ID NO: 12 (MVS), SEQ ID NO: 14 (WVS), SEQ ID NO: 16 (BVS) or a combination thereof, and a pharmaceutically acceptable excipient.
5. Use of the composition according to claim 3 or claim 4 in the manufacture of a vaccine for inducing an immune response to dengue virus in a subject.
6. A vector encoding a nucleic acid sequence represented by SEQ ID NO: 9 (Pre-master), SEQ ID NO: 11 (MVS), SEQ ID NO: 13 (WVS), SEQ ID NO: 15 (BVS) or a combination thereof.

7. A pharmaceutical composition comprising at least one nucleic acid chimera comprising a nucleic acid sequence encoding a polypeptide comprising a dengue-3/dengue-2 chimera comprising a nucleic acid sequence represented by SEQ ID NO: 17 (Pre-master), SEQ ID NO: 19 (MVS), SEQ ID NO: 21 (WVS), SEQ ID NO: 23 (BVS) or a combination thereof, and a pharmaceutically acceptable excipient.
8. Use of the composition according to claim 7 in the manufacture of a vaccine for inducing an immune response to dengue virus in a subject.
9. A pharmaceutical composition comprising at least one nucleic acid chimera comprising a nucleic acid sequence encoding a polypeptide- comprising a dengue-4/dengue-2 chimera comprising a nucleic acid sequence represented by SEQ ID NO: 25 (Pre-master), SEQ ID NO: 27 (MVS), SEQ ID NO: 29 (WVS), SEQ ID NO: 31 (BVS) or a combination thereof, and a pharmaceutically acceptable excipient.
10. Use of the composition according to claim 9 in the manufacture of a vaccine for inducing an immune response to dengue virus in a subject.
11. A method of inducing an immune response to dengue virus in a subject, comprising administering the composition according to any one of claims 1, 3, 4, 7 and 9 to the subject.
12. An immunogenic composition comprising one or more, live, attenuated dengue viruses having a nucleotide sequence encoding a dengue virus or dengue virus chimera represented by SEQ ID NOs: 1, 3, 5, or 7 for a dengue-1/dengue-2 chimera; SEQ ID NOs: 9, 11, 13, or 15 for a live, attenuated dengue-2 virus; SEQ ID NOs: 17, 19, 21, or 23 for a dengue-3/dengue-2 chimera; and SEQ ID NOs: 25, 27, 29 or 31 for a dengue-4/dengue-2 chimera; and a pharmaceutically acceptable carrier, wherein the composition contains at least one, live attenuated virus that represents each of the four dengue virus serotypes, a tetravalent composition.

13. The immunogenic composition of claim 12, wherein the live, attenuated dengue-2 virus is represented by the nucleic acid sequence of SEQ ID NO: 11.
14. The immunogenic composition of claim 12 or claim 13, further comprising an immunogenic composition comprising a flavivirus selected from the group consisting of yellow fever virus, tick-borne encephalitis virus, Japanese encephalitis virus, West Nile virus, hepatitis C virus, and a combination of two or more thereof.
15. A kit comprising at least one composition according to any one of claims 1, 3, 4, 7, 9, and 12-14; and a container.
16. The composition according to any one of claims 1, 3, 4, 7, 9, and 12-14, further comprising a pharmaceutically acceptable adjuvant.
17. A nucleic acid dengue-1 chimera comprising nucleic acid sequences represented by SEQ ID NO: 7 encoding a mixture of species containing nucleotides C and G at nucleotide position 2384 which encode a mixture of dengue viral species containing amino acids Gly and Ala at amino acid 483.
18. A dengue-2 nucleic acid sequence comprising nucleic acid sequences represented by SEQ ID NO:13 encoding a mixture of species containing nucleotides G and C at nucleotide position 6481 which encode a mixture of dengue viral species containing amino acids Ala and Pro in NS4A-36.
19. A dengue-2 nucleic acid sequence comprising nucleic acid sequences represented by SEQ ID NO: 13 encoding a mixture of species containing nucleotides C and T at nucleotide position 7156 which encode a mixture of dengue viral species containing Leu and Phe in NS4B-111.

20. A nucleic acid dengue 4 chimera comprising nucleic acid sequences represented by SEQ ID NO: 29 encoding a mixture of species containing nucleotides C and T at nucleotide position 7538 which encode a mixture of dengue viral species containing Ser and Phe in NS4B-238.
21. A nucleic acid dengue 4 chimera comprising nucleic acid sequences represented by SEQ ID NO: 29 encoding a mixture of species containing nucleotides A and G at nucleotide position 3773 which encode a mixture of dengue viral species containing Lys and Arg in NS2A-99.

Genetic variations among D2/4 chimeras (compared to wt D2 16681 and D4-1036)

the *hpa* gene at nt 15681 or nt 15686, resulting in open reading frames of 123 and 124 amino acids, respectively. The amino acid sequence of the 123 aa protein was identical to the 124 aa protein, except for the substitution of a serine for a leucine at position 123.

[illegible]

engaged in the study.

NO. 176797 (2074-54)

Fig. 2

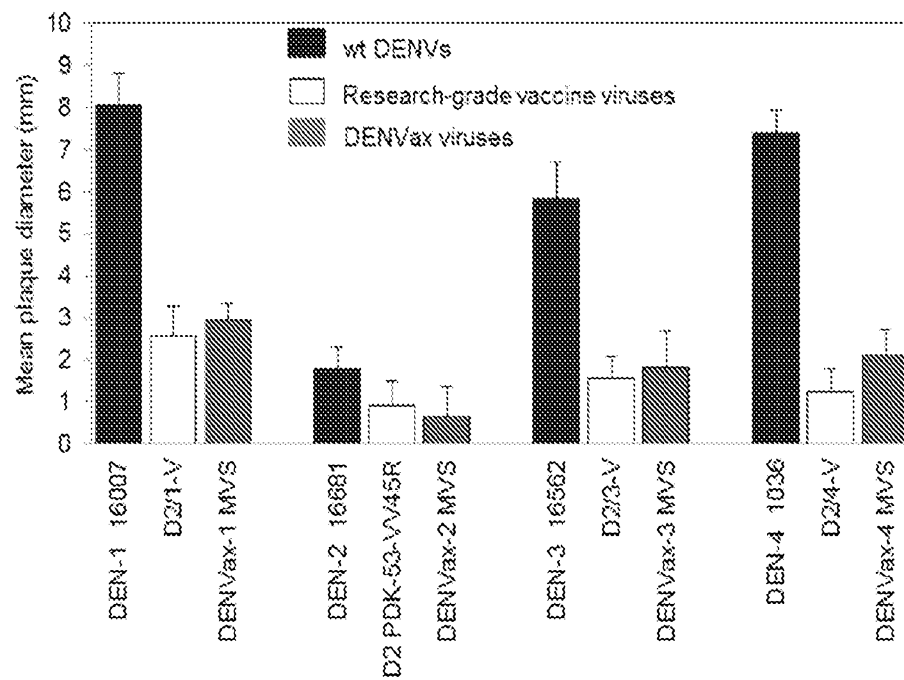


Fig. 3

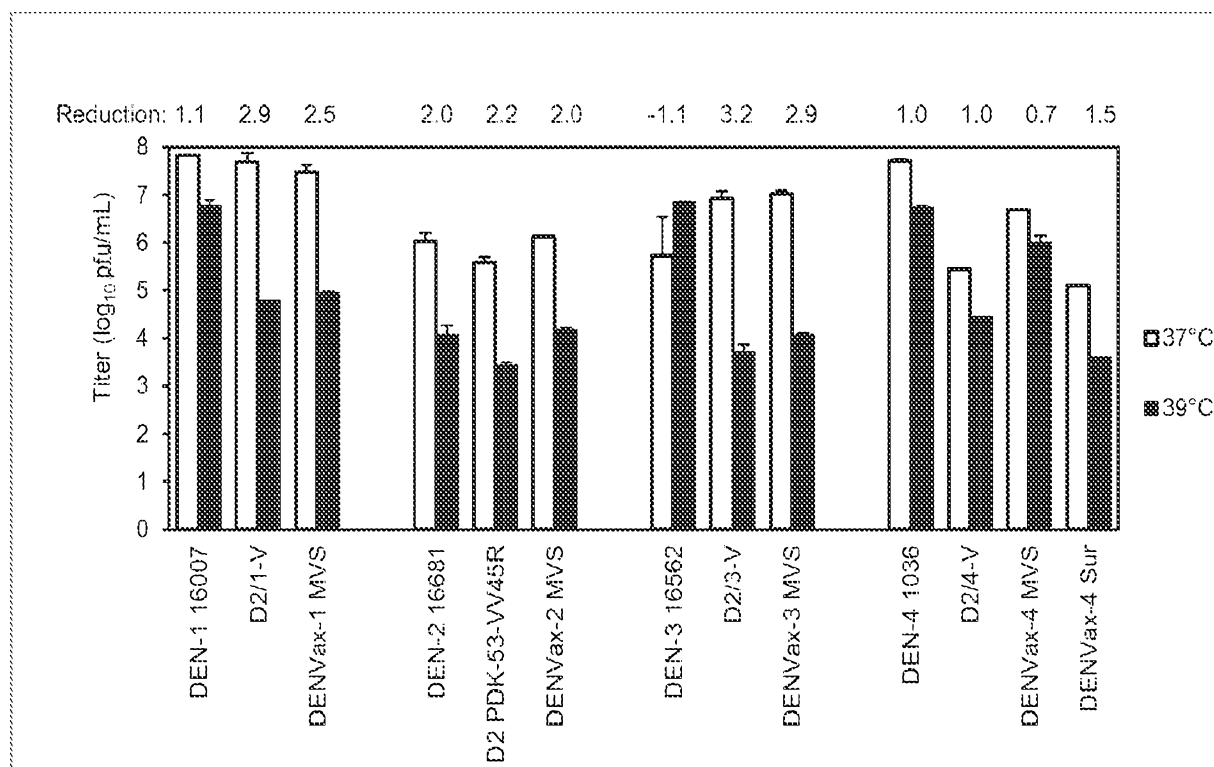


Fig. 4

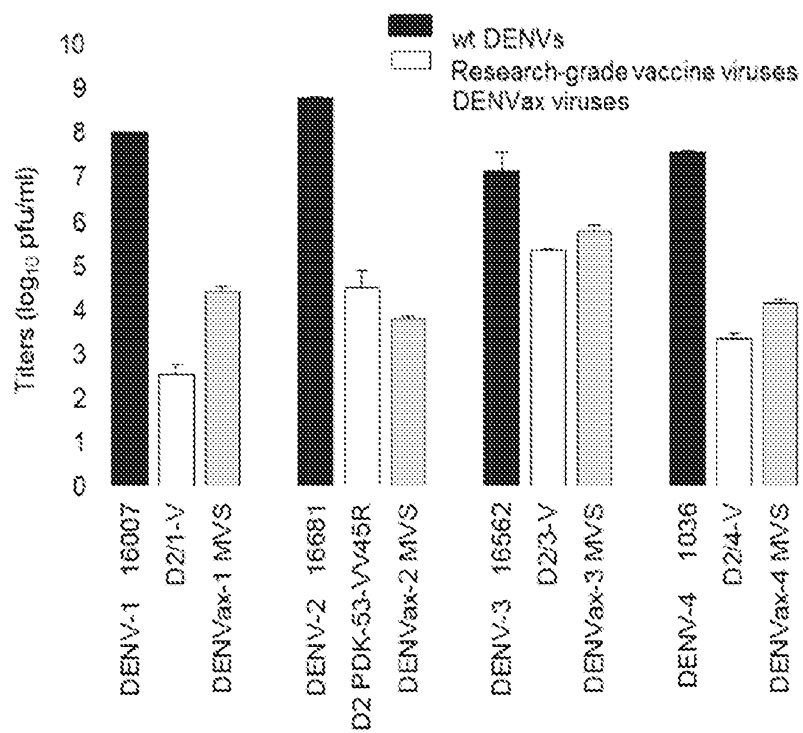


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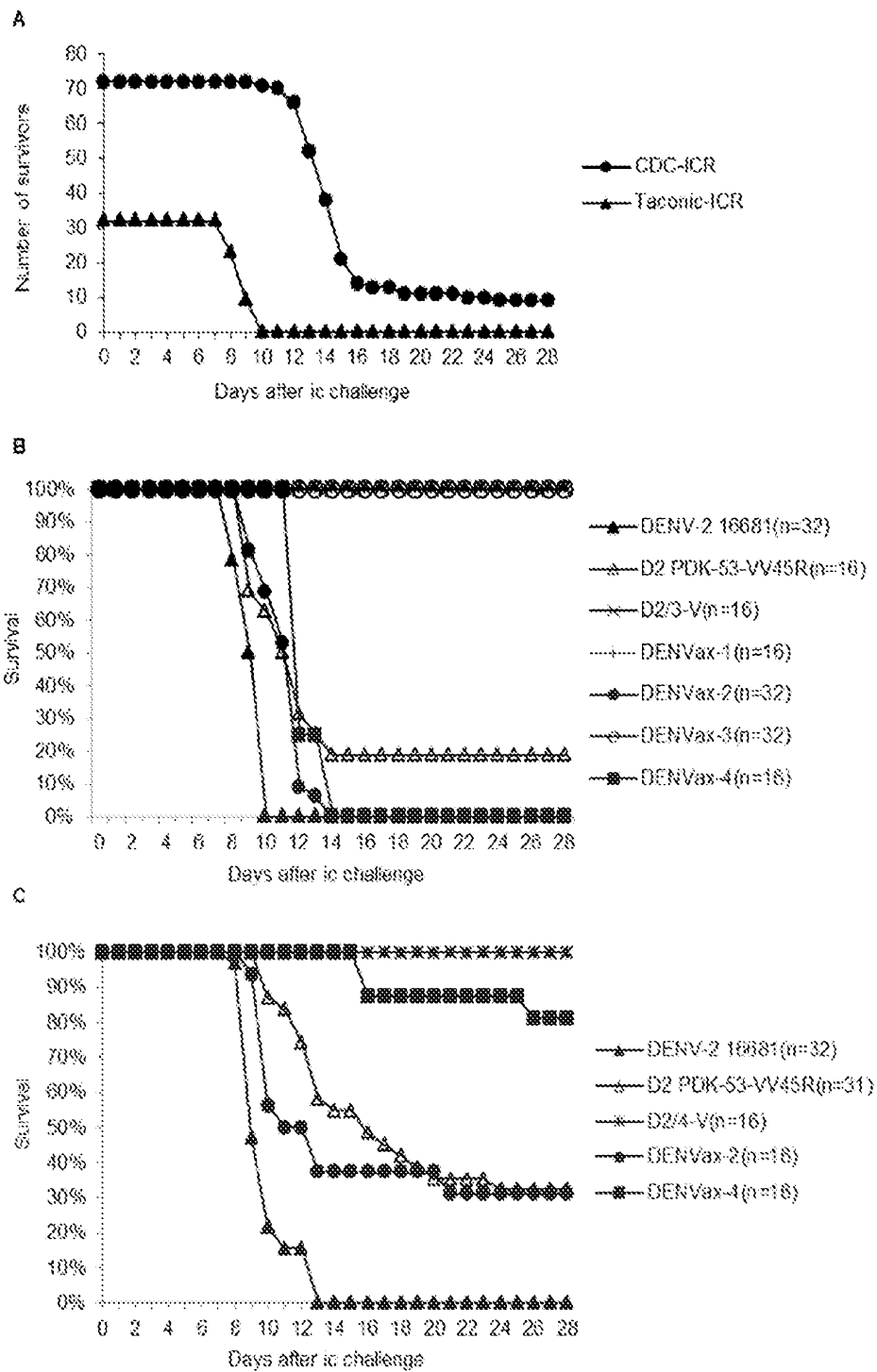


Fig. 6

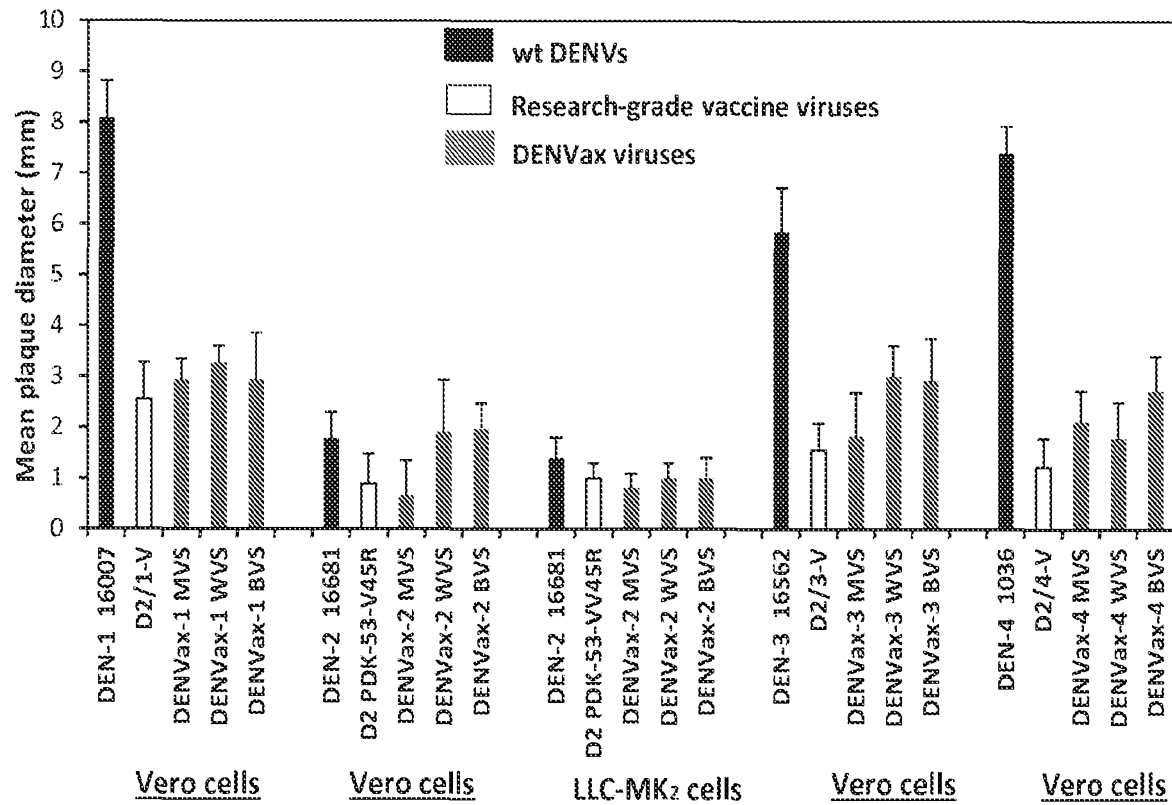


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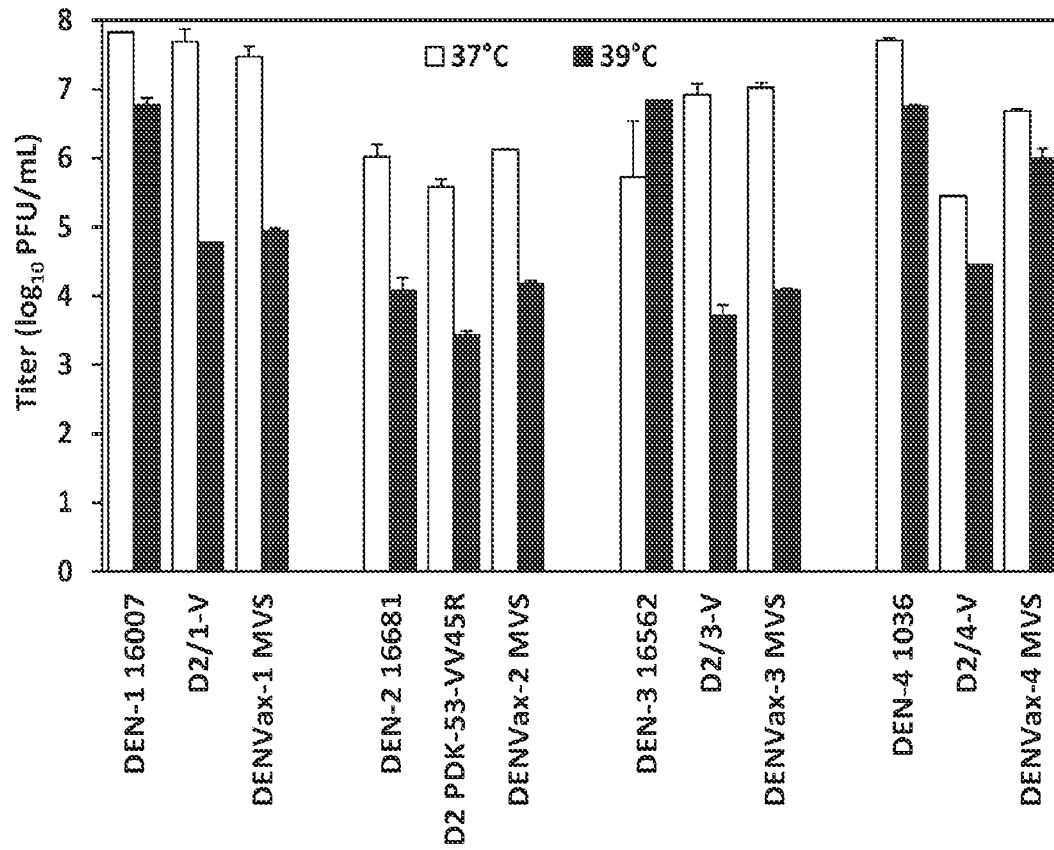


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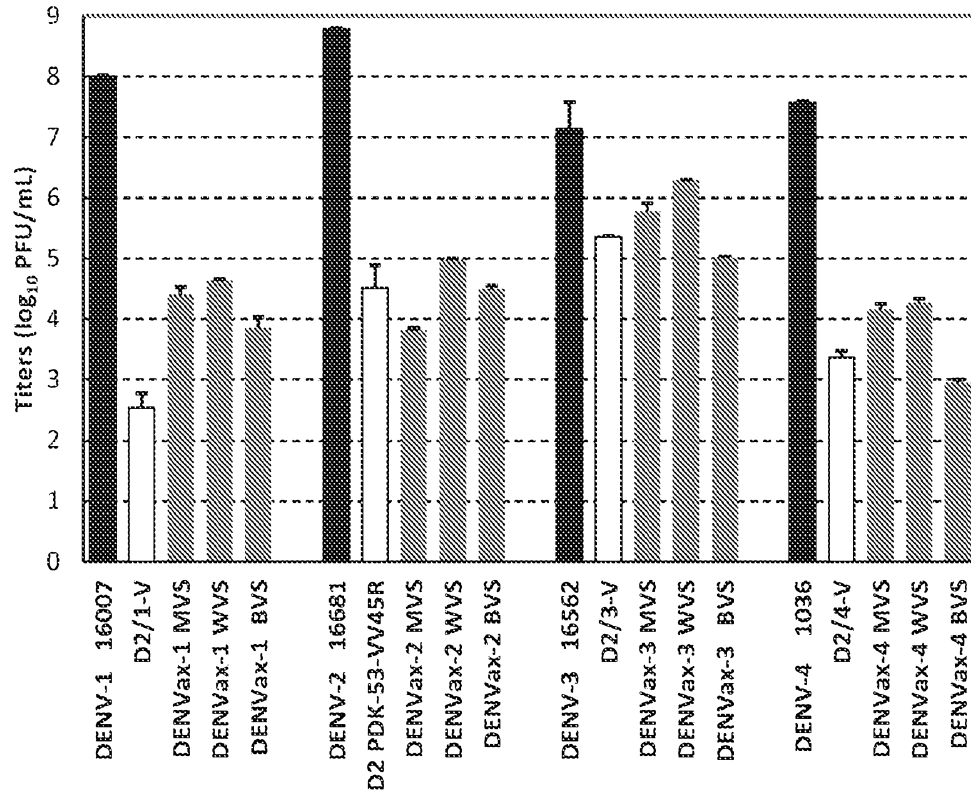


Fig. 9

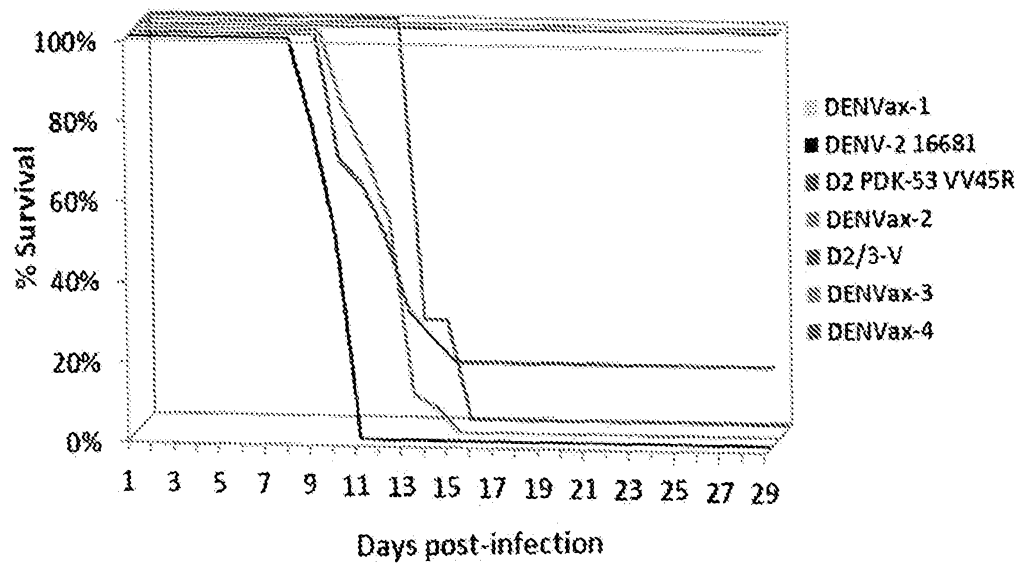
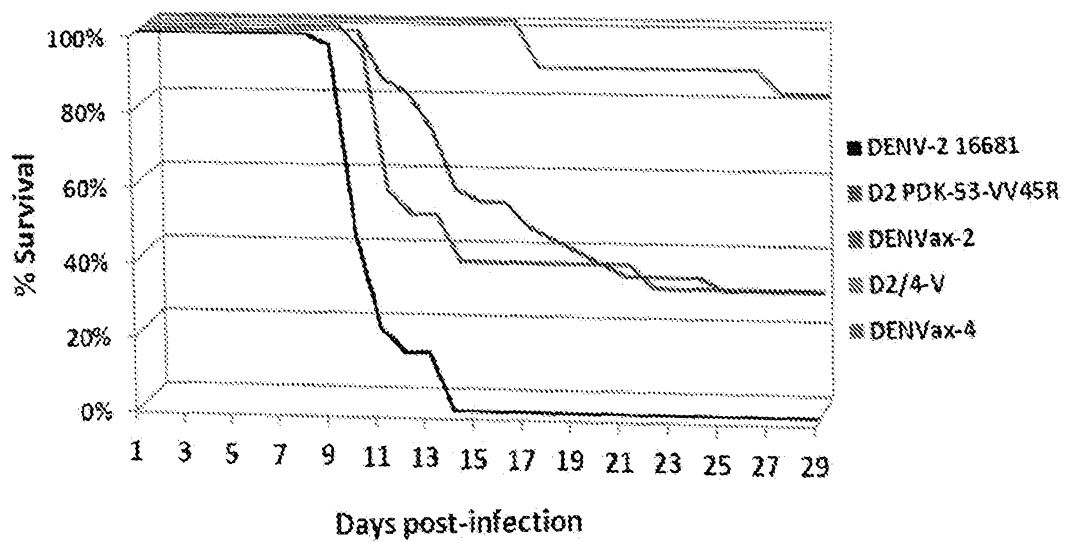
A**B**

Fig. 10

Sevotype	Strain	virus origin	C87T	A524T	T906C	C2059T	G2870A	C4018T	A5370A	T3547C	G6609C	C5571T
			PM-029V	M (virus)	E (silent)	N5345SD	N52A-1181	N53-E36V	N53 (silent)	N53 (silent)	N53 (silent)	N53 (silent)
16551		Isolate from human	A	T	C	G	C	A	T	T	G	C
PDK-53		PDK cell pass of 16551	T	..	t	A	T	T/A mix	c	c	C	t
DETV-2		Recombinant PDK-53-V	T	x	t	A	T	T	c	c	C	C
PDK-53-23(VT488)		Recombinant PDK-53-E	T	c	t	A	T	A	c	c	C	C

Underlined Mutations, the 3 most important mutations from PDK-53

Red font: PDK-53 specific sequence (change from 16551)

Bold font: Difference in sequence between PDK-53 and clone-derived X or E virus

* Engineered silent clone number to differentiate original PDK-53 and recombinant (clone-derived) viruses

20170306 478484.168 VAC-5035-AU Replacement Sequence Listing 34 sequences.txt
SEQUENCE LISTING

<110> Takeda Vaccines, Inc.
Stinchcomb, Dan
Kinney, Claire
Kinney, Richard M.
Livengood, Jill A.

<120> COMPOSITIONS AND METHODS FOR DENGUE VIRUS CHIMERIC CONSTRUCTS IN VACCINES

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 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Dengue virus serotype 1, Pre-Master

<400> 2

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Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
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Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45

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Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
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Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
65 70 75 80

Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
85 90 95

Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
100 105 110

Met Ala Phe His Leu Thr Thr Arg Gly Gly Glu Pro His Met Ile Val
115 120 125

Ser Lys Gln Glu Arg Gly Lys Ser Leu Leu Phe Lys Thr Ser Ala Gly
130 135 140

Val Asn Met Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Leu Cys Glu
145 150 155 160

Asp Thr Met Thr Tyr Lys Cys Pro Arg Ile Thr Glu Ala Glu Pro Asp
165 170 175

Asp Val Asp Cys Trp Cys Asn Ala Thr Asp Thr Trp Val Thr Tyr Gly
180 185 190

Thr Cys Ser Gln Thr Gly Glu His Arg Arg Asp Lys Arg Ser Val Ala
195 200 205

Leu Ala Pro His Val Gly Leu Gly Leu Glu Thr Arg Ala Glu Thr Trp
210 215 220

Met Ser Ser Glu Gly Ala Trp Lys Gln Ile Gln Lys Val Glu Thr Trp
225 230 235 240

Ala Leu Arg His Pro Gly Phe Thr Val Ile Ala Leu Phe Leu Ala His
245 250 255

Ala Ile Gly Thr Ser Ile Thr Gln Lys Gly Ile Ile Phe Ile Leu Leu
260 265 270

Met Leu Val Thr Pro Ser Met Ala Met Arg Cys Val Gly Ile Gly Asn
275 280 285

Arg Asp Phe Val Glu Gly Leu Ser Gly Ala Thr Trp Val Asp Val Val
290 295 300

Leu Glu His Gly Ser Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
305 310 315 320

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Leu Asp Ile Glu Leu₃₂₅ Leu Lys Thr Glu Val₃₃₀ Thr Asn Pro Ala Val₃₃₅ Leu
 Arg Lys Leu Cys₃₄₀ Ile Glu Ala Lys Ile₃₄₅ Ser Asn Thr Thr Thr₃₅₀ Asp Ser
 Arg Cys Pro₃₅₅ Thr Gln Gly Glu Ala₃₆₀ Thr Leu Val Glu Glu₃₆₅ Gln Asp Ala
 Asn Phe₃₇₀ Val Cys Arg Arg Thr₃₇₅ Phe Val Asp Arg Gly₃₈₀ Trp Gly Asn Gly
 Cys₃₈₅ Gly Leu Phe Gly Lys₃₉₀ Gly Ser Leu Ile Thr₃₉₅ Cys Ala Lys Phe Lys₄₀₀
 Cys Val Thr Lys Leu₄₀₅ Glu Gly Lys Ile Val₄₁₀ Gln Tyr Glu Asn Leu₄₁₅ Lys
 Tyr Ser Val Ile₄₂₀ Val Thr Val His Thr₄₂₅ Gly Asp Gln His Gln₄₃₀ Val Gly
 Asn Glu Thr₄₃₅ Thr Glu His Gly Thr₄₄₀ Thr Ala Thr Ile Thr₄₄₅ Pro Gln Ala
 Pro Thr₄₅₀ Ser Glu Ile Gln Leu₄₅₅ Thr Asp Tyr Gly Thr₄₆₀ Leu Thr Leu Asp
 Cys₄₆₅ Ser Pro Arg Thr Gly₄₇₀ Leu Asp Phe Asn Glu₄₇₅ Met Val Leu Leu Thr₄₈₀
 Met Lys Glu Arg Ser₄₈₅ Trp Leu Val His Lys₄₉₀ Gln Trp Phe Leu Asp₄₉₅ Leu
 Pro Leu Pro Trp₅₀₀ Thr Ser Gly Ala Ser₅₀₅ Thr Ser Gln Glu Thr₅₁₀ Trp Asn
 Arg Gln Asp₅₁₅ Leu Leu Val Thr Phe₅₂₀ Lys Thr Ala His Ala₅₂₅ Lys Lys Gln
 Glu Val₅₃₀ Val Val Leu Gly Ser₅₃₅ Gln Glu Gly Ala Met₅₄₀ His Thr Ala Leu
 Thr₅₄₅ Gly Ala Thr Glu Ile₅₅₀ Gln Thr Ser Gly Thr₅₅₅ Thr Thr Ile Phe Ala₅₆₀
 Gly His Leu Lys Cys₅₆₅ Arg Leu Lys Met Asp₅₇₀ Lys Leu Thr Leu Lys₅₇₅ Gly
 Met Ser Tyr Val₅₈₀ Met Cys Thr Gly Ser₅₈₅ Phe Lys Leu Glu Lys₅₉₀ Glu Val

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Ala Glu Thr Gln His Gly Thr Val Leu Val Gln Val Lys Tyr Glu Gly
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 Thr Asp Ala Pro Cys Lys Ile Pro Phe Ser Thr Gln Asp Glu Lys Gly
 610 615 620
 Ala Thr Gln Asn Gly Arg Leu Ile Thr Ala Asn Pro Ile Val Thr Asp
 625 630 635 640
 Lys Glu Lys Pro Val Asn Ile Glu Ala Glu Pro Pro Phe Gly Glu Ser
 645 650 655
 Tyr Ile Val Val Gly Ala Gly Glu Lys Ala Leu Lys Leu Ser Trp Phe
 660 665 670
 Lys Lys Gly Ser Ser Ile Gly Lys Met Phe Glu Ala Thr Ala Arg Gly
 675 680 685
 Ala Arg Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser
 690 695 700
 Ile Gly Gly Val Phe Thr Ser Met Gly Lys Leu Val His Gln Val Phe
 705 710 715 720
 Gly Thr Ala Tyr Gly Val Leu Phe Ser Gly Val Ser Trp Thr Met Lys
 725 730 735
 Ile Gly Ile Gly Ile Leu Leu Thr Trp Leu Gly Leu Asn Ser Arg Asn
 740 745 750
 Thr Ser Leu Ser Met Met Cys Ile Ala Ala Gly Ile Val Thr Leu Tyr
 755 760 765
 Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
 770 775 780
 Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
 785 790 795 800
 His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
 805 810 815
 Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
 820 825 830
 Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
 835 840 845
 Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
 850 855 860

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Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
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Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
 885 890 895

Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
 900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
 915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
 930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
 945 950 955 960

Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
 965 970 975

Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
 980 985 990

Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
 995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
 1010 1015 1020

Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
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Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
 1040 1045 1050

Phe Cys Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn
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Arg Gly Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile
 1070 1075 1080

Thr Glu Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr
 1085 1090 1095

Arg Gly Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu
 1100 1105 1110

Lys Glu Lys Glu Glu Asn Leu Val Asn Ser Leu Val Thr Ala Gly
 1115 1120 1125

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Ala	Ile 1160	Leu	Leu	Val	Ala	Val 1165	Ser	Phe	Val	Thr	Leu 1170	Ile	Thr	Gly
Asn	Met 1175	Ser	Phe	Arg	Asp	Leu 1180	Gly	Arg	Val	Met	Val 1185	Met	Val	Gly
Ala	Thr 1190	Met	Thr	Asp	Asp	Ile 1195	Gly	Met	Gly	Val	Thr 1200	Tyr	Leu	Ala
Leu	Leu 1205	Ala	Ala	Phe	Lys	Val 1210	Arg	Pro	Thr	Phe	Ala 1215	Ala	Gly	Leu
Leu	Leu 1220	Arg	Lys	Leu	Thr	Ser 1225	Lys	Glu	Leu	Met	Met 1230	Thr	Thr	Ile
Gly	Ile 1235	Val	Leu	Leu	Ser	Gln 1240	Ser	Thr	Leu	Pro	Glu 1245	Thr	Ile	Leu
Glu	Leu 1250	Thr	Asp	Ala	Leu	Ala 1255	Leu	Gly	Met	Met	Val 1260	Leu	Lys	Met
Val	Arg 1265	Asn	Met	Glu	Lys	Tyr 1270	Gln	Leu	Ala	Val	Thr 1275	Ile	Met	Ala
Ile	Leu 1280	Cys	Val	Pro	Asn	Ala 1285	Val	Ile	Leu	Gln	Asn 1290	Ala	Trp	Lys
Val	Ser 1295	Cys	Thr	Ile	Leu	Ala 1300	Val	Val	Ser	Val	Ser 1305	Pro	Leu	Phe
Leu	Thr 1310	Ser	Ser	Gln	Gln	Lys 1315	Thr	Asp	Trp	Ile	Pro 1320	Leu	Ala	Leu
Thr	Ile 1325	Lys	Gly	Leu	Asn	Pro 1330	Thr	Ala	Ile	Phe	Leu 1335	Thr	Thr	Leu
Ser	Arg 1340	Thr	Ser	Lys	Lys	Arg 1345	Ser	Trp	Pro	Leu	Asn 1350	Glu	Ala	Ile
Met	Ala 1355	Val	Gly	Met	Val	Ser 1360	Ile	Leu	Ala	Ser	Ser 1365	Leu	Leu	Lys
Asn	Asp 1370	Ile	Pro	Met	Thr	Gly 1375	Pro	Leu	Val	Ala	Gly 1380	Gly	Leu	Leu

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Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
	1385					1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
	1400					1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
	1415					1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Asp	Gln	Thr	Leu	Thr	Ile	Leu
	1430					1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
	1445					1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
	1460					1465					1470			
Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
	1475					1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
	1490					1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
	1505					1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
	1520					1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
	1535					1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
	1550					1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
	1565					1570					1575			
Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
	1580					1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
	1595					1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
	1610					1615					1620			
Leu	Tyr	Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser
	1625					1630					1635			

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Ala	Ile	Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile
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Glu	Asp	Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu
	1655					1660					1665			
His	Pro	Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val
	1670					1675					1680			
Arg	Glu	Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro
	1685					1690					1695			
Thr	Arg	Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu
	1700					1705					1710			
Pro	Ile	Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly
	1715					1720					1725			
Arg	Glu	Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg
	1730					1735					1740			
Leu	Leu	Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met
	1745					1750					1755			
Asp	Glu	Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly
	1760					1765					1770			
Tyr	Ile	Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe
	1775					1780					1785			
Met	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser
	1790					1795					1800			
Asn	Ala	Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser
	1805					1810					1815			
Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
	1820					1825					1830			
Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
	1835					1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
	1850					1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
	1865					1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
	1880					1885					1890			

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Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
	1895					1900					1905			
Leu	Thr	Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro
	1910					1915					1920			
Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
	1925					1930					1935			
Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
	1940					1945					1950			
Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
	1955					1960					1965			
Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
	1970					1975					1980			
Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
	1985					1990					1995			
Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
	2000					2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
	2015					2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
	2030					2035					2040			
Asn	Asn	Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr
	2045					2050					2055			
Lys	Glu	Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala
	2060					2065					2070			
Arg	Ile	Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe
	2075					2080					2085			
Ala	Ala	Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met
	2090					2095					2100			
Gly	Arg	Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Ala	Arg	Asp	Ala	Leu
	2105					2110					2115			
Asp	Asn	Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Ala	Gly	Gly	Arg	Ala
	2120					2125					2130			
Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
	2135					2140					2145			

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Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
	2150					2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
	2165					2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
	2180					2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
	2195					2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
	2210					2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
	2225					2230					2235			
Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
	2240					2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
	2255					2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
	2270					2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
	2285					2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
	2300					2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
	2315					2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
	2330					2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Thr	Ala	Ala	Leu	Phe	Leu	Leu	Val
	2345					2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
	2360					2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
	2375					2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
	2390					2395					2400			

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Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
	2405					2410					2415			
Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
	2420					2425					2430			
Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
	2435					2440					2445			
Glu	Gly	Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser
	2450					2455					2460			
Met	Ala	Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu
	2465					2470					2475			
Leu	Phe	Ser	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr
	2480					2485					2490			
Gly	Asn	Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu
	2495					2500					2505			
Asn	Ala	Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly
	2510					2515					2520			
Ile	Gln	Glu	Val	Asp	Arg	Thr	Leu	Ala	Lys	Glu	Gly	Ile	Lys	Arg
	2525					2530					2535			
Gly	Glu	Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu
	2540					2545					2550			
Arg	Trp	Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val
	2555					2560					2565			
Val	Asp	Leu	Gly	Cys	Gly	Arg	Gly	Gly	Trp	Ser	Tyr	Tyr	Cys	Gly
	2570					2575					2580			
Gly	Leu	Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly
	2585					2590					2595			
Pro	Gly	His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn
	2600					2605					2610			
Leu	Val	Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro
	2615					2620					2625			
Glu	Lys	Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro
	2630					2635					2640			
Asn	Pro	Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu
	2645					2650					2655			

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Val	Glu	Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val
	2660					2665					2670			
Leu	Asn	Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu
	2675					2680					2685			
Gln	Arg	Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg
	2690					2695					2700			
Asn	Ser	Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn
	2705					2710					2715			
Ile	Val	Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg
	2720					2725					2730			
Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
	2735					2740					2745			
Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
	2750					2755					2760			
Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
	2765					2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
	2780					2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
	2795					2800					2805			
Ser	Ser	Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp
	2810					2815					2820			
Asp	Val	Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr
	2825					2830					2835			
Pro	Phe	Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg
	2840					2845					2850			
Thr	Gln	Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr
	2855					2860					2865			
Ala	Glu	Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg
	2870					2875					2880			
Met	Cys	Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala
	2885					2890					2895			
Ala	Leu	Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
	2900					2905					2910			

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Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
	2915					2920					2925			
Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
	2930					2935					2940			
Asn	Met	Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys
	2945					2950					2955			
Ala	Lys	Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg
	2960					2965					2970			
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	2975					2980					2985			
Phe	Ser	Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu
	2990					2995					3000			
His	Lys	Leu	Gly	Tyr	Ile	Leu	Arg	Asp	Val	Ser	Lys	Lys	Glu	Gly
	3005					3010					3015			
Gly	Ala	Met	Tyr	Ala	Asp	Asp	Thr	Ala	Gly	Trp	Asp	Thr	Arg	Ile
	3020					3025					3030			
Thr	Leu	Glu	Asp	Leu	Lys	Asn	Glu	Glu	Met	Val	Thr	Asn	His	Met
	3035					3040					3045			
Glu	Gly	Glu	His	Lys	Lys	Leu	Ala	Glu	Ala	Ile	Phe	Lys	Leu	Thr
	3050					3055					3060			
Tyr	Gln	Asn	Lys	Val	Val	Arg	Val	Gln	Arg	Pro	Thr	Pro	Arg	Gly
	3065					3070					3075			
Thr	Val	Met	Asp	Ile	Ile	Ser	Arg	Arg	Asp	Gln	Arg	Gly	Ser	Gly
	3080					3085					3090			
Gln	Val	Gly	Thr	Tyr	Gly	Leu	Asn	Thr	Phe	Thr	Asn	Met	Glu	Ala
	3095					3100					3105			
Gln	Leu	Ile	Arg	Gln	Met	Glu	Gly	Glu	Gly	Val	Phe	Lys	Ser	Ile
	3110					3115					3120			
Gln	His	Leu	Thr	Ile	Thr	Glu	Glu	Ile	Ala	Val	Gln	Asn	Trp	Leu
	3125					3130					3135			
Ala	Arg	Val	Gly	Arg	Glu	Arg	Leu	Ser	Arg	Met	Ala	Ile	Ser	Gly
	3140					3145					3150			
Asp	Asp	Cys	Val	Val	Lys	Pro	Leu	Asp	Asp	Arg	Phe	Ala	Ser	Ala
	3155					3160					3165			

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 3185 3190 3195
 Phe Cys Ser His His Phe His Glu Leu Ile Met Lys Asp Gly Arg
 3200 3205 3210
 Val Leu Val Val Pro Cys Arg Asn Gln Asp Glu Leu Ile Gly Arg
 3215 3220 3225
 Ala Arg Ile Ser Gln Gly Ala Gly Trp Ser Leu Arg Glu Thr Ala
 3230 3235 3240
 Cys Leu Gly Lys Ser Tyr Ala Gln Met Trp Ser Leu Met Tyr Phe
 3245 3250 3255
 His Arg Arg Asp Leu Arg Leu Ala Ala Asn Ala Ile Cys Ser Ala
 3260 3265 3270
 Val Pro Ser His Trp Val Pro Thr Ser Arg Thr Thr Trp Ser Ile
 3275 3280 3285
 His Ala Lys His Glu Trp Met Thr Thr Glu Asp Met Leu Thr Val
 3290 3295 3300
 Trp Asn Arg Val Trp Ile Gln Glu Asn Pro Trp Met Glu Asp Lys
 3305 3310 3315
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 Glu Asp Gln Trp Cys Gly Ser Leu Ile Gly Leu Thr Ser Arg Ala
 3335 3340 3345
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 3380 3385 3390

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<220>

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 <223> Dengue virus serotype 1, MVS

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atggacaaac taactttaaa agggatgtca tatgtgatgt gcacaggctc attcaagtta     1860
gagaaagaag tggctgagac ccagcatgga actgttctgg tgcaggttaa atatgaagga     1920
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<220>
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 <400> 4

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Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
 50 55 60

Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
 65 70 75 80

Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
 85 90 95

Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
 100 105 110

Met Ala Phe His Leu Thr Thr Arg Gly Gly Glu Pro His Met Ile Val
 115 120 125

Ser Lys Gln Glu Arg Gly Lys Ser Leu Leu Phe Lys Thr Ser Ala Gly
 130 135 140

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	210					215					220				
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225					230					235					240
Ala	Leu	Arg	His	Pro	Gly	Phe	Thr	Val	Ile	Ala	Leu	Phe	Leu	Ala	His
				245					250					255	
Ala	Ile	Gly	Thr	Ser	Ile	Thr	Gln	Lys	Gly	Ile	Ile	Phe	Ile	Leu	Leu
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Met	Leu	Val	Thr	Pro	Ser	Met	Ala	Met	Arg	Cys	Val	Gly	Ile	Gly	Asn
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Arg	Asp	Phe	Val	Glu	Gly	Leu	Ser	Gly	Ala	Thr	Trp	Val	Asp	Val	Val
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305					310					315					320
Leu	Asp	Ile	Glu	Leu	Leu	Lys	Thr	Glu	Val	Thr	Asn	Pro	Ala	Val	Leu
				325					330					335	
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Cys	Val	Thr	Lys	Leu	Glu	Gly	Lys	Ile	Val	Gln	Tyr	Glu	Asn	Leu	Lys
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 Tyr Ser Val Ile Val Thr Val His Thr Gly Asp Gln His Gln Val Gly
 420 425 430

Asn Glu Thr Thr Glu His Gly Thr Thr Ala Thr Ile Thr Pro Gln Ala
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Pro Thr Ser Glu Ile Gln Leu Thr Asp Tyr Gly Thr Leu Thr Leu Asp
 450 455 460

Cys Ser Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Val Leu Leu Thr
 465 470 475 480

Met Lys Glu Arg Ser Trp Leu Val His Lys Gln Trp Phe Leu Asp Leu
 485 490 495

Pro Leu Pro Trp Thr Ser Gly Ala Ser Thr Ser Gln Glu Thr Trp Asn
 500 505 510

Arg Gln Asp Leu Leu Val Thr Phe Lys Thr Ala His Ala Lys Lys Gln
 515 520 525

Glu Val Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu
 530 535 540

Thr Gly Ala Thr Glu Ile Gln Thr Ser Gly Thr Thr Thr Ile Phe Ala
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Gly His Leu Lys Cys Arg Leu Lys Met Asp Lys Leu Thr Leu Lys Gly
 565 570 575

Met Ser Tyr Val Met Cys Thr Gly Ser Phe Lys Leu Glu Lys Glu Val
 580 585 590

Ala Glu Thr Gln His Gly Thr Val Leu Val Gln Val Lys Tyr Glu Gly
 595 600 605

Thr Asp Ala Pro Cys Lys Ile Pro Phe Ser Thr Gln Asp Glu Lys Gly
 610 615 620

Ala Thr Gln Asn Gly Arg Leu Ile Thr Ala Asn Pro Ile Val Thr Asp
 625 630 635 640

Lys Glu Lys Pro Val Asn Ile Glu Ala Glu Pro Pro Phe Gly Glu Ser
 645 650 655

Tyr Ile Val Val Gly Ala Gly Glu Lys Ala Leu Lys Leu Ser Trp Phe
 660 665 670

Lys Lys Gly Ser Ser Ile Gly Lys Met Phe Glu Ala Thr Ala Arg Gly
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 690 695 700

Ile Gly Gly Val Phe Thr Ser Met Gly Lys Leu Val His Gln Val Phe
 705 710 715 720

Gly Thr Ala Tyr Gly Val Leu Phe Ser Gly Val Ser Trp Thr Met Lys
 725 730 735

Ile Gly Ile Gly Ile Leu Leu Thr Trp Leu Gly Leu Asn Ser Arg Asn
 740 745 750

Thr Ser Leu Ser Met Met Cys Ile Ala Ala Gly Ile Val Thr Leu Tyr
 755 760 765

Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
 770 775 780

Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
 785 790 795 800

His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
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Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
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Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
 835 840 845

Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
 850 855 860

Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
 865 870 875 880

Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
 885 890 895

Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
 900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
 915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
 930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
 945 950 955 960

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Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
965 970 975

Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
980 985 990

Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
1010 1015 1020

Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
1025 1030 1035

Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
1040 1045 1050

Phe Cys Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn
1055 1060 1065

Arg Gly Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile
1070 1075 1080

Thr Glu Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr
1085 1090 1095

Arg Gly Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu
1100 1105 1110

Lys Glu Lys Glu Glu Asn Leu Val Asn Ser Leu Val Thr Ala Gly
1115 1120 1125

His Gly Gln Val Asp Asn Phe Ser Leu Gly Val Leu Gly Met Ala
1130 1135 1140

Leu Phe Leu Glu Glu Met Leu Arg Thr Arg Val Gly Thr Lys His
1145 1150 1155

Ala Ile Leu Leu Val Ala Val Ser Phe Val Thr Leu Ile Thr Gly
1160 1165 1170

Asn Met Ser Phe Arg Asp Leu Gly Arg Val Met Val Met Val Gly
1175 1180 1185

Ala Thr Met Thr Asp Asp Ile Gly Met Gly Val Thr Tyr Leu Ala
1190 1195 1200

Leu Leu Ala Ala Phe Lys Val Arg Pro Thr Phe Ala Ala Gly Leu
1205 1210 1215

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Leu	Leu	Arg	Lys	Leu	Thr	Ser	Lys	Glu	Leu	Met	Met	Thr	Thr	Ile
1220						1225					1230			
Gly	Ile	Val	Leu	Leu	Ser	Gln	Ser	Thr	Leu	Pro	Glu	Thr	Ile	Leu
1235						1240					1245			
Glu	Leu	Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met
1250						1255					1260			
Val	Arg	Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala
1265						1270					1275			
Ile	Leu	Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys
1280						1285					1290			
Val	Ser	Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe
1295						1300					1305			
Leu	Thr	Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu
1310						1315					1320			
Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
1325						1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
1340						1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
1355						1360					1365			
Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
1370						1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
1385						1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
1400						1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
1415						1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Asp	Gln	Thr	Leu	Thr	Ile	Leu
1430						1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
1445						1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
1460						1465					1470			

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Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
1475						1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
1490						1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
1505						1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
1520						1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
1535						1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
1550						1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
1565						1570					1575			
Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
1580						1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
1595						1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
1610						1615					1620			
Leu	Tyr	Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser
1625						1630					1635			
Ala	Ile	Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile
1640						1645					1650			
Glu	Asp	Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu
1655						1660					1665			
His	Pro	Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val
1670						1675					1680			
Arg	Glu	Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro
1685						1690					1695			
Thr	Arg	Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu
1700						1705					1710			
Pro	Ile	Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly
1715						1720					1725			

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Arg	Glu	Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg
	1730					1735					1740			
Leu	Leu	Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met
	1745					1750					1755			
Asp	Glu	Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly
	1760					1765					1770			
Tyr	Ile	Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe
	1775					1780					1785			
Met	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser
	1790					1795					1800			
Asn	Ala	Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser
	1805					1810					1815			
Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
	1820					1825					1830			
Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
	1835					1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
	1850					1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
	1865					1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
	1880					1885					1890			
Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
	1895					1900					1905			
Leu	Thr	Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro
	1910					1915					1920			
Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
	1925					1930					1935			
Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
	1940					1945					1950			
Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
	1955					1960					1965			
Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
	1970					1975					1980			

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Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
1985						1990					1995			
Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
2000						2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
2015						2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
2030						2035					2040			
Asn	Asn	Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr
2045						2050					2055			
Lys	Glu	Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala
2060						2065					2070			
Arg	Ile	Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe
2075						2080					2085			
Ala	Ala	Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met
2090						2095					2100			
Gly	Arg	Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Ala	Arg	Asp	Ala	Leu
2105						2110					2115			
Asp	Asn	Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Ala	Gly	Gly	Arg	Ala
2120						2125					2130			
Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
2135						2140					2145			
Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
2150						2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
2165						2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
2180						2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
2195						2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
2210						2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
2225						2230					2235			

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Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
2240						2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
2255						2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
2270						2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
2285						2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
2300						2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
2315						2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
2330						2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Thr	Ala	Ala	Leu	Phe	Leu	Leu	Val
2345						2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
2360						2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
2375						2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
2390						2395					2400			
Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
2405						2410					2415			
Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
2420						2425					2430			
Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
2435						2440					2445			
Glu	Gly	Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser
2450						2455					2460			
Met	Ala	Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu
2465						2470					2475			
Leu	Phe	Ser	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr
2480						2485					2490			

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Gly	Asn	Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu
	2495					2500					2505			
Asn	Ala	Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly
	2510					2515					2520			
Ile	Gln	Glu	Val	Asp	Arg	Thr	Leu	Ala	Lys	Glu	Gly	Ile	Lys	Arg
	2525					2530					2535			
Gly	Glu	Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu
	2540					2545					2550			
Arg	Trp	Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val
	2555					2560					2565			
Val	Asp	Leu	Gly	Cys	Gly	Arg	Gly	Gly	Trp	Ser	Tyr	Tyr	Cys	Gly
	2570					2575					2580			
Gly	Leu	Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly
	2585					2590					2595			
Pro	Gly	His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn
	2600					2605					2610			
Leu	Val	Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro
	2615					2620					2625			
Glu	Lys	Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro
	2630					2635					2640			
Asn	Pro	Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu
	2645					2650					2655			
Val	Glu	Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val
	2660					2665					2670			
Leu	Asn	Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu
	2675					2680					2685			
Gln	Arg	Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg
	2690					2695					2700			
Asn	Ser	Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn
	2705					2710					2715			
Ile	Val	Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg
	2720					2725					2730			
Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
	2735					2740					2745			

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Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
	2750					2755					2760			
Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
	2765					2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
	2780					2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
	2795					2800					2805			
Ser	Ser	Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp
	2810					2815					2820			
Asp	Val	Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr
	2825					2830					2835			
Pro	Phe	Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg
	2840					2845					2850			
Thr	Gln	Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr
	2855					2860					2865			
Ala	Glu	Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg
	2870					2875					2880			
Met	Cys	Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala
	2885					2890					2895			
Ala	Leu	Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
	2900					2905					2910			
Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
	2915					2920					2925			
Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
	2930					2935					2940			
Asn	Met	Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys
	2945					2950					2955			
Ala	Lys	Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg
	2960					2965					2970			
Phe	Leu	Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp
	2975					2980					2985			
Phe	Ser	Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu
	2990					2995					3000			

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 His Lys Leu Gly Tyr Ile Leu Arg Asp Val Ser Lys Lys Glu Gly
 3005 3010 3015

Gly Ala Met Tyr Ala Asp Asp Thr Ala Gly Trp Asp Thr Arg Ile
 3020 3025 3030

Thr Leu Glu Asp Leu Lys Asn Glu Glu Met Val Thr Asn His Met
 3035 3040 3045

Glu Gly Glu His Lys Lys Leu Ala Glu Ala Ile Phe Lys Leu Thr
 3050 3055 3060

Tyr Gln Asn Lys Val Val Arg Val Gln Arg Pro Thr Pro Arg Gly
 3065 3070 3075

Thr Val Met Asp Ile Ile Ser Arg Arg Asp Gln Arg Gly Ser Gly
 3080 3085 3090

Gln Val Gly Thr Tyr Gly Leu Asn Thr Phe Thr Asn Met Glu Ala
 3095 3100 3105

Gln Leu Ile Arg Gln Met Glu Gly Glu Gly Val Phe Lys Ser Ile
 3110 3115 3120

Gln His Leu Thr Ile Thr Glu Glu Ile Ala Val Gln Asn Trp Leu
 3125 3130 3135

Ala Arg Val Gly Arg Glu Arg Leu Ser Arg Met Ala Ile Ser Gly
 3140 3145 3150

Asp Asp Cys Val Val Lys Pro Leu Asp Asp Arg Phe Ala Ser Ala
 3155 3160 3165

Leu Thr Ala Leu Asn Asp Met Gly Lys Ile Arg Lys Asp Ile Gln
 3170 3175 3180

Gln Trp Glu Pro Ser Arg Gly Trp Asn Asp Trp Thr Gln Val Pro
 3185 3190 3195

Phe Cys Ser His His Phe His Glu Leu Ile Met Lys Asp Gly Arg
 3200 3205 3210

Val Leu Val Val Pro Cys Arg Asn Gln Asp Glu Leu Ile Gly Arg
 3215 3220 3225

Ala Arg Ile Ser Gln Gly Ala Gly Trp Ser Leu Arg Glu Thr Ala
 3230 3235 3240

Cys Leu Gly Lys Ser Tyr Ala Gln Met Trp Ser Leu Met Tyr Phe
 3245 3250 3255

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 His Arg Arg Asp Leu Arg Leu Ala Ala Asn Ala Ile Cys Ser Ala
 3260 3265 3270

Val Pro Ser His Trp Val Pro Thr Ser Arg Thr Thr Trp Ser Ile
 3275 3280 3285

His Ala Lys His Glu Trp Met Thr Thr Glu Asp Met Leu Thr Val
 3290 3295 3300

Trp Asn Arg Val Trp Ile Gln Glu Asn Pro Trp Met Glu Asp Lys
 3305 3310 3315

Thr Pro Val Glu Ser Trp Glu Glu Ile Pro Tyr Leu Gly Lys Arg
 3320 3325 3330

Glu Asp Gln Trp Cys Gly Ser Leu Ile Gly Leu Thr Ser Arg Ala
 3335 3340 3345

Thr Trp Ala Lys Asn Ile Gln Ala Ala Ile Asn Gln Val Arg Ser
 3350 3355 3360

Leu Ile Gly Asn Glu Glu Tyr Thr Asp Tyr Met Pro Ser Met Lys
 3365 3370 3375

Arg Phe Arg Arg Glu Glu Glu Glu Ala Gly Val Leu Trp
 3380 3385 3390

<210> 5
 <211> 10723
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Dengue virus serotype 1, WVS

<220>
 <221> misc_feature
 <222> (2384)..(2384)
 <223> n is either cytosine or guanine

<400> 5
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 gttctaacag tttttaatt agagagcaga tctctgatga ataaccaacg gaaaaaggcg 120
 aaaaacacgc ctttcaatat gctgaaacgc gagagaaacc gcgtgtcgac tgtgcaacag 180
 ctgacaaaga gattctcact tggaatgctg caggagcag gaccattaaa actgttcatg 240
 gccctggtgg cgttccttcg tttcctaaca atccaccaa cagcagggat attgaagaga 300
 tggggaacaa ttaaaaaatc aaaagctatt aatgttttga gagggttcag gaaagagatt 360
 ggaaggatgc tgaacatctt gaataggaga cgcagatctg caggcatgat cattatgctg 420
 attccaacag tgatggcggt ccatttaacc acgcgtgggg gagagccgca tatgatagtt 480
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 <213> Artificial Sequence

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 <221> misc_feature
 <222> (763)..(763)
 <223> Xaa is either alanine or glycine

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Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
 50 55 60

Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
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Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
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Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
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Ser Lys Gln Glu Arg Gly Lys Ser Leu Leu Phe Lys Thr Ser Ala Gly
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Val Asn Met Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Leu Cys Glu
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Asp Thr Met Thr Tyr Lys Cys Pro Arg Ile Thr Glu Ala Glu Pro Asp
 165 170 175

Asp Val Asp Cys Trp Cys Asn Ala Thr Asp Thr Trp Val Thr Tyr Gly
 180 185 190

Thr Cys Ser Gln Thr Gly Glu His Arg Arg Asp Lys Arg Ser Val Ala
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Met Ser Ser Glu Gly Ala Trp Lys Gln Ile Gln Lys Val Glu Thr Trp
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 245 250 255

Ala Ile Gly Thr Ser Ile Thr Gln Lys Gly Ile Ile Phe Ile Leu Leu
 260 265 270

Met Leu Val Thr Pro Ser Met Ala Met Arg Cys Val Gly Ile Gly Asn
 275 280 285

Arg Asp Phe Val Glu Gly Leu Ser Gly Ala Thr Trp Val Asp Val Val
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Leu Glu His Gly Ser Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
 305 310 315 320

Leu Asp Ile Glu Leu Leu Lys Thr Glu Val Thr Asn Pro Ala Val Leu
 325 330 335

Arg Lys Leu Cys Ile Glu Ala Lys Ile Ser Asn Thr Thr Thr Asp Ser
 340 345 350

Arg Cys Pro Thr Gln Gly Glu Ala Thr Leu Val Glu Glu Gln Asp Ala
 355 360 365

Asn Phe Val Cys Arg Arg Thr Phe Val Asp Arg Gly Trp Gly Asn Gly
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Cys Gly Leu Phe Gly Lys Gly Ser Leu Ile Thr Cys Ala Lys Phe Lys
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Cys Val Thr Lys Leu Glu Gly Lys Ile Val Gln Tyr Glu Asn Leu Lys
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Tyr Ser Val Ile Val Thr Val His Thr Gly Asp Gln His Gln Val Gly
 420 425 430

Asn Glu Thr Thr Glu His Gly Thr Thr Ala Thr Ile Thr Pro Gln Ala
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Pro Thr Ser Glu Ile Gln Leu Thr Asp Tyr Gly Thr Leu Thr Leu Asp
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Cys Ser Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Val Leu Leu Thr
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 500 505 510
 Arg Gln Asp Leu Leu Val Thr Phe Lys Thr Ala His Ala Lys Lys Gln
 515 520 525
 Glu Val Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu
 530 535 540
 Thr Gly Ala Thr Glu Ile Gln Thr Ser Gly Thr Thr Thr Ile Phe Ala
 545 550 555 560
 Gly His Leu Lys Cys Arg Leu Lys Met Asp Lys Leu Thr Leu Lys Gly
 565 570 575
 Met Ser Tyr Val Met Cys Thr Gly Ser Phe Lys Leu Glu Lys Glu Val
 580 585 590
 Ala Glu Thr Gln His Gly Thr Val Leu Val Gln Val Lys Tyr Glu Gly
 595 600 605
 Thr Asp Ala Pro Cys Lys Ile Pro Phe Ser Thr Gln Asp Glu Lys Gly
 610 615 620
 Ala Thr Gln Asn Gly Arg Leu Ile Thr Ala Asn Pro Ile Val Thr Asp
 625 630 635 640
 Lys Glu Lys Pro Val Asn Ile Glu Ala Glu Pro Pro Phe Gly Glu Ser
 645 650 655
 Tyr Ile Val Val Gly Ala Gly Glu Lys Ala Leu Lys Leu Ser Trp Phe
 660 665 670
 Lys Lys Gly Ser Ser Ile Gly Lys Met Phe Glu Ala Thr Ala Arg Gly
 675 680 685
 Ala Arg Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser
 690 695 700
 Ile Gly Gly Val Phe Thr Ser Met Gly Lys Leu Val His Gln Val Phe
 705 710 715 720
 Gly Thr Ala Tyr Gly Val Leu Phe Ser Gly Val Ser Trp Thr Met Lys
 725 730 735
 Ile Gly Ile Gly Ile Leu Leu Thr Trp Leu Gly Leu Asn Ser Arg Asn
 740 745 750

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Thr Ser Leu Ser Met Met Cys Ile Ala Ala Xaa Ile Val Thr Leu Tyr
 755 760 765
 Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
 770 775 780
 Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
 785 790 795 800
 His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
 805 810 815
 Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
 820 825 830
 Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
 835 840 845
 Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
 850 855 860
 Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
 865 870 875 880
 Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
 885 890 895
 Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
 900 905 910
 Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
 915 920 925
 Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
 930 935 940
 Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
 945 950 955 960
 Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
 965 970 975
 Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
 980 985 990
 Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
 995 1000 1005
 Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
 1010 1015 1020

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Gly	Pro	Val	Ser	Gln	His	Asn	Tyr	Arg	Pro	Gly	Tyr	His	Thr	Gln
	1025					1030					1035			
Ile	Thr	Gly	Pro	Trp	His	Leu	Gly	Lys	Leu	Glu	Met	Asp	Phe	Asp
	1040					1045					1050			
Phe	Cys	Asp	Gly	Thr	Thr	Val	Val	Val	Thr	Glu	Asp	Cys	Gly	Asn
	1055					1060					1065			
Arg	Gly	Pro	Ser	Leu	Arg	Thr	Thr	Thr	Ala	Ser	Gly	Lys	Leu	Ile
	1070					1075					1080			
Thr	Glu	Trp	Cys	Cys	Arg	Ser	Cys	Thr	Leu	Pro	Pro	Leu	Arg	Tyr
	1085					1090					1095			
Arg	Gly	Glu	Asp	Gly	Cys	Trp	Tyr	Gly	Met	Glu	Ile	Arg	Pro	Leu
	1100					1105					1110			
Lys	Glu	Lys	Glu	Glu	Asn	Leu	Val	Asn	Ser	Leu	Val	Thr	Ala	Gly
	1115					1120					1125			
His	Gly	Gln	Val	Asp	Asn	Phe	Ser	Leu	Gly	Val	Leu	Gly	Met	Ala
	1130					1135					1140			
Leu	Phe	Leu	Glu	Glu	Met	Leu	Arg	Thr	Arg	Val	Gly	Thr	Lys	His
	1145					1150					1155			
Ala	Ile	Leu	Leu	Val	Ala	Val	Ser	Phe	Val	Thr	Leu	Ile	Thr	Gly
	1160					1165					1170			
Asn	Met	Ser	Phe	Arg	Asp	Leu	Gly	Arg	Val	Met	Val	Met	Val	Gly
	1175					1180					1185			
Ala	Thr	Met	Thr	Asp	Asp	Ile	Gly	Met	Gly	Val	Thr	Tyr	Leu	Ala
	1190					1195					1200			
Leu	Leu	Ala	Ala	Phe	Lys	Val	Arg	Pro	Thr	Phe	Ala	Ala	Gly	Leu
	1205					1210					1215			
Leu	Leu	Arg	Lys	Leu	Thr	Ser	Lys	Glu	Leu	Met	Met	Thr	Thr	Ile
	1220					1225					1230			
Gly	Ile	Val	Leu	Leu	Ser	Gln	Ser	Thr	Leu	Pro	Glu	Thr	Ile	Leu
	1235					1240					1245			
Glu	Leu	Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met
	1250					1255					1260			
Val	Arg	Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala
	1265					1270					1275			

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Ile	Leu	Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys
	1280					1285					1290			
Val	Ser	Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe
	1295					1300					1305			
Leu	Thr	Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu
	1310					1315					1320			
Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
	1325					1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
	1340					1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
	1355					1360					1365			
Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
	1370					1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
	1385					1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
	1400					1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
	1415					1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Asp	Gln	Thr	Leu	Thr	Ile	Leu
	1430					1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
	1445					1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
	1460					1465					1470			
Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
	1475					1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
	1490					1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
	1505					1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
	1520					1525					1530			

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Met	His 1535	Lys	Gly	Lys	Arg	Ile 1540	Glu	Pro	Ser	Trp	Ala 1545	Asp	Val	Lys
Lys	Asp 1550	Leu	Ile	Ser	Tyr	Gly 1555	Gly	Gly	Trp	Lys	Leu 1560	Glu	Gly	Glu
Trp	Lys 1565	Glu	Gly	Glu	Glu	Val 1570	Gln	Val	Leu	Ala	Leu 1575	Glu	Pro	Gly
Lys	Asn 1580	Pro	Arg	Ala	Val	Gln 1585	Thr	Lys	Pro	Gly	Leu 1590	Phe	Lys	Thr
Asn	Ala 1595	Gly	Thr	Ile	Gly	Ala 1600	Val	Ser	Leu	Asp	Phe 1605	Ser	Pro	Gly
Thr	Ser 1610	Gly	Ser	Pro	Ile	Ile 1615	Asp	Lys	Lys	Gly	Lys 1620	Val	Val	Gly
Leu	Tyr 1625	Gly	Asn	Gly	Val	Val 1630	Thr	Arg	Ser	Gly	Ala 1635	Tyr	Val	Ser
Ala	Ile 1640	Ala	Gln	Thr	Glu	Lys 1645	Ser	Ile	Glu	Asp	Asn 1650	Pro	Glu	Ile
Glu	Asp 1655	Asp	Ile	Phe	Arg	Lys 1660	Arg	Arg	Leu	Thr	Ile 1665	Met	Asp	Leu
His	Pro 1670	Gly	Ala	Gly	Lys	Thr 1675	Lys	Arg	Tyr	Leu	Pro 1680	Ala	Ile	Val
Arg	Glu 1685	Ala	Ile	Lys	Arg	Gly 1690	Leu	Arg	Thr	Leu	Ile 1695	Leu	Ala	Pro
Thr	Arg 1700	Val	Val	Ala	Ala	Glu 1705	Met	Glu	Glu	Ala	Leu 1710	Arg	Gly	Leu
Pro	Ile 1715	Arg	Tyr	Gln	Thr	Pro 1720	Ala	Ile	Arg	Ala	Val 1725	His	Thr	Gly
Arg	Glu 1730	Ile	Val	Asp	Leu	Met 1735	Cys	His	Ala	Thr	Phe 1740	Thr	Met	Arg
Leu	Leu 1745	Ser	Pro	Val	Arg	Val 1750	Pro	Asn	Tyr	Asn	Leu 1755	Ile	Ile	Met
Asp	Glu 1760	Ala	His	Phe	Thr	Asp 1765	Pro	Ala	Ser	Ile	Ala 1770	Ala	Arg	Gly
Tyr	Ile 1775	Ser	Thr	Arg	Val	Glu 1780	Met	Gly	Glu	Ala	Ala 1785	Gly	Ile	Phe

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Met	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser
	1790					1795					1800			
Asn	Ala	Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser
	1805					1810					1815			
Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
	1820					1825					1830			
Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
	1835					1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
	1850					1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
	1865					1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
	1880					1885					1890			
Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
	1895					1900					1905			
Leu	Thr	Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro
	1910					1915					1920			
Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
	1925					1930					1935			
Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
	1940					1945					1950			
Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
	1955					1960					1965			
Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
	1970					1975					1980			
Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
	1985					1990					1995			
Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
	2000					2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
	2015					2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
	2030					2035					2040			

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Asn	Asn	Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr
	2045					2050					2055			
Lys	Glu	Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala
	2060					2065					2070			
Arg	Ile	Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe
	2075					2080					2085			
Ala	Ala	Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met
	2090					2095					2100			
Gly	Arg	Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Ala	Arg	Asp	Ala	Leu
	2105					2110					2115			
Asp	Asn	Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Ala	Gly	Gly	Arg	Ala
	2120					2125					2130			
Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
	2135					2140					2145			
Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
	2150					2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
	2165					2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
	2180					2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
	2195					2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
	2210					2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
	2225					2230					2235			
Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
	2240					2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
	2255					2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
	2270					2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
	2285					2290					2295			

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Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
	2300					2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
	2315					2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
	2330					2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Ile	Ala	Ala	Leu	Phe	Leu	Leu	Val
	2345					2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
	2360					2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
	2375					2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
	2390					2395					2400			
Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
	2405					2410					2415			
Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
	2420					2425					2430			
Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
	2435					2440					2445			
Glu	Gly	Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser
	2450					2455					2460			
Met	Ala	Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu
	2465					2470					2475			
Leu	Phe	Ser	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr
	2480					2485					2490			
Gly	Asn	Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu
	2495					2500					2505			
Asn	Ala	Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly
	2510					2515					2520			
Ile	Gln	Glu	Val	Asp	Arg	Thr	Leu	Ala	Lys	Glu	Gly	Ile	Lys	Arg
	2525					2530					2535			
Gly	Glu	Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu
	2540					2545					2550			

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Arg	Trp	Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val
	2555					2560					2565			
Val	Asp	Leu	Gly	Cys	Gly	Arg	Gly	Gly	Trp	Ser	Tyr	Tyr	Cys	Gly
	2570					2575					2580			
Gly	Leu	Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly
	2585					2590					2595			
Pro	Gly	His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn
	2600					2605					2610			
Leu	Val	Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro
	2615					2620					2625			
Glu	Lys	Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro
	2630					2635					2640			
Asn	Pro	Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu
	2645					2650					2655			
Val	Glu	Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val
	2660					2665					2670			
Leu	Asn	Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu
	2675					2680					2685			
Gln	Arg	Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg
	2690					2695					2700			
Asn	Ser	Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn
	2705					2710					2715			
Ile	Val	Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg
	2720					2725					2730			
Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
	2735					2740					2745			
Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
	2750					2755					2760			
Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
	2765					2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
	2780					2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
	2795					2800					2805			

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Ser	Ser	Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp
	2810					2815					2820			
Asp	Val	Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr
	2825					2830					2835			
Pro	Phe	Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg
	2840					2845					2850			
Thr	Gln	Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr
	2855					2860					2865			
Ala	Glu	Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg
	2870					2875					2880			
Met	Cys	Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala
	2885					2890					2895			
Ala	Leu	Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
	2900					2905					2910			
Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
	2915					2920					2925			
Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
	2930					2935					2940			
Asn	Met	Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys
	2945					2950					2955			
Ala	Lys	Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg
	2960					2965					2970			
Phe	Leu	Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp
	2975					2980					2985			
Phe	Ser	Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu
	2990					2995					3000			
His	Lys	Leu	Gly	Tyr	Ile	Leu	Arg	Asp	Val	Ser	Lys	Lys	Glu	Gly
	3005					3010					3015			
Gly	Ala	Met	Tyr	Ala	Asp	Asp	Thr	Ala	Gly	Trp	Asp	Thr	Arg	Ile
	3020					3025					3030			
Thr	Leu	Glu	Asp	Leu	Lys	Asn	Glu	Glu	Met	Val	Thr	Asn	His	Met
	3035					3040					3045			
Glu	Gly	Glu	His	Lys	Lys	Leu	Ala	Glu	Ala	Ile	Phe	Lys	Leu	Thr
	3050					3055					3060			

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Tyr	Gln	Asn	Lys	Val	Val	Arg	Val	Gln	Arg	Pro	Thr	Pro	Arg	Gly
	3065					3070					3075			
Thr	Val	Met	Asp	Ile	Ile	Ser	Arg	Arg	Asp	Gln	Arg	Gly	Ser	Gly
	3080					3085					3090			
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gaatacacag attacatgcc atccatgaaa agattcagaa gagaagagga agaagcagga     10260
gttctgtggg agaaagcaaa actaacatga aacaaggcta gaagtcaggc cggattaagc     10320
catagtacgg aaaaaactat gctacctgtg agccccgtcc aaggacgtta aaagaagtca     10380
ggccatcata aatgccatag cttgagtaaa ctatgcagcc tgtagctcca cctgagaagg     10440
tgtaaaaaat ccgggaggcc acaaaccatg gaagctgtac gcatggcgta gtggactagc     10500
ggtagagga gacctctccc ttacaaatcg cagcaacaat gggggcccaa ggcgagatga     10560
agctgtagtc tcgctggaag gactagaggt tagaggagac ccccccga aaacacag     10620
catattgacg ctgggaaaga ccagagatcc tgctgtctcc tcagcatcat tccaggcaca     10680
gaacgccaga aaatggaatg gtgctgttga atcaacaggt tct                        10723

```

```

<210> 8
<211> 3391
<212> PRT
<213> Artificial Sequence

```

```

<220>
<223> Dengue virus 1, BVS

```

```

<400> 8

```

```

Met Asn Asn Gln Arg Lys Lys Ala Lys Asn Thr Pro Phe Asn Met Leu
1          5          10          15

```

```

Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
          20          25          30

```

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Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45
 Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
 50 55 60
 Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
 65 70 75 80
 Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
 85 90 95
 Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
 100 105 110
 Met Ala Phe His Leu Thr Thr Arg Gly Gly Glu Pro His Met Ile Val
 115 120 125
 Ser Lys Gln Glu Arg Gly Lys Ser Leu Leu Phe Lys Thr Ser Ala Gly
 130 135 140
 Val Asn Met Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Leu Cys Glu
 145 150 155 160
 Asp Thr Met Thr Tyr Lys Cys Pro Arg Ile Thr Glu Ala Glu Pro Asp
 165 170 175
 Asp Val Asp Cys Trp Cys Asn Ala Thr Asp Thr Trp Val Thr Tyr Gly
 180 185 190
 Thr Cys Ser Gln Thr Gly Glu His Arg Arg Asp Lys Arg Ser Val Ala
 195 200 205
 Leu Ala Pro His Val Gly Leu Gly Leu Glu Thr Arg Ala Glu Thr Trp
 210 215 220
 Met Ser Ser Glu Gly Ala Trp Lys Gln Ile Gln Lys Val Glu Thr Trp
 225 230 235 240
 Ala Leu Arg His Pro Gly Phe Thr Val Ile Ala Leu Phe Leu Ala His
 245 250 255
 Ala Ile Gly Thr Ser Ile Thr Gln Lys Gly Ile Ile Phe Ile Leu Leu
 260 265 270
 Met Leu Val Thr Pro Ser Met Ala Met Arg Cys Val Gly Ile Gly Asn
 275 280 285
 Arg Asp Phe Val Glu Gly Leu Ser Gly Ala Thr Trp Val Asp Val Val
 290 295 300

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Leu Glu His Gly Ser Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
305          310          315          320

Leu Asp Ile Glu Leu Leu Lys Thr Glu Val Thr Asn Pro Ala Val Leu
          325          330          335

Arg Lys Leu Cys Ile Glu Ala Lys Ile Ser Asn Thr Thr Thr Asp Ser
          340          345          350

Arg Cys Pro Thr Gln Gly Glu Ala Thr Leu Val Glu Glu Gln Asp Ala
          355          360          365

Asn Phe Val Cys Arg Arg Thr Phe Val Asp Arg Gly Trp Gly Asn Gly
370          375          380

Cys Gly Leu Phe Gly Lys Gly Ser Leu Ile Thr Cys Ala Lys Phe Lys
385          390          395          400

Cys Val Thr Lys Leu Glu Gly Lys Ile Val Gln Tyr Glu Asn Leu Lys
          405          410          415

Tyr Ser Val Ile Val Thr Val His Thr Gly Asp Gln His Gln Val Gly
          420          425          430

Asn Glu Thr Thr Glu His Gly Thr Thr Ala Thr Ile Thr Pro Gln Ala
          435          440          445

Pro Thr Ser Glu Ile Gln Leu Thr Asp Tyr Gly Thr Leu Thr Leu Asp
          450          455          460

Cys Ser Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Val Leu Leu Thr
465          470          475          480

Met Lys Glu Arg Ser Trp Leu Val His Lys Gln Trp Phe Leu Asp Leu
          485          490          495

Pro Leu Pro Trp Thr Ser Gly Ala Ser Thr Ser Gln Glu Thr Trp Asn
          500          505          510

Arg Gln Asp Leu Leu Val Thr Phe Lys Thr Ala His Ala Lys Lys Gln
          515          520          525

Glu Val Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu
530          535          540

Thr Gly Ala Thr Glu Ile Gln Thr Ser Gly Thr Thr Thr Ile Phe Ala
545          550          555          560

Gly His Leu Lys Cys Arg Leu Lys Met Asp Lys Leu Thr Leu Lys Gly
          565          570          575

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Met Ser Tyr Val Met Cys Thr Gly Ser Phe Lys Leu Glu Lys Glu Val
580 585 590

Ala Glu Thr Gln His Gly Thr Val Leu Val Gln Val Lys Tyr Glu Gly
595 600 605

Thr Asp Ala Pro Cys Lys Ile Pro Phe Ser Thr Gln Asp Glu Lys Gly
610 615 620

Ala Thr Gln Asn Gly Arg Leu Ile Thr Ala Asn Pro Ile Val Thr Asp
625 630 635 640

Lys Glu Lys Pro Val Asn Ile Glu Ala Glu Pro Pro Phe Gly Glu Ser
645 650 655

Tyr Ile Val Val Gly Ala Gly Glu Lys Ala Leu Lys Leu Ser Trp Phe
660 665 670

Lys Lys Gly Ser Ser Ile Gly Lys Met Phe Glu Ala Thr Ala Arg Gly
675 680 685

Ala Arg Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser
690 695 700

Ile Gly Gly Val Phe Thr Ser Met Gly Lys Leu Val His Gln Val Phe
705 710 715 720

Gly Thr Ala Tyr Gly Val Leu Phe Ser Gly Val Ser Trp Thr Met Lys
725 730 735

Ile Gly Ile Gly Ile Leu Leu Thr Trp Leu Gly Leu Asn Ser Arg Asn
740 745 750

Thr Ser Leu Ser Met Met Cys Ile Ala Ala Ala Ile Val Thr Leu Tyr
755 760 765

Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
770 775 780

Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
785 790 795 800

His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
805 810 815

Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
820 825 830

Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
835 840 845

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Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
 850 855 860

Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
 865 870 875 880

Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
 885 890 895

Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
 900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
 915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
 930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
 945 950 955 960

Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
 965 970 975

Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
 980 985 990

Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
 995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
 1010 1015 1020

Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
 1025 1030 1035

Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
 1040 1045 1050

Phe Cys Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn
 1055 1060 1065

Arg Gly Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile
 1070 1075 1080

Thr Glu Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr
 1085 1090 1095

Arg Gly Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu
 1100 1105 1110

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Lys	Glu	Lys	Glu	Glu	Asn	Leu	Val	Asn	Ser	Leu	Val	Thr	Ala	Gly
1115						1120					1125			
His	Gly	Gln	Val	Asp	Asn	Phe	Ser	Leu	Gly	Val	Leu	Gly	Met	Ala
1130						1135					1140			
Leu	Phe	Leu	Glu	Glu	Met	Leu	Arg	Thr	Arg	Val	Gly	Thr	Lys	His
1145						1150					1155			
Ala	Ile	Leu	Leu	Val	Ala	Val	Ser	Phe	Val	Thr	Leu	Ile	Thr	Gly
1160						1165					1170			
Asn	Met	Ser	Phe	Arg	Asp	Leu	Gly	Arg	Val	Met	Val	Met	Val	Gly
1175						1180					1185			
Ala	Thr	Met	Thr	Asp	Asp	Ile	Gly	Met	Gly	Val	Thr	Tyr	Leu	Ala
1190						1195					1200			
Leu	Leu	Ala	Ala	Phe	Lys	Val	Arg	Pro	Thr	Phe	Ala	Ala	Gly	Leu
1205						1210					1215			
Leu	Leu	Arg	Lys	Leu	Thr	Ser	Lys	Glu	Leu	Met	Met	Thr	Thr	Ile
1220						1225					1230			
Gly	Ile	Val	Leu	Leu	Ser	Gln	Ser	Thr	Leu	Pro	Glu	Thr	Ile	Leu
1235						1240					1245			
Glu	Leu	Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met
1250						1255					1260			
Val	Arg	Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala
1265						1270					1275			
Ile	Leu	Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys
1280						1285					1290			
Val	Ser	Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe
1295						1300					1305			
Leu	Thr	Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu
1310						1315					1320			
Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
1325						1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
1340						1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
1355						1360					1365			

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Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
1370						1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
1385						1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
1400						1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
1415						1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Asp	Gln	Thr	Leu	Thr	Ile	Leu
1430						1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
1445						1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
1460						1465					1470			
Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
1475						1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
1490						1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
1505						1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
1520						1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
1535						1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
1550						1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
1565						1570					1575			
Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
1580						1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
1595						1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
1610						1615					1620			

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 Leu Tyr Gly Asn Gly Val Val Thr Arg Ser Gly Ala Tyr Val Ser
 1625 1630 1635

Ala Ile Ala Gln Thr Glu Lys Ser Ile Glu Asp Asn Pro Glu Ile
 1640 1645 1650

Glu Asp Asp Ile Phe Arg Lys Arg Arg Leu Thr Ile Met Asp Leu
 1655 1660 1665

His Pro Gly Ala Gly Lys Thr Lys Arg Tyr Leu Pro Ala Ile Val
 1670 1675 1680

Arg Glu Ala Ile Lys Arg Gly Leu Arg Thr Leu Ile Leu Ala Pro
 1685 1690 1695

Thr Arg Val Val Ala Ala Glu Met Glu Glu Ala Leu Arg Gly Leu
 1700 1705 1710

Pro Ile Arg Tyr Gln Thr Pro Ala Ile Arg Ala Val His Thr Gly
 1715 1720 1725

Arg Glu Ile Val Asp Leu Met Cys His Ala Thr Phe Thr Met Arg
 1730 1735 1740

Leu Leu Ser Pro Val Arg Val Pro Asn Tyr Asn Leu Ile Ile Met
 1745 1750 1755

Asp Glu Ala His Phe Thr Asp Pro Ala Ser Ile Ala Ala Arg Gly
 1760 1765 1770

Tyr Ile Ser Thr Arg Val Glu Met Gly Glu Ala Ala Gly Ile Phe
 1775 1780 1785

Met Thr Ala Thr Pro Pro Gly Ser Arg Asp Pro Phe Pro Gln Ser
 1790 1795 1800

Asn Ala Pro Ile Ile Asp Glu Glu Arg Glu Ile Pro Glu Arg Ser
 1805 1810 1815

Trp Asn Ser Gly His Glu Trp Val Thr Asp Phe Lys Gly Lys Thr
 1820 1825 1830

Val Trp Phe Val Pro Ser Ile Lys Ala Gly Asn Asp Ile Ala Ala
 1835 1840 1845

Cys Leu Arg Lys Asn Gly Lys Lys Val Ile Gln Leu Ser Arg Lys
 1850 1855 1860

Thr Phe Asp Ser Glu Tyr Val Lys Thr Arg Thr Asn Asp Trp Asp
 1865 1870 1875

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Phe Val 1880	Val Thr Thr Asp Ile 1885	Ser Glu Met Gly Ala 1890	Asn Phe Lys
Ala Glu 1895	Arg Val Ile Asp Pro 1900	Arg Arg Cys Met Lys 1905	Pro Val Ile
Leu Thr 1910	Asp Gly Glu Glu Arg 1915	Val Ile Leu Ala Gly 1920	Pro Met Pro
Val Thr 1925	His Ser Ser Ala Ala 1930	Gln Arg Arg Gly Arg 1935	Ile Gly Arg
Asn Pro 1940	Lys Asn Glu Asn Asp 1945	Gln Tyr Ile Tyr Met 1950	Gly Glu Pro
Leu Glu 1955	Asn Asp Glu Asp Cys 1960	Ala His Trp Lys Glu 1965	Ala Lys Met
Leu Leu 1970	Asp Asn Ile Asn Thr 1975	Pro Glu Gly Ile Ile 1980	Pro Ser Met
Phe Glu 1985	Pro Glu Arg Glu Lys 1990	Val Asp Ala Ile Asp 1995	Gly Glu Tyr
Arg Leu 2000	Arg Gly Glu Ala Arg 2005	Lys Thr Phe Val Asp 2010	Leu Met Arg
Arg Gly 2015	Asp Leu Pro Val Trp 2020	Leu Ala Tyr Arg Val 2025	Ala Ala Glu
Gly Ile 2030	Asn Tyr Ala Asp Arg 2035	Arg Trp Cys Phe Asp 2040	Gly Val Lys
Asn Asn 2045	Gln Ile Leu Glu Glu 2050	Asn Val Glu Val Glu 2055	Ile Trp Thr
Lys Glu 2060	Gly Glu Arg Lys Lys 2065	Leu Lys Pro Arg Trp 2070	Leu Asp Ala
Arg Ile 2075	Tyr Ser Asp Pro Leu 2080	Ala Leu Lys Glu Phe 2085	Lys Glu Phe
Ala Ala 2090	Gly Arg Lys Ser Leu 2095	Thr Leu Asn Leu Ile 2100	Thr Glu Met
Gly Arg 2105	Leu Pro Thr Phe Met 2110	Thr Gln Lys Ala Arg 2115	Asp Ala Leu
Asp Asn 2120	Leu Ala Val Leu His 2125	Thr Ala Glu Ala Gly 2130	Gly Arg Ala

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Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
2135						2140					2145			
Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
2150						2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
2165						2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
2180						2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
2195						2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
2210						2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
2225						2230					2235			
Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
2240						2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
2255						2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
2270						2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
2285						2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
2300						2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
2315						2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
2330						2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Ile	Ala	Ala	Leu	Phe	Leu	Leu	Val
2345						2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
2360						2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
2375						2380					2385			

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Thr Val 2390	Asp Gly Ile Thr Val 2395	Ile Asp Leu Asp Pro 2400	Ile Pro Tyr
Asp Pro 2405	Lys Phe Glu Lys Gln 2410	Leu Gly Gln Val Met 2415	Leu Leu Val
Leu Cys 2420	Val Thr Gln Val Leu 2425	Met Met Arg Thr Thr 2430	Trp Ala Leu
Cys Glu 2435	Ala Leu Thr Leu Ala 2440	Thr Gly Pro Ile Ser 2445	Thr Leu Trp
Glu Gly 2450	Asn Pro Gly Arg Phe 2455	Trp Asn Thr Thr Ile 2460	Ala Val Ser
Met Ala 2465	Asn Ile Phe Arg Gly 2470	Ser Tyr Leu Ala Gly 2475	Ala Gly Leu
Leu Phe 2480	Ser Ile Met Lys Asn 2485	Thr Thr Asn Thr Arg 2490	Arg Gly Thr
Gly Asn 2495	Ile Gly Glu Thr Leu 2500	Gly Glu Lys Trp Lys 2505	Ser Arg Leu
Asn Ala 2510	Leu Gly Lys Ser Glu 2515	Phe Gln Ile Tyr Lys 2520	Lys Ser Gly
Ile Gln 2525	Glu Val Asp Arg Thr 2530	Leu Ala Lys Glu Gly 2535	Ile Lys Arg
Gly Glu 2540	Thr Asp His His Ala 2545	Val Ser Arg Gly Ser 2550	Ala Lys Leu
Arg Trp 2555	Phe Val Glu Arg Asn 2560	Met Val Thr Pro Glu 2565	Gly Lys Val
Val Asp 2570	Leu Gly Cys Gly Arg 2575	Gly Gly Trp Ser Tyr 2580	Tyr Cys Gly
Gly Leu 2585	Lys Asn Val Arg Glu 2590	Val Lys Gly Leu Thr 2595	Lys Gly Gly
Pro Gly 2600	His Glu Glu Pro Ile 2605	Pro Met Ser Thr Tyr 2610	Gly Trp Asn
Leu Val 2615	Arg Leu Gln Ser Gly 2620	Val Asp Val Phe Phe 2625	Ile Pro Pro
Glu Lys 2630	Cys Asp Thr Leu Leu 2635	Cys Asp Ile Gly Glu 2640	Ser Ser Pro

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Asn 2645	Pro	Thr	Val	Glu	Ala	Gly 2650	Arg	Thr	Leu	Arg	Val 2655	Leu	Asn	Leu
Val 2660	Glu	Asn	Trp	Leu	Asn	Asn 2665	Asn	Thr	Gln	Phe	Cys 2670	Ile	Lys	Val
Leu 2675	Asn	Pro	Tyr	Met	Pro	Ser 2680	Val	Ile	Glu	Lys	Met 2685	Glu	Ala	Leu
Gln 2690	Arg	Lys	Tyr	Gly	Gly	Ala 2695	Leu	Val	Arg	Asn	Pro 2700	Leu	Ser	Arg
Asn 2705	Ser	Thr	His	Glu	Met	Tyr 2710	Trp	Val	Ser	Asn	Ala 2715	Ser	Gly	Asn
Ile 2720	Val	Ser	Ser	Val	Asn	Met 2725	Ile	Ser	Arg	Met	Leu 2730	Ile	Asn	Arg
Phe 2735	Thr	Met	Arg	Tyr	Lys	Lys 2740	Ala	Thr	Tyr	Glu	Pro 2745	Asp	Val	Asp
Leu 2750	Gly	Ser	Gly	Thr	Arg	Asn 2755	Ile	Gly	Ile	Glu	Ser 2760	Glu	Ile	Pro
Asn 2765	Leu	Asp	Ile	Ile	Gly	Lys 2770	Arg	Ile	Glu	Lys	Ile 2775	Lys	Gln	Glu
His 2780	Glu	Thr	Ser	Trp	His	Tyr 2785	Asp	Gln	Asp	His	Pro 2790	Tyr	Lys	Thr
Trp 2795	Ala	Tyr	His	Gly	Ser	Tyr 2800	Glu	Thr	Lys	Gln	Thr 2805	Gly	Ser	Ala
Ser 2810	Ser	Met	Val	Asn	Gly	Val 2815	Val	Arg	Leu	Leu	Thr 2820	Lys	Pro	Trp
Asp 2825	Val	Val	Pro	Met	Val	Thr 2830	Gln	Met	Ala	Met	Thr 2835	Asp	Thr	Thr
Pro 2840	Phe	Gly	Gln	Gln	Arg	Val 2845	Phe	Lys	Glu	Lys	Val 2850	Asp	Thr	Arg
Thr 2855	Gln	Glu	Pro	Lys	Glu	Gly 2860	Thr	Lys	Lys	Leu	Met 2865	Lys	Ile	Thr
Ala 2870	Glu	Trp	Leu	Trp	Lys	Glu 2875	Leu	Gly	Lys	Lys	Lys 2880	Thr	Pro	Arg
Met 2885	Cys	Thr	Arg	Glu	Glu	Phe 2890	Thr	Arg	Lys	Val	Arg 2895	Ser	Asn	Ala

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Ala	Leu	Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
2900						2905					2910			
Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
2915						2920					2925			
Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
2930						2935					2940			
Asn	Met	Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys
2945						2950					2955			
Ala	Lys	Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg
2960						2965					2970			
Phe	Leu	Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp
2975						2980					2985			
Phe	Ser	Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu
2990						2995					3000			
His	Lys	Leu	Gly	Tyr	Ile	Leu	Arg	Asp	Val	Ser	Lys	Lys	Glu	Gly
3005						3010					3015			
Gly	Ala	Met	Tyr	Ala	Asp	Asp	Thr	Ala	Gly	Trp	Asp	Thr	Arg	Ile
3020						3025					3030			
Thr	Leu	Glu	Asp	Leu	Lys	Asn	Glu	Glu	Met	Val	Thr	Asn	His	Met
3035						3040					3045			
Glu	Gly	Glu	His	Lys	Lys	Leu	Ala	Glu	Ala	Ile	Phe	Lys	Leu	Thr
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Phe Cys Ser His His Phe His Glu Leu Ile Met Lys Asp Gly Arg
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Val Leu Val Val Pro Cys Arg Asn Gln Asp Glu Leu Ile Gly Arg
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Ala Arg Ile Ser Gln Gly Ala Gly Trp Ser Leu Arg Glu Thr Ala
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Cys Leu Gly Lys Ser Tyr Ala Gln Met Trp Ser Leu Met Tyr Phe
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His Arg Arg Asp Leu Arg Leu Ala Ala Asn Ala Ile Cys Ser Ala
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Val Pro Ser His Trp Val Pro Thr Ser Arg Thr Thr Trp Ser Ile
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His Ala Lys His Glu Trp Met Thr Thr Glu Asp Met Leu Thr Val
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Trp Asn Arg Val Trp Ile Gln Glu Asn Pro Trp Met Glu Asp Lys
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<223> Dengue virus serotype 2, Pre-Master

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```
Met Asn Asn Gln Arg Lys Lys Ala Lys Asn Thr Pro Phe Asn Met Leu
1 5 10 15
```

```
Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
20 25 30
```

```
Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
35 40 45
```

```
Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
50 55 60
```

```
Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
65 70 75 80
```

```
Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
85 90 95
```

```
Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
100 105 110
```

```
Met Ala Phe His Leu Thr Thr Arg Asn Gly Glu Pro His Met Ile Val
115 120 125
```

```
Ser Arg Gln Glu Lys Gly Lys Ser Leu Leu Phe Lys Thr Glu Val Gly
130 135 140
```

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Val Asn Met Cys Thr Leu Met Ala Met Asp Leu Gly Glu Leu Cys Glu
 145 150 155 160
 Asp Thr Ile Thr Tyr Glu Cys Pro Leu Leu Arg Gln Asn Glu Pro Glu
 165 170 175
 Asp Ile Asp Cys Trp Cys Asn Ser Thr Ser Thr Trp Val Thr Tyr Gly
 180 185 190
 Thr Cys Thr Thr Met Gly Glu His Arg Arg Glu Lys Arg Ser Val Ala
 195 200 205
 Leu Val Pro His Val Gly Met Gly Leu Glu Thr Arg Thr Glu Thr Trp
 210 215 220
 Met Ser Ser Glu Gly Ala Trp Lys His Val Gln Arg Ile Glu Thr Trp
 225 230 235 240
 Ile Leu Arg His Pro Gly Phe Thr Met Met Ala Ala Ile Leu Ala Tyr
 245 250 255
 Thr Ile Gly Thr Thr His Phe Gln Arg Ala Leu Ile Phe Ile Leu Leu
 260 265 270
 Thr Ala Val Thr Pro Ser Met Thr Met Arg Cys Ile Gly Met Ser Asn
 275 280 285
 Arg Asp Phe Val Glu Gly Val Ser Gly Gly Ser Trp Val Asp Ile Val
 290 295 300
 Leu Glu His Gly Ser Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
 305 310 315 320
 Leu Asp Phe Glu Leu Ile Lys Thr Glu Ala Lys Gln Pro Ala Thr Leu
 325 330 335
 Arg Lys Tyr Cys Ile Glu Ala Lys Leu Thr Asn Thr Thr Thr Glu Ser
 340 345 350
 Arg Cys Pro Thr Gln Gly Glu Pro Ser Leu Asn Glu Glu Gln Asp Lys
 355 360 365
 Arg Phe Val Cys Lys His Ser Met Val Asp Arg Gly Trp Gly Asn Gly
 370 375 380
 Cys Gly Leu Phe Gly Lys Gly Gly Ile Val Thr Cys Ala Met Phe Arg
 385 390 395 400
 Cys Lys Lys Asn Met Glu Gly Lys Val Val Gln Pro Glu Asn Leu Glu
 405 410 415

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Tyr Thr Ile Val₄₂₀ Ile Thr Pro His Ser₄₂₅ Gly Glu Glu His Ala₄₃₀ Val Gly

Asn Asp Thr₄₃₅ Gly Lys His Gly Lys₄₄₀ Glu Ile Lys Ile Thr₄₄₅ Pro Gln Ser

Ser Ile Thr Glu Ala Glu Leu₄₅₅ Thr Gly Tyr Gly Thr₄₆₀ Val Thr Met Glu

Cys₄₆₅ Ser Pro Arg Thr Gly₄₇₀ Leu Asp Phe Asn Glu₄₇₅ Met Val Leu Leu Gln₄₈₀

Met Glu Asn Lys Ala₄₈₅ Trp Leu Val His Arg₄₉₀ Gln Trp Phe Leu Asp₄₉₅ Leu

Pro Leu Pro Trp₅₀₀ Leu Pro Gly Ala Asp₅₀₅ Thr Gln Gly Ser Asn₅₁₀ Trp Ile

Gln Lys Glu₅₁₅ Thr Leu Val Thr Phe₅₂₀ Lys Asn Pro His Ala₅₂₅ Lys Lys Gln

Asp Val₅₃₀ Val Val Leu Gly Ser₅₃₅ Gln Glu Gly Ala Met₅₄₀ His Thr Ala Leu

Thr₅₄₅ Gly Ala Thr Glu Ile₅₅₀ Gln Met Ser Ser Gly₅₅₅ Asn Leu Leu Phe Thr₅₆₀

Gly His Leu Lys Cys₅₆₅ Arg Leu Arg Met Asp₅₇₀ Lys Leu Gln Leu Lys₅₇₅ Gly

Met Ser Tyr Ser₅₈₀ Met Cys Thr Gly Lys₅₈₅ Phe Lys Val Val Lys₅₉₀ Glu Ile

Ala Glu Thr₅₉₅ Gln His Gly Thr Ile₆₀₀ Val Ile Arg Val Gln₆₀₅ Tyr Glu Gly

Asp Gly₆₁₀ Ser Pro Cys Lys Ile₆₁₅ Pro Phe Glu Ile Met₆₂₀ Asp Leu Glu Lys

Arg₆₂₅ His Val Leu Gly Arg₆₃₀ Leu Ile Thr Val Asn₆₃₅ Pro Ile Val Thr Glu₆₄₀

Lys Asp Ser Pro Val₆₄₅ Asn Ile Glu Ala Glu₆₅₀ Pro Pro Phe Gly Asp₆₅₅ Ser

Tyr Ile Ile Ile₆₆₀ Gly Val Glu Pro Gly₆₆₅ Gln Leu Lys Leu Asn₆₇₀ Trp Phe

Lys Lys Gly₆₇₅ Ser Ser Ile Gly Gln₆₈₀ Met Phe Glu Thr Thr₆₈₅ Met Arg Gly

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Ala Lys Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser
690 695 700

Leu Gly Gly Val Phe Thr Ser Ile Gly Lys Ala Leu His Gln Val Phe
705 710 715 720

Gly Ala Ile Tyr Gly Ala Ala Phe Ser Gly Val Ser Trp Thr Met Lys
725 730 735

Ile Leu Ile Gly Val Ile Ile Thr Trp Ile Gly Met Asn Ser Arg Ser
740 745 750

Thr Ser Leu Ser Val Thr Leu Val Leu Val Gly Ile Val Thr Leu Tyr
755 760 765

Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
770 775 780

Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
785 790 795 800

His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
805 810 815

Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
820 825 830

Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
835 840 845

Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
850 855 860

Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
865 870 875 880

Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
885 890 895

Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
945 950 955 960

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Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
 965 970 975

Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
 980 985 990

Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
 995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
 1010 1015 1020

Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
 1025 1030 1035

Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
 1040 1045 1050

Phe Cys Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn
 1055 1060 1065

Arg Gly Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile
 1070 1075 1080

Thr Glu Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr
 1085 1090 1095

Arg Gly Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu
 1100 1105 1110

Lys Glu Lys Glu Glu Asn Leu Val Asn Ser Leu Val Thr Ala Gly
 1115 1120 1125

His Gly Gln Val Asp Asn Phe Ser Leu Gly Val Leu Gly Met Ala
 1130 1135 1140

Leu Phe Leu Glu Glu Met Leu Arg Thr Arg Val Gly Thr Lys His
 1145 1150 1155

Ala Ile Leu Leu Val Ala Val Ser Phe Val Thr Leu Ile Thr Gly
 1160 1165 1170

Asn Met Ser Phe Arg Asp Leu Gly Arg Val Met Val Met Val Gly
 1175 1180 1185

Ala Thr Met Thr Asp Asp Ile Gly Met Gly Val Thr Tyr Leu Ala
 1190 1195 1200

Leu Leu Ala Ala Phe Lys Val Arg Pro Thr Phe Ala Ala Gly Leu
 1205 1210 1215

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Leu	Leu	Arg	Lys	Leu	Thr	Ser	Lys	Glu	Leu	Met	Met	Thr	Thr	Ile
	1220					1225					1230			
Gly	Ile	Val	Leu	Leu	Ser	Gln	Ser	Thr	Ile	Pro	Glu	Thr	Ile	Leu
	1235					1240					1245			
Glu	Leu	Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met
	1250					1255					1260			
Val	Arg	Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala
	1265					1270					1275			
Ile	Leu	Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys
	1280					1285					1290			
Val	Ser	Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe
	1295					1300					1305			
Leu	Thr	Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu
	1310					1315					1320			
Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
	1325					1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
	1340					1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
	1355					1360					1365			
Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
	1370					1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
	1385					1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
	1400					1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
	1415					1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Glu	Gln	Thr	Leu	Thr	Ile	Leu
	1430					1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
	1445					1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
	1460					1465					1470			

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Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
	1475					1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
	1490					1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
	1505					1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
	1520					1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
	1535					1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
	1550					1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
	1565					1570					1575			
Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
	1580					1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
	1595					1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
	1610					1615					1620			
Leu	Tyr	Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser
	1625					1630					1635			
Ala	Ile	Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile
	1640					1645					1650			
Glu	Asp	Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu
	1655					1660					1665			
His	Pro	Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val
	1670					1675					1680			
Arg	Glu	Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro
	1685					1690					1695			
Thr	Arg	Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu
	1700					1705					1710			
Pro	Ile	Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly
	1715					1720					1725			

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Arg	Glu	Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg
	1730					1735					1740			
Leu	Leu	Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met
	1745					1750					1755			
Asp	Glu	Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly
	1760					1765					1770			
Tyr	Ile	Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe
	1775					1780					1785			
Met	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser
	1790					1795					1800			
Asn	Ala	Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser
	1805					1810					1815			
Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
	1820					1825					1830			
Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
	1835					1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
	1850					1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
	1865					1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
	1880					1885					1890			
Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
	1895					1900					1905			
Leu	Thr	Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro
	1910					1915					1920			
Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
	1925					1930					1935			
Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
	1940					1945					1950			
Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
	1955					1960					1965			
Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
	1970					1975					1980			

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Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
	1985					1990					1995			
Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
	2000					2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
	2015					2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
	2030					2035					2040			
Asn	Asn	Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr
	2045					2050					2055			
Lys	Glu	Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala
	2060					2065					2070			
Arg	Ile	Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe
	2075					2080					2085			
Ala	Ala	Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met
	2090					2095					2100			
Gly	Arg	Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Ala	Arg	Asp	Ala	Leu
	2105					2110					2115			
Asp	Asn	Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Ala	Gly	Gly	Arg	Ala
	2120					2125					2130			
Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
	2135					2140					2145			
Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
	2150					2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
	2165					2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
	2180					2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
	2195					2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
	2210					2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
	2225					2230					2235			

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Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
	2240					2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
	2255					2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
	2270					2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
	2285					2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
	2300					2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
	2315					2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
	2330					2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Thr	Ala	Ala	Leu	Phe	Leu	Leu	Val
	2345					2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
	2360					2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
	2375					2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
	2390					2395					2400			
Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
	2405					2410					2415			
Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
	2420					2425					2430			
Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
	2435					2440					2445			
Glu	Gly	Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser
	2450					2455					2460			
Met	Ala	Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu
	2465					2470					2475			
Leu	Phe	Ser	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr
	2480					2485					2490			

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Gly	Asn 2495	Ile	Gly	Glu	Thr	Leu 2500	Gly	Glu	Lys	Trp	Lys 2505	Ser	Arg	Leu
Asn	Ala 2510	Leu	Gly	Lys	Ser	Glu 2515	Phe	Gln	Ile	Tyr	Lys 2520	Lys	Ser	Gly
Ile	Gln 2525	Glu	Val	Asp	Arg	Thr 2530	Leu	Ala	Lys	Glu	Gly 2535	Ile	Lys	Arg
Gly	Glu 2540	Thr	Asp	His	His	Ala 2545	Val	Ser	Arg	Gly	Ser 2550	Ala	Lys	Leu
Arg	Trp 2555	Phe	Val	Glu	Arg	Asn 2560	Met	Val	Thr	Pro	Glu 2565	Gly	Lys	Val
Val	Asp 2570	Leu	Gly	Cys	Gly	Arg 2575	Gly	Gly	Trp	Ser	Tyr 2580	Tyr	Cys	Gly
Gly	Leu 2585	Lys	Asn	Val	Arg	Glu 2590	Val	Lys	Gly	Leu	Thr 2595	Lys	Gly	Gly
Pro	Gly 2600	His	Glu	Glu	Pro	Ile 2605	Pro	Met	Ser	Thr	Tyr 2610	Gly	Trp	Asn
Leu	Val 2615	Arg	Leu	Gln	Ser	Gly 2620	Val	Asp	Val	Phe	Phe 2625	Ile	Pro	Pro
Glu	Lys 2630	Cys	Asp	Thr	Leu	Leu 2635	Cys	Asp	Ile	Gly	Glu 2640	Ser	Ser	Pro
Asn	Pro 2645	Thr	Val	Glu	Ala	Gly 2650	Arg	Thr	Leu	Arg	Val 2655	Leu	Asn	Leu
Val	Glu 2660	Asn	Trp	Leu	Asn	Asn 2665	Asn	Thr	Gln	Phe	Cys 2670	Ile	Lys	Val
Leu	Asn 2675	Pro	Tyr	Met	Pro	Ser 2680	Val	Ile	Glu	Lys	Met 2685	Glu	Ala	Leu
Gln	Arg 2690	Lys	Tyr	Gly	Gly	Ala 2695	Leu	Val	Arg	Asn	Pro 2700	Leu	Ser	Arg
Asn	Ser 2705	Thr	His	Glu	Met	Tyr 2710	Trp	Val	Ser	Asn	Ala 2715	Ser	Gly	Asn
Ile	Val 2720	Ser	Ser	Val	Asn	Met 2725	Ile	Ser	Arg	Met	Leu 2730	Ile	Asn	Arg
Phe	Thr 2735	Met	Arg	Tyr	Lys	Lys 2740	Ala	Thr	Tyr	Glu	Pro 2745	Asp	Val	Asp

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Leu	Gly 2750	Ser	Gly	Thr	Arg	Asn 2755	Ile	Gly	Ile	Glu	Ser 2760	Glu	Ile	Pro
Asn	Leu 2765	Asp	Ile	Ile	Gly	Lys 2770	Arg	Ile	Glu	Lys	Ile 2775	Lys	Gln	Glu
His	Glu 2780	Thr	Ser	Trp	His	Tyr 2785	Asp	Gln	Asp	His	Pro 2790	Tyr	Lys	Thr
Trp	Ala 2795	Tyr	His	Gly	Ser	Tyr 2800	Glu	Thr	Lys	Gln	Thr 2805	Gly	Ser	Ala
Ser	Ser 2810	Met	Val	Asn	Gly	Val 2815	Val	Arg	Leu	Leu	Thr 2820	Lys	Pro	Trp
Asp	Val 2825	Val	Pro	Met	Val	Thr 2830	Gln	Met	Ala	Met	Thr 2835	Asp	Thr	Thr
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Thr	Val 3080	Met	Asp	Ile	Ile	Ser 3085	Arg	Arg	Asp	Gln	Arg 3090	Gly	Ser	Gly
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Gln	His 3125	Leu	Thr	Ile	Thr	Glu 3130	Glu	Ile	Ala	Val	Gln 3135	Asn	Trp	Leu
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Asp	Asp 3155	Cys	Val	Val	Lys	Pro 3160	Leu	Asp	Asp	Arg	Phe 3165	Ala	Ser	Ala
Leu	Thr 3170	Ala	Leu	Asn	Asp	Met 3175	Gly	Lys	Ile	Arg	Lys 3180	Asp	Ile	Gln
Gln	Trp 3185	Glu	Pro	Ser	Arg	Gly 3190	Trp	Asn	Asp	Trp	Thr 3195	Gln	Val	Pro
Phe	Cys 3200	Ser	His	His	Phe	His 3205	Glu	Leu	Ile	Met	Lys 3210	Asp	Gly	Arg
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Cys	Leu 3245	Gly	Lys	Ser	Tyr	Ala 3250	Gln	Met	Trp	Ser	Leu 3255	Met	Tyr	Phe

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His Ala Lys His Glu Trp Met Thr Thr Glu Asp Met Leu Thr Val
3290 3295 3300

Trp Asn Arg Val Trp Ile Gln Glu Asn Pro Trp Met Glu Asp Lys
3305 3310 3315

Thr Pro Val Glu Ser Trp Glu Glu Ile Pro Tyr Leu Gly Lys Arg
3320 3325 3330

Glu Asp Gln Trp Cys Gly Ser Leu Ile Gly Leu Thr Ser Arg Ala
3335 3340 3345

Thr Trp Ala Lys Asn Ile Gln Ala Ala Ile Asn Gln Val Arg Ser
3350 3355 3360

Leu Ile Gly Asn Glu Glu Tyr Thr Asp Tyr Met Pro Ser Met Lys
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ctgacaaaga gattctcact tggaatgctg cagggacgag gaccattaaa actgttcatg 240
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ttaacagctc	taaatgacat	gggaaagatt	aggaaagaca	tacaacaatg	ggaaccttca	9660
agaggatgga	atgattggac	acaagtggcc	ttctgttcac	accattttcca	tgagttaatc	9720
atgaaagacg	gtcgcgtact	cgttggtcca	tgtagaaacc	aagatgaact	gattggcaga	9780
gcccgaatct	cccaaggagc	agggtggtct	ttgcgggaga	cggcctgttt	ggggaagtct	9840
tacgccccaa	tgtggagctt	gatgtacttc	cacagacgcg	acctcaggct	ggcggcaaat	9900
gctatttgct	cggcagtacc	atcacattgg	gttccaacaa	gtcgaacaac	ctggtccata	9960
catgctaaac	atgaatggat	gacaacggaa	gacatgctga	cagtctggaa	caggggtgtgg	10020
attcaagaaa	acccatggat	ggaagacaaa	actccagtgg	aatcatggga	ggaaatccca	10080
tacttgggga	aaagagaaga	ccaatgggtc	ggctcattga	ttgggttaac	aagcaggggcc	10140
acctggggca	agaacatcca	agcagcaata	aatcaagtta	gatcccttat	aggcaatgaa	10200
gaatacacag	attacatgcc	atccatgaaa	agattcagaa	gagaagagga	agaagcagga	10260
gttctgtggt	agaaagcaaa	actaacatga	aacaaggcta	gaagtcagggt	cggattaagc	10320
catagtacgg	aaaaaactat	gctacctgtg	agccccgtcc	aaggacgtta	aaagaagtca	10380
ggccatcata	aatgccatag	cttgagtaaa	ctatgcagcc	tgtagctcca	cctgagaagg	10440
tgtaaaaaat	ccgggaggcc	acaaaccatg	gaagctgtac	gcatggcgta	gtggactagc	10500
ggtagagga	gacccctccc	ttacaaatcg	cagcaacaat	gggggcccac	ggcgagatga	10560
agctgtagtc	tcgctggaag	gactagaggt	tagaggagac	cccccgaaa	caaaaaacag	10620
catattgacg	ctgggaaaga	ccagagatcc	tgctgtctcc	tcagcatcat	tccaggcaca	10680
gaacgccaga	aaatggaatg	gtgctgttga	atcaacaggt	tct		10723

<210> 12
 <211> 3391

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<212> PRT

<213> Artificial Sequence

<220>

<223> Dengue virus serotype 2, MVS

<400> 12

Met Asn Asn Gln Arg Lys Lys Ala Lys Asn Thr Pro Phe Asn Met Leu
1 5 10 15

Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
20 25 30

Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
50 55 60

Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
65 70 75 80

Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
85 90 95

Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
100 105 110

Met Ala Phe His Leu Thr Thr Arg Asn Gly Glu Pro His Met Ile Val
115 120 125

Ser Arg Gln Glu Lys Gly Lys Ser Leu Leu Phe Lys Thr Glu Val Gly
130 135 140

Val Asn Met Cys Thr Leu Met Ala Met Asp Leu Gly Glu Leu Cys Glu
145 150 155 160

Asp Thr Ile Thr Tyr Glu Cys Pro Leu Leu Arg Gln Asn Glu Pro Glu
165 170 175

Asp Ile Asp Cys Trp Cys Asn Ser Thr Ser Thr Trp Val Thr Tyr Gly
180 185 190

Thr Cys Thr Thr Met Gly Glu His Arg Arg Glu Lys Arg Ser Val Ala
195 200 205

Leu Val Pro His Val Gly Met Gly Leu Glu Thr Arg Thr Glu Thr Trp
210 215 220

Met Ser Ser Glu Gly Ala Trp Lys His Val Gln Arg Ile Glu Thr Trp
225 230 235 240

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Ile Leu Arg His Pro Gly Phe Thr Met Met Ala Ala Ile Leu Ala Tyr
245 250 255

Thr Ile Gly Thr Thr His Phe Gln Arg Ala Leu Ile Phe Ile Leu Leu
260 265 270

Thr Ala Val Thr Pro Ser Met Thr Met Arg Cys Ile Gly Met Ser Asn
275 280 285

Arg Asp Phe Val Glu Gly Val Ser Gly Gly Ser Trp Val Asp Ile Val
290 295 300

Leu Glu His Gly Ser Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
305 310 315 320

Leu Asp Phe Glu Leu Ile Lys Thr Glu Ala Lys Gln Pro Ala Thr Leu
325 330 335

Arg Lys Tyr Cys Ile Glu Ala Lys Leu Thr Asn Thr Thr Thr Glu Ser
340 345 350

Arg Cys Pro Thr Gln Gly Glu Pro Ser Leu Asn Glu Glu Gln Asp Lys
355 360 365

Arg Phe Val Cys Lys His Ser Met Val Asp Arg Gly Trp Gly Asn Gly
370 375 380

Cys Gly Leu Phe Gly Lys Gly Gly Ile Val Thr Cys Ala Met Phe Arg
385 390 395 400

Cys Lys Lys Asn Met Glu Gly Lys Val Val Gln Pro Glu Asn Leu Glu
405 410 415

Tyr Thr Ile Val Ile Thr Pro His Ser Gly Glu Glu His Ala Val Gly
420 425 430

Asn Asp Thr Gly Lys His Gly Lys Glu Ile Lys Ile Thr Pro Gln Ser
435 440 445

Ser Ile Thr Glu Ala Glu Leu Thr Gly Tyr Gly Thr Val Thr Met Glu
450 455 460

Cys Ser Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Val Leu Leu Gln
465 470 475 480

Met Glu Asn Lys Ala Trp Leu Val His Arg Gln Trp Phe Leu Asp Leu
485 490 495

Pro Leu Pro Trp Leu Pro Gly Ala Asp Thr Gln Gly Ser Asn Trp Ile
500 505 510

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Gln Lys Glu Thr Leu Val Thr Phe Lys Asn Pro His Ala Lys Lys Gln
515 520 525

Asp Val Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu
530 535 540

Thr Gly Ala Thr Glu Ile Gln Met Ser Ser Gly Asn Leu Leu Phe Thr
545 550 555 560

Gly His Leu Lys Cys Arg Leu Arg Met Asp Lys Leu Gln Leu Lys Gly
565 570 575

Met Ser Tyr Ser Met Cys Thr Gly Lys Phe Lys Val Val Lys Glu Ile
580 585 590

Ala Glu Thr Gln His Gly Thr Ile Val Ile Arg Val Gln Tyr Glu Gly
595 600 605

Asp Gly Ser Pro Cys Lys Ile Pro Phe Glu Ile Met Asp Leu Glu Lys
610 615 620

Arg His Val Leu Gly Arg Leu Ile Thr Val Asn Pro Ile Val Thr Glu
625 630 635 640

Lys Asp Ser Pro Val Asn Ile Glu Ala Glu Pro Pro Phe Gly Asp Ser
645 650 655

Tyr Ile Ile Ile Gly Val Glu Pro Gly Gln Leu Lys Leu Asn Trp Phe
660 665 670

Lys Lys Gly Ser Ser Ile Gly Gln Met Phe Glu Thr Thr Met Arg Gly
675 680 685

Ala Lys Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser
690 695 700

Leu Gly Gly Val Phe Thr Ser Ile Gly Lys Ala Leu His Gln Val Phe
705 710 715 720

Gly Ala Ile Tyr Gly Ala Ala Phe Ser Gly Val Ser Trp Thr Met Lys
725 730 735

Ile Leu Ile Gly Val Ile Ile Thr Trp Ile Gly Met Asn Ser Arg Ser
740 745 750

Thr Ser Leu Ser Val Thr Leu Val Leu Val Gly Ile Val Thr Leu Tyr
755 760 765

Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
770 775 780

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Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
785 790 795 800

His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
805 810 815

Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
820 825 830

Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
835 840 845

Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
850 855 860

Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
865 870 875 880

Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
885 890 895

Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
945 950 955 960

Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
965 970 975

Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
980 985 990

Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
1010 1015 1020

Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
1025 1030 1035

Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
1040 1045 1050

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Phe	Cys	Asp	Gly	Thr	Thr	Val	Val	Val	Thr	Glu	Asp	Cys	Gly	Asn
	1055					1060					1065			
Arg	Gly	Pro	Ser	Leu	Arg	Thr	Thr	Thr	Ala	Ser	Gly	Lys	Leu	Ile
	1070					1075					1080			
Thr	Glu	Trp	Cys	Cys	Arg	Ser	Cys	Thr	Leu	Pro	Pro	Leu	Arg	Tyr
	1085					1090					1095			
Arg	Gly	Glu	Asp	Gly	Cys	Trp	Tyr	Gly	Met	Glu	Ile	Arg	Pro	Leu
	1100					1105					1110			
Lys	Glu	Lys	Glu	Glu	Asn	Leu	Val	Asn	Ser	Leu	Val	Thr	Ala	Gly
	1115					1120					1125			
His	Gly	Gln	Val	Asp	Asn	Phe	Ser	Leu	Gly	Val	Leu	Gly	Met	Ala
	1130					1135					1140			
Leu	Phe	Leu	Glu	Glu	Met	Leu	Arg	Thr	Arg	Val	Gly	Thr	Lys	His
	1145					1150					1155			
Ala	Ile	Leu	Leu	Val	Ala	Val	Ser	Phe	Val	Thr	Leu	Ile	Thr	Gly
	1160					1165					1170			
Asn	Met	Ser	Phe	Arg	Asp	Leu	Gly	Arg	Val	Met	Val	Met	Val	Gly
	1175					1180					1185			
Ala	Thr	Met	Thr	Asp	Asp	Ile	Gly	Met	Gly	Val	Thr	Tyr	Leu	Ala
	1190					1195					1200			
Leu	Leu	Ala	Ala	Phe	Lys	Val	Arg	Pro	Thr	Phe	Ala	Ala	Gly	Leu
	1205					1210					1215			
Leu	Leu	Arg	Lys	Leu	Thr	Ser	Lys	Glu	Leu	Met	Met	Thr	Thr	Ile
	1220					1225					1230			
Gly	Ile	Val	Leu	Leu	Ser	Gln	Ser	Thr	Ile	Pro	Glu	Thr	Ile	Leu
	1235					1240					1245			
Glu	Leu	Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met
	1250					1255					1260			
Val	Arg	Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala
	1265					1270					1275			
Ile	Leu	Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys
	1280					1285					1290			
Val	Ser	Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe
	1295					1300					1305			

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Leu	Thr	Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu
1310						1315					1320			
Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
1325						1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
1340						1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
1355						1360					1365			
Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
1370						1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
1385						1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
1400						1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
1415						1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Glu	Gln	Thr	Leu	Thr	Ile	Leu
1430						1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
1445						1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
1460						1465					1470			
Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
1475						1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
1490						1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
1505						1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
1520						1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
1535						1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
1550						1555					1560			

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Trp Lys Glu Gly Glu Glu Val Gln Val Leu Ala Leu Glu Pro Gly
1565 1570 1575

Lys Asn Pro Arg Ala Val Gln Thr Lys Pro Gly Leu Phe Lys Thr
1580 1585 1590

Asn Ala Gly Thr Ile Gly Ala Val Ser Leu Asp Phe Ser Pro Gly
1595 1600 1605

Thr Ser Gly Ser Pro Ile Ile Asp Lys Lys Gly Lys Val Val Gly
1610 1615 1620

Leu Tyr Gly Asn Gly Val Val Thr Arg Ser Gly Ala Tyr Val Ser
1625 1630 1635

Ala Ile Ala Gln Thr Glu Lys Ser Ile Glu Asp Asn Pro Glu Ile
1640 1645 1650

Glu Asp Asp Ile Phe Arg Lys Arg Arg Leu Thr Ile Met Asp Leu
1655 1660 1665

His Pro Gly Ala Gly Lys Thr Lys Arg Tyr Leu Pro Ala Ile Val
1670 1675 1680

Arg Glu Ala Ile Lys Arg Gly Leu Arg Thr Leu Ile Leu Ala Pro
1685 1690 1695

Thr Arg Val Val Ala Ala Glu Met Glu Glu Ala Leu Arg Gly Leu
1700 1705 1710

Pro Ile Arg Tyr Gln Thr Pro Ala Ile Arg Ala Val His Thr Gly
1715 1720 1725

Arg Glu Ile Val Asp Leu Met Cys His Ala Thr Phe Thr Met Arg
1730 1735 1740

Leu Leu Ser Pro Val Arg Val Pro Asn Tyr Asn Leu Ile Ile Met
1745 1750 1755

Asp Glu Ala His Phe Thr Asp Pro Ala Ser Ile Ala Ala Arg Gly
1760 1765 1770

Tyr Ile Ser Thr Arg Val Glu Met Gly Glu Ala Ala Gly Ile Phe
1775 1780 1785

Met Thr Ala Thr Pro Pro Gly Ser Arg Asp Pro Phe Pro Gln Ser
1790 1795 1800

Asn Ala Pro Ile Ile Asp Glu Glu Arg Glu Ile Pro Glu Arg Ser
1805 1810 1815

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Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
1820						1825					1830			
Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
1835						1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
1850						1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
1865						1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
1880						1885					1890			
Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
1895						1900					1905			
Leu	Thr	Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro
1910						1915					1920			
Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
1925						1930					1935			
Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
1940						1945					1950			
Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
1955						1960					1965			
Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
1970						1975					1980			
Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
1985						1990					1995			
Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
2000						2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
2015						2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
2030						2035					2040			
Asn	Asn	Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr
2045						2050					2055			
Lys	Glu	Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala
2060						2065					2070			

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Arg	Ile	Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe
2075						2080					2085			
Ala	Ala	Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met
2090						2095					2100			
Gly	Arg	Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Ala	Arg	Asp	Ala	Leu
2105						2110					2115			
Asp	Asn	Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Ala	Gly	Gly	Arg	Ala
2120						2125					2130			
Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
2135						2140					2145			
Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
2150						2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
2165						2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
2180						2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
2195						2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
2210						2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
2225						2230					2235			
Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
2240						2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
2255						2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
2270						2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
2285						2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
2300						2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
2315						2320					2325			

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Lys Met 2330	Asp Ile Gly Val	Pro 2335	Leu Leu Ala Ile	Gly Cys Tyr Ser 2340						
Gln Val 2345	Asn Pro Ile Thr	Leu 2350	Thr Ala Ala Leu	Phe 2355	Leu Leu Val					
Ala His 2360	Tyr Ala Ile Ile	Gly 2365	Pro Gly Leu Gln	Ala 2370	Lys Ala Thr					
Arg Glu 2375	Ala Gln Lys Arg	Ala 2380	Ala Ala Gly Ile	Met 2385	Lys Asn Pro					
Thr Val 2390	Asp Gly Ile Thr	Val 2395	Ile Asp Leu Asp	Pro 2400	Ile Pro Tyr					
Asp Pro 2405	Lys Phe Glu Lys	Gln 2410	Leu Gly Gln Val	Met 2415	Leu Leu Val					
Leu Cys 2420	Val Thr Gln Val	Leu 2425	Met Met Arg Thr	Thr 2430	Trp Ala Leu					
Cys Glu 2435	Ala Leu Thr Leu	Ala 2440	Thr Gly Pro Ile	Ser 2445	Thr Leu Trp					
Glu Gly 2450	Asn Pro Gly Arg	Phe 2455	Trp Asn Thr Thr	Ile 2460	Ala Val Ser					
Met Ala 2465	Asn Ile Phe Arg	Gly 2470	Ser Tyr Leu Ala	Gly 2475	Ala Gly Leu					
Leu Phe 2480	Ser Ile Met Lys	Asn 2485	Thr Thr Asn Thr	Arg 2490	Arg Gly Thr					
Gly Asn 2495	Ile Gly Glu Thr	Leu 2500	Gly Glu Lys Trp	Lys 2505	Ser Arg Leu					
Asn Ala 2510	Leu Gly Lys Ser	Glu 2515	Phe Gln Ile Tyr	Lys 2520	Lys Ser Gly					
Ile Gln 2525	Glu Val Asp Arg	Thr 2530	Leu Ala Lys Glu	Gly 2535	Ile Lys Arg					
Gly Glu 2540	Thr Asp His His	Ala 2545	Val Ser Arg Gly	Ser 2550	Ala Lys Leu					
Arg Trp 2555	Phe Val Glu Arg	Asn 2560	Met Val Thr Pro	Glu 2565	Gly Lys Val					
Val Asp 2570	Leu Gly Cys Gly	Arg 2575	Gly Gly Trp Ser	Tyr 2580	Tyr Cys Gly					

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Gly	Leu	Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly
2585						2590					2595			
Pro	Gly	His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn
2600						2605					2610			
Leu	Val	Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro
2615						2620					2625			
Glu	Lys	Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro
2630						2635					2640			
Asn	Pro	Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu
2645						2650					2655			
Val	Glu	Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val
2660						2665					2670			
Leu	Asn	Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu
2675						2680					2685			
Gln	Arg	Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg
2690						2695					2700			
Asn	Ser	Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn
2705						2710					2715			
Ile	Val	Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg
2720						2725					2730			
Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
2735						2740					2745			
Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
2750						2755					2760			
Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
2765						2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
2780						2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
2795						2800					2805			
Ser	Ser	Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp
2810						2815					2820			
Asp	Val	Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr
2825						2830					2835			

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Thr	Gln	Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr
	2855					2860					2865			
Ala	Glu	Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg
	2870					2875					2880			
Met	Cys	Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala
	2885					2890					2895			
Ala	Leu	Gly	Ala	Val	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
	2900					2905					2910			
Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
	2915					2920					2925			
Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
	2930					2935					2940			
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	2945					2950					2955			
Ala	Lys	Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg
	2960					2965					2970			
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	2975					2980					2985			
Phe	Ser	Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu
	2990					2995					3000			
His	Lys	Leu	Gly	Tyr	Ile	Leu	Arg	Asp	Val	Ser	Lys	Lys	Glu	Gly
	3005					3010					3015			
Gly	Ala	Met	Tyr	Ala	Asp	Asp	Thr	Ala	Gly	Trp	Asp	Thr	Arg	Ile
	3020					3025					3030			
Thr	Leu	Glu	Asp	Leu	Lys	Asn	Glu	Glu	Met	Val	Thr	Asn	His	Met
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Glu	Gly	Glu	His	Lys	Lys	Leu	Ala	Glu	Ala	Ile	Phe	Lys	Leu	Thr
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Tyr	Gln	Asn	Lys	Val	Val	Arg	Val	Gln	Arg	Pro	Thr	Pro	Arg	Gly
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Thr	Val	Met	Asp	Ile	Ile	Ser	Arg	Arg	Asp	Gln	Arg	Gly	Ser	Gly
	3080					3085					3090			

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Gln Leu 3110	Ile Arg Gln Met	Glu Gly Glu Gly Val	Phe Lys Ser Ile 3120
Gln His 3125	Leu Thr Ile Thr	Glu Glu Ile Ala Val	Gln Asn Trp Leu 3135
Ala Arg 3140	Val Gly Arg Glu	Arg Leu Ser Arg Met	Ala Ile Ser Gly 3150
Asp Asp 3155	Cys Val Val Lys	Pro Leu Asp Asp Arg	Phe Ala Ser Ala 3165
Leu Thr 3170	Ala Leu Asn Asp	Met Gly Lys Ile Arg	Lys Asp Ile Gln 3180
Gln Trp 3185	Glu Pro Ser Arg	Gly Trp Asn Asp Trp	Thr Gln Val Pro 3195
Phe Cys 3200	Ser His His Phe	His Glu Leu Ile Met	Lys Asp Gly Arg 3210
Val Leu 3215	Val Val Pro Cys	Arg Asn Gln Asp Glu	Leu Ile Gly Arg 3225
Ala Arg 3230	Ile Ser Gln Gly	Ala Gly Trp Ser Leu	Arg Glu Thr Ala 3240
Cys Leu 3245	Gly Lys Ser Tyr	Ala Gln Met Trp Ser	Leu Met Tyr Phe 3255
His Arg 3260	Arg Asp Leu Arg	Leu Ala Ala Asn Ala	Ile Cys Ser Ala 3270
Val Pro 3275	Ser His Trp Val	Pro Thr Ser Arg Thr	Thr Trp Ser Ile 3285
His Ala 3290	Lys His Glu Trp	Met Thr Thr Glu Asp	Met Leu Thr Val 3300
Trp Asn 3305	Arg Val Trp Ile	Gln Glu Asn Pro Trp	Met Glu Asp Lys 3315
Thr Pro 3320	Val Glu Ser Trp	Glu Glu Ile Pro Tyr	Leu Gly Lys Arg 3330
Glu Asp 3335	Gln Trp Cys Gly	Ser Leu Ile Gly Leu	Thr Ser Arg Ala 3345

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 Thr Trp Ala Lys Asn Ile Gln Ala Ala Ile Asn Gln Val Arg Ser
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Leu Ile Gly Asn Glu Glu Tyr Thr Asp Tyr Met Pro Ser Met Lys
 3365 3370 3375

Arg Phe Arg Arg Glu Glu Glu Glu Ala Gly Val Leu Trp
 3380 3385 3390

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 <212> DNA
 <213> Artificial Sequence

<220>
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 <222> (6481)..(6481)
 <223> n is either cytosine or guanine

<220>
 <221> misc_feature
 <222> (7156)..(7156)
 <223> n is either cytosine or thymine

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 aaaaacacgc ctttcaatat gctgaaacgc gagagaaacc gcgtgtcgac tgtgcaacag 180
 ctgacaaaga gattctcact tggaatgctg cagggacgag gaccattaaa actgttcagt 240
 gccctggtgg cgttccttcg tttcctaaca atcccaccaa cagcagggat attgaagaga 300
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tgggatacaa	gaatcacact	agaagaccta	aaaaatgaag	aatggtaac	aaaccacatg	9240

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gaaggagaac acaagaaact agccgaggcc attttcaaac taacgtacca aaacaagggtg 9300
gtgctgtgtc aaagaccaac accaagaggc acagtaatgg acatcatatc gagaagagac 9360
caaagaggta gtggacaagt tggcacctat ggactcaata ctttcaccaa tatggaagcc 9420
caactaatca gacagatgga gggagaagga gtcttttaaaa gcattcagca cctaacaatc 9480
acagaagaaa tcgctgtgca aaactgggtta gcaagagtgg ggcgcgaaag gttatcaaga 9540
atggccatca gtggagatga ttgtgtttgtg aaaccttttag atgacagggtt cgcaagcgct 9600
ttaacagctc taaatgacat gggaaagatt aggaaagaca tacaacaatg ggaaccttca 9660
agaggatgga atgattggac acaagtggcc ttctgttcac accattttcca tgagttaatc 9720
atgaaagacg gtcgcgtact cgttgtttcca tgtagaaacc aagatgaact gattggcaga 9780
gcccgaatct cccaaggagc aggggtggtct ttgcgggaga cggcctgttt ggggaagtct 9840
tacgccccaa tgtggagctt gatgtacttc cacagacgag acctcaggct ggcggcaaat 9900
gctatttgct cggcagtacc atcacattgg gttccaacaa gtcgaacaac ctggtccata 9960
catgctaaac atgaatggat gacaacggaa gacatgctga cagtctggaa cagggtgtgg 10020
attcaagaaa acccatggat ggaagacaaa actccagtgg aatcatggga ggaaatccca 10080
tacttgggga aaagagaaga ccaatgggtc ggctcattga ttgggttaac aagcagggcc 10140
acctgggcaa agaacatcca agcagcaata aatcaagtta gatcccttat aggcaatgaa 10200
gaatacacag attacatgcc atccatgaaa agattcagaa gagaagagga agaagcagga 10260
gttctgtggt agaaagcaaa actaacatga aacaaggcta gaagtcaggc cggattaagc 10320
catagtacgg aaaaaactat gctacctgtg agccccgtcc aaggacgtta aaagaagtca 10380
ggccatcata aatgccatag cttgagtaaa ctatgcagcc tgtagctcca cctgagaagg 10440
tgtaaaaaat ccgggaggcc acaaaccatg gaagctgtac gcatggcgta gtggactagc 10500
ggttagagga gaccctccc ttacaaatcg cagcaacaat gggggcccaa ggcgagatga 10560
agctgtagtc tcgctggaag gactagaggt tagaggagac cccccgaaa caaaaaacag 10620
catattgacg ctgggaaaga ccagagatcc tgctgtctcc tcagcatcat tccaggcaca 10680
gaacgcgaga aaatggaatg gtgctgttga atcaacaggt tct 10723

<210> 14
<211> 3391
<212> PRT
<213> Artificial Sequence

<220>
<223> Dengue virus serotype 2, WVS

<220>
<221> misc_feature
<222> (2129)..(2129)
<223> Xaa is either alanine or proline

<220>
<221> misc_feature
<222> (2354)..(2354)

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 <223> Xaa is either leucine or phenylalanine

<400> 14

Met Asn Asn Gln Arg Lys Lys Ala Lys Asn Thr Pro Phe Asn Met Leu
 1 5 10 15

Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
 20 25 30

Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
 50 55 60

Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
 65 70 75 80

Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
 85 90 95

Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
 100 105 110

Met Ala Phe His Leu Thr Thr Arg Asn Gly Glu Pro His Met Ile Val
 115 120 125

Ser Arg Gln Glu Lys Gly Lys Ser Leu Leu Phe Lys Thr Glu Val Gly
 130 135 140

Val Asn Met Cys Thr Leu Met Ala Met Asp Leu Gly Glu Leu Cys Glu
 145 150 155 160

Asp Thr Ile Thr Tyr Glu Cys Pro Leu Leu Arg Gln Asn Glu Pro Glu
 165 170 175

Asp Ile Asp Cys Trp Cys Asn Ser Thr Ser Thr Trp Val Thr Tyr Gly
 180 185 190

Thr Cys Thr Thr Met Gly Glu His Arg Arg Glu Lys Arg Ser Val Ala
 195 200 205

Leu Val Pro His Val Gly Met Gly Leu Glu Thr Arg Thr Glu Thr Trp
 210 215 220

Met Ser Ser Glu Gly Ala Trp Lys His Val Gln Arg Ile Glu Thr Trp
 225 230 235 240

Ile Leu Arg His Pro Gly Phe Thr Met Met Ala Ala Ile Leu Ala Tyr
 245 250 255

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Thr Ile Gly Thr Thr His Phe Gln Arg Ala Leu Ile Phe Ile Leu Leu
260 265 270

Thr Ala Val Thr Pro Ser Met Thr Met Arg Cys Ile Gly Met Ser Asn
275 280 285

Arg Asp Phe Val Glu Gly Val Ser Gly Gly Ser Trp Val Asp Ile Val
290 295 300

Leu Glu His Gly Ser Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
305 310 315 320

Leu Asp Phe Glu Leu Ile Lys Thr Glu Ala Lys Gln Pro Ala Thr Leu
325 330 335

Arg Lys Tyr Cys Ile Glu Ala Lys Leu Thr Asn Thr Thr Thr Glu Ser
340 345 350

Arg Cys Pro Thr Gln Gly Glu Pro Ser Leu Asn Glu Glu Gln Asp Lys
355 360 365

Arg Phe Val Cys Lys His Ser Met Val Asp Arg Gly Trp Gly Asn Gly
370 375 380

Cys Gly Leu Phe Gly Lys Gly Gly Ile Val Thr Cys Ala Met Phe Arg
385 390 395 400

Cys Lys Lys Asn Met Glu Gly Lys Val Val Gln Pro Glu Asn Leu Glu
405 410 415

Tyr Thr Ile Val Ile Thr Pro His Ser Gly Glu Glu His Ala Val Gly
420 425 430

Asn Asp Thr Gly Lys His Gly Lys Glu Ile Lys Ile Thr Pro Gln Ser
435 440 445

Ser Ile Thr Glu Ala Glu Leu Thr Gly Tyr Gly Thr Val Thr Met Glu
450 455 460

Cys Ser Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Val Leu Leu Gln
465 470 475 480

Met Glu Asn Lys Ala Trp Leu Val His Arg Gln Trp Phe Leu Asp Leu
485 490 495

Pro Leu Pro Trp Leu Pro Gly Ala Asp Thr Gln Gly Ser Asn Trp Ile
500 505 510

Gln Lys Glu Thr Leu Val Thr Phe Lys Asn Pro His Ala Lys Lys Gln
515 520 525

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Asp Val Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu
530 535 540

Thr Gly Ala Thr Glu Ile Gln Met Ser Ser Gly Asn Leu Leu Phe Thr
545 550 555 560

Gly His Leu Lys Cys Arg Leu Arg Met Asp Lys Leu Gln Leu Lys Gly
565 570 575

Met Ser Tyr Ser Met Cys Thr Gly Lys Phe Lys Val Val Lys Glu Ile
580 585 590

Ala Glu Thr Gln His Gly Thr Ile Val Ile Arg Val Gln Tyr Glu Gly
595 600 605

Asp Gly Ser Pro Cys Lys Ile Pro Phe Glu Ile Met Asp Leu Glu Lys
610 615 620

Arg His Val Leu Gly Arg Leu Ile Thr Val Asn Pro Ile Val Thr Glu
625 630 635 640

Lys Asp Ser Pro Val Asn Ile Glu Ala Glu Pro Pro Phe Gly Asp Ser
645 650 655

Tyr Ile Ile Ile Gly Val Glu Pro Gly Gln Leu Lys Leu Asn Trp Phe
660 665 670

Lys Lys Gly Ser Ser Ile Gly Gln Met Phe Glu Thr Thr Met Arg Gly
675 680 685

Ala Lys Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser
690 695 700

Leu Gly Gly Val Phe Thr Ser Ile Gly Lys Ala Leu His Gln Val Phe
705 710 715 720

Gly Ala Ile Tyr Gly Ala Ala Phe Ser Gly Val Ser Trp Thr Met Lys
725 730 735

Ile Leu Ile Gly Val Ile Ile Thr Trp Ile Gly Met Asn Ser Arg Ser
740 745 750

Thr Ser Leu Ser Val Thr Leu Val Leu Val Gly Ile Val Thr Leu Tyr
755 760 765

Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
770 775 780

Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
785 790 795 800

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His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
805 810 815

Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
820 825 830

Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
835 840 845

Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
850 855 860

Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
865 870 875 880

Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
885 890 895

Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
945 950 955 960

Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
965 970 975

Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
980 985 990

Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
1010 1015 1020

Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
1025 1030 1035

Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
1040 1045 1050

Phe Cys Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn
1055 1060 1065

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Arg Gly 1070	Pro Ser Leu Arg Thr 1075	Thr Thr Ala Ser Gly 1080	Lys Leu Ile
Thr Glu 1085	Trp Cys Cys Arg Ser 1090	Cys Thr Leu Pro Pro 1095	Leu Arg Tyr
Arg Gly 1100	Glu Asp Gly Cys Trp 1105	Tyr Gly Met Glu Ile 1110	Arg Pro Leu
Lys Glu 1115	Lys Glu Glu Asn Leu 1120	Val Asn Ser Leu Val 1125	Thr Ala Gly
His Gly 1130	Gln Val Asp Asn Phe 1135	Ser Leu Gly Val Leu 1140	Gly Met Ala
Leu Phe 1145	Leu Glu Glu Met Leu 1150	Arg Thr Arg Val Gly 1155	Thr Lys His
Ala Ile 1160	Leu Leu Val Ala Val 1165	Ser Phe Val Thr Leu 1170	Ile Thr Gly
Asn Met 1175	Ser Phe Arg Asp Leu 1180	Gly Arg Val Met Val 1185	Met Val Gly
Ala Thr 1190	Met Thr Asp Asp Ile 1195	Gly Met Gly Val Thr 1200	Tyr Leu Ala
Leu Leu 1205	Ala Ala Phe Lys Val 1210	Arg Pro Thr Phe Ala 1215	Ala Gly Leu
Leu Leu 1220	Arg Lys Leu Thr Ser 1225	Lys Glu Leu Met Met 1230	Thr Thr Ile
Gly Ile 1235	Val Leu Leu Ser Gln 1240	Ser Thr Ile Pro Glu 1245	Thr Ile Leu
Glu Leu 1250	Thr Asp Ala Leu Ala 1255	Leu Gly Met Met Val 1260	Leu Lys Met
Val Arg 1265	Asn Met Glu Lys Tyr 1270	Gln Leu Ala Val Thr 1275	Ile Met Ala
Ile Leu 1280	Cys Val Pro Asn Ala 1285	Val Ile Leu Gln Asn 1290	Ala Trp Lys
Val Ser 1295	Cys Thr Ile Leu Ala 1300	Val Val Ser Val Ser 1305	Pro Leu Phe
Leu Thr 1310	Ser Ser Gln Gln Lys 1315	Thr Asp Trp Ile Pro 1320	Leu Ala Leu

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Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
1325						1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
1340						1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
1355						1360					1365			
Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
1370						1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
1385						1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
1400						1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
1415						1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Glu	Gln	Thr	Leu	Thr	Ile	Leu
1430						1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
1445						1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
1460						1465					1470			
Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
1475						1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
1490						1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
1505						1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
1520						1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
1535						1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
1550						1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
1565						1570					1575			

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Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
1580						1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
1595						1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
1610						1615					1620			
Leu	Tyr	Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser
1625						1630					1635			
Ala	Ile	Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile
1640						1645					1650			
Glu	Asp	Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu
1655						1660					1665			
His	Pro	Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val
1670						1675					1680			
Arg	Glu	Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro
1685						1690					1695			
Thr	Arg	Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu
1700						1705					1710			
Pro	Ile	Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly
1715						1720					1725			
Arg	Glu	Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg
1730						1735					1740			
Leu	Leu	Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met
1745						1750					1755			
Asp	Glu	Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly
1760						1765					1770			
Tyr	Ile	Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe
1775						1780					1785			
Met	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser
1790						1795					1800			
Asn	Ala	Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser
1805						1810					1815			
Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
1820						1825					1830			

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Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
1835						1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
1850						1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
1865						1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
1880						1885					1890			
Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
1895						1900					1905			
Leu	Thr	Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro
1910						1915					1920			
Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
1925						1930					1935			
Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
1940						1945					1950			
Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
1955						1960					1965			
Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
1970						1975					1980			
Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
1985						1990					1995			
Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
2000						2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
2015						2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
2030						2035					2040			
Asn	Asn	Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr
2045						2050					2055			
Lys	Glu	Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala
2060						2065					2070			
Arg	Ile	Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe
2075						2080					2085			

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Ala	Ala	Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met
2090						2095					2100			
Gly	Arg	Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Ala	Arg	Asp	Ala	Leu
2105						2110					2115			
Asp	Asn	Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Xaa	Gly	Gly	Arg	Ala
2120						2125					2130			
Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
2135						2140					2145			
Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
2150						2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
2165						2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
2180						2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
2195						2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
2210						2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
2225						2230					2235			
Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
2240						2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
2255						2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
2270						2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
2285						2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
2300						2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
2315						2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
2330						2335					2340			

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Gln	Val	Asn	Pro	Ile	Thr	Leu	Thr	Ala	Ala	Xaa	Phe	Leu	Leu	Val
2345						2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
2360						2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
2375						2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
2390						2395					2400			
Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
2405						2410					2415			
Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
2420						2425					2430			
Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
2435						2440					2445			
Glu	Gly	Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser
2450						2455					2460			
Met	Ala	Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu
2465						2470					2475			
Leu	Phe	Ser	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr
2480						2485					2490			
Gly	Asn	Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu
2495						2500					2505			
Asn	Ala	Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly
2510						2515					2520			
Ile	Gln	Glu	Val	Asp	Arg	Thr	Leu	Ala	Lys	Glu	Gly	Ile	Lys	Arg
2525						2530					2535			
Gly	Glu	Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu
2540						2545					2550			
Arg	Trp	Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val
2555						2560					2565			
Val	Asp	Leu	Gly	Cys	Gly	Arg	Gly	Gly	Trp	Ser	Tyr	Tyr	Cys	Gly
2570						2575					2580			
Gly	Leu	Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly
2585						2590					2595			

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Pro	Gly	His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn
	2600					2605					2610			
Leu	Val	Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro
	2615					2620					2625			
Glu	Lys	Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro
	2630					2635					2640			
Asn	Pro	Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu
	2645					2650					2655			
Val	Glu	Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val
	2660					2665					2670			
Leu	Asn	Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu
	2675					2680					2685			
Gln	Arg	Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg
	2690					2695					2700			
Asn	Ser	Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn
	2705					2710					2715			
Ile	Val	Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg
	2720					2725					2730			
Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
	2735					2740					2745			
Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
	2750					2755					2760			
Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
	2765					2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
	2780					2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
	2795					2800					2805			
Ser	Ser	Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp
	2810					2815					2820			
Asp	Val	Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr
	2825					2830					2835			
Pro	Phe	Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg
	2840					2845					2850			

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Thr	Gln	Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr
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Ala	Glu	Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg
	2870					2875					2880			
Met	Cys	Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala
	2885					2890					2895			
Ala	Leu	Gly	Ala	Val	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
	2900					2905					2910			
Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
	2915					2920					2925			
Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
	2930					2935					2940			
Asn	Met	Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys
	2945					2950					2955			
Ala	Lys	Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg
	2960					2965					2970			
Phe	Leu	Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp
	2975					2980					2985			
Phe	Ser	Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu
	2990					2995					3000			
His	Lys	Leu	Gly	Tyr	Ile	Leu	Arg	Asp	Val	Ser	Lys	Lys	Glu	Gly
	3005					3010					3015			
Gly	Ala	Met	Tyr	Ala	Asp	Asp	Thr	Ala	Gly	Trp	Asp	Thr	Arg	Ile
	3020					3025					3030			
Thr	Leu	Glu	Asp	Leu	Lys	Asn	Glu	Glu	Met	Val	Thr	Asn	His	Met
	3035					3040					3045			
Glu	Gly	Glu	His	Lys	Lys	Leu	Ala	Glu	Ala	Ile	Phe	Lys	Leu	Thr
	3050					3055					3060			
Tyr	Gln	Asn	Lys	Val	Val	Arg	Val	Gln	Arg	Pro	Thr	Pro	Arg	Gly
	3065					3070					3075			
Thr	Val	Met	Asp	Ile	Ile	Ser	Arg	Arg	Asp	Gln	Arg	Gly	Ser	Gly
	3080					3085					3090			
Gln	Val	Gly	Thr	Tyr	Gly	Leu	Asn	Thr	Phe	Thr	Asn	Met	Glu	Ala
	3095					3100					3105			

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Gln	Leu	Ile	Arg	Gln	Met	Glu	Gly	Glu	Gly	Val	Phe	Lys	Ser	Ile
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3125						3130					3135			
Ala	Arg	Val	Gly	Arg	Glu	Arg	Leu	Ser	Arg	Met	Ala	Ile	Ser	Gly
3140						3145					3150			
Asp	Asp	Cys	Val	Val	Lys	Pro	Leu	Asp	Asp	Arg	Phe	Ala	Ser	Ala
3155						3160					3165			
Leu	Thr	Ala	Leu	Asn	Asp	Met	Gly	Lys	Ile	Arg	Lys	Asp	Ile	Gln
3170						3175					3180			
Gln	Trp	Glu	Pro	Ser	Arg	Gly	Trp	Asn	Asp	Trp	Thr	Gln	Val	Pro
3185						3190					3195			
Phe	Cys	Ser	His	His	Phe	His	Glu	Leu	Ile	Met	Lys	Asp	Gly	Arg
3200						3205					3210			
Val	Leu	Val	Val	Pro	Cys	Arg	Asn	Gln	Asp	Glu	Leu	Ile	Gly	Arg
3215						3220					3225			
Ala	Arg	Ile	Ser	Gln	Gly	Ala	Gly	Trp	Ser	Leu	Arg	Glu	Thr	Ala
3230						3235					3240			
Cys	Leu	Gly	Lys	Ser	Tyr	Ala	Gln	Met	Trp	Ser	Leu	Met	Tyr	Phe
3245						3250					3255			
His	Arg	Arg	Asp	Leu	Arg	Leu	Ala	Ala	Asn	Ala	Ile	Cys	Ser	Ala
3260						3265					3270			
Val	Pro	Ser	His	Trp	Val	Pro	Thr	Ser	Arg	Thr	Thr	Trp	Ser	Ile
3275						3280					3285			
His	Ala	Lys	His	Glu	Trp	Met	Thr	Thr	Glu	Asp	Met	Leu	Thr	Val
3290						3295					3300			
Trp	Asn	Arg	Val	Trp	Ile	Gln	Glu	Asn	Pro	Trp	Met	Glu	Asp	Lys
3305						3310					3315			
Thr	Pro	Val	Glu	Ser	Trp	Glu	Glu	Ile	Pro	Tyr	Leu	Gly	Lys	Arg
3320						3325					3330			
Glu	Asp	Gln	Trp	Cys	Gly	Ser	Leu	Ile	Gly	Leu	Thr	Ser	Arg	Ala
3335						3340					3345			
Thr	Trp	Ala	Lys	Asn	Ile	Gln	Ala	Ala	Ile	Asn	Gln	Val	Arg	Ser
3350						3355					3360			

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 3365 3370 3375

Arg Phe Arg Arg Glu Glu Glu Glu Ala Gly Val Leu Trp
 3380 3385 3390

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 <211> 10723
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Dengue virus serotype 2, BVS

<400> 15
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 gttctaacag tttttaatt agagagcaga tctctgatga ataaccaacg gaaaaaggcg 120
 aaaaacacgc ctttcaatat gctgaaacgc gagagaaacc gcgtgtcgac tgtgcaacag 180
 ctgacaaaga gattctcact tggaatgctg cagggacgag gaccattaaa actgttcatg 240
 gccctggtgg cgttccttcg tttcctaaca atcccaccaa cagcagggat attgaagaga 300
 tggggaacaa ttaaaaaatc aaaagctatt aatgttttga gaggggttcag gaaagagatt 360
 ggaaggatgc tgaacatctt gaataggaga cgcagatctg caggcatgat cattatgctg 420
 attccaacag tgatggcggt ccatttaacc acacgtaacg gagaaccaca catgatcgtc 480
 agcagacaag agaaagggaa aagtcttctg tttaaaacag aggttggcgt gaacatgtgt 540
 accctcatgg ccatggacct tggatgaattg tgtgaagaca caatcacgta cgagtgtccc 600
 cttctcaggc agaatgagcc agaagacata gactgttggg gcaactctac gtccacgtgg 660
 gtaacttatg ggacgtgtac caccatggga gaacatagaa gagaaaaaag atcagtggca 720
 ctcgttccac atgtgggaat gggactggag acacgaactg aaacatggat gtcatcagaa 780
 ggggcctgga aacatgtcca gagaattgaa acttggatct tgagacatcc aggcttcacc 840
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 ttcattctac tgacagctgt cactccttca atgacaatgc gttgcatagg aatgtcaaat 960
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 aggttcgtct gcaaacactc catggtagac agaggatggg gaaatggatg tggactatct 1260
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 catgcagtcg gaaatgacac aggaaaacat ggcaaggaaa tcaaaataac accacagagt 1440
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gatgttggtg	ttttaggatc	ccaagaaggg	gccatgcaca	cagcacttac	aggggccaca	1740
gaaatccaaa	tgtcatcagg	aaacttactc	ttcacaggac	atctcaagtg	caggctgaga	1800
atggacaagc	tacagctcaa	aggaatgtca	tactctatgt	gcacaggaaa	gtttaaagtt	1860
gtgaaggaaa	tagcagaaac	acaacatgga	acaatagtta	tcagagtgc	atatgaaggg	1920
gacggctctc	catgcaagat	cccttttgag	ataatggatt	tggaaaaaag	acatgtctta	1980
ggtcgcctga	ttacagtcaa	cccaattgtg	acagaaaaag	atagcccagt	caacatagaa	2040
gcagaacctc	catttgagga	cagctacatc	atcataggag	tagagccggg	acaactgaag	2100
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gcgaagagaa	tggccatttt	aggtgacaca	gcctgggatt	ttggatcctt	gggaggagt	2220
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atttgtggaa	tccgctcagt	aacaagactg	gagaatctga	tgtggaaaca	aataacacca	2640
gaattgaatc	acattctatc	agaaaatgag	gtgaagttaa	ctattatgac	aggagacatc	2700
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agaggatgga	atgattggac	acaagtggcc	ttctgttcac	accattttcca	tgagttaatc	9720

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atgaaagacg gtcgcgtact cgttggtcca tgtagaaacc aagatgaact gattggcaga      9780
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tacgccccaa tgtggagctt gatgtacttc cacagacgcg acctcaggct ggcggcaaatt      9900
gctatttgct cggcagtacc atcacattgg gttccaacaa gtcgaacaac ctggtccata      9960
catgctaaac atgaatggat gacaacggaa gacatgctga cagtctggaa cagggtgtgg      10020
attcaagaaa acccatggat ggaagacaaa actccagtgg aatcatggga ggaaatccca      10080
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acctgggcaa agaacatcca agcagcaata aatcaagtta gatcccttat aggcaatgaa      10200
gaatacacag attacatgcc atccatgaaa agattcagaa gagaagagga agaagcagga      10260
gttctgtggt agaaagcaaa actaacatga aacaaggcta gaagtcaggt cggattaagc      10320
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 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Dengue virus serotype 2, BVS

<400> 16

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Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
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Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
 50 55 60

Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
 65 70 75 80

Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
 85 90 95

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Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
 100 105 110

Met Ala Phe His Leu Thr Thr Arg Asn Gly Glu Pro His Met Ile Val
 115 120 125

Ser Arg Gln Glu Lys Gly Lys Ser Leu Leu Phe Lys Thr Glu Val Gly
 130 135 140

Val Asn Met Cys Thr Leu Met Ala Met Asp Leu Gly Glu Leu Cys Glu
 145 150 155 160

Asp Thr Ile Thr Tyr Glu Cys Pro Leu Leu Arg Gln Asn Glu Pro Glu
 165 170 175

Asp Ile Asp Cys Trp Cys Asn Ser Thr Ser Thr Trp Val Thr Tyr Gly
 180 185 190

Thr Cys Thr Thr Met Gly Glu His Arg Arg Glu Lys Arg Ser Val Ala
 195 200 205

Leu Val Pro His Val Gly Met Gly Leu Glu Thr Arg Thr Glu Thr Trp
 210 215 220

Met Ser Ser Glu Gly Ala Trp Lys His Val Gln Arg Ile Glu Thr Trp
 225 230 235 240

Ile Leu Arg His Pro Gly Phe Thr Met Met Ala Ala Ile Leu Ala Tyr
 245 250 255

Thr Ile Gly Thr Thr His Phe Gln Arg Ala Leu Ile Phe Ile Leu Leu
 260 265 270

Thr Ala Val Thr Pro Ser Met Thr Met Arg Cys Ile Gly Met Ser Asn
 275 280 285

Arg Asp Phe Val Glu Gly Val Ser Gly Gly Ser Trp Val Asp Ile Val
 290 295 300

Leu Glu His Gly Ser Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
 305 310 315 320

Leu Asp Phe Glu Leu Ile Lys Thr Glu Ala Lys Gln Pro Ala Thr Leu
 325 330 335

Arg Lys Tyr Cys Ile Glu Ala Lys Leu Thr Asn Thr Thr Thr Glu Ser
 340 345 350

Arg Cys Pro Thr Gln Gly Glu Pro Ser Leu Asn Glu Glu Gln Asp Lys
 355 360 365

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Arg Phe Val Cys Lys His Ser Met Val Asp Arg Gly Trp Gly Asn Gly
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 Cys Gly Leu Phe Gly Lys Gly Gly Ile Val Thr Cys Ala Met Phe Arg
 385 390 395 400
 Cys Lys Lys Asn Met Glu Gly Lys Val Val Gln Pro Glu Asn Leu Glu
 405 410 415
 Tyr Thr Ile Val Ile Thr Pro His Ser Gly Glu Glu His Ala Val Gly
 420 425 430
 Asn Asp Thr Gly Lys His Gly Lys Glu Ile Lys Ile Thr Pro Gln Ser
 435 440 445
 Ser Ile Thr Glu Ala Glu Leu Thr Gly Tyr Gly Thr Val Thr Met Glu
 450 455 460
 Cys Ser Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Val Leu Leu Gln
 465 470 475 480
 Met Glu Asn Lys Ala Trp Leu Val His Arg Gln Trp Phe Leu Asp Leu
 485 490 495
 Pro Leu Pro Trp Leu Pro Gly Ala Asp Thr Gln Gly Ser Asn Trp Ile
 500 505 510
 Gln Lys Glu Thr Leu Val Thr Phe Lys Asn Pro His Ala Lys Lys Gln
 515 520 525
 Asp Val Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu
 530 535 540
 Thr Gly Ala Thr Glu Ile Gln Met Ser Ser Gly Asn Leu Leu Phe Thr
 545 550 555 560
 Gly His Leu Lys Cys Arg Leu Arg Met Asp Lys Leu Gln Leu Lys Gly
 565 570 575
 Met Ser Tyr Ser Met Cys Thr Gly Lys Phe Lys Val Val Lys Glu Ile
 580 585 590
 Ala Glu Thr Gln His Gly Thr Ile Val Ile Arg Val Gln Tyr Glu Gly
 595 600 605
 Asp Gly Ser Pro Cys Lys Ile Pro Phe Glu Ile Met Asp Leu Glu Lys
 610 615 620
 Arg His Val Leu Gly Arg Leu Ile Thr Val Asn Pro Ile Val Thr Glu
 625 630 635 640

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Lys Asp Ser Pro Val₆₄₅ Asn Ile Glu Ala Glu₆₅₀ Pro Pro Phe Gly Asp₆₅₅ Ser

Tyr Ile Ile Ile₆₆₀ Gly Val Glu Pro Gly₆₆₅ Gln Leu Lys Leu Asn₆₇₀ Trp Phe

Lys Lys Gly₆₇₅ Ser Ser Ile Gly Gln₆₈₀ Met Phe Glu Thr Thr₆₈₅ Met Arg Gly

Ala Lys₆₉₀ Arg Met Ala Ile Leu₆₉₅ Gly Asp Thr Ala Trp₇₀₀ Asp Phe Gly Ser

Leu₇₀₅ Gly Gly Val Phe Thr₇₁₀ Ser Ile Gly Lys Ala₇₁₅ Leu His Gln Val Phe₇₂₀

Gly Ala Ile Tyr Gly₇₂₅ Ala Ala Phe Ser Gly₇₃₀ Val Ser Trp Thr Met₇₃₅ Lys

Ile Leu Ile Gly₇₄₀ Val Ile Ile Thr Trp₇₄₅ Ile Gly Met Asn Ser₇₅₀ Arg Ser

Thr Ser Leu₇₅₅ Ser Val Thr Leu Val₇₆₀ Leu Val Gly Ile Val₇₆₅ Thr Leu Tyr

Leu Gly₇₇₀ Val Met Val Gln Ala₇₇₅ Asp Ser Gly Cys Val₇₈₀ Val Ser Trp Lys

Asn₇₈₅ Lys Glu Leu Lys Cys₇₉₀ Gly Ser Gly Ile Phe₇₉₅ Ile Thr Asp Asn Val₈₀₀

His Thr Trp Thr Glu₈₀₅ Gln Tyr Lys Phe Gln₈₁₀ Pro Glu Ser Pro Ser₈₁₅ Lys

Leu Ala Ser Ala₈₂₀ Ile Gln Lys Ala His₈₂₅ Glu Glu Asp Ile Cys₈₃₀ Gly Ile

Arg Ser Val₈₃₅ Thr Arg Leu Glu Asn₈₄₀ Leu Met Trp Lys Gln₈₄₅ Ile Thr Pro

Glu Leu₈₅₀ Asn His Ile Leu Ser₈₅₅ Glu Asn Glu Val Lys₈₆₀ Leu Thr Ile Met

Thr₈₆₅ Gly Asp Ile Lys Gly₈₇₀ Ile Met Gln Ala Gly₈₇₅ Lys Arg Ser Leu Arg₈₈₀

Pro Gln Pro Thr Glu₈₈₅ Leu Lys Tyr Ser Trp₈₉₀ Lys Thr Trp Gly Lys₈₉₅ Ala

Lys Met Leu Ser₉₀₀ Thr Glu Ser His Asn₉₀₅ Gln Thr Phe Leu Ile₉₁₀ Asp Gly

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Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
 915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
 930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
 945 950 955 960

Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
 965 970 975

Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
 980 985 990

Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
 995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
 1010 1015 1020

Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
 1025 1030 1035

Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
 1040 1045 1050

Phe Cys Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn
 1055 1060 1065

Arg Gly Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile
 1070 1075 1080

Thr Glu Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr
 1085 1090 1095

Arg Gly Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu
 1100 1105 1110

Lys Glu Lys Glu Glu Asn Leu Val Asn Ser Leu Val Thr Ala Gly
 1115 1120 1125

His Gly Gln Val Asp Asn Phe Ser Leu Gly Val Leu Gly Met Ala
 1130 1135 1140

Leu Phe Leu Glu Glu Met Leu Arg Thr Arg Val Gly Thr Lys His
 1145 1150 1155

Ala Ile Leu Leu Val Ala Val Ser Phe Val Thr Leu Ile Thr Gly
 1160 1165 1170

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Asn	Met	Ser	Phe	Arg	Asp	Leu	Gly	Arg	Val	Met	Val	Met	Val	Gly
	1175					1180					1185			
Ala	Thr	Met	Thr	Asp	Asp	Ile	Gly	Met	Gly	Val	Thr	Tyr	Leu	Ala
	1190					1195					1200			
Leu	Leu	Ala	Ala	Phe	Lys	Val	Arg	Pro	Thr	Phe	Ala	Ala	Gly	Leu
	1205					1210					1215			
Leu	Leu	Arg	Lys	Leu	Thr	Ser	Lys	Glu	Leu	Met	Met	Thr	Thr	Ile
	1220					1225					1230			
Gly	Ile	Val	Leu	Leu	Ser	Gln	Ser	Thr	Ile	Pro	Glu	Thr	Ile	Leu
	1235					1240					1245			
Glu	Leu	Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met
	1250					1255					1260			
Val	Arg	Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala
	1265					1270					1275			
Ile	Leu	Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys
	1280					1285					1290			
Val	Ser	Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe
	1295					1300					1305			
Leu	Thr	Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu
	1310					1315					1320			
Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
	1325					1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
	1340					1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
	1355					1360					1365			
Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
	1370					1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
	1385					1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
	1400					1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
	1415					1420					1425			

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Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Glu	Gln	Thr	Leu	Thr	Ile	Leu
	1430					1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
	1445					1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
	1460					1465					1470			
Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
	1475					1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
	1490					1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
	1505					1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
	1520					1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
	1535					1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
	1550					1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
	1565					1570					1575			
Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
	1580					1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
	1595					1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
	1610					1615					1620			
Leu	Tyr	Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser
	1625					1630					1635			
Ala	Ile	Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile
	1640					1645					1650			
Glu	Asp	Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu
	1655					1660					1665			
His	Pro	Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val
	1670					1675					1680			

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Arg	Glu	Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro
	1685					1690					1695			
Thr	Arg	Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu
	1700					1705					1710			
Pro	Ile	Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly
	1715					1720					1725			
Arg	Glu	Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg
	1730					1735					1740			
Leu	Leu	Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met
	1745					1750					1755			
Asp	Glu	Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly
	1760					1765					1770			
Tyr	Ile	Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe
	1775					1780					1785			
Met	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser
	1790					1795					1800			
Asn	Ala	Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser
	1805					1810					1815			
Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
	1820					1825					1830			
Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
	1835					1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
	1850					1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
	1865					1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
	1880					1885					1890			
Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
	1895					1900					1905			
Leu	Thr	Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro
	1910					1915					1920			
Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
	1925					1930					1935			

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Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
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Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
	1955					1960					1965			
Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
	1970					1975					1980			
Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
	1985					1990					1995			
Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
	2000					2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
	2015					2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
	2030					2035					2040			
Asn	Asn	Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr
	2045					2050					2055			
Lys	Glu	Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala
	2060					2065					2070			
Arg	Ile	Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe
	2075					2080					2085			
Ala	Ala	Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met
	2090					2095					2100			
Gly	Arg	Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Ala	Arg	Asp	Ala	Leu
	2105					2110					2115			
Asp	Asn	Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Pro	Gly	Gly	Arg	Ala
	2120					2125					2130			
Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
	2135					2140					2145			
Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
	2150					2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
	2165					2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
	2180					2185					2190			

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Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
	2195					2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
	2210					2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
	2225					2230					2235			
Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
	2240					2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
	2255					2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
	2270					2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
	2285					2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
	2300					2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
	2315					2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
	2330					2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Thr	Ala	Ala	Phe	Phe	Leu	Leu	Val
	2345					2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
	2360					2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
	2375					2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
	2390					2395					2400			
Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
	2405					2410					2415			
Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
	2420					2425					2430			
Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
	2435					2440					2445			

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Glu	Gly 2450	Asn	Pro	Gly	Arg	Phe 2455	Trp	Asn	Thr	Thr	Ile 2460	Ala	Val	Ser
Met	Ala 2465	Asn	Ile	Phe	Arg	Gly 2470	Ser	Tyr	Leu	Ala	Gly 2475	Ala	Gly	Leu
Leu	Phe 2480	Ser	Ile	Met	Lys	Asn 2485	Thr	Thr	Asn	Thr	Arg 2490	Arg	Gly	Thr
Gly	Asn 2495	Ile	Gly	Glu	Thr	Leu 2500	Gly	Glu	Lys	Trp	Lys 2505	Ser	Arg	Leu
Asn	Ala 2510	Leu	Gly	Lys	Ser	Glu 2515	Phe	Gln	Ile	Tyr	Lys 2520	Lys	Ser	Gly
Ile	Gln 2525	Glu	Val	Asp	Arg	Thr 2530	Leu	Ala	Lys	Glu	Gly 2535	Ile	Lys	Arg
Gly	Glu 2540	Thr	Asp	His	His	Ala 2545	Val	Ser	Arg	Gly	Ser 2550	Ala	Lys	Leu
Arg	Trp 2555	Phe	Val	Glu	Arg	Asn 2560	Met	Val	Thr	Pro	Glu 2565	Gly	Lys	Val
Val	Asp 2570	Leu	Gly	Cys	Gly	Arg 2575	Gly	Gly	Trp	Ser	Tyr 2580	Tyr	Cys	Gly
Gly	Leu 2585	Lys	Asn	Val	Arg	Glu 2590	Val	Lys	Gly	Leu	Thr 2595	Lys	Gly	Gly
Pro	Gly 2600	His	Glu	Glu	Pro	Ile 2605	Pro	Met	Ser	Thr	Tyr 2610	Gly	Trp	Asn
Leu	Val 2615	Arg	Leu	Gln	Ser	Gly 2620	Val	Asp	Val	Phe	Phe 2625	Ile	Pro	Pro
Glu	Lys 2630	Cys	Asp	Thr	Leu	Leu 2635	Cys	Asp	Ile	Gly	Glu 2640	Ser	Ser	Pro
Asn	Pro 2645	Thr	Val	Glu	Ala	Gly 2650	Arg	Thr	Leu	Arg	Val 2655	Leu	Asn	Leu
Val	Glu 2660	Asn	Trp	Leu	Asn	Asn 2665	Asn	Thr	Gln	Phe	Cys 2670	Ile	Lys	Val
Leu	Asn 2675	Pro	Tyr	Met	Pro	Ser 2680	Val	Ile	Glu	Lys	Met 2685	Glu	Ala	Leu
Gln	Arg 2690	Lys	Tyr	Gly	Gly	Ala 2695	Leu	Val	Arg	Asn	Pro 2700	Leu	Ser	Arg

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Asn	Ser	Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn
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Ile	Val	Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg
2720						2725					2730			
Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
2735						2740					2745			
Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
2750						2755					2760			
Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
2765						2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
2780						2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
2795						2800					2805			
Ser	Ser	Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp
2810						2815					2820			
Asp	Val	Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr
2825						2830					2835			
Pro	Phe	Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg
2840						2845					2850			
Thr	Gln	Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr
2855						2860					2865			
Ala	Glu	Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg
2870						2875					2880			
Met	Cys	Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala
2885						2890					2895			
Ala	Leu	Gly	Ala	Val	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
2900						2905					2910			
Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
2915						2920					2925			
Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
2930						2935					2940			
Asn	Met	Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys
2945						2950					2955			

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Ala	Lys 2960	Gly	Ser	Arg	Ala	Ile 2965	Trp	Tyr	Met	Trp	Leu 2970	Gly	Ala	Arg
Phe	Leu 2975	Glu	Phe	Glu	Ala	Leu 2980	Gly	Phe	Leu	Asn	Glu 2985	Asp	His	Trp
Phe	Ser 2990	Arg	Glu	Asn	Ser	Leu 2995	Ser	Gly	Val	Glu	Gly 3000	Glu	Gly	Leu
His	Lys 3005	Leu	Gly	Tyr	Ile	Leu 3010	Arg	Asp	Val	Ser	Lys 3015	Lys	Glu	Gly
Gly	Ala 3020	Met	Tyr	Ala	Asp	Asp 3025	Thr	Ala	Gly	Trp	Asp 3030	Thr	Arg	Ile
Thr	Leu 3035	Glu	Asp	Leu	Lys	Asn 3040	Glu	Glu	Met	Val	Thr 3045	Asn	His	Met
Glu	Gly 3050	Glu	His	Lys	Lys	Leu 3055	Ala	Glu	Ala	Ile	Phe 3060	Lys	Leu	Thr
Tyr	Gln 3065	Asn	Lys	Val	Val	Arg 3070	Val	Gln	Arg	Pro	Thr 3075	Pro	Arg	Gly
Thr	Val 3080	Met	Asp	Ile	Ile	Ser 3085	Arg	Arg	Asp	Gln	Arg 3090	Gly	Ser	Gly
Gln	Val 3095	Gly	Thr	Tyr	Gly	Leu 3100	Asn	Thr	Phe	Thr	Asn 3105	Met	Glu	Ala
Gln	Leu 3110	Ile	Arg	Gln	Met	Glu 3115	Gly	Glu	Gly	Val	Phe 3120	Lys	Ser	Ile
Gln	His 3125	Leu	Thr	Ile	Thr	Glu 3130	Glu	Ile	Ala	Val	Gln 3135	Asn	Trp	Leu
Ala	Arg 3140	Val	Gly	Arg	Glu	Arg 3145	Leu	Ser	Arg	Met	Ala 3150	Ile	Ser	Gly
Asp	Asp 3155	Cys	Val	Val	Lys	Pro 3160	Leu	Asp	Asp	Arg	Phe 3165	Ala	Ser	Ala
Leu	Thr 3170	Ala	Leu	Asn	Asp	Met 3175	Gly	Lys	Ile	Arg	Lys 3180	Asp	Ile	Gln
Gln	Trp 3185	Glu	Pro	Ser	Arg	Gly 3190	Trp	Asn	Asp	Trp	Thr 3195	Gln	Val	Pro
Phe	Cys 3200	Ser	His	His	Phe	His 3205	Glu	Leu	Ile	Met	Lys 3210	Asp	Gly	Arg

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Val Leu Val Val Pro Cys Arg Asn Gln Asp Glu Leu Ile Gly Arg
 3215 3220 3225
 Ala Arg Ile Ser Gln Gly Ala Gly Trp Ser Leu Arg Glu Thr Ala
 3230 3235 3240
 Cys Leu Gly Lys Ser Tyr Ala Gln Met Trp Ser Leu Met Tyr Phe
 3245 3250 3255
 His Arg Arg Asp Leu Arg Leu Ala Ala Asn Ala Ile Cys Ser Ala
 3260 3265 3270
 Val Pro Ser His Trp Val Pro Thr Ser Arg Thr Thr Trp Ser Ile
 3275 3280 3285
 His Ala Lys His Glu Trp Met Thr Thr Glu Asp Met Leu Thr Val
 3290 3295 3300
 Trp Asn Arg Val Trp Ile Gln Glu Asn Pro Trp Met Glu Asp Lys
 3305 3310 3315
 Thr Pro Val Glu Ser Trp Glu Glu Ile Pro Tyr Leu Gly Lys Arg
 3320 3325 3330
 Glu Asp Gln Trp Cys Gly Ser Leu Ile Gly Leu Thr Ser Arg Ala
 3335 3340 3345
 Thr Trp Ala Lys Asn Ile Gln Ala Ala Ile Asn Gln Val Arg Ser
 3350 3355 3360
 Leu Ile Gly Asn Glu Glu Tyr Thr Asp Tyr Met Pro Ser Met Lys
 3365 3370 3375
 Arg Phe Arg Arg Glu Glu Glu Glu Ala Gly Val Leu Trp
 3380 3385 3390

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 <211> 10717
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Dengue virus serotype 3, Pre-Master

<400> 17
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 gttctaacag tttttaatt agagagcaga tctctgatga ataaccaacg gaaaaaggcg 120
 aaaaacacgc ctttcaatat gctgaaacgc gagagaaacc gcgtgtcgac tgtgcaacag 180
 ctgacaaaga gattctcact tggaatgctg cagggacgag gaccattaaa actgttcatg 240
 gccctggtgg cgttccttcg tttcctaaca atcccaccaa cagcagggat attgaagaga 300

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tggggaacaa	ttaaaaaatc	aaaagctatt	aatgttttga	gagggttcag	gaaagagatt	360
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attccaacag	tgatggcggt	ccatttaacc	acgcgtgatg	gagagccgcg	catgattgtg	480
gggaagaatg	aaagaggaaa	atccctactt	ttcaagacag	cctctggaat	caacatgtgc	540
acactcatag	ctatggatct	gggagagatg	tgtgatgaca	cggtcactta	caaagtcccc	600
cacattaccg	aagtggagcc	tgaagacatt	gactgctggt	gcaaccttac	atcgacatgg	660
gtgacttatg	gaacatgcaa	tcaagctgga	gagcatagac	gcgataagag	atcagtggcg	720
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ggagcttggg	gacaagtcga	gaaggtagag	acatgggccc	ttaggcaccc	agggtttacc	840
atactagccc	tatttcttgc	ccattacata	ggcacttcct	tgaccagaa	agtggttatt	900
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agagattttg	tggaaggcct	atcgggagct	acgtgggttg	acgtggtgct	cgagcacggt	1020
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gaggccaccc	aactggcgac	cctaaggaag	ctatgcattg	agggaaaaat	taccaacata	1140
acaaccgact	caagatgtcc	caccaaggg	gaagcgattt	tacctgagga	gcaggaccag	1200
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gtggtgcaac	atgagaacct	caaatacacc	gtcatcatca	cagtgcacac	aggagaccaa	1380
caccaggtgg	gaaatgaaac	gcagggagtc	acggctgaga	taacacccca	ggcatcaacc	1440
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caatggttct	ttgacttacc	cctaccatgg	acatcaggag	cttcagcaga	aacaccaact	1620
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gttgttcttg	gatcacaaga	gggagcaatg	catacagcac	tgacaggagc	tacagagatc	1740
caaacctcag	gaggcacaag	tatctttgcg	gggcacttaa	aatgtagact	caagatggac	1800
aaattggaac	tcaaggggat	gagctatgca	atgtgcttga	gtagctttgt	gttgaagaaa	1860
gaagtctccg	aaacgcagca	tgggacaata	ctcattaagg	ttgagtacaa	aggggaagat	1920
gcaccctgca	agattccttt	ctccacggag	gatggacaag	gaaaagctct	caatggcaga	1980
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tcattagggg	aaatggtcca	ccaaatattt	gggagtgcct	acacagccct	atttggtgga	2280
gtctcctgga	tgatgaaaat	tggaataggt	gtcctcttaa	cctggatagg	gttgaactca	2340

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ggcagtggga	ttttcatcac	agacaacgtg	cacacatgga	cagaacaata	caagttccaa	2520
ccagaatccc	cttcaaaact	agcttcagct	atccagaaag	cccatgaaga	ggacatttgt	2580
ggaatccgct	cagtaacaag	actggagaat	ctgatgtgga	aacaaataac	accagaattg	2640
aatcacattc	tatcagaaaa	tgaggtgaag	ttaactatta	tgacaggaga	catcaaagga	2700
atcatgcagg	caggaaaacg	atctctgcgg	cctcagccca	ctgagctgaa	gtattcatgg	2760
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atcggagccg	gagtttaca	agaaggaaca	ttccatacaa	tgtggcatgt	cacacgtggc	4680
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gcacaaatac	agccacactg	gatagcagct	tcaataatac	tggagttttt	tctcatagtt	6720
ttgcttattc	cagaacctga	aaaacagaga	acaccccaag	acaaccaact	gacctacgtt	6780
gtcatagcca	tcctcacagt	ggtggccgca	accatggcaa	acgagatggg	tttcctagaa	6840
aaaacgaaga	aagatctcgg	attgggaagc	attgcaaccc	agcaacccga	gagcaacatc	6900
ctggacatag	atctacgtcc	tgcatcagca	tggacgctgt	atgccgtggc	cacaacatth	6960
gttacaccaa	tgttgagaca	tagcattgaa	aattcctcag	tgaatgtgtc	cctaacagct	7020
atagccaacc	aagccacagt	gttaatgggt	ctcgggaaag	gatggccatt	gtcaaagatg	7080
gacatcggag	ttcccccttc	cgccattgga	tgctactcac	aagtcaaccc	cataactctc	7140
acagcagctc	ttttcttatt	ggtagcacat	tatgccatca	tagggccagg	actccaagca	7200
aaagcaacca	gagaagctca	gaaaagagca	gcggcgggca	tcataaaaaa	cccaactgtc	7260
gatggaataa	cagtgattga	cctagatcca	ataccttatg	atccaaagtt	tgaaaagcag	7320
ttgggacaag	taatgctcct	agtcctctgc	gtgactcaag	tattgatgat	gaggactaca	7380
tgggctctgt	gtgaggcttt	aaccttagct	accgggcccc	tctccacatt	gtgggaagga	7440
aatccagggg	ggttttggaa	cactaccatt	gcggtgtcaa	tggctaacat	tttttagaggg	7500
agttacttgg	ccggagctgg	acttctcttt	tctattatga	agaacacaac	caacacaaga	7560
aggggaactg	gcaacatagg	agagacgctt	ggagagaaat	ggaaaagccg	attgaacgcg	7620
ttgggaaaaa	gtgaattcca	gatctacaag	aaaagtggaa	tccaggaagt	ggatagaacc	7680
ttagcaaaaag	aaggcattaa	aagaggagaa	acggaccatc	acgctgtgtc	gcgaggctca	7740
gcaaaactga	gatgggttcgt	tgagagaaac	atggctcacac	cagaagggaa	agtagtgagc	7800
ctcggttgtg	gcagaggagg	ctggtcatac	tattgtggag	gactaaagaa	tgtaagagaa	7860
gtcaaaggcc	taacaaaagg	aggaccagga	cacgaagaac	ccatcccat	gtcaacatat	7920
gggtggaatc	tagtgctgtc	tcaaagtgga	gttgacgttt	tcttcatccc	gccagaaaag	7980
tgtgacacat	tattgtgtga	cataggggag	tcataccaa	atcccacagt	ggaagcagga	8040
cgaacactca	gagtccttaa	cttagtagaa	aattggttga	acaacaacac	tcaattttgc	8100
ataaagggtc	tcaaccata	tatgccctca	gtcatagaaa	aaatggaagc	actacaaagg	8160
aaatatggag	gagccttagt	gaggaatcca	ctctcacgaa	actccacaca	tgagatgtac	8220
tgggtatcca	atgcttccgg	gaacatagtg	tcatacgtga	acatgatttc	aaggatgttg	8280
atcaacagat	ttacaatgag	atacaagaaa	gccacttacg	agccggatgt	tgacctcgga	8340
agcggaaccc	gtaacatcgg	gattgaaagt	gagataccaa	acctagatat	aattgggaaa	8400
agaatagaaa	aaataaagca	agagcatgaa	acatcatggc	actatgacca	agaccaccca	8460

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tacaaaacgt	gggcatacca	tggtagctat	gaaacaaaac	agactggatc	agcatcatcc	8520
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cagatggcaa	tgacagacac	gactccattt	ggacaacagc	gcgtttttta	agagaaagtg	8640
gacacgagaa	cccaagaacc	gaaagaaggc	acgaagaaac	taatgaaaat	aacagcagag	8700
tggcttttga	aagaattagg	gaagaaaaag	acaccagga	tgtgcaccag	agaagaattc	8760
acaagaaagg	tgagaagcaa	tgcagccttg	ggggccatat	tcactgatga	gaacaagtgg	8820
aagtcggcac	gtgaggctgt	tgaagatagt	aggttttggg	agctggttga	caaggaaagg	8880
aatctccatc	ttgaaggaaa	gtgtgaaaca	tgtgtgtaca	acatgatggg	aaaaagagag	8940
aagaagctag	gggaattcgg	caaggcaaaa	ggcagcagag	ccatatggta	catgtggctt	9000
ggagcacgct	tcttagagtt	tgaagcccta	ggattcttaa	atgaagatca	ctggttctcc	9060
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acaagaatca	cactagaaga	cctaaaaaat	gaagaaatgg	taacaaacca	catggaagga	9240
gaacacaaga	aactagccga	ggccattttc	aaactaacgt	accaaacaac	ggtggtgcgt	9300
gtgcaaagac	caacaccaag	aggcacagta	atggacatca	tatcgagaag	agaccaaaga	9360
ggtagtggac	aagttagcac	ctatggactc	aatactttca	ccaatatgga	agcccaacta	9420
atcagacaga	tggagggaga	aggagtcttt	aaaagcattc	agcacctaac	aatcacagaa	9480
gaaatcgctg	tgcaaaactg	gttagcaaga	gtggggcgcg	aaaggttatc	aagaatggcc	9540
atcagtggag	atgatttgtt	tgtgaaacct	ttagatgaca	ggttcgcaag	cgctttaaca	9600
gctctaaatg	acatgggaaa	gattaggaaa	gacatacaac	aatgggaacc	ttcaagagga	9660
tggaatgatt	ggacacaagt	gcccttctgt	tcacaccatt	tccatgagtt	aatcatgaaa	9720
gacggtcgcg	tactcgttgt	tccatgtaga	aaccaagatg	aactgattgg	cagagcccga	9780
atctcccaag	gagcaggggt	gtctttgcgg	gagacggcct	gtttggggaa	gtcttacgcc	9840
caaatgtgga	gcttgatgta	cttccacaga	cgcgacctca	ggctggcggc	aaatgctatt	9900
tgctcggcag	taccatcaca	ttgggttcca	acaagtcgaa	caacctggtc	catacatgct	9960
aaacatgaat	ggatgacaac	ggaagacatg	ctgacagtct	ggaacagggt	gtggattcaa	10020
gaaaacccat	ggatggaaga	caaaactcca	gtggaatcat	gggaggaaat	cccatacttg	10080
gggaaaagag	aagaccaatg	gtgcgggtca	ttgattgggt	taacaagcag	ggccacctgg	10140
gcaaagaaca	tccaagcagc	aataaatcaa	gttagatccc	ttataggcaa	tgaagaatac	10200
acagattaca	tgccatccat	gaaaagattc	agaagagaag	aggaagaagc	aggagtctctg	10260
tggtagaaaag	caaaactaac	atgaaacaag	gctagaagtc	aggtcggatt	aagccatagt	10320
acggaaaaaa	ctatgctacc	tgtgagcccc	gtccaaggac	gttaaaagaa	gtcaggccat	10380
cataaatgcc	atagcttgag	taaactatgc	agcctgtagc	tccacctgag	aaggtgtaaa	10440
aaatccggga	ggccacaaac	catggaagct	gtacgcatgg	cgtagtggac	tagcggttag	10500

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```
aggagacccc tcccttataa atcgagcaa caatgggggc ccaaggcgag atgaagctgt      10560
agtctcgctg gaaggactag aggttagagg agaccccccc gaaacaaaaa acagcatatt      10620
gacgctggga aagaccagag atcctgctgt ctcctcagca tcattccagg cacagaacgc      10680
cagaaaatgg aatggtgctg ttgaatcaac aggttctt                                10717
```

```
<210> 18
<211> 3389
<212> PRT
<213> Artificial Sequence
```

```
<220>
<223> Dengue virus serotype 3, Pre-Master
<400> 18
```

```
Met Asn Asn Gln Arg Lys Lys Ala Lys Asn Thr Pro Phe Asn Met Leu
 1          5          10          15
```

```
Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
          20          25          30
```

```
Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
          35          40          45
```

```
Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
          50          55          60
```

```
Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
        65          70          75          80
```

```
Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
          85          90          95
```

```
Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
          100          105          110
```

```
Met Ala Phe His Leu Thr Thr Arg Asp Gly Glu Pro Arg Met Ile Val
          115          120          125
```

```
Gly Lys Asn Glu Arg Gly Lys Ser Leu Leu Phe Lys Thr Ala Ser Gly
          130          135          140
```

```
Ile Asn Met Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Met Cys Asp
          145          150          155          160
```

```
Asp Thr Val Thr Tyr Lys Cys Pro His Ile Thr Glu Val Glu Pro Glu
          165          170          175
```

```
Asp Ile Asp Cys Trp Cys Asn Leu Thr Ser Thr Trp Val Thr Tyr Gly
          180          185          190
```

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```

Thr Cys Asn Gln Ala Gly Glu His Arg Arg Asp Lys Arg Ser Val Ala
      195                               200               205

Leu Ala Pro His Val Gly Met Gly Leu Asp Thr Arg Thr Gln Thr Trp
      210                               215               220

Met Ser Ala Glu Gly Ala Trp Arg Gln Val Glu Lys Val Glu Thr Trp
      225                               230               235               240

Ala Leu Arg His Pro Gly Phe Thr Ile Leu Ala Leu Phe Leu Ala His
      245                               250               255

Tyr Ile Gly Thr Ser Leu Thr Gln Lys Val Val Ile Phe Ile Leu Leu
      260                               265               270

Met Leu Val Thr Pro Ser Met Thr Met Arg Cys Val Gly Val Gly Asn
      275                               280               285

Arg Asp Phe Val Glu Gly Leu Ser Gly Ala Thr Trp Val Asp Val Val
      290                               295               300

Leu Glu His Gly Gly Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
      305                               310               315               320

Leu Asp Ile Glu Leu Gln Lys Thr Glu Ala Thr Gln Leu Ala Thr Leu
      325                               330               335

Arg Lys Leu Cys Ile Glu Gly Lys Ile Thr Asn Ile Thr Thr Asp Ser
      340                               345               350

Arg Cys Pro Thr Gln Gly Glu Ala Ile Leu Pro Glu Glu Gln Asp Gln
      355                               360               365

Asn Tyr Val Cys Lys His Thr Tyr Val Asp Arg Gly Trp Gly Asn Gly
      370                               375               380

Cys Gly Leu Phe Gly Lys Gly Ser Leu Val Thr Cys Ala Lys Phe Gln
      385                               390               395               400

Cys Leu Glu Ser Ile Glu Gly Lys Val Val Gln His Glu Asn Leu Lys
      405                               410               415

Tyr Thr Val Ile Ile Thr Val His Thr Gly Asp Gln His Gln Val Gly
      420                               425               430

Asn Glu Thr Gln Gly Val Thr Ala Glu Ile Thr Pro Gln Ala Ser Thr
      435                               440               445

Ala Glu Ala Ile Leu Pro Glu Tyr Gly Thr Leu Gly Leu Glu Cys Ser
      450                               455               460

```

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```

Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Ile Ser Leu Thr Met Lys
465                               470                               475                               480

Asn Lys Ala Trp Met Val His Arg Gln Trp Phe Phe Asp Leu Pro Leu
                               485                               490                               495

Pro Trp Thr Ser Gly Ala Ser Ala Glu Thr Pro Thr Trp Asn Arg Lys
                               500                               505                               510

Glu Leu Leu Val Thr Phe Lys Asn Ala His Ala Lys Lys Gln Glu Val
                               515                               520                               525

Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu Thr Gly
530                               535                               540

Ala Thr Glu Ile Gln Thr Ser Gly Gly Thr Ser Ile Phe Ala Gly His
545                               550                               555                               560

Leu Lys Cys Arg Leu Lys Met Asp Lys Leu Glu Leu Lys Gly Met Ser
                               565                               570                               575

Tyr Ala Met Cys Leu Ser Ser Phe Val Leu Lys Lys Glu Val Ser Glu
                               580                               585                               590

Thr Gln His Gly Thr Ile Leu Ile Lys Val Glu Tyr Lys Gly Glu Asp
                               595                               600                               605

Ala Pro Cys Lys Ile Pro Phe Ser Thr Glu Asp Gly Gln Gly Lys Ala
610                               615                               620

Leu Asn Gly Arg Leu Ile Thr Ala Asn Pro Val Val Thr Lys Lys Glu
625                               630                               635                               640

Glu Pro Val Asn Ile Glu Ala Glu Pro Pro Phe Gly Glu Ser Asn Ile
                               645                               650                               655

Val Ile Gly Ile Gly Asp Lys Ala Leu Lys Ile Asn Trp Tyr Lys Lys
                               660                               665                               670

Gly Ser Ser Ile Gly Lys Met Phe Glu Ala Thr Ala Arg Gly Ala Arg
                               675                               680                               685

Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser Val Gly
690                               695                               700

Gly Val Leu Asn Ser Leu Gly Lys Met Val His Gln Ile Phe Gly Ser
705                               710                               715                               720

Ala Tyr Thr Ala Leu Phe Gly Gly Val Ser Trp Met Met Lys Ile Gly
                               725                               730                               735

```

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```

Ile Gly Val Leu Leu Thr Trp Ile Gly Leu Asn Ser Lys Asn Thr Ser
              740              745              750

Met Ser Phe Ser Cys Ile Ala Ala Gly Ile Val Thr Leu Tyr Leu Gly
              755              760              765

Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys Asn Lys
              770              775              780

Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val His Thr
785              790              795              800

Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys Leu Ala
              805              810              815

Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile Arg Ser
              820              825              830

Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro Glu Leu
              835              840              845

Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met Thr Gly
              850              855              860

Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg Pro Gln
865              870              875              880

Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala Lys Met
              885              890              895

Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly Pro Glu
              900              905              910

Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu Glu Val
              915              920              925

Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu Lys Leu
930              935              940

Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser Ala Ala
945              950              955              960

Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp Ile Glu
              965              970              975

Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe Ile Glu
              980              985              990

Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser Asn Gly
              995              1000              1005

```

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Val	Leu	Glu	Ser	Glu	Met	Ile	Ile	Pro	Lys	Asn	Leu	Ala	Gly	Pro
	1010					1015					1020			
Val	Ser	Gln	His	Asn	Tyr	Arg	Pro	Gly	Tyr	His	Thr	Gln	Ile	Thr
	1025					1030					1035			
Gly	Pro	Trp	His	Leu	Gly	Lys	Leu	Glu	Met	Asp	Phe	Asp	Phe	Cys
	1040					1045					1050			
Asp	Gly	Thr	Thr	Val	Val	Val	Thr	Glu	Asp	Cys	Gly	Asn	Arg	Gly
	1055					1060					1065			
Pro	Ser	Leu	Arg	Thr	Thr	Thr	Ala	Ser	Gly	Lys	Leu	Ile	Thr	Glu
	1070					1075					1080			
Trp	Cys	Cys	Arg	Ser	Cys	Thr	Leu	Pro	Pro	Leu	Arg	Tyr	Arg	Gly
	1085					1090					1095			
Glu	Asp	Gly	Cys	Trp	Tyr	Gly	Met	Glu	Ile	Arg	Pro	Leu	Lys	Glu
	1100					1105					1110			
Lys	Glu	Glu	Asn	Leu	Val	Asn	Ser	Leu	Val	Thr	Ala	Gly	His	Gly
	1115					1120					1125			
Gln	Val	Asp	Asn	Phe	Ser	Leu	Gly	Val	Leu	Gly	Met	Ala	Leu	Phe
	1130					1135					1140			
Leu	Glu	Glu	Met	Leu	Arg	Thr	Arg	Val	Gly	Thr	Lys	His	Ala	Ile
	1145					1150					1155			
Leu	Leu	Val	Ala	Val	Ser	Phe	Val	Thr	Leu	Ile	Thr	Gly	Asn	Met
	1160					1165					1170			
Ser	Phe	Arg	Asp	Leu	Gly	Arg	Val	Met	Val	Met	Val	Gly	Ala	Thr
	1175					1180					1185			
Met	Thr	Asp	Asp	Ile	Gly	Met	Gly	Val	Thr	Tyr	Leu	Ala	Leu	Leu
	1190					1195					1200			
Ala	Ala	Phe	Lys	Val	Arg	Pro	Thr	Phe	Ala	Ala	Gly	Leu	Leu	Leu
	1205					1210					1215			
Arg	Lys	Leu	Thr	Ser	Lys	Glu	Leu	Met	Met	Thr	Thr	Ile	Gly	Ile
	1220					1225					1230			
Val	Leu	Leu	Ser	Gln	Ser	Thr	Ile	Pro	Glu	Thr	Ile	Leu	Glu	Leu
	1235					1240					1245			
Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met	Val	Arg
	1250					1255					1260			

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Asn Met 1265	Glu Lys Tyr Gln Leu 1270	Ala Val Thr Ile Met 1275	Ala Ile Leu
Cys Val 1280	Pro Asn Ala Val Ile 1285	Leu Gln Asn Ala Trp 1290	Lys Val Ser
Cys Thr 1295	Ile Leu Ala Val Val 1300	Ser Val Ser Pro Leu 1305	Phe Leu Thr
Ser Ser 1310	Gln Gln Lys Thr Asp 1315	Trp Ile Pro Leu Ala 1320	Leu Thr Ile
Lys Gly 1325	Leu Asn Pro Thr Ala 1330	Ile Phe Leu Thr Thr 1335	Leu Ser Arg
Thr Ser 1340	Lys Lys Arg Ser Trp 1345	Pro Leu Asn Glu Ala 1350	Ile Met Ala
Val Gly 1355	Met Val Ser Ile Leu 1360	Ala Ser Ser Leu Leu 1365	Lys Asn Asp
Ile Pro 1370	Met Thr Gly Pro Leu 1375	Val Ala Gly Gly Leu 1380	Leu Thr Val
Cys Tyr 1385	Val Leu Thr Gly Arg 1390	Ser Ala Asp Leu Glu 1395	Leu Glu Arg
Ala Ala 1400	Asp Val Lys Trp Glu 1405	Asp Gln Ala Glu Ile 1410	Ser Gly Ser
Ser Pro 1415	Ile Leu Ser Ile Thr 1420	Ile Ser Glu Asp Gly 1425	Ser Met Ser
Ile Lys 1430	Asn Glu Glu Glu Glu 1435	Gln Thr Leu Thr Ile 1440	Leu Ile Arg
Thr Gly 1445	Leu Leu Val Ile Ser 1450	Gly Leu Phe Pro Val 1455	Ser Ile Pro
Ile Thr 1460	Ala Ala Ala Trp Tyr 1465	Leu Trp Glu Val Lys 1470	Lys Gln Arg
Ala Gly 1475	Val Leu Trp Asp Val 1480	Pro Ser Pro Pro Pro 1485	Met Gly Lys
Ala Glu 1490	Leu Glu Asp Gly Ala 1495	Tyr Arg Ile Lys Gln 1500	Lys Gly Ile
Leu Gly 1505	Tyr Ser Gln Ile Gly 1510	Ala Gly Val Tyr Lys 1515	Glu Gly Thr

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Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu	Met	His
1520						1525					1530			
Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys	Lys	Asp
1535						1540					1545			
Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu	Trp	Lys
1550						1555					1560			
Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly	Lys	Asn
1565						1570					1575			
Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr	Asn	Ala
1580						1585					1590			
Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly	Thr	Ser
1595						1600					1605			
Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly	Leu	Tyr
1610						1615					1620			
Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser	Ala	Ile
1625						1630					1635			
Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile	Glu	Asp
1640						1645					1650			
Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu	His	Pro
1655						1660					1665			
Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val	Arg	Glu
1670						1675					1680			
Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro	Thr	Arg
1685						1690					1695			
Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu	Pro	Ile
1700						1705					1710			
Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly	Arg	Glu
1715						1720					1725			
Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg	Leu	Leu
1730						1735					1740			
Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met	Asp	Glu
1745						1750					1755			
Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly	Tyr	Ile
1760						1765					1770			

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Ser Thr	Arg Val	Glu Met	Gly	Glu Ala	Ala Gly	Ile	Phe Met	Thr			
1775			1780			1785					
Ala Thr	Pro Pro	Gly Ser	Arg	Asp Pro	Phe Pro	Gln	Ser Asn	Ala			
1790			1795			1800					
Pro Ile	Ile Asp	Glu Glu	Arg	Glu Ile	Pro Glu	Arg	Ser Trp	Asn			
1805			1810			1815					
Ser Gly	His Glu	Trp Val	Thr	Asp Phe	Lys Gly	Lys	Thr Val	Trp			
1820			1825			1830					
Phe Val	Pro Ser	Ile Lys	Ala	Gly Asn	Asp Ile	Ala	Ala Cys	Leu			
1835			1840			1845					
Arg Lys	Asn Gly	Lys Lys	Val	Ile Gln	Leu Ser	Arg	Lys Thr	Phe			
1850			1855			1860					
Asp Ser	Glu Tyr	Val Lys	Thr	Arg Thr	Asn Asp	Trp	Asp Phe	Val			
1865			1870			1875					
Val Thr	Thr Asp	Ile Ser	Glu	Met Gly	Ala Asn	Phe	Lys Ala	Glu			
1880			1885			1890					
Arg Val	Ile Asp	Pro Arg	Arg	Cys Met	Lys Pro	Val	Ile Leu	Thr			
1895			1900			1905					
Asp Gly	Glu Glu	Arg Val	Ile	Leu Ala	Gly Pro	Met	Pro Val	Thr			
1910			1915			1920					
His Ser	Ser Ala	Ala Gln	Arg	Arg Gly	Arg Ile	Gly	Arg Asn	Pro			
1925			1930			1935					
Lys Asn	Glu Asn	Asp Gln	Tyr	Ile Tyr	Met Gly	Glu	Pro Leu	Glu			
1940			1945			1950					
Asn Asp	Glu Asp	Cys Ala	His	Trp Lys	Glu Ala	Lys	Met Leu	Leu			
1955			1960			1965					
Asp Asn	Ile Asn	Thr Pro	Glu	Gly Ile	Ile Pro	Ser	Met Phe	Glu			
1970			1975			1980					
Pro Glu	Arg Glu	Lys Val	Asp	Ala Ile	Asp Gly	Glu	Tyr Arg	Leu			
1985			1990			1995					
Arg Gly	Glu Ala	Arg Lys	Thr	Phe Val	Asp Leu	Met	Arg Arg	Gly			
2000			2005			2010					
Asp Leu	Pro Val	Trp Leu	Ala	Tyr Arg	Val Ala	Ala	Glu Gly	Ile			
2015			2020			2025					

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Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys	Asn	Asn
2030						2035					2040			
Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr	Lys	Glu
2045						2050					2055			
Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala	Arg	Ile
2060						2065					2070			
Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe	Ala	Ala
2075						2080					2085			
Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met	Gly	Arg
2090						2095					2100			
Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Ala	Arg	Asp	Ala	Leu	Asp	Asn
2105						2110					2115			
Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Ala	Gly	Gly	Arg	Ala	Tyr	Asn
2120						2125					2130			
His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu	Leu	Leu
2135						2140					2145			
Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu	Phe	Leu
2150						2155					2160			
Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met	Cys	Cys
2165						2170					2175			
Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile	Gln	Pro
2180						2185					2190			
His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu	Ile	Val
2195						2200					2205			
Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln	Asp	Asn
2210						2215					2220			
Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val	Ala	Ala
2225						2230					2235			
Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys	Lys	Asp
2240						2245					2250			
Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser	Asn	Ile
2255						2260					2265			
Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu	Tyr	Ala
2270						2275					2280			

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Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser	Ile	Glu
2285						2290					2295			
Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn	Gln	Ala
2300						2305					2310			
Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser	Lys	Met
2315						2320					2325			
Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser	Gln	Val
2330						2335					2340			
Asn	Pro	Ile	Thr	Leu	Thr	Ala	Ala	Leu	Phe	Leu	Leu	Val	Ala	His
2345						2350					2355			
Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr	Arg	Glu
2360						2365					2370			
Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro	Thr	Val
2375						2380					2385			
Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr	Asp	Pro
2390						2395					2400			
Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val	Leu	Cys
2405						2410					2415			
Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu	Cys	Glu
2420						2425					2430			
Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp	Glu	Gly
2435						2440					2445			
Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser	Met	Ala
2450						2455					2460			
Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu	Leu	Phe
2465						2470					2475			
Ser	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr	Gly	Asn
2480						2485					2490			
Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu	Asn	Ala
2495						2500					2505			
Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly	Ile	Gln
2510						2515					2520			
Glu	Val	Asp	Arg	Thr	Leu	Ala	Lys	Glu	Gly	Ile	Lys	Arg	Gly	Glu
2525						2530					2535			

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Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu	Arg	Trp
	2540					2545					2550			
Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val	Val	Asp
	2555					2560					2565			
Leu	Gly	Cys	Gly	Arg	Gly	Gly	Trp	Ser	Tyr	Tyr	Cys	Gly	Gly	Leu
	2570					2575					2580			
Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly	Pro	Gly
	2585					2590					2595			
His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn	Leu	Val
	2600					2605					2610			
Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro	Glu	Lys
	2615					2620					2625			
Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro	Asn	Pro
	2630					2635					2640			
Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu	Val	Glu
	2645					2650					2655			
Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val	Leu	Asn
	2660					2665					2670			
Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu	Gln	Arg
	2675					2680					2685			
Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg	Asn	Ser
	2690					2695					2700			
Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn	Ile	Val
	2705					2710					2715			
Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg	Phe	Thr
	2720					2725					2730			
Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp	Leu	Gly
	2735					2740					2745			
Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro	Asn	Leu
	2750					2755					2760			
Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu	His	Glu
	2765					2770					2775			
Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr	Trp	Ala
	2780					2785					2790			

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Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala	Ser	Ser
2795						2800					2805			
Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp	Asp	Val
2810						2815					2820			
Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr	Pro	Phe
2825						2830					2835			
Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg	Thr	Gln
2840						2845					2850			
Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr	Ala	Glu
2855						2860					2865			
Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg	Met	Cys
2870						2875					2880			
Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala	Ala	Leu
2885						2890					2895			
Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala	Arg	Glu
2900						2905					2910			
Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys	Glu	Arg
2915						2920					2925			
Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr	Asn	Met
2930						2935					2940			
Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys	Ala	Lys
2945						2950					2955			
Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg	Phe	Leu
2960						2965					2970			
Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp	Phe	Ser
2975						2980					2985			
Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu	His	Lys
2990						2995					3000			
Leu	Gly	Tyr	Ile	Leu	Arg	Asp	Val	Ser	Lys	Lys	Glu	Gly	Gly	Ala
3005						3010					3015			
Met	Tyr	Ala	Asp	Asp	Thr	Ala	Gly	Trp	Asp	Thr	Arg	Ile	Thr	Leu
3020						3025					3030			
Glu	Asp	Leu	Lys	Asn	Glu	Glu	Met	Val	Thr	Asn	His	Met	Glu	Gly
3035						3040					3045			

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 Glu His 3050 Lys Lys Leu Ala Glu 3055 Ala Ile Phe Lys Leu 3060 Thr Tyr Gln
 Asn Lys 3065 Val Val Arg Val Gln 3070 Arg Pro Thr Pro Arg 3075 Gly Thr Val
 Met Asp 3080 Ile Ile Ser Arg Arg 3085 Asp Gln Arg Gly Ser 3090 Gly Gln Val
 Gly Thr 3095 Tyr Gly Leu Asn Thr 3100 Phe Thr Asn Met Glu 3105 Ala Gln Leu
 Ile Arg 3110 Gln Met Glu Gly Glu 3115 Gly Val Phe Lys Ser 3120 Ile Gln His
 Leu Thr 3125 Ile Thr Glu Glu Ile 3130 Ala Val Gln Asn Trp 3135 Leu Ala Arg
 Val Gly 3140 Arg Glu Arg Leu Ser 3145 Arg Met Ala Ile Ser 3150 Gly Asp Asp
 Cys Val 3155 Val Lys Pro Leu Asp 3160 Asp Arg Phe Ala Ser 3165 Ala Leu Thr
 Ala Leu 3170 Asn Asp Met Gly Lys 3175 Ile Arg Lys Asp Ile 3180 Gln Gln Trp
 Glu Pro 3185 Ser Arg Gly Trp Asn 3190 Asp Trp Thr Gln Val 3195 Pro Phe Cys
 Ser His 3200 His Phe His Glu Leu 3205 Ile Met Lys Asp Gly 3210 Arg Val Leu
 Val Val 3215 Pro Cys Arg Asn Gln 3220 Asp Glu Leu Ile Gly 3225 Arg Ala Arg
 Ile Ser 3230 Gln Gly Ala Gly Trp 3235 Ser Leu Arg Glu Thr 3240 Ala Cys Leu
 Gly Lys 3245 Ser Tyr Ala Gln Met 3250 Trp Ser Leu Met Tyr 3255 Phe His Arg
 Arg Asp 3260 Leu Arg Leu Ala Ala 3265 Asn Ala Ile Cys Ser 3270 Ala Val Pro
 Ser His 3275 Trp Val Pro Thr Ser 3280 Arg Thr Thr Trp Ser 3285 Ile His Ala
 Lys His 3290 Glu Trp Met Thr Thr 3295 Glu Asp Met Leu Thr 3300 Val Trp Asn

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 Arg Val Trp Ile Gln Glu Asn Pro Trp Met Glu Asp Lys Thr Pro
 3305 3310 3315

Val Glu Ser Trp Glu Glu Ile Pro Tyr Leu Gly Lys Arg Glu Asp
 3320 3325 3330

Gln Trp Cys Gly Ser Leu Ile Gly Leu Thr Ser Arg Ala Thr Trp
 3335 3340 3345

Ala Lys Asn Ile Gln Ala Ala Ile Asn Gln Val Arg Ser Leu Ile
 3350 3355 3360

Gly Asn Glu Glu Tyr Thr Asp Tyr Met Pro Ser Met Lys Arg Phe
 3365 3370 3375

Arg Arg Glu Glu Glu Glu Ala Gly Val Leu Trp
 3380 3385

<210> 19
 <211> 10717
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Dengue virus serotype 3, MVS

<400> 19
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 gttctaacag tttttaatt agagagcaga tctctgatga ataaccaacg gaaaaaggcg 120
 aaaaacacgc ctttcaatat gctgaaacgc gagagaaacc gcgtgtcgac tgtgcaacag 180
 ctgacaaaga gattctcact tggaatgctg cagggacgag gaccattaaa actgttcattg 240
 gccctggtgg cgttccttcg tttcctaaca atcccaccaa cagcagggat attgaagaga 300
 tggggaacaa ttaaaaaatc aaaagctatt aatgttttga gaggggttcag gaaagagatt 360
 ggaaggatgc tgaacatctt gaataggaga cgcagatctg caggcatgat cattatgctg 420
 attccaacag tgatggcggt ccatttaacc acgcgtgatg gagagccgcg catgattgtg 480
 gggaagaatg aaagaggaaa atccctactt ttcaagacag cctctggaat caacatgtgc 540
 acactcatag ctatggatct gggagagatg tgtgatgaca cggtcactta caaatgcccc 600
 cacattaccg aagtggagcc tgaagacatt gactgctggt gcaaccttac atcgacatgg 660
 gtgacttatg gaacatgcaa tcaagctgga gagcatagac gcgataagag atcagtggcg 720
 ttagctcccc atgttggcat gggactggac acacgcactc aaacctggat gtcggctgaa 780
 ggagcttgga gacaagtcga gaaggtagag acatgggccc ttaggcaccc agggtttacc 840
 atactagccc tatttcttgc ccattacata ggcacttcct tgaccagaa agtggttatt 900
 tttatactat taatgctggt taccccatcc atgacaatga gatgtgtagg agtaggaaac 960
 agagattttg tggaaggcct atcgggagct acgtgggttg acgtggtgct cgagcacggt 1020
 ggggtgtgtga ctaccatggc taagaacaag cccacgtgg acatagagct tcagaagacc 1080

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gaggccaccc	aactggcgac	cctaaggaag	ctatgcattg	agggaaaaat	taccaacata	1140
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aactacgtgt	gtaagcatac	atacgtggac	agaggctggg	gaaacggttg	tggtttgttt	1260
ggcaagggaa	gcttggtgac	atgcgcgaaa	tttcaatggt	tagaatcaat	agagggaaaa	1320
gtggtgcaac	atgagaacct	caaatacacc	gtcatcatca	cagtgcacac	aggagaccaa	1380
caccaggtgg	gaaatgaaac	gcagggagtc	acggctgaga	taacacccca	ggcatcaacc	1440
gctgaagcca	ttttacctga	atatggaacc	ctcgggctag	aatgctcacc	acggacaggt	1500
ttggatttca	atgaaatgat	ctcattgaca	atgaagaaca	aagcatggat	ggtacataga	1560
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aaattggaac	tcaaggggat	gagctatgca	atgtgcttga	gtagctttgt	gttgaagaaa	1860
gaagtctccg	aaacgcagca	tgggacaata	ctcattaagg	ttgagtacaa	aggggaagat	1920
gcaccctgca	agattccttt	ctccacggag	gatggacaag	gaaaagctct	caatggcaga	1980
ctgatcacag	ccaatccagt	ggtgaccaag	aaggaggagc	ctgtcaacat	tgaggctgaa	2040
cctccttttg	gagaaagtaa	catagtaatt	ggaattggag	acaaagccct	gaaaatcaac	2100
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ggcagtggga	ttttcatcac	agacaacgtg	cacacatgga	cagaacaata	caagttccaa	2520
ccagaatccc	cttcaaaaact	agcttcagct	atccagaaag	cccatgaaga	ggacatttgt	2580
ggaatccgct	cagtaacaag	actggagaat	ctgatgtgga	aacaaataac	accagaattg	2640
aatcacattc	tatcagaaaa	tgaggtgaag	ttaactatta	tgacaggaga	catcaaagga	2700
atcatgcagg	caggaaaacg	atctctgcgg	cctcagccca	ctgagctgaa	gtattcatgg	2760
aaaacatggg	gcaaagcaaa	aatgctctct	acagagtctc	ataaccagac	ctttctcatt	2820
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gccgatatgg	gttattggat	agaaagtgca	ctcaatgaca	catggaagat	agagaaagcc	3060
tctttcattg	aagttaaaaa	ctgccactgg	ccaaaatcac	acaccctctg	gagcaatgga	3120

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ggagcgggaa	agacgaagag	ataccttccg	gccatagtca	gagaagctat	aaaacggggt	5160

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atcagtggag atgatttgtt tgtgaaacct ttagatgaca ggttcgcaag cgctttaaca      9600
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 <213> Artificial Sequence

<220>
 <223> Dengue virus serotype 3, MVS

<400> 20

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Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
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Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45
 Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
 50 55 60
 Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
 65 70 75 80
 Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
 85 90 95
 Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
 100 105 110
 Met Ala Phe His Leu Thr Thr Arg Asp Gly Glu Pro Arg Met Ile Val
 115 120 125
 Gly Lys Asn Glu Arg Gly Lys Ser Leu Leu Phe Lys Thr Ala Ser Gly
 130 135 140
 Ile Asn Met Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Met Cys Asp
 145 150 155 160
 Asp Thr Val Thr Tyr Lys Cys Pro His Ile Thr Glu Val Glu Pro Glu
 165 170 175
 Asp Ile Asp Cys Trp Cys Asn Leu Thr Ser Thr Trp Val Thr Tyr Gly
 180 185 190
 Thr Cys Asn Gln Ala Gly Glu His Arg Arg Asp Lys Arg Ser Val Ala
 195 200 205
 Leu Ala Pro His Val Gly Met Gly Leu Asp Thr Arg Thr Gln Thr Trp
 210 215 220
 Met Ser Ala Glu Gly Ala Trp Arg Gln Val Glu Lys Val Glu Thr Trp
 225 230 235 240
 Ala Leu Arg His Pro Gly Phe Thr Ile Leu Ala Leu Phe Leu Ala His
 245 250 255
 Tyr Ile Gly Thr Ser Leu Thr Gln Lys Val Val Ile Phe Ile Leu Leu
 260 265 270
 Met Leu Val Thr Pro Ser Met Thr Met Arg Cys Val Gly Val Gly Asn
 275 280 285
 Arg Asp Phe Val Glu Gly Leu Ser Gly Ala Thr Trp Val Asp Val Val
 290 295 300

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Leu Glu His Gly Gly Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
 305 310 315 320

Leu Asp Ile Glu Leu Gln Lys Thr Glu Ala Thr Gln Leu Ala Thr Leu
 325 330 335

Arg Lys Leu Cys Ile Glu Gly Lys Ile Thr Asn Ile Thr Thr Asp Ser
 340 345 350

Arg Cys Pro Thr Gln Gly Glu Ala Ile Leu Pro Glu Glu Gln Asp Gln
 355 360 365

Asn Tyr Val Cys Lys His Thr Tyr Val Asp Arg Gly Trp Gly Asn Gly
 370 375 380

Cys Gly Leu Phe Gly Lys Gly Ser Leu Val Thr Cys Ala Lys Phe Gln
 385 390 395 400

Cys Leu Glu Ser Ile Glu Gly Lys Val Val Gln His Glu Asn Leu Lys
 405 410 415

Tyr Thr Val Ile Ile Thr Val His Thr Gly Asp Gln His Gln Val Gly
 420 425 430

Asn Glu Thr Gln Gly Val Thr Ala Glu Ile Thr Pro Gln Ala Ser Thr
 435 440 445

Ala Glu Ala Ile Leu Pro Glu Tyr Gly Thr Leu Gly Leu Glu Cys Ser
 450 455 460

Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Ile Ser Leu Thr Met Lys
 465 470 475 480

Asn Lys Ala Trp Met Val His Arg Gln Trp Phe Phe Asp Leu Pro Leu
 485 490 495

Pro Trp Thr Ser Gly Ala Ser Ala Glu Thr Pro Thr Trp Asn Arg Lys
 500 505 510

Glu Leu Leu Val Thr Phe Lys Asn Ala His Ala Lys Lys Gln Glu Val
 515 520 525

Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu Thr Gly
 530 535 540

Ala Thr Glu Ile Gln Thr Ser Gly Gly Thr Ser Ile Phe Ala Gly His
 545 550 555 560

Leu Lys Cys Arg Leu Lys Met Asp Lys Leu Glu Leu Lys Gly Met Ser
 565 570 575

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Tyr Ala Met Cys₅₈₀ Leu Ser Ser Phe Val₅₈₅ Leu Lys Lys Glu Val₅₉₀ Ser Glu
 Thr Gln His₅₉₅ Gly Thr Ile Leu Ile₆₀₀ Lys Val Glu Tyr Lys₆₀₅ Gly Glu Asp
 Ala Pro₆₁₀ Cys Lys Ile Pro Phe₆₁₅ Ser Thr Glu Asp Gly₆₂₀ Gln Gly Lys Ala
 Leu₆₂₅ Asn Gly Arg Leu Ile₆₃₀ Thr Ala Asn Pro Val₆₃₅ Val Thr Lys Lys Glu₆₄₀
 Glu Pro Val Asn₆₄₅ Ile Glu Ala Glu Pro Pro₆₅₀ Phe Gly Glu Ser Asn₆₅₅ Ile
 Val Ile Gly Ile₆₆₀ Gly Asp Lys Ala Leu₆₆₅ Lys Ile Asn Trp Tyr₆₇₀ Lys Lys
 Gly Ser Ser₆₇₅ Ile Gly Lys Met Phe₆₈₀ Glu Ala Thr Ala Arg₆₈₅ Gly Ala Arg
 Arg Met₆₉₀ Ala Ile Leu Gly Asp₆₉₅ Thr Ala Trp Asp Phe₇₀₀ Gly Ser Val Gly
 Gly₇₀₅ Val Leu Asn Ser Leu₇₁₀ Gly Lys Met Val His₇₁₅ Gln Ile Phe Gly Ser₇₂₀
 Ala Tyr Thr Ala Leu₇₂₅ Phe Gly Gly Val Ser₇₃₀ Trp Met Met Lys Ile₇₃₅ Gly
 Ile Gly Val Leu₇₄₀ Leu Thr Trp Ile Gly₇₄₅ Leu Asn Ser Lys Asn₇₅₀ Thr Ser
 Met Ser Phe₇₅₅ Ser Cys Ile Ala Ala₇₆₀ Gly Ile Val Thr Leu₇₆₅ Tyr Leu Gly
 Val Met₇₇₀ Val Gln Ala Asp Ser₇₇₅ Gly Cys Val Val Ser₇₈₀ Trp Lys Asn Lys
 Glu₇₈₅ Leu Lys Cys Gly Ser₇₉₀ Gly Ile Phe Ile Thr₇₉₅ Asp Asn Val His Thr₈₀₀
 Trp Thr Glu Gln Tyr₈₀₅ Lys Phe Gln Pro Glu₈₁₀ Ser Pro Ser Lys Leu₈₁₅ Ala
 Ser Ala Ile Gln₈₂₀ Lys Ala His Glu Glu₈₂₅ Asp Ile Cys Gly Ile₈₃₀ Arg Ser
 Val Thr Arg₈₃₅ Leu Glu Asn Leu Met₈₄₀ Trp Lys Gln Ile Thr₈₄₅ Pro Glu Leu

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Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met Thr Gly
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Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg Pro Gln
 865 870 875 880

Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala Lys Met
 885 890 895

Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly Pro Glu
 900 905 910

Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu Glu Val
 915 920 925

Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu Lys Leu
 930 935 940

Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser Ala Ala
 945 950 955 960

Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp Ile Glu
 965 970 975

Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe Ile Glu
 980 985 990

Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser Asn Gly
 995 1000 1005

Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala Gly Pro
 1010 1015 1020

Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln Ile Thr
 1025 1030 1035

Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp Phe Cys
 1040 1045 1050

Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn Arg Gly
 1055 1060 1065

Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile Thr Glu
 1070 1075 1080

Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr Arg Gly
 1085 1090 1095

Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu Lys Glu
 1100 1105 1110

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Gln	Val	Asp	Asn	Phe	Ser	Leu	Gly	Val	Leu	Gly	Met	Ala	Leu	Phe
	1130					1135					1140			
Leu	Glu	Glu	Met	Leu	Arg	Thr	Arg	Val	Gly	Thr	Lys	His	Ala	Ile
	1145					1150					1155			
Leu	Leu	Val	Ala	Val	Ser	Phe	Val	Thr	Leu	Ile	Thr	Gly	Asn	Met
	1160					1165					1170			
Ser	Phe	Arg	Asp	Leu	Gly	Arg	Val	Met	Val	Met	Val	Gly	Ala	Thr
	1175					1180					1185			
Met	Thr	Asp	Asp	Ile	Gly	Met	Gly	Val	Thr	Tyr	Leu	Ala	Leu	Leu
	1190					1195					1200			
Ala	Ala	Phe	Lys	Val	Arg	Pro	Thr	Phe	Ala	Ala	Gly	Leu	Leu	Leu
	1205					1210					1215			
Arg	Lys	Leu	Thr	Ser	Lys	Glu	Leu	Met	Met	Thr	Thr	Ile	Gly	Ile
	1220					1225					1230			
Val	Leu	Leu	Ser	Gln	Ser	Thr	Ile	Pro	Glu	Thr	Ile	Leu	Glu	Leu
	1235					1240					1245			
Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met	Val	Arg
	1250					1255					1260			
Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala	Ile	Leu
	1265					1270					1275			
Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys	Val	Ser
	1280					1285					1290			
Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe	Leu	Thr
	1295					1300					1305			
Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu	Thr	Ile
	1310					1315					1320			
Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu	Ser	Arg
	1325					1330					1335			
Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile	Met	Ala
	1340					1345					1350			
Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys	Asn	Asp
	1355					1360					1365			

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Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu	Thr	Val
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Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu	Glu	Arg
	1385					1390					1395			
Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser	Gly	Ser
	1400					1405					1410			
Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser	Met	Ser
	1415					1420					1425			
Ile	Lys	Asn	Glu	Glu	Glu	Glu	Gln	Thr	Leu	Thr	Ile	Leu	Ile	Arg
	1430					1435					1440			
Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser	Ile	Pro
	1445					1450					1455			
Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys	Gln	Arg
	1460					1465					1470			
Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met	Gly	Lys
	1475					1480					1485			
Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys	Gly	Ile
	1490					1495					1500			
Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu	Gly	Thr
	1505					1510					1515			
Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu	Met	His
	1520					1525					1530			
Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys	Lys	Asp
	1535					1540					1545			
Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu	Trp	Lys
	1550					1555					1560			
Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly	Lys	Asn
	1565					1570					1575			
Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr	Asn	Ala
	1580					1585					1590			
Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly	Thr	Ser
	1595					1600					1605			
Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly	Leu	Tyr
	1610					1615					1620			

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Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser	Ala	Ile
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Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile	Glu	Asp
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Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu	His	Pro
	1655					1660					1665			
Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val	Arg	Glu
	1670					1675					1680			
Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro	Thr	Arg
	1685					1690					1695			
Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu	Pro	Ile
	1700					1705					1710			
Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly	Arg	Glu
	1715					1720					1725			
Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg	Leu	Leu
	1730					1735					1740			
Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met	Asp	Glu
	1745					1750					1755			
Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly	Tyr	Ile
	1760					1765					1770			
Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe	Met	Thr
	1775					1780					1785			
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	1790					1795					1800			
Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser	Trp	Asn
	1805					1810					1815			
Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr	Val	Trp
	1820					1825					1830			
Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala	Cys	Leu
	1835					1840					1845			
Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys	Thr	Phe
	1850					1855					1860			
Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp	Phe	Val
	1865					1870					1875			

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Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys	Ala	Glu
	1880					1885					1890			
Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile	Leu	Thr
	1895					1900					1905			
Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro	Val	Thr
	1910					1915					1920			
His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg	Asn	Pro
	1925					1930					1935			
Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro	Leu	Glu
	1940					1945					1950			
Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met	Leu	Leu
	1955					1960					1965			
Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met	Phe	Glu
	1970					1975					1980			
Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr	Arg	Leu
	1985					1990					1995			
Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg	Arg	Gly
	2000					2005					2010			
Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu	Gly	Ile
	2015					2020					2025			
Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys	Asn	Asn
	2030					2035					2040			
Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr	Lys	Glu
	2045					2050					2055			
Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala	Arg	Ile
	2060					2065					2070			
Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe	Ala	Ala
	2075					2080					2085			
Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met	Gly	Arg
	2090					2095					2100			
Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Ala	Arg	Asp	Ala	Leu	Asp	Asn
	2105					2110					2115			
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	2120					2125					2130			

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His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu	Leu	Leu
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	2150					2155					2160			
Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met	Cys	Cys
	2165					2170					2175			
Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile	Gln	Pro
	2180					2185					2190			
His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu	Ile	Val
	2195					2200					2205			
Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln	Asp	Asn
	2210					2215					2220			
Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val	Ala	Ala
	2225					2230					2235			
Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys	Lys	Asp
	2240					2245					2250			
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	2255					2260					2265			
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	2270					2275					2280			
Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser	Ile	Glu
	2285					2290					2295			
Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn	Gln	Ala
	2300					2305					2310			
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	2315					2320					2325			
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	2330					2335					2340			
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	2345					2350					2355			
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	2360					2365					2370			
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	2375					2380					2385			

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Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr	Asp	Pro
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Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu	Cys	Glu
	2420					2425					2430			
Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp	Glu	Gly
	2435					2440					2445			
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	2450					2455					2460			
Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu	Leu	Phe
	2465					2470					2475			
Ser	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr	Gly	Asn
	2480					2485					2490			
Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu	Asn	Ala
	2495					2500					2505			
Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly	Ile	Gln
	2510					2515					2520			
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	2525					2530					2535			
Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu	Arg	Trp
	2540					2545					2550			
Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val	Val	Asp
	2555					2560					2565			
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	2570					2575					2580			
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	2585					2590					2595			
His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn	Leu	Val
	2600					2605					2610			
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	2675					2680					2685			
Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg	Asn	Ser
	2690					2695					2700			
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	2705					2710					2715			
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	2735					2740					2745			
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Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr	Ala	Glu
	2855					2860					2865			
Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg	Met	Cys
	2870					2875					2880			
Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala	Ala	Leu
	2885					2890					2895			

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	3050					3055					3060			
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Gly	Thr	Tyr	Gly	Leu	Asn	Thr	Phe	Thr	Asn	Met	Glu	Ala	Gln	Leu
	3095					3100					3105			
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Val	Gly	Arg	Glu	Arg	Leu	Ser	Arg	Met	Ala	Ile	Ser	Gly	Asp	Asp
	3140					3145					3150			

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 Glu Pro Ser Arg Gly Trp Asn Asp Trp Thr Gln Val Pro Phe Cys
 3185 3190 3195
 Ser His His Phe His Glu Leu Ile Met Lys Asp Gly Arg Val Leu
 3200 3205 3210
 Val Val Pro Cys Arg Asn Gln Asp Glu Leu Ile Gly Arg Ala Arg
 3215 3220 3225
 Ile Ser Gln Gly Ala Gly Trp Ser Leu Arg Glu Thr Ala Cys Leu
 3230 3235 3240
 Gly Lys Ser Tyr Ala Gln Met Trp Ser Leu Met Tyr Phe His Arg
 3245 3250 3255
 Arg Asp Leu Arg Leu Ala Ala Asn Ala Ile Cys Ser Ala Val Pro
 3260 3265 3270
 Ser His Trp Val Pro Thr Ser Arg Thr Thr Trp Ser Ile His Ala
 3275 3280 3285
 Lys His Glu Trp Met Thr Thr Glu Asp Met Leu Thr Val Trp Asn
 3290 3295 3300
 Arg Val Trp Ile Gln Glu Asn Pro Trp Met Glu Asp Lys Thr Pro
 3305 3310 3315
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 Ala Lys Asn Ile Gln Ala Ala Ile Asn Gln Val Arg Ser Leu Ile
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<212> DNA

<213> Artificial Sequence

<220>

<223> Dengue virus serotype 3, WVS

<400> 21

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gccctggtgg cgttccttcg tttcctaaca atcccaccaa cagcagggat attgaagaga      300
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 <400> 22

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Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
 50 55 60

Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
 65 70 75 80

Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
 85 90 95

Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
 100 105 110

Met Ala Phe His Leu Thr Thr Arg Asp Gly Glu Pro Arg Met Ile Val
 115 120 125

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 Gly Lys Asn Glu Arg Gly Lys Ser Leu Leu Phe Lys Thr Ala Ser Gly
 130 135 140

Ile Asn Met Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Met Cys Asp
 145 150 155 160

Asp Thr Val Thr Tyr Lys Cys Pro His Ile Thr Glu Val Glu Pro Glu
 165 170 175

Asp Ile Asp Cys Trp Cys Asn Leu Thr Ser Thr Trp Val Thr Tyr Gly
 180 185 190

Thr Cys Asn Gln Ala Gly Glu His Arg Arg Asp Lys Arg Ser Val Ala
 195 200 205

Leu Ala Pro His Val Gly Met Gly Leu Asp Thr Arg Thr Gln Thr Trp
 210 215 220

Met Ser Ala Glu Gly Ala Trp Arg Gln Val Glu Lys Val Glu Thr Trp
 225 230 235 240

Ala Leu Arg His Pro Gly Phe Thr Ile Leu Ala Leu Phe Leu Ala His
 245 250 255

Tyr Ile Gly Thr Ser Leu Thr Gln Lys Val Val Ile Phe Ile Leu Leu
 260 265 270

Met Leu Val Thr Pro Ser Met Thr Met Arg Cys Val Gly Val Gly Asn
 275 280 285

Arg Asp Phe Val Glu Gly Leu Ser Gly Ala Thr Trp Val Asp Val Val
 290 295 300

Leu Glu His Gly Gly Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
 305 310 315 320

Leu Asp Ile Glu Leu Gln Lys Thr Glu Ala Thr Gln Leu Ala Thr Leu
 325 330 335

Arg Lys Leu Cys Ile Glu Gly Lys Ile Thr Asn Ile Thr Thr Asp Ser
 340 345 350

Arg Cys Pro Thr Gln Gly Glu Ala Ile Leu Pro Glu Glu Gln Asp Gln
 355 360 365

Asn Tyr Val Cys Lys His Thr Tyr Val Asp Arg Gly Trp Gly Asn Gly
 370 375 380

Cys Gly Leu Phe Gly Lys Gly Ser Leu Val Thr Cys Ala Lys Phe Gln
 385 390 395 400

20170306 478484.168 VAC-5035-AU Replacement Sequence Listing 34 sequences.txt
 Cys Leu Glu Ser Ile Glu Gly Lys Val Val Gln His Glu Asn Leu Lys
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Tyr Thr Val Ile Ile Thr Val His Thr Gly Asp Gln His Gln Val Gly
 420 425 430

Asn Glu Thr Gln Gly Val Thr Ala Glu Ile Thr Pro Gln Ala Ser Thr
 435 440 445

Ala Glu Ala Ile Leu Pro Glu Tyr Gly Thr Leu Gly Leu Glu Cys Ser
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Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Ile Ser Leu Thr Met Lys
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Asn Lys Ala Trp Met Val His Arg Gln Trp Phe Phe Asp Leu Pro Leu
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Pro Trp Thr Ser Gly Ala Ser Ala Glu Thr Pro Thr Trp Asn Arg Lys
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Glu Leu Leu Val Thr Phe Lys Asn Ala His Ala Lys Lys Gln Glu Val
 515 520 525

Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu Thr Gly
 530 535 540

Ala Thr Glu Ile Gln Thr Ser Gly Gly Thr Ser Ile Phe Ala Gly His
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Leu Lys Cys Arg Leu Lys Met Asp Lys Leu Glu Leu Lys Gly Met Ser
 565 570 575

Tyr Ala Met Cys Leu Ser Ser Phe Val Leu Lys Lys Glu Val Ser Glu
 580 585 590

Thr Gln His Gly Thr Ile Leu Ile Lys Val Glu Tyr Lys Gly Glu Asp
 595 600 605

Ala Pro Cys Lys Ile Pro Phe Ser Thr Glu Asp Gly Gln Gly Lys Ala
 610 615 620

Leu Asn Gly Arg Leu Ile Thr Ala Asn Pro Val Val Thr Lys Lys Glu
 625 630 635 640

Glu Pro Val Asn Ile Glu Ala Glu Pro Pro Phe Gly Glu Ser Asn Ile
 645 650 655

Val Ile Gly Ile Gly Asp Lys Ala Leu Lys Ile Asn Trp Tyr Lys Lys
 660 665 670

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Gly Ser Ser Ile Gly Lys Met Phe Glu Ala Thr Ala Arg Gly Ala Arg
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Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser Val Gly
690 695 700

Gly Val Leu Asn Ser Leu Gly Lys Met Val His Gln Ile Phe Gly Ser
705 710 715 720

Ala Tyr Thr Ala Leu Phe Gly Gly Val Ser Trp Met Met Lys Ile Gly
725 730 735

Ile Gly Val Leu Leu Thr Trp Ile Gly Leu Asn Ser Lys Asn Thr Ser
740 745 750

Met Ser Phe Ser Cys Ile Ala Ala Gly Ile Val Thr Leu Tyr Leu Gly
755 760 765Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys Asn Lys
770 775 780

Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val His Thr
785 790 795 800

Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys Leu Ala
805 810 815

Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile Arg Ser
820 825 830

Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro Glu Leu
835 840 845

Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met Thr Gly
850 855 860

Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg Pro Gln
865 870 875 880

Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala Lys Met
885 890 895

Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly Pro Glu
900 905 910

Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu Glu Val
915 920 925

Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu Lys Leu
930 935 940

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 Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser Ala Ala
 945 950 955 960

Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp Ile Glu
 965 970 975

Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe Ile Glu
 980 985 990

Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser Asn Gly
 995 1000 1005

Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala Gly Pro
 1010 1015 1020

Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln Ile Thr
 1025 1030 1035

Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp Phe Cys
 1040 1045 1050

Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn Arg Gly
 1055 1060 1065

Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile Thr Glu
 1070 1075 1080

Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr Arg Gly
 1085 1090 1095

Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu Lys Glu
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Lys Glu Glu Asn Leu Val Asn Ser Leu Val Thr Ala Gly His Gly
 1115 1120 1125

Gln Val Asp Asn Phe Ser Leu Gly Val Leu Gly Met Ala Leu Phe
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Leu Glu Glu Met Leu Arg Thr Arg Val Gly Thr Lys His Ala Ile
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Leu Leu Val Ala Val Ser Phe Val Thr Leu Ile Thr Gly Asn Met
 1160 1165 1170

Ser Phe Arg Asp Leu Gly Arg Val Met Val Met Val Gly Ala Thr
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Met Thr Asp Asp Ile Gly Met Gly Val Thr Tyr Leu Ala Leu Leu
 1190 1195 1200

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	1235					1240					1245			
Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met	Val	Arg
	1250					1255					1260			
Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala	Ile	Leu
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	1280					1285					1290			
Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe	Leu	Thr
	1295					1300					1305			
Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu	Thr	Ile
	1310					1315					1320			
Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu	Ser	Arg
	1325					1330					1335			
Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile	Met	Ala
	1340					1345					1350			
Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys	Asn	Asp
	1355					1360					1365			
Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu	Thr	Val
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Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu	Glu	Arg
	1385					1390					1395			
Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser	Gly	Ser
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Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser	Met	Ser
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Ile	Lys	Asn	Glu	Glu	Glu	Glu	Gln	Thr	Leu	Thr	Ile	Leu	Ile	Arg
	1430					1435					1440			
Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser	Ile	Pro
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1490		1495		1500	
Leu Gly	Tyr Ser Gln Ile	Gly	Ala Gly Val Tyr	Lys	Glu Gly Thr
1505		1510		1515	
Phe His	Thr Met Trp His	Val	Thr Arg Gly Ala	Val	Leu Met His
1520		1525		1530	
Lys Gly	Lys Arg Ile Glu	Pro	Ser Trp Ala Asp	Val	Lys Lys Asp
1535		1540		1545	
Leu Ile	Ser Tyr Gly Gly	Gly	Trp Lys Leu Glu	Gly	Glu Trp Lys
1550		1555		1560	
Glu Gly	Glu Glu Val Gln	Val	Leu Ala Leu Glu	Pro	Gly Lys Asn
1565		1570		1575	
Pro Arg	Ala Val Gln Thr	Lys	Pro Gly Leu Phe	Lys	Thr Asn Ala
1580		1585		1590	
Gly Thr	Ile Gly Ala Val	Ser	Leu Asp Phe Ser	Pro	Gly Thr Ser
1595		1600		1605	
Gly Ser	Pro Ile Ile Asp	Lys	Lys Gly Lys Val	Val	Gly Leu Tyr
1610		1615		1620	
Gly Asn	Gly Val Val Thr	Arg	Ser Gly Ala Tyr	Val	Ser Ala Ile
1625		1630		1635	
Ala Gln	Thr Glu Lys Ser	Ile	Glu Asp Asn Pro	Glu	Ile Glu Asp
1640		1645		1650	
Asp Ile	Phe Arg Lys Arg	Arg	Leu Thr Ile Met	Asp	Leu His Pro
1655		1660		1665	
Gly Ala	Gly Lys Thr Lys	Arg	Tyr Leu Pro Ala	Ile	Val Arg Glu
1670		1675		1680	
Ala Ile	Lys Arg Gly Leu	Arg	Thr Leu Ile Leu	Ala	Pro Thr Arg
1685		1690		1695	
Val Val	Ala Ala Glu Met	Glu	Glu Ala Leu Arg	Gly	Leu Pro Ile
1700		1705		1710	

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Arg Tyr 1715	Gln Thr Pro Ala Ile 1720	Arg Ala Val His Thr 1725	Gly Arg Glu
Ile Val 1730	Asp Leu Met Cys His 1735	Ala Thr Phe Thr Met 1740	Arg Leu Leu
Ser Pro 1745	Val Arg Val Pro Asn 1750	Tyr Asn Leu Ile Ile 1755	Met Asp Glu
Ala His 1760	Phe Thr Asp Pro Ala 1765	Ser Ile Ala Ala Arg 1770	Gly Tyr Ile
Ser Thr 1775	Arg Val Glu Met Gly 1780	Glu Ala Ala Gly Ile 1785	Phe Met Thr
Ala Thr 1790	Pro Pro Gly Ser Arg 1795	Asp Pro Phe Pro Gln 1800	Ser Asn Ala
Pro Ile 1805	Ile Asp Glu Glu Arg 1810	Glu Ile Pro Glu Arg 1815	Ser Trp Asn
Ser Gly 1820	His Glu Trp Val Thr 1825	Asp Phe Lys Gly Lys 1830	Thr Val Trp
Phe Val 1835	Pro Ser Ile Lys Ala 1840	Gly Asn Asp Ile Ala 1845	Ala Cys Leu
Arg Lys 1850	Asn Gly Lys Lys Val 1855	Ile Gln Leu Ser Arg 1860	Lys Thr Phe
Asp Ser 1865	Glu Tyr Val Lys Thr 1870	Arg Thr Asn Asp Trp 1875	Asp Phe Val
Val Thr 1880	Thr Asp Ile Ser Glu 1885	Met Gly Ala Asn Phe 1890	Lys Ala Glu
Arg Val 1895	Ile Asp Pro Arg Arg 1900	Cys Met Lys Pro Val 1905	Ile Leu Thr
Asp Gly 1910	Glu Glu Arg Val Ile 1915	Leu Ala Gly Pro Met 1920	Pro Val Thr
His Ser 1925	Ser Ala Ala Gln Arg 1930	Arg Gly Arg Ile Gly 1935	Arg Asn Pro
Lys Asn 1940	Glu Asn Asp Gln Tyr 1945	Ile Tyr Met Gly Glu 1950	Pro Leu Glu
Asn Asp 1955	Glu Asp Cys Ala His 1960	Trp Lys Glu Ala Lys 1965	Met Leu Leu

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Asp 1970	Asn	Ile	Asn	Thr	Pro	Glu 1975	Gly	Ile	Ile	Pro	Ser 1980	Met	Phe	Glu
Pro	Glu 1985	Arg	Glu	Lys	Val	Asp 1990	Ala	Ile	Asp	Gly	Glu 1995	Tyr	Arg	Leu
Arg	Gly 2000	Glu	Ala	Arg	Lys	Thr 2005	Phe	Val	Asp	Leu	Met 2010	Arg	Arg	Gly
Asp	Leu 2015	Pro	Val	Trp	Leu	Ala 2020	Tyr	Arg	Val	Ala	Ala 2025	Glu	Gly	Ile
Asn	Tyr 2030	Ala	Asp	Arg	Arg	Trp 2035	Cys	Phe	Asp	Gly	Val 2040	Lys	Asn	Asn
Gln	Ile 2045	Leu	Glu	Glu	Asn	Val 2050	Glu	Val	Glu	Ile	Trp 2055	Thr	Lys	Glu
Gly	Glu 2060	Arg	Lys	Lys	Leu	Lys 2065	Pro	Arg	Trp	Leu	Asp 2070	Ala	Arg	Ile
Tyr	Ser 2075	Asp	Pro	Leu	Ala	Leu 2080	Lys	Glu	Phe	Lys	Glu 2085	Phe	Ala	Ala
Gly	Arg 2090	Lys	Ser	Leu	Thr	Leu 2095	Asn	Leu	Ile	Thr	Glu 2100	Met	Gly	Arg
Leu	Pro 2105	Thr	Phe	Met	Thr	Gln 2110	Lys	Ala	Arg	Asn	Ala 2115	Leu	Asp	Asn
Leu	Ala 2120	Val	Leu	His	Thr	Ala 2125	Glu	Ala	Gly	Gly	Arg 2130	Ala	Tyr	Asn
His	Ala 2135	Leu	Ser	Glu	Leu	Pro 2140	Glu	Thr	Leu	Glu	Thr 2145	Leu	Leu	Leu
Leu	Thr 2150	Leu	Leu	Ala	Thr	Val 2155	Thr	Gly	Gly	Ile	Phe 2160	Leu	Phe	Leu
Met	Ser 2165	Ala	Arg	Gly	Ile	Gly 2170	Lys	Met	Thr	Leu	Gly 2175	Met	Cys	Cys
Ile	Ile 2180	Thr	Ala	Ser	Ile	Leu 2185	Leu	Trp	Tyr	Ala	Gln 2190	Ile	Gln	Pro
His	Trp 2195	Ile	Ala	Ala	Ser	Ile 2200	Ile	Leu	Glu	Phe	Phe 2205	Leu	Ile	Val
Leu	Leu 2210	Ile	Pro	Glu	Pro	Glu 2215	Lys	Gln	Arg	Thr	Pro 2220	Gln	Asp	Asn

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Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val	Ala	Ala
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Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys	Lys	Asp
2240						2245					2250			
Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser	Asn	Ile
2255						2260					2265			
Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu	Tyr	Ala
2270						2275					2280			
Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser	Ile	Glu
2285						2290					2295			
Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn	Gln	Ala
2300						2305					2310			
Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser	Lys	Met
2315						2320					2325			
Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser	Gln	Val
2330						2335					2340			
Asn	Pro	Ile	Thr	Leu	Thr	Ala	Ala	Leu	Phe	Leu	Leu	Val	Ala	His
2345						2350					2355			
Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr	Arg	Glu
2360						2365					2370			
Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro	Thr	Val
2375						2380					2385			
Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr	Asp	Pro
2390						2395					2400			
Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val	Leu	Cys
2405						2410					2415			
Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu	Cys	Glu
2420						2425					2430			
Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp	Glu	Gly
2435						2440					2445			
Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser	Met	Ala
2450						2455					2460			
Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu	Leu	Phe
2465						2470					2475			

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Ser	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr	Gly	Asn
2480						2485					2490			
Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu	Asn	Ala
2495						2500					2505			
Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly	Ile	Gln
2510						2515					2520			
Glu	Val	Asp	Arg	Thr	Leu	Ala	Lys	Glu	Gly	Ile	Lys	Arg	Gly	Glu
2525						2530					2535			
Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu	Arg	Trp
2540						2545					2550			
Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val	Val	Asp
2555						2560					2565			
Leu	Gly	Cys	Gly	Arg	Gly	Gly	Trp	Ser	Tyr	Tyr	Cys	Gly	Gly	Leu
2570						2575					2580			
Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly	Pro	Gly
2585						2590					2595			
His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn	Leu	Val
2600						2605					2610			
Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro	Glu	Lys
2615						2620					2625			
Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro	Asn	Pro
2630						2635					2640			
Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu	Val	Glu
2645						2650					2655			
Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val	Leu	Asn
2660						2665					2670			
Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu	Gln	Arg
2675						2680					2685			
Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg	Asn	Ser
2690						2695					2700			
Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn	Ile	Val
2705						2710					2715			
Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg	Phe	Thr
2720						2725					2730			

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Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp	Leu	Gly
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Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro	Asn	Leu
	2750					2755					2760			
Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu	His	Glu
	2765					2770					2775			
Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr	Trp	Ala
	2780					2785					2790			
Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala	Ser	Ser
	2795					2800					2805			
Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp	Asp	Val
	2810					2815					2820			
Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr	Pro	Phe
	2825					2830					2835			
Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg	Thr	Gln
	2840					2845					2850			
Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr	Ala	Glu
	2855					2860					2865			
Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg	Met	Cys
	2870					2875					2880			
Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala	Ala	Leu
	2885					2890					2895			
Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala	Arg	Glu
	2900					2905					2910			
Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys	Glu	Arg
	2915					2920					2925			
Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr	Asn	Met
	2930					2935					2940			
Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys	Ala	Lys
	2945					2950					2955			
Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg	Phe	Leu
	2960					2965					2970			
Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp	Phe	Ser
	2975					2980					2985			

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Arg Glu Asn Ser Leu Ser Gly Val Glu Gly Glu Gly Leu His Lys
2990 2995 3000

Leu Gly Tyr Ile Leu Arg Asp Val Ser Lys Lys Glu Gly Gly Ala
3005 3010 3015

Met Tyr Ala Asp Asp Thr Ala Gly Trp Asp Thr Arg Ile Thr Leu
3020 3025 3030

Glu Asp Leu Lys Asn Glu Glu Met Val Thr Asn His Met Glu Gly
3035 3040 3045

Glu His Lys Lys Leu Ala Glu Ala Ile Phe Lys Leu Thr Tyr Gln
3050 3055 3060

Asn Lys Val Val Arg Val Gln Arg Pro Thr Pro Arg Gly Thr Val
3065 3070 3075

Met Asp Ile Ile Ser Arg Arg Asp Gln Arg Gly Ser Gly Gln Val
3080 3085 3090

Gly Thr Tyr Gly Leu Asn Thr Phe Thr Asn Met Glu Ala Gln Leu
3095 3100 3105

Ile Arg Gln Met Glu Gly Glu Gly Val Phe Lys Ser Ile Gln His
3110 3115 3120

Leu Thr Ile Thr Glu Glu Ile Ala Val Gln Asn Trp Leu Ala Arg
3125 3130 3135

Val Gly Arg Glu Arg Leu Ser Arg Met Ala Ile Ser Gly Asp Asp
3140 3145 3150

Cys Val Val Lys Pro Leu Asp Asp Arg Phe Ala Ser Ala Leu Thr
3155 3160 3165

Ala Leu Asn Asp Met Gly Lys Ile Arg Lys Asp Ile Gln Gln Trp
3170 3175 3180

Glu Pro Ser Arg Gly Trp Asn Asp Trp Thr Gln Val Pro Phe Cys
3185 3190 3195

Ser His His Phe His Glu Leu Ile Met Lys Asp Gly Arg Val Leu
3200 3205 3210

Val Val Pro Cys Arg Asn Gln Asp Glu Leu Ile Gly Arg Ala Arg
3215 3220 3225

Ile Ser Gln Gly Ala Gly Trp Ser Leu Arg Glu Thr Ala Cys Leu
3230 3235 3240

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 Gly Lys Ser Tyr Ala Gln Met Trp Ser Leu Met Tyr Phe His Arg
 3245 3250 3255

Arg Asp Leu Arg Leu Ala Ala Asn Ala Ile Cys Ser Ala Val Pro
 3260 3265 3270

Ser His Trp Val Pro Thr Ser Arg Thr Thr Trp Ser Ile His Ala
 3275 3280 3285

Lys His Glu Trp Met Thr Thr Glu Asp Met Leu Thr Val Trp Asn
 3290 3295 3300

Arg Val Trp Ile Gln Glu Asn Pro Trp Met Glu Asp Lys Thr Pro
 3305 3310 3315

Val Glu Ser Trp Glu Glu Ile Pro Tyr Leu Gly Lys Arg Glu Asp
 3320 3325 3330

Gln Trp Cys Gly Ser Leu Ile Gly Leu Thr Ser Arg Ala Thr Trp
 3335 3340 3345

Ala Lys Asn Ile Gln Ala Ala Ile Asn Gln Val Arg Ser Leu Ile
 3350 3355 3360

Gly Asn Glu Glu Tyr Thr Asp Tyr Met Pro Ser Met Lys Arg Phe
 3365 3370 3375

Arg Arg Glu Glu Glu Glu Ala Gly Val Leu Trp
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 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Dengue virus serotype 3, BVS

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 gttctaacag ttttttaatt agagagcaga tctctgatga ataaccaacg gaaaaaggcg 120
 aaaaacacgc ctttcaatat gctgaaacgc gagagaaacc gcgtgtcgac tgtgcaacag 180
 ctgacaaaga gattctcact tggaatgctg cagggacgag gaccattaaa actgttcatg 240
 gccctggtgg cgttccttcg tttcctaaca atcccaccaa cagcagggat attgaagaga 300
 tggggaacaa ttaaaaaatc aaaagctatt aatgttttga gagggttcag gaaagagatt 360
 ggaaggatgc tgaacatctt gaataggaga cgcagatctg caggcatgat cattatgctg 420
 attccaacag tgatggcggt ccatttaacc acgcgtgatg gagagccgcg catgattgtg 480
 gggaagaatg aaagaggaaa atccctactt ttcaagacag cctctggaat caacatgtgc 540
 acactcatag ctatggatct gggagagatg tgtgatgaca cggtcactta caaatgcccc 600

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cacattaccg	aagtggagcc	tgaagacatt	gactgctggt	gcaaccttac	atcgacatgg	660
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ttagctcccc	atgttggcat	gggactggac	acacgcactc	aaacctggat	gtcggctgaa	780
ggagcttggg	gacaagtcga	gaaggtagag	acatgggccc	ttaggcaccc	agggtttacc	840
atactagccc	tatttcttgc	ccattacata	ggcacttcct	tgaccagaa	agtggttatt	900
tttatactat	taatgctggt	taccccatcc	atgacaatga	gatgtgtagg	agtaggaaac	960
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gggtgtgtga	ctaccatggc	taagaacaag	cccacgtgg	acatagagct	tcagaagacc	1080
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acaaccgact	caagatgtcc	caccaaggg	gaagcgattt	tacctgagga	gcaggaccag	1200
aactacgtgt	gtaagcatc	atacgtggac	agaggctggg	gaaacggttg	tggtttgttt	1260
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caccaggtgg	gaaatgaaac	gcagggagtc	acggctgaga	taacacccca	ggcatcaacc	1440
gctgaagcca	ttttacctga	atatggaacc	ctcgggctag	aatgctcacc	acggacaggt	1500
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ccagaatccc	cttcaaaact	agcttcagct	atccagaaag	cccatgaaga	ggacatttgt	2580
ggaatccgct	cagtaacaag	actgggagaat	ctgatgtgga	aacaaataac	accagaattg	2640

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gctgaactgg	aagatggagc	ctatagaatt	aagcaaaaag	ggattcttgg	atattcccag	4620
atcggagccg	gagtttacaa	agaaggaaca	ttccatacaa	tgtggcatgt	cacacgtggc	4680

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gctgttctaa	tgcataaagg	aaagaggatt	gaaccatcat	gggcggaagt	caagaaagac	4740
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gacacgagaa	ccaagaacc	gaaagaaggc	acgaagaaac	taatgaaaat	aacagcagag	8700
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<210> 24

<211> 3389

<212> PRT

<213> Artificial Sequence

<220>

<223> Dengue virus serotype 3, BVS

<400> 24

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Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
20 25 30

Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
50 55 60

Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
65 70 75 80

Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
85 90 95

Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
100 105 110

Met Ala Phe His Leu Thr Thr Arg Asp Gly Glu Pro Arg Met Ile Val
115 120 125

Gly Lys Asn Glu Arg Gly Lys Ser Leu Leu Phe Lys Thr Ala Ser Gly
130 135 140

Ile Asn Met Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Met Cys Asp
145 150 155 160

Asp Thr Val Thr Tyr Lys Cys Pro His Ile Thr Glu Val Glu Pro Glu
165 170 175

Asp Ile Asp Cys Trp Cys Asn Leu Thr Ser Thr Trp Val Thr Tyr Gly
180 185 190

Thr Cys Asn Gln Ala Gly Glu His Arg Arg Asp Lys Arg Ser Val Ala
195 200 205

Leu Ala Pro His Val Gly Met Gly Leu Asp Thr Arg Thr Gln Thr Trp
210 215 220

Met Ser Ala Glu Gly Ala Trp Arg Gln Val Glu Lys Val Glu Thr Trp
225 230 235 240

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Ala Leu Arg His Pro Gly Phe Thr Ile Leu Ala Leu Phe Leu Ala His
245 250 255

Tyr Ile Gly Thr Ser Leu Thr Gln Lys Val Val Ile Phe Ile Leu Leu
260 265 270

Met Leu Val Thr Pro Ser Met Thr Met Arg Cys Val Gly Val Gly Asn
275 280 285

Arg Asp Phe Val Glu Gly Leu Ser Gly Ala Thr Trp Val Asp Val Val
290 295 300

Leu Glu His Gly Gly Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
305 310 315 320

Leu Asp Ile Glu Leu Gln Lys Thr Glu Ala Thr Gln Leu Ala Thr Leu
325 330 335

Arg Lys Leu Cys Ile Glu Gly Lys Ile Thr Asn Ile Thr Thr Asp Ser
340 345 350

Arg Cys Pro Thr Gln Gly Glu Ala Ile Leu Pro Glu Glu Gln Asp Gln
355 360 365

Asn Tyr Val Cys Lys His Thr Tyr Val Asp Arg Gly Trp Gly Asn Gly
370 375 380

Cys Gly Leu Phe Gly Lys Gly Ser Leu Val Thr Cys Ala Lys Phe Gln
385 390 395 400

Cys Leu Glu Ser Ile Glu Gly Lys Val Val Gln His Glu Asn Leu Lys
405 410 415

Tyr Thr Val Ile Ile Thr Val His Thr Gly Asp Gln His Gln Val Gly
420 425 430

Asn Glu Thr Gln Gly Val Thr Ala Glu Ile Thr Pro Gln Ala Ser Thr
435 440 445

Ala Glu Ala Ile Leu Pro Glu Tyr Gly Thr Leu Gly Leu Glu Cys Ser
450 455 460

Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Ile Ser Leu Thr Met Lys
465 470 475 480

Asn Lys Ala Trp Met Val His Arg Gln Trp Phe Phe Asp Leu Pro Leu
485 490 495

Pro Trp Thr Ser Gly Ala Ser Ala Glu Thr Pro Thr Trp Asn Arg Lys
500 505 510

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Glu Leu Leu Val Thr Phe Lys Asn Ala His Ala Lys Lys Gln Glu Val
 515 520 525
 Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu Thr Gly
 530 535 540
 Ala Thr Glu Ile Gln Thr Ser Gly Gly Thr Ser Ile Phe Ala Gly His
 545 550 555 560
 Leu Lys Cys Arg Leu Lys Met Asp Lys Leu Glu Leu Lys Gly Met Ser
 565 570 575
 Tyr Ala Met Cys Leu Ser Ser Phe Val Leu Lys Lys Glu Val Ser Glu
 580 585 590
 Thr Gln His Gly Thr Ile Leu Ile Lys Val Glu Tyr Lys Gly Glu Asp
 595 600 605
 Ala Pro Cys Lys Ile Pro Phe Ser Thr Glu Asp Gly Gln Gly Lys Ala
 610 615 620
 Leu Asn Gly Arg Leu Ile Thr Ala Asn Pro Val Val Thr Lys Lys Glu
 625 630 635 640
 Glu Pro Val Asn Ile Glu Ala Glu Pro Pro Phe Gly Glu Ser Asn Ile
 645 650 655
 Val Ile Gly Ile Gly Asp Lys Ala Leu Lys Ile Asn Trp Tyr Lys Lys
 660 665 670
 Gly Ser Ser Ile Gly Lys Met Phe Glu Ala Thr Ala Arg Gly Ala Arg
 675 680 685
 Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser Val Gly
 690 695 700
 Gly Val Leu Asn Ser Leu Gly Lys Met Val His Gln Ile Phe Gly Ser
 705 710 715 720
 Ala Tyr Thr Ala Leu Phe Gly Gly Val Ser Trp Met Met Lys Ile Gly
 725 730 735
 Ile Gly Val Leu Leu Thr Trp Ile Gly Leu Asn Ser Lys Asn Thr Ser
 740 745 750
 Met Ser Phe Ser Cys Ile Ala Ala Gly Ile Val Thr Leu Tyr Leu Gly
 755 760 765
 Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys Asn Lys
 770 775 780

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Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val His Thr
 785 790 795 800
 Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys Leu Ala
 805 810 815
 Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile Arg Ser
 820 825 830
 Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro Glu Leu
 835 840 845
 Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met Thr Gly
 850 855 860
 Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg Pro Gln
 865 870 875 880
 Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala Lys Met
 885 890 895
 Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly Pro Glu
 900 905 910
 Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu Glu Val
 915 920 925
 Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu Lys Leu
 930 935 940
 Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser Ala Ala
 945 950 955 960
 Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp Ile Glu
 965 970 975
 Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe Ile Glu
 980 985 990
 Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser Asn Gly
 995 1000 1005
 Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala Gly Pro
 1010 1015 1020
 Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln Ile Thr
 1025 1030 1035
 Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp Phe Cys
 1040 1045 1050

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Pro	Ser 1070	Leu	Arg	Thr	Thr	Thr 1075	Ala	Ser	Gly	Lys	Leu 1080	Ile	Thr	Glu
Trp	Cys 1085	Cys	Arg	Ser	Cys	Thr 1090	Leu	Pro	Pro	Leu	Arg 1095	Tyr	Arg	Gly
Glu	Asp 1100	Gly	Cys	Trp	Tyr	Gly 1105	Met	Glu	Ile	Arg	Pro 1110	Leu	Lys	Glu
Lys	Glu 1115	Glu	Asn	Leu	Val	Asn 1120	Ser	Leu	Val	Thr	Ala 1125	Gly	His	Gly
Gln	Val 1130	Asp	Asn	Phe	Ser	Leu 1135	Gly	Val	Leu	Gly	Met 1140	Ala	Leu	Phe
Leu	Glu 1145	Glu	Met	Leu	Arg	Thr 1150	Arg	Val	Gly	Thr	Lys 1155	His	Ala	Ile
Leu	Leu 1160	Val	Ala	Val	Ser	Phe 1165	Val	Thr	Leu	Ile	Thr 1170	Gly	Asn	Met
Ser	Phe 1175	Arg	Asp	Leu	Gly	Arg 1180	Val	Met	Val	Met	Val 1185	Gly	Ala	Thr
Met	Thr 1190	Asp	Asp	Ile	Gly	Met 1195	Gly	Val	Thr	Tyr	Leu 1200	Ala	Leu	Leu
Ala	Ala 1205	Phe	Lys	Val	Arg	Pro 1210	Thr	Phe	Ala	Ala	Gly 1215	Leu	Leu	Leu
Arg	Lys 1220	Leu	Thr	Ser	Lys	Glu 1225	Leu	Met	Met	Thr	Thr 1230	Ile	Gly	Ile
Val	Leu 1235	Leu	Ser	Gln	Ser	Thr 1240	Ile	Pro	Glu	Thr	Ile 1245	Leu	Glu	Leu
Thr	Asp 1250	Ala	Leu	Ala	Leu	Gly 1255	Met	Met	Val	Leu	Lys 1260	Met	Val	Arg
Asn	Met 1265	Glu	Lys	Tyr	Gln	Leu 1270	Ala	Val	Thr	Ile	Met 1275	Ala	Ile	Leu
Cys	Val 1280	Pro	Asn	Ala	Val	Ile 1285	Leu	Gln	Asn	Ala	Trp 1290	Lys	Val	Ser
Cys	Thr 1295	Ile	Leu	Ala	Val	Val 1300	Ser	Val	Ser	Pro	Leu 1305	Phe	Leu	Thr

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Lys	Gly 1325	Leu	Asn	Pro	Thr	Ala 1330	Ile	Phe	Leu	Thr	Thr 1335	Leu	Ser	Arg
Thr	Ser 1340	Lys	Lys	Arg	Ser	Trp 1345	Pro	Leu	Asn	Glu	Ala 1350	Ile	Met	Ala
Val	Gly 1355	Met	Val	Ser	Ile	Leu 1360	Ala	Ser	Ser	Leu	Leu 1365	Lys	Asn	Asp
Ile	Pro 1370	Met	Thr	Gly	Pro	Leu 1375	Val	Ala	Gly	Gly	Leu 1380	Leu	Thr	Val
Cys	Tyr 1385	Val	Leu	Thr	Gly	Arg 1390	Ser	Ala	Asp	Leu	Glu 1395	Leu	Glu	Arg
Ala	Ala 1400	Asp	Val	Lys	Trp	Glu 1405	Asp	Gln	Ala	Glu	Ile 1410	Ser	Gly	Ser
Ser	Pro 1415	Ile	Leu	Ser	Ile	Thr 1420	Ile	Ser	Glu	Asp	Gly 1425	Ser	Met	Ser
Ile	Lys 1430	Asn	Glu	Glu	Glu	Glu 1435	Gln	Thr	Leu	Thr	Ile 1440	Leu	Ile	Arg
Thr	Gly 1445	Leu	Leu	Val	Ile	Ser 1450	Gly	Leu	Phe	Pro	Val 1455	Ser	Ile	Pro
Ile	Thr 1460	Ala	Ala	Ala	Trp	Tyr 1465	Leu	Trp	Glu	Val	Lys 1470	Lys	Gln	Arg
Ala	Gly 1475	Val	Leu	Trp	Asp	Val 1480	Pro	Ser	Pro	Pro	Pro 1485	Met	Gly	Lys
Ala	Glu 1490	Leu	Glu	Asp	Gly	Ala 1495	Tyr	Arg	Ile	Lys	Gln 1500	Lys	Gly	Ile
Leu	Gly 1505	Tyr	Ser	Gln	Ile	Gly 1510	Ala	Gly	Val	Tyr	Lys 1515	Glu	Gly	Thr
Phe	His 1520	Thr	Met	Trp	His	Val 1525	Thr	Arg	Gly	Ala	Val 1530	Leu	Met	His
Lys	Gly 1535	Lys	Arg	Ile	Glu	Pro 1540	Ser	Trp	Ala	Asp	Val 1545	Lys	Lys	Asp
Leu	Ile 1550	Ser	Tyr	Gly	Gly	Gly 1555	Trp	Lys	Leu	Glu	Gly 1560	Glu	Trp	Lys

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	1580					1585					1590			
Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly	Thr	Ser
	1595					1600					1605			
Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly	Leu	Tyr
	1610					1615					1620			
Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser	Ala	Ile
	1625					1630					1635			
Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile	Glu	Asp
	1640					1645					1650			
Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu	His	Pro
	1655					1660					1665			
Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val	Arg	Glu
	1670					1675					1680			
Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro	Thr	Arg
	1685					1690					1695			
Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu	Pro	Ile
	1700					1705					1710			
Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly	Arg	Glu
	1715					1720					1725			
Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg	Leu	Leu
	1730					1735					1740			
Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met	Asp	Glu
	1745					1750					1755			
Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly	Tyr	Ile
	1760					1765					1770			
Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe	Met	Thr
	1775					1780					1785			
Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser	Asn	Ala
	1790					1795					1800			
Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser	Trp	Asn
	1805					1810					1815			

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Ser	Gly 1820	His	Glu	Trp	Val	Thr 1825	Asp	Phe	Lys	Gly	Lys 1830	Thr	Val	Trp
Phe	Val 1835	Pro	Ser	Ile	Lys	Ala 1840	Gly	Asn	Asp	Ile	Ala 1845	Ala	Cys	Leu
Arg	Lys 1850	Asn	Gly	Lys	Lys	Val 1855	Ile	Gln	Leu	Ser	Arg 1860	Lys	Thr	Phe
Asp	Ser 1865	Glu	Tyr	Val	Lys	Thr 1870	Arg	Thr	Asn	Asp	Trp 1875	Asp	Phe	Val
Val	Thr 1880	Thr	Asp	Ile	Ser	Glu 1885	Met	Gly	Ala	Asn	Phe 1890	Lys	Ala	Glu
Arg	Val 1895	Ile	Asp	Pro	Arg	Arg 1900	Cys	Met	Lys	Pro	Val 1905	Ile	Leu	Thr
Asp	Gly 1910	Glu	Glu	Arg	Val	Ile 1915	Leu	Ala	Gly	Pro	Met 1920	Pro	Val	Thr
His	Ser 1925	Ser	Ala	Ala	Gln	Arg 1930	Arg	Gly	Arg	Ile	Gly 1935	Arg	Asn	Pro
Lys	Asn 1940	Glu	Asn	Asp	Gln	Tyr 1945	Ile	Tyr	Met	Gly	Glu 1950	Pro	Leu	Glu
Asn	Asp 1955	Glu	Asp	Cys	Ala	His 1960	Trp	Lys	Glu	Ala	Lys 1965	Met	Leu	Leu
Asp	Asn 1970	Ile	Asn	Thr	Pro	Glu 1975	Gly	Ile	Ile	Pro	Ser 1980	Met	Phe	Glu
Pro	Glu 1985	Arg	Glu	Lys	Val	Asp 1990	Ala	Ile	Asp	Gly	Glu 1995	Tyr	Arg	Leu
Arg	Gly 2000	Glu	Ala	Arg	Lys	Thr 2005	Phe	Val	Asp	Leu	Met 2010	Arg	Arg	Gly
Asp	Leu 2015	Pro	Val	Trp	Leu	Ala 2020	Tyr	Arg	Val	Ala	Ala 2025	Glu	Gly	Ile
Asn	Tyr 2030	Ala	Asp	Arg	Arg	Trp 2035	Cys	Phe	Asp	Gly	Val 2040	Lys	Asn	Asn
Gln	Ile 2045	Leu	Glu	Glu	Asn	Val 2050	Glu	Val	Glu	Ile	Trp 2055	Thr	Lys	Glu
Gly	Glu 2060	Arg	Lys	Lys	Leu	Lys 2065	Pro	Arg	Trp	Leu	Asp 2070	Ala	Arg	Ile

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Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe	Ala	Ala
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Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met	Gly	Arg
	2090					2095					2100			
Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Ala	Arg	Asn	Ala	Leu	Asp	Asn
	2105					2110					2115			
Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Ala	Gly	Gly	Arg	Ala	Tyr	Asn
	2120					2125					2130			
His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu	Leu	Leu
	2135					2140					2145			
Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu	Phe	Leu
	2150					2155					2160			
Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met	Cys	Cys
	2165					2170					2175			
Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile	Gln	Pro
	2180					2185					2190			
His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu	Ile	Val
	2195					2200					2205			
Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln	Asp	Asn
	2210					2215					2220			
Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val	Ala	Ala
	2225					2230					2235			
Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys	Lys	Asp
	2240					2245					2250			
Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser	Asn	Ile
	2255					2260					2265			
Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu	Tyr	Ala
	2270					2275					2280			
Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser	Ile	Glu
	2285					2290					2295			
Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn	Gln	Ala
	2300					2305					2310			
Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser	Lys	Met
	2315					2320					2325			

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Asp	Ile 2330	Gly	Val	Pro	Leu	Leu 2335	Ala	Ile	Gly	Cys	Tyr 2340	Ser	Gln	Val
Asn	Pro 2345	Ile	Thr	Leu	Thr	Ala 2350	Ala	Leu	Phe	Leu	Leu 2355	Val	Ala	His
Tyr	Ala 2360	Ile	Ile	Gly	Pro	Gly 2365	Leu	Gln	Ala	Lys	Ala 2370	Thr	Arg	Glu
Ala	Gln 2375	Lys	Arg	Ala	Ala	Ala 2380	Gly	Ile	Met	Lys	Asn 2385	Pro	Thr	Val
Asp	Gly 2390	Ile	Thr	Val	Ile	Asp 2395	Leu	Asp	Pro	Ile	Pro 2400	Tyr	Asp	Pro
Lys	Phe 2405	Glu	Lys	Gln	Leu	Gly 2410	Gln	Val	Met	Leu	Leu 2415	Val	Leu	Cys
Val	Thr 2420	Gln	Val	Leu	Met	Met 2425	Arg	Thr	Thr	Trp	Ala 2430	Leu	Cys	Glu
Ala	Leu 2435	Thr	Leu	Ala	Thr	Gly 2440	Pro	Ile	Ser	Thr	Leu 2445	Trp	Glu	Gly
Asn	Pro 2450	Gly	Arg	Phe	Trp	Asn 2455	Thr	Thr	Ile	Ala	Val 2460	Ser	Met	Ala
Asn	Ile 2465	Phe	Arg	Gly	Ser	Tyr 2470	Leu	Ala	Gly	Ala	Gly 2475	Leu	Leu	Phe
Ser	Ile 2480	Met	Lys	Asn	Thr	Thr 2485	Asn	Thr	Arg	Arg	Gly 2490	Thr	Gly	Asn
Ile	Gly 2495	Glu	Thr	Leu	Gly	Glu 2500	Lys	Trp	Lys	Ser	Arg 2505	Leu	Asn	Ala
Leu	Gly 2510	Lys	Ser	Glu	Phe	Gln 2515	Ile	Tyr	Lys	Lys	Ser 2520	Gly	Ile	Gln
Glu	Val 2525	Asp	Arg	Thr	Leu	Ala 2530	Lys	Glu	Gly	Ile	Lys 2535	Arg	Gly	Glu
Thr	Asp 2540	His	His	Ala	Val	Ser 2545	Arg	Gly	Ser	Ala	Lys 2550	Leu	Arg	Trp
Phe	Val 2555	Glu	Arg	Asn	Met	Val 2560	Thr	Pro	Glu	Gly	Lys 2565	Val	Val	Asp
Leu	Gly 2570	Cys	Gly	Arg	Gly	Gly 2575	Trp	Ser	Tyr	Tyr	Cys 2580	Gly	Gly	Leu

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Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly	Pro	Gly
	2585					2590					2595			
His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn	Leu	Val
	2600					2605					2610			
Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro	Glu	Lys
	2615					2620					2625			
Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro	Asn	Pro
	2630					2635					2640			
Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu	Val	Glu
	2645					2650					2655			
Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val	Leu	Asn
	2660					2665					2670			
Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu	Gln	Arg
	2675					2680					2685			
Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg	Asn	Ser
	2690					2695					2700			
Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn	Ile	Val
	2705					2710					2715			
Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg	Phe	Thr
	2720					2725					2730			
Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp	Leu	Gly
	2735					2740					2745			
Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro	Asn	Leu
	2750					2755					2760			
Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu	His	Glu
	2765					2770					2775			
Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr	Trp	Ala
	2780					2785					2790			
Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala	Ser	Ser
	2795					2800					2805			
Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp	Asp	Val
	2810					2815					2820			
Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr	Pro	Phe
	2825					2830					2835			

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Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg	Thr	Gln
	2840					2845					2850			
Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr	Ala	Glu
	2855					2860					2865			
Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg	Met	Cys
	2870					2875					2880			
Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala	Ala	Leu
	2885					2890					2895			
Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala	Arg	Glu
	2900					2905					2910			
Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys	Glu	Arg
	2915					2920					2925			
Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr	Asn	Met
	2930					2935					2940			
Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys	Ala	Lys
	2945					2950					2955			
Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg	Phe	Leu
	2960					2965					2970			
Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp	Phe	Ser
	2975					2980					2985			
Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu	His	Lys
	2990					2995					3000			
Leu	Gly	Tyr	Ile	Leu	Arg	Asp	Val	Ser	Lys	Lys	Glu	Gly	Gly	Ala
	3005					3010					3015			
Met	Tyr	Ala	Asp	Asp	Thr	Ala	Gly	Trp	Asp	Thr	Arg	Ile	Thr	Leu
	3020					3025					3030			
Glu	Asp	Leu	Lys	Asn	Glu	Glu	Met	Val	Thr	Asn	His	Met	Glu	Gly
	3035					3040					3045			
Glu	His	Lys	Lys	Leu	Ala	Glu	Ala	Ile	Phe	Lys	Leu	Thr	Tyr	Gln
	3050					3055					3060			
Asn	Lys	Val	Val	Arg	Val	Gln	Arg	Pro	Thr	Pro	Arg	Gly	Thr	Val
	3065					3070					3075			
Met	Asp	Ile	Ile	Ser	Arg	Arg	Asp	Gln	Arg	Gly	Ser	Gly	Gln	Val
	3080					3085					3090			

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Gly	Thr	Tyr	Gly	Leu	Asn	Thr	Phe	Thr	Asn	Met	Glu	Ala	Gln	Leu
	3095					3100					3105			
Ile	Arg	Gln	Met	Glu	Gly	Glu	Gly	Val	Phe	Lys	Ser	Ile	Gln	His
	3110					3115					3120			
Leu	Thr	Ile	Thr	Glu	Glu	Ile	Ala	Val	Gln	Asn	Trp	Leu	Ala	Arg
	3125					3130					3135			
Val	Gly	Arg	Glu	Arg	Leu	Ser	Arg	Met	Ala	Ile	Ser	Gly	Asp	Asp
	3140					3145					3150			
Cys	Val	Val	Lys	Pro	Leu	Asp	Asp	Arg	Phe	Ala	Ser	Ala	Leu	Thr
	3155					3160					3165			
Ala	Leu	Asn	Asp	Met	Gly	Lys	Ile	Arg	Lys	Asp	Ile	Gln	Gln	Trp
	3170					3175					3180			
Glu	Pro	Ser	Arg	Gly	Trp	Asn	Asp	Trp	Thr	Gln	Val	Pro	Phe	Cys
	3185					3190					3195			
Ser	His	His	Phe	His	Glu	Leu	Ile	Met	Lys	Asp	Gly	Arg	Val	Leu
	3200					3205					3210			
Val	Val	Pro	Cys	Arg	Asn	Gln	Asp	Glu	Leu	Ile	Gly	Arg	Ala	Arg
	3215					3220					3225			
Ile	Ser	Gln	Gly	Ala	Gly	Trp	Ser	Leu	Arg	Glu	Thr	Ala	Cys	Leu
	3230					3235					3240			
Gly	Lys	Ser	Tyr	Ala	Gln	Met	Trp	Ser	Leu	Met	Tyr	Phe	His	Arg
	3245					3250					3255			
Arg	Asp	Leu	Arg	Leu	Ala	Ala	Asn	Ala	Ile	Cys	Ser	Ala	Val	Pro
	3260					3265					3270			
Ser	His	Trp	Val	Pro	Thr	Ser	Arg	Thr	Thr	Trp	Ser	Ile	His	Ala
	3275					3280					3285			
Lys	His	Glu	Trp	Met	Thr	Thr	Glu	Asp	Met	Leu	Thr	Val	Trp	Asn
	3290					3295					3300			
Arg	Val	Trp	Ile	Gln	Glu	Asn	Pro	Trp	Met	Glu	Asp	Lys	Thr	Pro
	3305					3310					3315			
Val	Glu	Ser	Trp	Glu	Glu	Ile	Pro	Tyr	Leu	Gly	Lys	Arg	Glu	Asp
	3320					3325					3330			
Gln	Trp	Cys	Gly	Ser	Leu	Ile	Gly	Leu	Thr	Ser	Arg	Ala	Thr	Trp
	3335					3340					3345			

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Ala Lys Asn Ile Gln Ala Ala Ile Asn Gln Val Arg Ser Leu Ile
 3350 3355 3360

Gly Asn Glu Glu Tyr Thr Asp Tyr Met Pro Ser Met Lys Arg Phe
 3365 3370 3375

Arg Arg Glu Glu Glu Glu Ala Gly Val Leu Trp
 3380 3385

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 <211> 10723
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Dengue virus serotype 4, Pre-Master

<400> 25
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 gttctaacag tttttaatt agagagcaga tctctgatga ataaccaacg gaaaaaggcg 120
 aaaaacacgc ctttcaatat gctgaaacgc gagagaaacc gcgtgtcgac tgtgcaacag 180
 ctgacaaaga gattctcact tggaatgctg cagggacgag gacctttaa actgttcatg 240
 gccctggtgg cgttccttcg tttcctaaca atcccaccaa cagcagggat attgaagaga 300
 tggggaacaa ttaaaaaatc aaaagctatt aatgttttga gaggggttcag gaaagagatt 360
 ggaaggatgc tgaacatctt gaataggaga cgcagctctg caggcatgat cattatgctg 420
 attccaacag tgatggcggt ccatttaacc acgcgtgatg gcgaaccct catgatagtg 480
 gcaaaacatg aaagggggag acctctcttg tttaagacaa cagaggggat caacaaatgc 540
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 ttactggtca ataccgaacc tgaagacatt gattgctggt gcaatctcac gtctacctgg 660
 gtcattgatg ggacatgcac ccagagcgga gaacggagac gagagaagcg ctcatgtatg 720
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 ggaaaaggag gagttgtgac atgtgcgaag ttttcatgtt cggggaagat aacaggcaat 1320
 ttggtccaaa ttgagaacct tgaatacaca gtggttgtaa cagtccacaa tggagacacc 1380

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tctggaattg	actttaatga	gatgattctg	atgaaaatga	aaaagaaaac	atggcttgtg	1560
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gacaaagaga	tggcagaaac	acagcatggg	acaacagtgg	tgaaagtcaa	gtatgaaggt	1920
gctggagctc	cgtgtaaagt	ccccatagag	ataagagatg	tgaacaagga	aaaagtggtt	1980
gggcgtatca	tctcatccac	ccctttggct	gagaatacca	acagtgtaac	caacatagag	2040
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 <212> PRT
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<220>
 <223> Dengue virus serotype 4, Pre-Master

<400> 26

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Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
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Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
 50 55 60

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Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
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Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
      85      90      95

Arg Arg Arg Ser Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
      100      105      110

Met Ala Phe His Leu Thr Thr Arg Asp Gly Glu Pro Leu Met Ile Val
      115      120      125

Ala Lys His Glu Arg Gly Arg Pro Leu Leu Phe Lys Thr Thr Glu Gly
      130      135      140

Ile Asn Lys Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Met Cys Glu
145      150      155      160

Asp Thr Val Thr Tyr Lys Cys Pro Leu Leu Val Asn Thr Glu Pro Glu
      165      170      175

Asp Ile Asp Cys Trp Cys Asn Leu Thr Ser Thr Trp Val Met Tyr Gly
      180      185      190

Thr Cys Thr Gln Ser Gly Glu Arg Arg Arg Glu Lys Arg Ser Val Ala
      195      200      205

Leu Thr Pro His Ser Gly Met Gly Leu Glu Thr Arg Ala Glu Thr Trp
      210      215      220

Met Ser Ser Glu Gly Ala Trp Lys His Ala Gln Arg Val Glu Ser Trp
225      230      235      240

Ile Leu Arg Asn Pro Gly Phe Ala Leu Leu Ala Gly Phe Met Ala Tyr
      245      250      255

Met Ile Gly Gln Thr Gly Ile Gln Arg Thr Val Phe Phe Val Leu Met
      260      265      270

Met Leu Val Ala Pro Ser Tyr Gly Met Arg Cys Val Gly Val Gly Asn
      275      280      285

Arg Asp Phe Val Glu Gly Val Ser Gly Gly Ala Trp Val Asp Leu Val
      290      295      300

Leu Glu His Gly Gly Cys Val Thr Thr Met Ala Gln Gly Lys Pro Thr
305      310      315      320

Leu Asp Phe Glu Leu Thr Lys Thr Thr Ala Lys Glu Val Ala Leu Leu
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Arg Thr Tyr Cys Ile Glu Ala Ser Ile Ser Asn Ile Thr Thr Ala Thr
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Arg Cys Pro Thr Gln Gly Glu Pro Tyr Leu Lys Glu Glu Gln Asp Gln
355 360 365

Gln Tyr Ile Cys Arg Arg Asp Val Val Asp Arg Gly Trp Gly Asn Gly
370 375 380

Cys Gly Leu Phe Gly Lys Gly Gly Val Val Thr Cys Ala Lys Phe Ser
385 390 395 400

Cys Ser Gly Lys Ile Thr Gly Asn Leu Val Gln Ile Glu Asn Leu Glu
405 410 415

Tyr Thr Val Val Val Thr Val His Asn Gly Asp Thr His Ala Val Gly
420 425 430

Asn Asp Thr Ser Asn His Gly Val Thr Ala Thr Ile Thr Pro Arg Ser
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Pro Ser Val Glu Val Lys Leu Pro Asp Tyr Gly Glu Leu Thr Leu Asp
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Cys Glu Pro Arg Ser Gly Ile Asp Phe Asn Glu Met Ile Leu Met Lys
465 470 475 480

Met Lys Lys Lys Thr Trp Leu Val His Lys Gln Trp Phe Leu Asp Leu
485 490 495

Pro Leu Pro Trp Thr Ala Gly Ala Asp Thr Ser Glu Val His Trp Asn
500 505 510

Tyr Lys Glu Arg Met Val Thr Phe Lys Val Pro His Ala Lys Arg Gln
515 520 525

Asp Val Thr Val Leu Gly Ser Gln Glu Gly Ala Met His Ser Ala Leu
530 535 540

Ala Gly Ala Thr Glu Val Asp Ser Gly Asp Gly Asn His Met Phe Ala
545 550 555 560

Gly His Leu Lys Cys Lys Val Arg Met Glu Lys Leu Arg Ile Lys Gly
565 570 575

Met Ser Tyr Thr Met Cys Ser Gly Lys Phe Ser Ile Asp Lys Glu Met
580 585 590

Ala Glu Thr Gln His Gly Thr Thr Val Val Lys Val Lys Tyr Glu Gly
595 600 605

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Ala Gly Ala Pro Cys Lys Val Pro Ile Glu Ile Arg Asp Val Asn Lys
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Glu Lys Val Val Gly Arg Ile Ile Ser Ser Thr Pro Leu Ala Glu Asn
625 630 635

Thr Asn Ser Val Thr Asn Ile Glu Leu Glu Pro Pro Phe Gly Asp Ser
645 650 655

Tyr Ile Val Ile Gly Val Gly Asn Ser Ala Leu Thr Leu His Trp Phe
660 665 670

Arg Lys Gly Ser Ser Ile Gly Lys Met Phe Glu Ser Thr Tyr Arg Gly
675 680 685

Ala Lys Arg Met Ala Ile Leu Gly Glu Thr Ala Trp Asp Phe Gly Ser
690 695 700

Val Gly Gly Leu Phe Thr Ser Leu Gly Lys Ala Val His Gln Val Phe
705 710 715 720

Gly Ser Val Tyr Thr Thr Leu Phe Gly Gly Val Ser Trp Met Ile Arg
725 730 735

Ile Leu Ile Gly Phe Leu Val Leu Trp Ile Gly Thr Asn Ser Arg Asn
740 745 750

Thr Ser Met Ala Met Thr Cys Ile Ala Ala Gly Ile Val Thr Leu Tyr
755 760 765

Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
770 775 780

Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
785 790 795 800

His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
805 810 815

Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
820 825 830

Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
835 840 845

Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
850 855 860

Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
865 870 875 880

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Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
885 890 895

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900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
945 950 955 960

Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
965 970 975

Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
980 985 990

Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
1010 1015 1020

Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
1025 1030 1035

Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
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Phe Cys Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn
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Arg Gly Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile
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Thr Glu Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr
1085 1090 1095

Arg Gly Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu
1100 1105 1110

Lys Glu Lys Glu Glu Asn Leu Val Asn Ser Leu Val Thr Ala Gly
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His Gly Gln Val Asp Asn Phe Ser Leu Gly Val Leu Gly Met Ala
1130 1135 1140

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Asn Met 1175	Ser Phe Arg Asp 1180	Gly Arg Val Met 1185	Val Met Val Gly
Ala Thr 1190	Met Thr Gly Asp 1195	Gly Met Gly Val 1200	Thr Tyr Leu Ala
Leu Leu 1205	Ala Ala Phe Lys 1210	Arg Pro Thr Phe 1215	Ala Ala Gly Leu
Leu Leu 1220	Arg Lys Leu Thr 1225	Lys Glu Leu Met 1230	Met Thr Thr Ile
Gly Ile 1235	Val Leu Leu Ser 1240	Ser Thr Ile Pro 1245	Glu Thr Ile Leu
Glu Leu 1250	Thr Asp Ala Leu 1255	Leu Gly Met Met 1260	Val Leu Lys Met
Val Arg 1265	Asn Met Glu Lys 1270	Gln Leu Ala Val 1275	Thr Ile Met Ala
Ile Leu 1280	Cys Val Pro Asn 1285	Val Ile Leu Gln 1290	Asn Ala Trp Lys
Val Ser 1295	Cys Thr Ile Leu 1300	Val Val Ser Val 1305	Ser Pro Leu Phe
Leu Thr 1310	Ser Ser Gln Gln 1315	Lys Thr Asp Trp Ile 1320	Pro Leu Ala Leu
Thr Ile 1325	Lys Gly Leu Asn 1330	Pro Thr Ala Ile Phe 1335	Leu Thr Thr Leu
Ser Arg 1340	Thr Ser Lys Lys 1345	Arg Ser Trp Pro Leu 1350	Asn Glu Ala Ile
Met Ala 1355	Val Gly Met Val 1360	Ser Ile Leu Ala Ser 1365	Ser Leu Leu Lys
Asn Asp 1370	Ile Pro Met Thr 1375	Gly Pro Leu Val Ala 1380	Gly Gly Leu Leu
Thr Val 1385	Cys Tyr Val Leu 1390	Thr Gly Arg Ser Ala 1395	Asp Leu Glu Leu

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1415						1420					1425			
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1430						1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
1445						1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
1460						1465					1470			
Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
1475						1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
1490						1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
1505						1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
1520						1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
1535						1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
1550						1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
1565						1570					1575			
Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
1580						1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
1595						1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
1610						1615					1620			
Leu	Tyr	Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser
1625						1630					1635			
Ala	Ile	Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile
1640						1645					1650			

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Glu	Asp	Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu
1655						1660					1665			
His	Pro	Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val
1670						1675					1680			
Arg	Glu	Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro
1685						1690					1695			
Thr	Arg	Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu
1700						1705					1710			
Pro	Ile	Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly
1715						1720					1725			
Arg	Glu	Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg
1730						1735					1740			
Leu	Leu	Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met
1745						1750					1755			
Asp	Glu	Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly
1760						1765					1770			
Tyr	Ile	Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe
1775						1780					1785			
Met	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser
1790						1795					1800			
Asn	Ala	Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser
1805						1810					1815			
Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
1820						1825					1830			
Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
1835						1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
1850						1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
1865						1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
1880						1885					1890			
Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
1895						1900					1905			

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Leu Thr 1910	Asp Gly Glu Glu Arg 1915	Val Ile Leu Ala Gly 1920	Pro Met Pro
Val Thr 1925	His Ser Ser Ala Ala 1930	Gln Arg Arg Gly Arg 1935	Ile Gly Arg
Asn Pro 1940	Lys Asn Glu Asn Asp 1945	Gln Tyr Ile Tyr Met 1950	Gly Glu Pro
Leu Glu 1955	Asn Asp Glu Asp Cys 1960	Ala His Trp Lys Glu 1965	Ala Lys Met
Leu Leu 1970	Asp Asn Ile Asn Thr 1975	Pro Glu Gly Ile Ile 1980	Pro Ser Met
Phe Glu 1985	Pro Glu Arg Glu Lys 1990	Val Asp Ala Ile Asp 1995	Gly Glu Tyr
Arg Leu 2000	Arg Gly Glu Ala Arg 2005	Lys Thr Phe Val Asp 2010	Leu Met Arg
Arg Gly 2015	Asp Leu Pro Val Trp 2020	Leu Ala Tyr Arg Val 2025	Ala Ala Glu
Gly Ile 2030	Asn Tyr Ala Asp Arg 2035	Arg Trp Cys Phe Asp 2040	Gly Val Lys
Asn Asn 2045	Gln Ile Leu Glu Glu 2050	Asn Val Glu Val Glu 2055	Ile Trp Thr
Lys Glu 2060	Gly Glu Arg Lys Lys 2065	Leu Lys Pro Arg Trp 2070	Leu Asp Ala
Arg Ile 2075	Tyr Ser Asp Pro Leu 2080	Ala Leu Lys Glu Phe 2085	Lys Glu Phe
Ala Ala 2090	Gly Arg Lys Ser Leu 2095	Thr Leu Asn Leu Ile 2100	Thr Glu Met
Gly Arg 2105	Leu Pro Thr Phe Met 2110	Thr Gln Lys Val Arg 2115	Asp Ala Leu
Asp Asn 2120	Leu Ala Val Leu His 2125	Thr Ala Glu Ala Gly 2130	Gly Arg Ala
Tyr Asn 2135	His Ala Leu Ser Glu 2140	Leu Pro Glu Thr Leu 2145	Glu Thr Leu
Leu Leu 2150	Leu Thr Leu Leu Ala 2155	Thr Val Thr Gly Gly 2160	Ile Phe Leu

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Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
2165						2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
2180						2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
2195						2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
2210						2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
2225						2230					2235			
Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
2240						2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
2255						2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
2270						2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
2285						2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
2300						2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
2315						2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
2330						2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Thr	Ala	Ala	Leu	Phe	Leu	Leu	Val
2345						2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
2360						2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
2375						2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
2390						2395					2400			
Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
2405						2410					2415			

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Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
	2420					2425					2430			
Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
	2435					2440					2445			
Glu	Gly	Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser
	2450					2455					2460			
Met	Ala	Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu
	2465					2470					2475			
Leu	Phe	Ser	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr
	2480					2485					2490			
Gly	Asn	Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu
	2495					2500					2505			
Asn	Ala	Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly
	2510					2515					2520			
Ile	Gln	Glu	Val	Asp	Arg	Thr	Leu	Ala	Lys	Glu	Gly	Ile	Lys	Arg
	2525					2530					2535			
Gly	Glu	Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu
	2540					2545					2550			
Arg	Trp	Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val
	2555					2560					2565			
Val	Asp	Leu	Gly	Cys	Gly	Arg	Gly	Gly	Trp	Ser	Tyr	Tyr	Cys	Gly
	2570					2575					2580			
Gly	Leu	Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly
	2585					2590					2595			
Pro	Gly	His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn
	2600					2605					2610			
Leu	Val	Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro
	2615					2620					2625			
Glu	Lys	Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro
	2630					2635					2640			
Asn	Pro	Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu
	2645					2650					2655			
Val	Glu	Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val
	2660					2665					2670			

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Leu	Asn	Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu
	2675					2680					2685			
Gln	Arg	Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg
	2690					2695					2700			
Asn	Ser	Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn
	2705					2710					2715			
Ile	Val	Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg
	2720					2725					2730			
Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
	2735					2740					2745			
Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
	2750					2755					2760			
Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
	2765					2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
	2780					2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
	2795					2800					2805			
Ser	Ser	Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp
	2810					2815					2820			
Asp	Val	Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr
	2825					2830					2835			
Pro	Phe	Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg
	2840					2845					2850			
Thr	Gln	Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr
	2855					2860					2865			
Ala	Glu	Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg
	2870					2875					2880			
Met	Cys	Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala
	2885					2890					2895			
Ala	Leu	Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
	2900					2905					2910			
Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
	2915					2920					2925			

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Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
2930						2935					2940			
Asn	Met	Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys
2945						2950					2955			
Ala	Lys	Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg
2960						2965					2970			
Phe	Leu	Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp
2975						2980					2985			
Phe	Ser	Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu
2990						2995					3000			
His	Lys	Leu	Gly	Tyr	Ile	Leu	Arg	Asp	Val	Ser	Lys	Lys	Glu	Gly
3005						3010					3015			
Gly	Ala	Met	Tyr	Ala	Asp	Asp	Thr	Ala	Gly	Trp	Asp	Thr	Arg	Ile
3020						3025					3030			
Thr	Leu	Glu	Asp	Leu	Lys	Asn	Glu	Glu	Met	Val	Thr	Asn	His	Met
3035						3040					3045			
Glu	Gly	Glu	His	Lys	Lys	Leu	Ala	Glu	Ala	Ile	Phe	Lys	Leu	Thr
3050						3055					3060			
Tyr	Gln	Asn	Lys	Val	Val	Arg	Val	Gln	Arg	Pro	Thr	Pro	Arg	Gly
3065						3070					3075			
Thr	Val	Met	Asp	Ile	Ile	Ser	Arg	Arg	Asp	Gln	Arg	Gly	Ser	Gly
3080						3085					3090			
Gln	Val	Gly	Thr	Tyr	Gly	Leu	Asn	Thr	Phe	Thr	Asn	Met	Glu	Ala
3095						3100					3105			
Gln	Leu	Ile	Arg	Gln	Met	Glu	Gly	Glu	Gly	Val	Phe	Lys	Ser	Ile
3110						3115					3120			
Gln	His	Leu	Thr	Ile	Thr	Glu	Glu	Ile	Ala	Val	Gln	Asn	Trp	Leu
3125						3130					3135			
Ala	Arg	Val	Gly	Arg	Glu	Arg	Leu	Ser	Arg	Met	Ala	Ile	Ser	Gly
3140						3145					3150			
Asp	Asp	Cys	Val	Val	Lys	Pro	Leu	Asp	Asp	Arg	Phe	Ala	Ser	Ala
3155						3160					3165			
Leu	Thr	Ala	Leu	Asn	Asp	Met	Gly	Lys	Ile	Arg	Lys	Asp	Ile	Gln
3170						3175					3180			

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Gln Trp 3185 Glu Pro Ser Arg Gly 3190 Trp Asn Asp Trp Thr 3195 Gln Val Pro

Phe Cys 3200 Ser His His Phe His 3205 Glu Leu Ile Met Lys 3210 Asp Gly Arg

Val Leu 3215 Val Val Pro Cys Arg 3220 Asn Gln Asp Glu Leu 3225 Ile Gly Arg

Ala Arg 3230 Ile Ser Gln Gly Ala 3235 Gly Trp Ser Leu Arg 3240 Glu Thr Ala

Cys Leu 3245 Gly Lys Ser Tyr Ala 3250 Gln Met Trp Ser Leu 3255 Met Tyr Phe

His Arg 3260 Arg Asp Leu Arg Leu 3265 Ala Ala Asn Ala Ile 3270 Cys Ser Ala

Val Pro 3275 Ser His Trp Val Pro 3280 Thr Ser Arg Thr Thr 3285 Trp Ser Ile

His Ala 3290 Lys His Glu Trp Met 3295 Thr Thr Glu Asp Met 3300 Leu Thr Val

Trp Asn 3305 Arg Val Trp Ile Gln 3310 Glu Asn Pro Trp Met 3315 Glu Asp Lys

Thr Pro 3320 Val Glu Ser Trp Glu 3325 Glu Ile Pro Tyr Leu 3330 Gly Lys Arg

Glu Asp 3335 Gln Trp Cys Gly Ser 3340 Leu Ile Gly Leu Thr 3345 Ser Arg Ala

Thr Trp 3350 Ala Lys Asn Ile Gln 3355 Ala Ala Ile Asn Gln 3360 Val Arg Ser

Leu Ile 3365 Gly Asn Glu Glu Tyr 3370 Thr Asp Tyr Met Pro 3375 Ser Met Lys

Arg Phe 3380 Arg Arg Glu Glu Glu 3385 Glu Ala Gly Val Leu 3390 Trp

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 <211> 10723
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Dengue virus serotype 4, MVS

<220>
 <221> misc_feature
 <222> (3773)..(3773)

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 <223> n is either adenine or guanine

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aaaaacacgc ctttcaatat gctgaaacgc gagagaaacc gcgtgtcgac tgtgcaacag      180
ctgacaaaga gattctcact tggaatgctg cagggacgag gacctttaaa actgttcatg      240
gccctggtgg cgttccttcg tttcctaaca atcccaccaa cagcagggat attgaagaga      300
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gagatggact ttgatttctg tgatggaaca acagtggtag tgactgagga ctgcggaaat      3300
agaggaccct ctttgagaac aaccactgcc tctggaaaac tcataacaga atggtgctgc      3360
cgatcttgca cattaccacc gctaagatac agaggtgagg atgggtgctg gtacgggatg      3420
gaaatcagac cattgaagga gaaagaagag aatttgggtca actccttgggt cacagctgga      3480
catgggcagg tcgacaactt ttcactagga gtcttgggaa tggcattgtt cctggaggaa      3540
atgcttagga cccgagtagg aacgaaacat gcaatactac tagttgcagt ttcttttgtg      3600
acattgatca cagggaacat gtcctttaga gacctgggaa gagtgatggt tatggtaggc      3660
gccactatga cgggtgacat aggtatgggc gtgacttatc ttgccctact agcagccttc      3720
aaagtacagc caacttttgc agctggacta ctcttgagaa agctgacctc canggaattg      3780
atgatgacta ctataggaat tgtactcttc tcccagagca ccataccaga gaccattctt      3840
gagttgactg atgcgttagc cttaggcatg atggctctca aaatggtgag aaatatggaa      3900
aagtatcaat tggcagtac tatcatggct atcttgtgctg tcccaaacgc agtgatatta      3960
caaaacgcat ggaaagttag ttgcacaata ttggcagtgg tgtccgtttc cccactgttc      4020

```

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ttaacatcct	cacagcaaaa	aacagattgg	ataccattag	cattgacgat	caaaggtctc	4080
aatccaacag	ctatTTTTtct	aacaaccctc	tcaagaacca	gcaagaaaag	gagctggcca	4140
ttaaattgagg	ctatcatggc	agtcgggatg	gtgagcattt	tagccagttc	tctcctaaaa	4200
aatgatattc	ccatgacagg	accattagtg	gctggagggc	tcctcactgt	gtgctacgtg	4260
ctcactggac	gatcggccga	tttggaaactg	gagagagcag	ccgatgtcaa	atgggaagac	4320
caggcagaga	tatcaggaag	cagtccaatc	ctgtcaataa	caatatcaga	agatggtagc	4380
atgtcgataa	aaaatgaaga	ggaagaacaa	acactgacca	tactcattag	aacaggattg	4440
ctggtgatct	caggactttt	tcctgtatca	ataccaatca	cggcagcagc	atggtacctg	4500
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ggaaaggctg	aactggaaga	tggagcctat	agaattaagc	aaaaagggat	tcttgatat	4620
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cgtggcgctg	ttctaattgca	taaaggaaag	aggattgaac	catcatgggc	ggacgtcaag	4740
aaagacctaa	tatcatatgg	aggaggctgg	aagttagaag	gagaatggaa	ggaaggagaa	4800
gaagtccagg	tattggcact	ggagcctgga	aaaaatccaa	gagccgtcca	aacgaaacct	4860
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acgtcaggat	ctccaattat	cgacaaaaaa	ggaaaagttg	tgggtcttta	tggtaatggt	4980
gttggttaca	ggagtggagc	atatgtgagt	gctatagccc	agactgaaaa	aagcattgaa	5040
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gcccttagag	gacttccaat	aagataccag	accccagcca	tcagagctgt	gcacaccggg	5280
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tatgtcaaga	ctagaaccaa	tgattgggac	ttcgtggtta	caactgacat	ttcagaaatg	5760
ggtgccaat	tcaaggctga	gagggttata	gaccccagac	gctgcatgaa	accagtcata	5820
ctaacagatg	gtgaagagcg	ggtgattctg	gcaggaccta	tgccagtgac	ccactctagt	5880
gcagcacaaa	gaagaggagg	aataggaaga	aatccaaaaa	atgagaatga	ccagtacata	5940
tacatggggg	aacctctgga	aatgatgaa	gactgtgcac	actggaaaga	agctaaaatg	6000
ctcctagata	acatcaacac	gccagaagga	atcatttccta	gcatgttcga	accagagcgt	6060

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gaaaagggtg	atgccattga	tggcgaatac	cgcttgagag	gagaagcaag	gaaaaccttt	6120
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ggcatcaact	acgcagacag	aagggtggtg	tttgatggag	tcaagaacaa	ccaaatccta	6240
gaagaaaacg	tggaagttga	aatctggaca	aaagaagggg	aaaggaagaa	attgaaaccc	6300
agatggtttg	atgctaggat	ctattctgac	ccactggcgc	taaaagaatt	taaggaattt	6360
gcagccggaa	gaaagtctct	gaccctgaac	ctaatacag	aaatgggtag	gctcccaacc	6420
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acaagaaggg	gaactggcaa	cataggagag	acgcttgag	agaaatggaa	aagccgattg	7620
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acatatgggt	ggaatctagt	gcgtcttcaa	agtggagttg	acgttttctt	catcccgcca	7980
gaaaagtgtg	acacattatt	gtgtgacata	ggggagtcac	caccaaattc	cacagtggaa	8040
gcaggacgaa	cactcagagt	ccttaactta	gtagaaaatt	ggttgaacaa	caacactcaa	8100

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atgttgatca	acagatttac	aatgagatac	aagaaagcca	cttacgagcc	ggatgttgac	8340
ctcgggaagcg	gaacccgtaa	catcgggatt	gaaagtgaga	taccaaacct	agatataatt	8400
gggaaaagaa	tagaaaaaat	aaagcaagag	catgaaacat	catggcacta	tgaccaagac	8460
caccataca	aaacgtgggc	ataccatggg	agctatgaaa	caaaacagac	tggatcagca	8520
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gcagagtggc	tttggaagaa	attaggggaag	aaaaagacac	ccaggatgtg	caccagagaa	8760
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catgctaaac	atgaatggat	gacaacggaa	gacatgctga	cagtctggaa	cagggtgtgg	10020
attcaagaaa	acccatggat	ggaagacaaa	actccagtgg	aatcatggga	ggaaatccca	10080
tacttggggga	aaagagaaga	ccaatgggtgc	ggctcattga	ttgggttaac	aagcaggggcc	10140

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```
acctgggcaa agaacatcca agcagcaata aatcaagtta gatcccttat aggcaatgaa      10200
gaatacacag attacatgcc atccatgaaa agattcagaa gagaagagga agaagcagga      10260
gttctgtggt agaaagcaaa actaacatga aacaaggcta gaagtcaggt cggattaagc      10320
catagtacgg aaaaaactat gctacctgtg agccccgtcc aaggacgtta aaagaagtca      10380
ggccatcata aatgccatag cttgagtaaa ctatgcagcc tgtagctcca cctgagaagg      10440
tgtaaaaaat ccgggaggcc acaaaccatg gaagctgtac gcatggcgta gtggactagc      10500
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catattgacg ctgggaaaga ccagagatcc tgctgtctcc tcagcatcat tccaggcaca      10680
gaacgccaga aaatggaatg gtgctgttga atcaacaggt tct                        10723
```

```
<210> 28
<211> 3391
<212> PRT
<213> Artificial Sequence
```

```
<220>
<223> Dengue virus serotype 4, MVS
```

```
<220>
<221> misc_feature
<222> (1226)..(1226)
<223> Xaa is either lysine or arginine
```

```
<400> 28
```

```
Met Asn Asn Gln Arg Lys Lys Ala Lys Asn Thr Pro Phe Asn Met Leu
1          5          10          15
```

```
Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
          20          25          30
```

```
Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
          35          40          45
```

```
Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
          50          55          60
```

```
Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
65          70          75          80
```

```
Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
          85          90          95
```

```
Arg Arg Arg Ser Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
          100          105          110
```

```
Met Ala Phe His Leu Thr Thr Arg Asp Gly Glu Pro Leu Met Ile Val
          115          120          125
```

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Ala Lys His Glu Arg Gly Arg Pro Leu Leu Phe Lys Thr Thr Glu Gly
 130 135 140
 Ile Asn Lys Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Met Cys Glu
 145 150 155 160
 Asp Thr Val Thr Tyr Lys Cys Pro Leu Leu Val Asn Thr Glu Pro Glu
 165 170 175
 Asp Ile Asp Cys Trp Cys Asn Leu Thr Ser Thr Trp Val Met Tyr Gly
 180 185 190
 Thr Cys Thr Gln Ser Gly Glu Arg Arg Arg Glu Lys Arg Ser Val Ala
 195 200 205
 Leu Thr Pro His Ser Gly Met Gly Leu Glu Thr Arg Ala Glu Thr Trp
 210 215 220
 Met Ser Ser Glu Gly Ala Trp Lys His Ala Gln Arg Val Glu Ser Trp
 225 230 235 240
 Ile Leu Arg Asn Pro Gly Phe Ala Leu Leu Ala Gly Phe Met Ala Tyr
 245 250 255
 Met Ile Gly Gln Thr Gly Ile Gln Arg Thr Val Phe Phe Val Leu Met
 260 265 270
 Met Leu Val Ala Pro Ser Tyr Gly Met Arg Cys Val Gly Val Gly Asn
 275 280 285
 Arg Asp Phe Val Glu Gly Val Ser Gly Gly Ala Trp Val Asp Leu Val
 290 295 300
 Leu Glu His Gly Gly Cys Val Thr Thr Met Ala Gln Gly Lys Pro Thr
 305 310 315 320
 Leu Asp Phe Glu Leu Thr Lys Thr Thr Ala Lys Glu Val Ala Leu Leu
 325 330 335
 Arg Thr Tyr Cys Ile Glu Ala Ser Ile Ser Asn Ile Thr Thr Ala Thr
 340 345 350
 Arg Cys Pro Thr Gln Gly Glu Pro Tyr Leu Lys Glu Glu Gln Asp Gln
 355 360 365
 Gln Tyr Ile Cys Arg Arg Asp Val Val Asp Arg Gly Trp Gly Asn Gly
 370 375 380
 Cys Gly Leu Phe Gly Lys Gly Gly Val Val Thr Cys Ala Lys Phe Ser
 385 390 395 400

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Cys Ser Gly Lys Ile Thr Gly Asn Leu Val Gln Ile Glu Asn Leu Glu
405 410 415

Tyr Thr Val Val Thr Val His Asn Gly Asp Thr His Ala Val Gly
420 425 430

Asn Asp Thr Ser Asn His Gly Val Thr Ala Thr Ile Thr Pro Arg Ser
435 440 445

Pro Ser Val Glu Val Lys Leu Pro Asp Tyr Gly Glu Leu Thr Leu Asp
450 455 460

Cys Glu Pro Arg Ser Gly Ile Asp Phe Asn Glu Met Ile Leu Met Lys
465 470 475 480

Met Lys Lys Lys Thr Trp Leu Val His Lys Gln Trp Phe Leu Asp Leu
485 490 495

Pro Leu Pro Trp Thr Ala Gly Ala Asp Thr Ser Glu Val His Trp Asn
500 505 510

Tyr Lys Glu Arg Met Val Thr Phe Lys Val Pro His Ala Lys Arg Gln
515 520 525

Asp Val Thr Val Leu Gly Ser Gln Glu Gly Ala Met His Ser Ala Leu
530 535 540

Ala Gly Ala Thr Glu Val Asp Ser Gly Asp Gly Asn His Met Phe Ala
545 550 555 560

Gly His Leu Lys Cys Lys Val Arg Met Glu Lys Leu Arg Ile Lys Gly
565 570 575

Met Ser Tyr Thr Met Cys Ser Gly Lys Phe Ser Ile Asp Lys Glu Met
580 585 590

Ala Glu Thr Gln His Gly Thr Thr Val Val Lys Val Lys Tyr Glu Gly
595 600 605

Ala Gly Ala Pro Cys Lys Val Pro Ile Glu Ile Arg Asp Val Asn Lys
610 615 620

Glu Lys Val Val Gly Arg Ile Ile Ser Ser Thr Pro Leu Ala Glu Asn
625 630 635 640

Thr Asn Ser Val Thr Asn Ile Glu Leu Glu Pro Pro Phe Gly Asp Ser
645 650 655

Tyr Ile Val Ile Gly Val Gly Asn Ser Ala Leu Thr Leu His Trp Phe
660 665 670

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Arg Lys Gly Ser Ser Ile Gly Lys Met Phe Glu Ser Thr Tyr Arg Gly
675 680 685

Ala Lys Arg Met Ala Ile Leu Gly Glu Thr Ala Trp Asp Phe Gly Ser
690 695 700

Val Gly Gly Leu Phe Thr Ser Leu Gly Lys Ala Val His Gln Val Phe
705 710 715 720

Gly Ser Val Tyr Thr Thr Leu Phe Gly Gly Val Ser Trp Met Ile Arg
725 730 735

Ile Leu Ile Gly Phe Leu Val Leu Trp Ile Gly Thr Asn Ser Arg Asn
740 745 750

Thr Ser Met Ala Met Thr Cys Ile Ala Ala Gly Ile Val Thr Leu Tyr
755 760 765

Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
770 775 780

Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
785 790 795 800

His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
805 810 815

Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
820 825 830

Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
835 840 845

Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
850 855 860

Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
865 870 875 880

Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
885 890 895

Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
930 935 940

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Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
 945 950 955 960
 Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
 965 970 975
 Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
 980 985 990
 Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
 995 1000 1005
 Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
 1010 1015 1020
 Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
 1025 1030 1035
 Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
 1040 1045 1050
 Phe Cys Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn
 1055 1060 1065
 Arg Gly Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile
 1070 1075 1080
 Thr Glu Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr
 1085 1090 1095
 Arg Gly Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu
 1100 1105 1110
 Lys Glu Lys Glu Glu Asn Leu Val Asn Ser Leu Val Thr Ala Gly
 1115 1120 1125
 His Gly Gln Val Asp Asn Phe Ser Leu Gly Val Leu Gly Met Ala
 1130 1135 1140
 Leu Phe Leu Glu Glu Met Leu Arg Thr Arg Val Gly Thr Lys His
 1145 1150 1155
 Ala Ile Leu Leu Val Ala Val Ser Phe Val Thr Leu Ile Thr Gly
 1160 1165 1170
 Asn Met Ser Phe Arg Asp Leu Gly Arg Val Met Val Met Val Gly
 1175 1180 1185
 Ala Thr Met Thr Gly Asp Ile Gly Met Gly Val Thr Tyr Leu Ala
 1190 1195 1200

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Leu	Leu	Ala	Ala	Phe	Lys	Val	Arg	Pro	Thr	Phe	Ala	Ala	Gly	Leu
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Leu	Leu	Arg	Lys	Leu	Thr	Ser	Xaa	Glu	Leu	Met	Met	Thr	Thr	Ile
	1220					1225					1230			
Gly	Ile	Val	Leu	Leu	Ser	Gln	Ser	Thr	Ile	Pro	Glu	Thr	Ile	Leu
	1235					1240					1245			
Glu	Leu	Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met
	1250					1255					1260			
Val	Arg	Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala
	1265					1270					1275			
Ile	Leu	Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys
	1280					1285					1290			
Val	Ser	Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe
	1295					1300					1305			
Leu	Thr	Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu
	1310					1315					1320			
Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
	1325					1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
	1340					1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
	1355					1360					1365			
Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
	1370					1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
	1385					1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
	1400					1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
	1415					1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Glu	Gln	Thr	Leu	Thr	Ile	Leu
	1430					1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
	1445					1450					1455			

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Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
	1460					1465					1470			
Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
	1475					1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
	1490					1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
	1505					1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
	1520					1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
	1535					1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
	1550					1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
	1565					1570					1575			
Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
	1580					1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
	1595					1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
	1610					1615					1620			
Leu	Tyr	Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser
	1625					1630					1635			
Ala	Ile	Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile
	1640					1645					1650			
Glu	Asp	Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu
	1655					1660					1665			
His	Pro	Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val
	1670					1675					1680			
Arg	Glu	Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro
	1685					1690					1695			
Thr	Arg	val	val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu
	1700					1705					1710			

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Pro	Ile	Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly
	1715					1720					1725			
Arg	Glu	Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg
	1730					1735					1740			
Leu	Leu	Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met
	1745					1750					1755			
Asp	Glu	Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly
	1760					1765					1770			
Tyr	Ile	Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe
	1775					1780					1785			
Met	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser
	1790					1795					1800			
Asn	Ala	Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser
	1805					1810					1815			
Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
	1820					1825					1830			
Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
	1835					1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
	1850					1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
	1865					1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
	1880					1885					1890			
Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
	1895					1900					1905			
Leu	Thr	Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro
	1910					1915					1920			
Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
	1925					1930					1935			
Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
	1940					1945					1950			
Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
	1955					1960					1965			

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Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
	1970					1975					1980			
Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
	1985					1990					1995			
Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
	2000					2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
	2015					2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
	2030					2035					2040			
Asn	Asn	Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr
	2045					2050					2055			
Lys	Glu	Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala
	2060					2065					2070			
Arg	Ile	Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe
	2075					2080					2085			
Ala	Ala	Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met
	2090					2095					2100			
Gly	Arg	Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Val	Arg	Asp	Ala	Leu
	2105					2110					2115			
Asp	Asn	Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Ala	Gly	Gly	Arg	Ala
	2120					2125					2130			
Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
	2135					2140					2145			
Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
	2150					2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
	2165					2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
	2180					2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
	2195					2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
	2210					2215					2220			

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Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
	2225					2230					2235			
Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
	2240					2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
	2255					2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
	2270					2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
	2285					2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
	2300					2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
	2315					2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
	2330					2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Thr	Ala	Ala	Leu	Phe	Leu	Leu	Val
	2345					2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
	2360					2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
	2375					2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
	2390					2395					2400			
Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
	2405					2410					2415			
Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
	2420					2425					2430			
Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
	2435					2440					2445			
Glu	Gly	Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser
	2450					2455					2460			
Met	Ala	Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu
	2465					2470					2475			

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Leu	Phe 2480	Ser	Ile	Met	Lys	Asn 2485	Thr	Thr	Asn	Thr	Arg 2490	Arg	Gly	Thr
Gly	Asn 2495	Ile	Gly	Glu	Thr	Leu 2500	Gly	Glu	Lys	Trp	Lys 2505	Ser	Arg	Leu
Asn	Ala 2510	Leu	Gly	Lys	Ser	Glu 2515	Phe	Gln	Ile	Tyr	Lys 2520	Lys	Ser	Gly
Ile	Gln 2525	Glu	Val	Asp	Arg	Thr 2530	Leu	Ala	Lys	Glu	Gly 2535	Ile	Lys	Arg
Gly	Glu 2540	Thr	Asp	His	His	Ala 2545	Val	Ser	Arg	Gly	Ser 2550	Ala	Lys	Leu
Arg	Trp 2555	Phe	Val	Glu	Arg	Asn 2560	Met	Val	Thr	Pro	Glu 2565	Gly	Lys	Val
Val	Asp 2570	Leu	Gly	Cys	Gly	Arg 2575	Gly	Gly	Trp	Ser	Tyr 2580	Tyr	Cys	Gly
Gly	Leu 2585	Lys	Asn	Val	Arg	Glu 2590	Val	Lys	Gly	Leu	Thr 2595	Lys	Gly	Gly
Pro	Gly 2600	His	Glu	Glu	Pro	Ile 2605	Pro	Met	Ser	Thr	Tyr 2610	Gly	Trp	Asn
Leu	Val 2615	Arg	Leu	Gln	Ser	Gly 2620	Val	Asp	Val	Phe	Phe 2625	Ile	Pro	Pro
Glu	Lys 2630	Cys	Asp	Thr	Leu	Leu 2635	Cys	Asp	Ile	Gly	Glu 2640	Ser	Ser	Pro
Asn	Pro 2645	Thr	Val	Glu	Ala	Gly 2650	Arg	Thr	Leu	Arg	Val 2655	Leu	Asn	Leu
Val	Glu 2660	Asn	Trp	Leu	Asn	Asn 2665	Asn	Thr	Gln	Phe	Cys 2670	Ile	Lys	Val
Leu	Asn 2675	Pro	Tyr	Met	Pro	Ser 2680	Val	Ile	Glu	Lys	Met 2685	Glu	Ala	Leu
Gln	Arg 2690	Lys	Tyr	Gly	Gly	Ala 2695	Leu	Val	Arg	Asn	Pro 2700	Leu	Ser	Arg
Asn	Ser 2705	Thr	His	Glu	Met	Tyr 2710	Trp	Val	Ser	Asn	Ala 2715	Ser	Gly	Asn
Ile	Val 2720	Ser	Ser	Val	Asn	Met 2725	Ile	Ser	Arg	Met	Leu 2730	Ile	Asn	Arg

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Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
	2735					2740					2745			
Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
	2750					2755					2760			
Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
	2765					2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
	2780					2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
	2795					2800					2805			
Ser	Ser	Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp
	2810					2815					2820			
Asp	Val	Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr
	2825					2830					2835			
Pro	Phe	Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg
	2840					2845					2850			
Thr	Gln	Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr
	2855					2860					2865			
Ala	Glu	Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg
	2870					2875					2880			
Met	Cys	Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala
	2885					2890					2895			
Ala	Leu	Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
	2900					2905					2910			
Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
	2915					2920					2925			
Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
	2930					2935					2940			
Asn	Met	Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys
	2945					2950					2955			
Ala	Lys	Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg
	2960					2965					2970			
Phe	Leu	Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp
	2975					2980					2985			

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Phe	Ser 2990	Arg	Glu	Asn	Ser	Leu 2995	Ser	Gly	Val	Glu	Gly 3000	Glu	Gly	Leu
His	Lys 3005	Leu	Gly	Tyr	Ile	Leu 3010	Arg	Asp	Val	Ser	Lys 3015	Lys	Glu	Gly
Gly	Ala 3020	Met	Tyr	Ala	Asp	Asp 3025	Thr	Ala	Gly	Trp	Asp 3030	Thr	Arg	Ile
Thr	Leu 3035	Glu	Asp	Leu	Lys	Asn 3040	Glu	Glu	Met	Val	Thr 3045	Asn	His	Met
Glu	Gly 3050	Glu	His	Lys	Lys	Leu 3055	Ala	Glu	Ala	Ile	Phe 3060	Lys	Leu	Thr
Tyr	Gln 3065	Asn	Lys	Val	Val	Arg 3070	Val	Gln	Arg	Pro	Thr 3075	Pro	Arg	Gly
Thr	Val 3080	Met	Asp	Ile	Ile	Ser 3085	Arg	Arg	Asp	Gln	Arg 3090	Gly	Ser	Gly
Gln	Val 3095	Gly	Thr	Tyr	Gly	Leu 3100	Asn	Thr	Phe	Thr	Asn 3105	Met	Glu	Ala
Gln	Leu 3110	Ile	Arg	Gln	Met	Glu 3115	Gly	Glu	Gly	Val	Phe 3120	Lys	Ser	Ile
Gln	His 3125	Leu	Thr	Ile	Thr	Glu 3130	Glu	Ile	Ala	Val	Gln 3135	Asn	Trp	Leu
Ala	Arg 3140	Val	Gly	Arg	Glu	Arg 3145	Leu	Ser	Arg	Met	Ala 3150	Ile	Ser	Gly
Asp	Asp 3155	Cys	Val	Val	Lys	Pro 3160	Leu	Asp	Asp	Arg	Phe 3165	Ala	Ser	Ala
Leu	Thr 3170	Ala	Leu	Asn	Asp	Met 3175	Gly	Lys	Ile	Arg	Lys 3180	Asp	Ile	Gln
Gln	Trp 3185	Glu	Pro	Ser	Arg	Gly 3190	Trp	Asn	Asp	Trp	Thr 3195	Gln	Val	Pro
Phe	Cys 3200	Ser	His	His	Phe	His 3205	Glu	Leu	Ile	Met	Lys 3210	Asp	Gly	Arg
Val	Leu 3215	Val	Val	Pro	Cys	Arg 3220	Asn	Gln	Asp	Glu	Leu 3225	Ile	Gly	Arg
Ala	Arg 3230	Ile	Ser	Gln	Gly	Ala 3235	Gly	Trp	Ser	Leu	Arg 3240	Glu	Thr	Ala

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Cys Leu Gly Lys Ser Tyr Ala Gln Met Trp Ser Leu Met Tyr Phe
3245 3250 3255

His Arg Arg Asp Leu Arg Leu Ala Ala Asn Ala Ile Cys Ser Ala
3260 3265 3270

Val Pro Ser His Trp Val Pro Thr Ser Arg Thr Thr Trp Ser Ile
3275 3280 3285

His Ala Lys His Glu Trp Met Thr Thr Glu Asp Met Leu Thr Val
3290 3295 3300

Trp Asn Arg Val Trp Ile Gln Glu Asn Pro Trp Met Glu Asp Lys
3305 3310 3315

Thr Pro Val Glu Ser Trp Glu Glu Ile Pro Tyr Leu Gly Lys Arg
3320 3325 3330

Glu Asp Gln Trp Cys Gly Ser Leu Ile Gly Leu Thr Ser Arg Ala
3335 3340 3345

Thr Trp Ala Lys Asn Ile Gln Ala Ala Ile Asn Gln Val Arg Ser
3350 3355 3360

Leu Ile Gly Asn Glu Glu Tyr Thr Asp Tyr Met Pro Ser Met Lys
3365 3370 3375

Arg Phe Arg Arg Glu Glu Glu Glu Ala Gly Val Leu Trp
3380 3385 3390

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<211> 10723
<212> DNA
<213> Artificial Sequence

<220>
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<222> (3773)..(3773)
<223> n is either adenine or guanine

<220>
<221> misc_feature
<222> (7538)..(7538)
<223> n is either cytosine or thymine

<400> 29
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gttctaacag tttttaatt agagagcaga tctctgatga ataaccaacg gaaaaaggcg 120
aaaaacacgc ctttcaatat gctgaaacgc gagagaaacc gcgtgtcgac tgtgcaacag 180

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ctgacaaaga gattctcact tggaatgctg cagggacgag gacctttaaa actgttcatg	240
gccctggtgg cgttccttcg tttcctaaca atcccaccaa cagcagggat attgaagaga	300
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ggaaggatgc tgaacatctt gaataggaga cgcagctctg caggcatgat cattatgctg	420
attccaacag tgatggcggt ccatttaacc acgcgtgatg gcgaaccctt catgatagtg	480
gcaaaacatg aaagggggag acctctcttg tttaagacaa cagaggggat caacaaatgc	540
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ttactggtca ataccgaacc tgaagacatt gattgctggt gcaatctcac gtctacctgg	660
gtcatgtatg ggacatgcac ccagagcgga gaacggagac gagagaagcg ctcagtagct	720
ttaacaccac attcaggaat gggattggaa acaagagctg agacatggat gtcacggaa	780
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ggatgctgca caaccatggc ccagggaaaa ccaaccttgg attttgaact gactaagaca	1080
acagccaagg aagtggctct gttaagaacc tattgcattg aagcctcaat atcaaacata	1140
accacggcaa caagatgtcc aacgcaagga gagccttatc taaaagagga acaagaccaa	1200
cagtacattt gccggagaga tgtggttagac agaggggtgg gcaatggctg tggcttgttt	1260
ggaaaaggag gagttgtgac atgtgcgaag ttttcatgtt cggggaagat aacaggcaat	1320
ttggtccaaa ttgagaacct tgaatacaca gtggttgtaa cagtccacaa tggagacacc	1380
catgcagtag gaaatgacac gtccaatcat ggagttacag ccacgataac tcccagggtca	1440
ccatcgggtg aagtcaaatt gccggactat ggagaactaa cactcgattg tgaaccagg	1500
tctggaattg actttaatga gatgattctg atgaaaatga aaaagaaaac atggcttgtg	1560
cataagcaat ggttttttga tctacctcta ccatggacag caggagcaga cacatcagag	1620
gttacttggg attacaaaga gagaatggtg acatttaagg ttcctcatgc caagagacag	1680
gatgtgacag tgctgggatc tcaggaagga gccatgcatt ctgccctcgc tggagccaca	1740
gaagtggact ccggtgatgg aaatcacatg tttgcaggac atctcaagtg caaagtccgt	1800
atggagaaat tgagaatcaa gggaatgtca tacacgatgt gttcaggaaa gttctcaatt	1860
gacaaagaga tggcagaaac acagcatggg acaacagtgg tgaaagtcaa gtatgaaggt	1920
gctggagctc cgtgtaaagt ccccatagag ataagagatg tgaacaagga aaaagtgggt	1980
gggcgtatca tctcatccac ccctttggct gagaatacca acagtgtaac caacatagag	2040
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20170306 478484.168 VAC-5035-AU Replacement Sequence Listing 34 sequences.txt
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20170306 478484.168 VAC-5035-AU Replacement Sequence Listing 34 sequences.txt
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 <211> 3391
 <212> PRT
 <213> Artificial Sequence
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 <222> (1226)..(1226)
 <223> Xaa is either lysine or arginine

<220>
 <221> misc_feature
 <222> (2481)..(2481)
 <223> Xaa is either serine or phenylalanine

<400> 30

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Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
 20 25 30

Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
 50 55 60

Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
 65 70 75 80

Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
 85 90 95

Arg Arg Arg Ser Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
 100 105 110

Met Ala Phe His Leu Thr Thr Arg Asp Gly Glu Pro Leu Met Ile Val
 115 120 125

Ala Lys His Glu Arg Gly Arg Pro Leu Leu Phe Lys Thr Thr Glu Gly
 130 135 140

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Ile Asn Lys Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Met Cys Glu
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Asp Thr Val Thr Tyr Lys Cys Pro Leu Leu Val Asn Thr Glu Pro Glu
      165      170      175

Asp Ile Asp Cys Trp Cys Asn Leu Thr Ser Thr Trp Val Met Tyr Gly
      180      185      190

Thr Cys Thr Gln Ser Gly Glu Arg Arg Arg Glu Lys Arg Ser Val Ala
      195      200      205

Leu Thr Pro His Ser Gly Met Gly Leu Glu Thr Arg Ala Glu Thr Trp
      210      215      220

Met Ser Ser Glu Gly Ala Trp Lys His Ala Gln Arg Val Glu Ser Trp
225      230      235      240

Ile Leu Arg Asn Pro Gly Phe Ala Leu Leu Ala Gly Phe Met Ala Tyr
      245      250      255

Met Ile Gly Gln Thr Gly Ile Gln Arg Thr Val Phe Phe Val Leu Met
      260      265      270

Met Leu Val Ala Pro Ser Tyr Gly Met Arg Cys Val Gly Val Gly Asn
      275      280      285

Arg Asp Phe Val Glu Gly Val Ser Gly Gly Ala Trp Val Asp Leu Val
      290      295      300

Leu Glu His Gly Gly Cys Val Thr Thr Met Ala Gln Gly Lys Pro Thr
305      310      315      320

Leu Asp Phe Glu Leu Thr Lys Thr Thr Ala Lys Glu Val Ala Leu Leu
      325      330      335

Arg Thr Tyr Cys Ile Glu Ala Ser Ile Ser Asn Ile Thr Thr Ala Thr
      340      345      350

Arg Cys Pro Thr Gln Gly Glu Pro Tyr Leu Lys Glu Glu Gln Asp Gln
      355      360      365

Gln Tyr Ile Cys Arg Arg Asp Val Val Asp Arg Gly Trp Gly Asn Gly
      370      375      380

Cys Gly Leu Phe Gly Lys Gly Gly Val Val Thr Cys Ala Lys Phe Ser
385      390      395      400

Cys Ser Gly Lys Ile Thr Gly Asn Leu Val Gln Ile Glu Asn Leu Glu
      405      410      415

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Tyr Thr Val Val Thr Val His Asn Gly Asp Thr His Ala Val Gly
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 Asn Asp Thr Ser Asn His Gly Val Thr Ala Thr Ile Thr Pro Arg Ser
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 450 455 460
 Cys Glu Pro Arg Ser Gly Ile Asp Phe Asn Glu Met Ile Leu Met Lys
 465 470 475 480
 Met Lys Lys Lys Thr Trp Leu Val His Lys Gln Trp Phe Leu Asp Leu
 485 490 495
 Pro Leu Pro Trp Thr Ala Gly Ala Asp Thr Ser Glu Val His Trp Asn
 500 505 510
 Tyr Lys Glu Arg Met Val Thr Phe Lys Val Pro His Ala Lys Arg Gln
 515 520 525
 Asp Val Thr Val Leu Gly Ser Gln Glu Gly Ala Met His Ser Ala Leu
 530 535 540
 Ala Gly Ala Thr Glu Val Asp Ser Gly Asp Gly Asn His Met Phe Ala
 545 550 555 560
 Gly His Leu Lys Cys Lys Val Arg Met Glu Lys Leu Arg Ile Lys Gly
 565 570 575
 Met Ser Tyr Thr Met Cys Ser Gly Lys Phe Ser Ile Asp Lys Glu Met
 580 585 590
 Ala Glu Thr Gln His Gly Thr Thr Val Val Lys Val Lys Tyr Glu Gly
 595 600 605
 Ala Gly Ala Pro Cys Lys Val Pro Ile Glu Ile Arg Asp Val Asn Lys
 610 615 620
 Glu Lys Val Val Gly Arg Ile Ile Ser Ser Thr Pro Leu Ala Glu Asn
 625 630 635 640
 Thr Asn Ser Val Thr Asn Ile Glu Leu Glu Pro Pro Phe Gly Asp Ser
 645 650 655
 Tyr Ile Val Ile Gly Val Gly Asn Ser Ala Leu Thr Leu His Trp Phe
 660 665 670
 Arg Lys Gly Ser Ser Ile Gly Lys Met Phe Glu Ser Thr Tyr Arg Gly
 675 680 685

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Ala Lys Arg Met Ala Ile Leu Gly Glu Thr Ala Trp Asp Phe Gly Ser
690 695 700

Val Gly Gly Leu Phe Thr Ser Leu Gly Lys Ala Val His Gln Val Phe
705 710 715 720

Gly Ser Val Tyr Thr Thr Leu Phe Gly Gly Val Ser Trp Met Ile Arg
725 730 735

Ile Leu Ile Gly Phe Leu Val Leu Trp Ile Gly Thr Asn Ser Arg Asn
740 745 750

Thr Ser Met Ala Met Thr Cys Ile Ala Ala Gly Ile Val Thr Leu Tyr
755 760 765

Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
770 775 780

Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
785 790 795 800

His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
805 810 815

Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
820 825 830

Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
835 840 845

Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
850 855 860

Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
865 870 875 880

Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
885 890 895

Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
945 950 955 960

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Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
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Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
 980 985 990

Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
 995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
 1010 1015 1020

Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
 1025 1030 1035

Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
 1040 1045 1050

Phe Cys Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn
 1055 1060 1065

Arg Gly Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile
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Thr Glu Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr
 1085 1090 1095

Arg Gly Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu
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Lys Glu Lys Glu Glu Asn Leu Val Asn Ser Leu Val Thr Ala Gly
 1115 1120 1125

His Gly Gln Val Asp Asn Phe Ser Leu Gly Val Leu Gly Met Ala
 1130 1135 1140

Leu Phe Leu Glu Glu Met Leu Arg Thr Arg Val Gly Thr Lys His
 1145 1150 1155

Ala Ile Leu Leu Val Ala Val Ser Phe Val Thr Leu Ile Thr Gly
 1160 1165 1170

Asn Met Ser Phe Arg Asp Leu Gly Arg Val Met Val Met Val Gly
 1175 1180 1185

Ala Thr Met Thr Gly Asp Ile Gly Met Gly Val Thr Tyr Leu Ala
 1190 1195 1200

Leu Leu Ala Ala Phe Lys Val Arg Pro Thr Phe Ala Ala Gly Leu
 1205 1210 1215

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	1235					1240					1245			
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	1250					1255					1260			
Val	Arg	Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala
	1265					1270					1275			
Ile	Leu	Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys
	1280					1285					1290			
Val	Ser	Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe
	1295					1300					1305			
Leu	Thr	Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu
	1310					1315					1320			
Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
	1325					1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
	1340					1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
	1355					1360					1365			
Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
	1370					1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
	1385					1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
	1400					1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
	1415					1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Glu	Gln	Thr	Leu	Thr	Ile	Leu
	1430					1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
	1445					1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
	1460					1465					1470			

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Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
	1475					1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
	1490					1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
	1505					1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
	1520					1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
	1535					1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
	1550					1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
	1565					1570					1575			
Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
	1580					1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
	1595					1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
	1610					1615					1620			
Leu	Tyr	Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser
	1625					1630					1635			
Ala	Ile	Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile
	1640					1645					1650			
Glu	Asp	Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu
	1655					1660					1665			
His	Pro	Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val
	1670					1675					1680			
Arg	Glu	Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro
	1685					1690					1695			
Thr	Arg	Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu
	1700					1705					1710			
Pro	Ile	Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly
	1715					1720					1725			

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Arg	Glu	Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg
	1730					1735					1740			
Leu	Leu	Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met
	1745					1750					1755			
Asp	Glu	Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly
	1760					1765					1770			
Tyr	Ile	Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe
	1775					1780					1785			
Met	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser
	1790					1795					1800			
Asn	Ala	Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser
	1805					1810					1815			
Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
	1820					1825					1830			
Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
	1835					1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
	1850					1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
	1865					1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
	1880					1885					1890			
Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
	1895					1900					1905			
Leu	Thr	Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro
	1910					1915					1920			
Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
	1925					1930					1935			
Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
	1940					1945					1950			
Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
	1955					1960					1965			
Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
	1970					1975					1980			

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Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
	1985					1990					1995			
Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
	2000					2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
	2015					2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
	2030					2035					2040			
Asn	Asn	Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr
	2045					2050					2055			
Lys	Glu	Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala
	2060					2065					2070			
Arg	Ile	Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe
	2075					2080					2085			
Ala	Ala	Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met
	2090					2095					2100			
Gly	Arg	Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Val	Arg	Asp	Ala	Leu
	2105					2110					2115			
Asp	Asn	Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Ala	Gly	Gly	Arg	Ala
	2120					2125					2130			
Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
	2135					2140					2145			
Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
	2150					2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
	2165					2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
	2180					2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
	2195					2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
	2210					2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
	2225					2230					2235			

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Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
	2240					2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
	2255					2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
	2270					2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
	2285					2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
	2300					2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
	2315					2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
	2330					2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Thr	Ala	Ala	Leu	Phe	Leu	Leu	Val
	2345					2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
	2360					2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
	2375					2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
	2390					2395					2400			
Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
	2405					2410					2415			
Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
	2420					2425					2430			
Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
	2435					2440					2445			
Glu	Gly	Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser
	2450					2455					2460			
Met	Ala	Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu
	2465					2470					2475			
Leu	Phe	Xaa	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr
	2480					2485					2490			

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Gly	Asn	Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu
	2495					2500					2505			
Asn	Ala	Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly
	2510					2515					2520			
Ile	Gln	Glu	Val	Asp	Arg	Thr	Leu	Ala	Lys	Glu	Gly	Ile	Lys	Arg
	2525					2530					2535			
Gly	Glu	Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu
	2540					2545					2550			
Arg	Trp	Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val
	2555					2560					2565			
Val	Asp	Leu	Gly	Cys	Gly	Arg	Gly	Gly	Trp	Ser	Tyr	Tyr	Cys	Gly
	2570					2575					2580			
Gly	Leu	Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly
	2585					2590					2595			
Pro	Gly	His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn
	2600					2605					2610			
Leu	Val	Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro
	2615					2620					2625			
Glu	Lys	Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro
	2630					2635					2640			
Asn	Pro	Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu
	2645					2650					2655			
Val	Glu	Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val
	2660					2665					2670			
Leu	Asn	Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu
	2675					2680					2685			
Gln	Arg	Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg
	2690					2695					2700			
Asn	Ser	Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn
	2705					2710					2715			
Ile	Val	Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg
	2720					2725					2730			
Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
	2735					2740					2745			

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Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
	2750					2755					2760			
Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
	2765					2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
	2780					2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
	2795					2800					2805			
Ser	Ser	Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp
	2810					2815					2820			
Asp	Val	Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr
	2825					2830					2835			
Pro	Phe	Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg
	2840					2845					2850			
Thr	Gln	Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr
	2855					2860					2865			
Ala	Glu	Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg
	2870					2875					2880			
Met	Cys	Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala
	2885					2890					2895			
Ala	Leu	Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
	2900					2905					2910			
Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
	2915					2920					2925			
Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
	2930					2935					2940			
Asn	Met	Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys
	2945					2950					2955			
Ala	Lys	Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg
	2960					2965					2970			
Phe	Leu	Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp
	2975					2980					2985			
Phe	Ser	Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu
	2990					2995					3000			

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His	Lys 3005	Leu	Gly	Tyr	Ile	Leu 3010	Arg	Asp	Val	Ser	Lys 3015	Lys	Glu	Gly
Gly	Ala 3020	Met	Tyr	Ala	Asp	Asp 3025	Thr	Ala	Gly	Trp	Asp 3030	Thr	Arg	Ile
Thr	Leu 3035	Glu	Asp	Leu	Lys	Asn 3040	Glu	Glu	Met	Val	Thr 3045	Asn	His	Met
Glu	Gly 3050	Glu	His	Lys	Lys	Leu 3055	Ala	Glu	Ala	Ile	Phe 3060	Lys	Leu	Thr
Tyr	Gln 3065	Asn	Lys	Val	Val	Arg 3070	Val	Gln	Arg	Pro	Thr 3075	Pro	Arg	Gly
Thr	Val 3080	Met	Asp	Ile	Ile	Ser 3085	Arg	Arg	Asp	Gln	Arg 3090	Gly	Ser	Gly
Gln	Val 3095	Gly	Thr	Tyr	Gly	Leu 3100	Asn	Thr	Phe	Thr	Asn 3105	Met	Glu	Ala
Gln	Leu 3110	Ile	Arg	Gln	Met	Glu 3115	Gly	Glu	Gly	Val	Phe 3120	Lys	Ser	Ile
Gln	His 3125	Leu	Thr	Ile	Thr	Glu 3130	Glu	Ile	Ala	Val	Gln 3135	Asn	Trp	Leu
Ala	Arg 3140	Val	Gly	Arg	Glu	Arg 3145	Leu	Ser	Arg	Met	Ala 3150	Ile	Ser	Gly
Asp	Asp 3155	Cys	Val	Val	Lys	Pro 3160	Leu	Asp	Asp	Arg	Phe 3165	Ala	Ser	Ala
Leu	Thr 3170	Ala	Leu	Asn	Asp	Met 3175	Gly	Lys	Ile	Arg	Lys 3180	Asp	Ile	Gln
Gln	Trp 3185	Glu	Pro	Ser	Arg	Gly 3190	Trp	Asn	Asp	Trp	Thr 3195	Gln	Val	Pro
Phe	Cys 3200	Ser	His	His	Phe	His 3205	Glu	Leu	Ile	Met	Lys 3210	Asp	Gly	Arg
Val	Leu 3215	Val	Val	Pro	Cys	Arg 3220	Asn	Gln	Asp	Glu	Leu 3225	Ile	Gly	Arg
Ala	Arg 3230	Ile	Ser	Gln	Gly	Ala 3235	Gly	Trp	Ser	Leu	Arg 3240	Glu	Thr	Ala
Cys	Leu 3245	Gly	Lys	Ser	Tyr	Ala 3250	Gln	Met	Trp	Ser	Leu 3255	Met	Tyr	Phe

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His Arg Arg Asp Leu Arg Leu Ala Ala Asn Ala Ile Cys Ser Ala
3260 3265 3270

Val Pro Ser His Trp Val Pro Thr Ser Arg Thr Thr Trp Ser Ile
3275 3280 3285

His Ala Lys His Glu Trp Met Thr Thr Glu Asp Met Leu Thr Val
3290 3295 3300

Trp Asn Arg Val Trp Ile Gln Glu Asn Pro Trp Met Glu Asp Lys
3305 3310 3315

Thr Pro Val Glu Ser Trp Glu Glu Ile Pro Tyr Leu Gly Lys Arg
3320 3325 3330

Glu Asp Gln Trp Cys Gly Ser Leu Ile Gly Leu Thr Ser Arg Ala
3335 3340 3345

Thr Trp Ala Lys Asn Ile Gln Ala Ala Ile Asn Gln Val Arg Ser
3350 3355 3360

Leu Ile Gly Asn Glu Glu Tyr Thr Asp Tyr Met Pro Ser Met Lys
3365 3370 3375

Arg Phe Arg Arg Glu Glu Glu Glu Ala Gly Val Leu Trp
3380 3385 3390

<210> 31
<211> 10723
<212> DNA
<213> Artificial Sequence

<220>
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<220>
<221> misc_feature
<222> (3773)..(3773)
<223> n is either adenine or guanine

<220>
<221> misc_feature
<222> (7538)..(7538)
<223> n is either cytosine or thymine

<400> 31
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gttctaacag tttttaatt agagagcaga tctctgatga ataaccaacg gaaaaaggcg 120
aaaaacacgc ctttcaatat gctgaaacgc gagagaaacc gcgtgtcgac tgtgcaacag 180
ctgacaaaga gattctcact tggaatgctg cagggacgag gacctttaaa actgttcatg 240
gccctggtgg cgttccttcg tttcctaaca atccaccaa cagcagggat attgaagaga 300

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 ggaaggatgc tgaacatctt gaataggaga cgcagctctg caggcatgat cattatgctg 420
 attccaacag tgatggcggt ccatttaacc acgcgtgatg gcgaaccctt catgatagt 480
 gcaaaacatg aaagggggag acctctcttg tttaagacaa cagaggggat caacaaatgc 540
 actctcattg ccatggactt gggtgaaatg tgtgaggaca ctgtcacgta taaatgcccc 600
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 ggggcttgga agcatgctca gagagtagag agctggatac tcagaaaccc aggattcgcg 840
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 agagactttg tggaaggagt ctcagggtga gcatgggtcg atctggtgct agaacatgga 1020
 ggatgctca caacctggc ccagggaata ccaaccttg attttgaact gactaagaca 1080
 acagccaagg aagtggctct gttaagaacc tattgcattg aagcctcaat atcaaacata 1140
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 <213> Artificial Sequence

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 <223> Xaa is either lysine or arginine

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 <222> (2481)..(2481)
 <223> Xaa is either serine or phenylalanine

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Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
 50 55 60

Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
 65 70 75 80

Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
 85 90 95

Arg Arg Arg Ser Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
 100 105 110

Met Ala Phe His Leu Thr Thr Arg Asp Gly Glu Pro Leu Met Ile Val
 115 120 125

Ala Lys His Glu Arg Gly Arg Pro Leu Leu Phe Lys Thr Thr Glu Gly
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Ile Asn Lys Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Met Cys Glu
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 Thr Cys Thr Gln Ser Gly Glu Arg Arg Arg Glu Lys Arg Ser Val Ala
 195 200 205
 Leu Thr Pro His Ser Gly Met Gly Leu Glu Thr Arg Ala Glu Thr Trp
 210 215 220
 Met Ser Ser Glu Gly Ala Trp Lys His Ala Gln Arg Val Glu Ser Trp
 225 230 235 240
 Ile Leu Arg Asn Pro Gly Phe Ala Leu Leu Ala Gly Phe Met Ala Tyr
 245 250 255
 Met Ile Gly Gln Thr Gly Ile Gln Arg Thr Val Phe Phe Val Leu Met
 260 265 270
 Met Leu Val Ala Pro Ser Tyr Gly Met Arg Cys Val Gly Val Gly Asn
 275 280 285
 Arg Asp Phe Val Glu Gly Val Ser Gly Gly Ala Trp Val Asp Leu Val
 290 295 300
 Leu Glu His Gly Gly Cys Val Thr Thr Met Ala Gln Gly Lys Pro Thr
 305 310 315 320
 Leu Asp Phe Glu Leu Thr Lys Thr Thr Ala Lys Glu Val Ala Leu Leu
 325 330 335
 Arg Thr Tyr Cys Ile Glu Ala Ser Ile Ser Asn Ile Thr Thr Ala Thr
 340 345 350
 Arg Cys Pro Thr Gln Gly Glu Pro Tyr Leu Lys Glu Glu Gln Asp Gln
 355 360 365
 Gln Tyr Ile Cys Arg Arg Asp Val Val Asp Arg Gly Trp Gly Asn Gly
 370 375 380
 Cys Gly Leu Phe Gly Lys Gly Gly Val Val Thr Cys Ala Lys Phe Ser
 385 390 395 400
 Cys Ser Gly Lys Ile Thr Gly Asn Leu Val Gln Ile Glu Asn Leu Glu
 405 410 415
 Tyr Thr Val Val Val Thr Val His Asn Gly Asp Thr His Ala Val Gly
 420 425 430

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Asn Asp Thr Ser Asn His Gly Val Thr Ala Thr Ile Thr Pro Arg Ser
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Pro Ser Val Glu Val Lys Leu Pro Asp Tyr Gly Glu Leu Thr Leu Asp
450 455 460

Cys Glu Pro Arg Ser Gly Ile Asp Phe Asn Glu Met Ile Leu Met Lys
465 470 475 480

Met Lys Lys Lys Thr Trp Leu Val His Lys Gln Trp Phe Leu Asp Leu
485 490 495

Pro Leu Pro Trp Thr Ala Gly Ala Asp Thr Ser Glu Val His Trp Asn
500 505 510

Tyr Lys Glu Arg Met Val Thr Phe Lys Val Pro His Ala Lys Arg Gln
515 520 525

Asp Val Thr Val Leu Gly Ser Gln Glu Gly Ala Met His Ser Ala Leu
530 535 540

Ala Gly Ala Thr Glu Val Asp Ser Gly Asp Gly Asn His Met Phe Ala
545 550 555 560

Gly His Leu Lys Cys Lys Val Arg Met Glu Lys Leu Arg Ile Lys Gly
565 570 575

Met Ser Tyr Thr Met Cys Ser Gly Lys Phe Ser Ile Asp Lys Glu Met
580 585 590

Ala Glu Thr Gln His Gly Thr Thr Val Val Lys Val Lys Tyr Glu Gly
595 600 605

Ala Gly Ala Pro Cys Lys Val Pro Ile Glu Ile Arg Asp Val Asn Lys
610 615 620

Glu Lys Val Val Gly Arg Ile Ile Ser Ser Thr Pro Leu Ala Glu Asn
625 630 635 640

Thr Asn Ser Val Thr Asn Ile Glu Leu Glu Pro Pro Phe Gly Asp Ser
645 650 655

Tyr Ile Val Ile Gly Val Gly Asn Ser Ala Leu Thr Leu His Trp Phe
660 665 670

Arg Lys Gly Ser Ser Ile Gly Lys Met Phe Glu Ser Thr Tyr Arg Gly
675 680 685

Ala Lys Arg Met Ala Ile Leu Gly Glu Thr Ala Trp Asp Phe Gly Ser
690 695 700

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Val Gly Gly Leu Phe Thr Ser Leu Gly Lys Ala Val His Gln Val Phe
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Gly Ser Val Tyr Thr Leu Phe Gly Gly Val Ser Trp Met Ile Arg
725 730 735

Ile Leu Ile Gly Phe Leu Val Leu Trp Ile Gly Thr Asn Ser Arg Asn
740 745 750

Thr Ser Met Ala Met Thr Cys Ile Ala Ala Gly Ile Val Thr Leu Tyr
755 760 765

Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
770 775 780

Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
785 790 795 800

His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
805 810 815

Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
820 825 830

Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
835 840 845

Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
850 855 860

Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
865 870 875 880

Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
885 890 895

Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
945 950 955 960

Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
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Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
 995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
 1010 1015 1020

Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
 1025 1030 1035

Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
 1040 1045 1050

Phe Cys Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn
 1055 1060 1065

Arg Gly Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile
 1070 1075 1080

Thr Glu Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr
 1085 1090 1095

Arg Gly Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu
 1100 1105 1110

Lys Glu Lys Glu Glu Asn Leu Val Asn Ser Leu Val Thr Ala Gly
 1115 1120 1125

His Gly Gln Val Asp Asn Phe Ser Leu Gly Val Leu Gly Met Ala
 1130 1135 1140

Leu Phe Leu Glu Glu Met Leu Arg Thr Arg Val Gly Thr Lys His
 1145 1150 1155

Ala Ile Leu Leu Val Ala Val Ser Phe Val Thr Leu Ile Thr Gly
 1160 1165 1170

Asn Met Ser Phe Arg Asp Leu Gly Arg Val Met Val Met Val Gly
 1175 1180 1185

Ala Thr Met Thr Gly Asp Ile Gly Met Gly Val Thr Tyr Leu Ala
 1190 1195 1200

Leu Leu Ala Ala Phe Lys Val Arg Pro Thr Phe Ala Ala Gly Leu
 1205 1210 1215

Leu Leu Arg Lys Leu Thr Ser Xaa Glu Leu Met Met Thr Thr Ile
 1220 1225 1230

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Gly	Ile	Val	Leu	Leu	Ser	Gln	Ser	Thr	Ile	Pro	Glu	Thr	Ile	Leu
	1235					1240					1245			
Glu	Leu	Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met
	1250					1255					1260			
Val	Arg	Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala
	1265					1270					1275			
Ile	Leu	Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys
	1280					1285					1290			
Val	Ser	Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe
	1295					1300					1305			
Leu	Thr	Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu
	1310					1315					1320			
Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
	1325					1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
	1340					1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
	1355					1360					1365			
Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
	1370					1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
	1385					1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
	1400					1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
	1415					1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Glu	Gln	Thr	Leu	Thr	Ile	Leu
	1430					1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
	1445					1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
	1460					1465					1470			
Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
	1475					1480					1485			

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Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
	1490					1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
	1505					1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
	1520					1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
	1535					1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
	1550					1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
	1565					1570					1575			
Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
	1580					1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
	1595					1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
	1610					1615					1620			
Leu	Tyr	Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser
	1625					1630					1635			
Ala	Ile	Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile
	1640					1645					1650			
Glu	Asp	Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu
	1655					1660					1665			
His	Pro	Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val
	1670					1675					1680			
Arg	Glu	Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro
	1685					1690					1695			
Thr	Arg	Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu
	1700					1705					1710			
Pro	Ile	Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly
	1715					1720					1725			
Arg	Glu	Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg
	1730					1735					1740			

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Leu	Leu	Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met
	1745					1750					1755			
Asp	Glu	Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly
	1760					1765					1770			
Tyr	Ile	Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe
	1775					1780					1785			
Met	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser
	1790					1795					1800			
Asn	Ala	Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser
	1805					1810					1815			
Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
	1820					1825					1830			
Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
	1835					1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
	1850					1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
	1865					1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
	1880					1885					1890			
Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
	1895					1900					1905			
Leu	Thr	Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro
	1910					1915					1920			
Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
	1925					1930					1935			
Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
	1940					1945					1950			
Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
	1955					1960					1965			
Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
	1970					1975					1980			
Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
	1985					1990					1995			

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Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
	2000					2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
	2015					2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
	2030					2035					2040			
Asn	Asn	Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr
	2045					2050					2055			
Lys	Glu	Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala
	2060					2065					2070			
Arg	Ile	Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe
	2075					2080					2085			
Ala	Ala	Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met
	2090					2095					2100			
Gly	Arg	Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Val	Arg	Asp	Ala	Leu
	2105					2110					2115			
Asp	Asn	Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Ala	Gly	Gly	Arg	Ala
	2120					2125					2130			
Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
	2135					2140					2145			
Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
	2150					2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
	2165					2170					2175			
Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
	2180					2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
	2195					2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
	2210					2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
	2225					2230					2235			
Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
	2240					2245					2250			

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Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
	2255					2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
	2270					2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
	2285					2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
	2300					2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
	2315					2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
	2330					2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Thr	Ala	Ala	Leu	Phe	Leu	Leu	Val
	2345					2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
	2360					2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
	2375					2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
	2390					2395					2400			
Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
	2405					2410					2415			
Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
	2420					2425					2430			
Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
	2435					2440					2445			
Glu	Gly	Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser
	2450					2455					2460			
Met	Ala	Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu
	2465					2470					2475			
Leu	Phe	Xaa	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr
	2480					2485					2490			
Gly	Asn	Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu
	2495					2500					2505			

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Asn	Ala	Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly
2510						2515					2520			
Ile	Gln	Glu	Val	Asp	Arg	Thr	Leu	Ala	Lys	Glu	Gly	Ile	Lys	Arg
2525						2530					2535			
Gly	Glu	Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu
2540						2545					2550			
Arg	Trp	Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val
2555						2560					2565			
Val	Asp	Leu	Gly	Cys	Gly	Arg	Gly	Gly	Trp	Ser	Tyr	Tyr	Cys	Gly
2570						2575					2580			
Gly	Leu	Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly
2585						2590					2595			
Pro	Gly	His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn
2600						2605					2610			
Leu	Val	Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro
2615						2620					2625			
Glu	Lys	Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro
2630						2635					2640			
Asn	Pro	Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu
2645						2650					2655			
Val	Glu	Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val
2660						2665					2670			
Leu	Asn	Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu
2675						2680					2685			
Gln	Arg	Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg
2690						2695					2700			
Asn	Ser	Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn
2705						2710					2715			
Ile	Val	Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg
2720						2725					2730			
Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
2735						2740					2745			
Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
2750						2755					2760			

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Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
	2765					2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
	2780					2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
	2795					2800					2805			
Ser	Ser	Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp
	2810					2815					2820			
Asp	Val	Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr
	2825					2830					2835			
Pro	Phe	Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg
	2840					2845					2850			
Thr	Gln	Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr
	2855					2860					2865			
Ala	Glu	Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg
	2870					2875					2880			
Met	Cys	Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala
	2885					2890					2895			
Ala	Leu	Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
	2900					2905					2910			
Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
	2915					2920					2925			
Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
	2930					2935					2940			
Asn	Met	Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys
	2945					2950					2955			
Ala	Lys	Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg
	2960					2965					2970			
Phe	Leu	Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp
	2975					2980					2985			
Phe	Ser	Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu
	2990					2995					3000			
His	Lys	Leu	Gly	Tyr	Ile	Leu	Arg	Asp	Val	Ser	Lys	Lys	Glu	Gly
	3005					3010					3015			

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Gly	Ala	Met	Tyr	Ala	Asp	Asp	Thr	Ala	Gly	Trp	Asp	Thr	Arg	Ile
	3020					3025					3030			
Thr	Leu	Glu	Asp	Leu	Lys	Asn	Glu	Glu	Met	Val	Thr	Asn	His	Met
	3035					3040					3045			
Glu	Gly	Glu	His	Lys	Lys	Leu	Ala	Glu	Ala	Ile	Phe	Lys	Leu	Thr
	3050					3055					3060			
Tyr	Gln	Asn	Lys	Val	Val	Arg	Val	Gln	Arg	Pro	Thr	Pro	Arg	Gly
	3065					3070					3075			
Thr	Val	Met	Asp	Ile	Ile	Ser	Arg	Arg	Asp	Gln	Arg	Gly	Ser	Gly
	3080					3085					3090			
Gln	Val	Gly	Thr	Tyr	Gly	Leu	Asn	Thr	Phe	Thr	Asn	Met	Glu	Ala
	3095					3100					3105			
Gln	Leu	Ile	Arg	Gln	Met	Glu	Gly	Glu	Gly	Val	Phe	Lys	Ser	Ile
	3110					3115					3120			
Gln	His	Leu	Thr	Ile	Thr	Glu	Glu	Ile	Ala	Val	Gln	Asn	Trp	Leu
	3125					3130					3135			
Ala	Arg	Val	Gly	Arg	Glu	Arg	Leu	Ser	Arg	Met	Ala	Ile	Ser	Gly
	3140					3145					3150			
Asp	Asp	Cys	Val	Val	Lys	Pro	Leu	Asp	Asp	Arg	Phe	Ala	Ser	Ala
	3155					3160					3165			
Leu	Thr	Ala	Leu	Asn	Asp	Met	Gly	Lys	Ile	Arg	Lys	Asp	Ile	Gln
	3170					3175					3180			
Gln	Trp	Glu	Pro	Ser	Arg	Gly	Trp	Asn	Asp	Trp	Thr	Gln	Val	Pro
	3185					3190					3195			
Phe	Cys	Ser	His	His	Phe	His	Glu	Leu	Ile	Met	Lys	Asp	Gly	Arg
	3200					3205					3210			
Val	Leu	Val	Val	Pro	Cys	Arg	Asn	Gln	Asp	Glu	Leu	Ile	Gly	Arg
	3215					3220					3225			
Ala	Arg	Ile	Ser	Gln	Gly	Ala	Gly	Trp	Ser	Leu	Arg	Glu	Thr	Ala
	3230					3235					3240			
Cys	Leu	Gly	Lys	Ser	Tyr	Ala	Gln	Met	Trp	Ser	Leu	Met	Tyr	Phe
	3245					3250					3255			
His	Arg	Arg	Asp	Leu	Arg	Leu	Ala	Ala	Asn	Ala	Ile	Cys	Ser	Ala
	3260					3265					3270			

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Val Pro Ser His Trp Val Pro Thr Ser Arg Thr Thr Trp Ser Ile
3275 3280 3285

His Ala Lys His Glu Trp Met Thr Thr Glu Asp Met Leu Thr Val
3290 3295 3300

Trp Asn Arg Val Trp Ile Gln Glu Asn Pro Trp Met Glu Asp Lys
3305 3310 3315

Thr Pro Val Glu Ser Trp Glu Glu Ile Pro Tyr Leu Gly Lys Arg
3320 3325 3330

Glu Asp Gln Trp Cys Gly Ser Leu Ile Gly Leu Thr Ser Arg Ala
3335 3340 3345

Thr Trp Ala Lys Asn Ile Gln Ala Ala Ile Asn Gln Val Arg Ser
3350 3355 3360

Leu Ile Gly Asn Glu Glu Tyr Thr Asp Tyr Met Pro Ser Met Lys
3365 3370 3375

Arg Phe Arg Arg Glu Glu Glu Glu Ala Gly Val Leu Trp
3380 3385 3390

<210> 33
<211> 3464
<212> PRT
<213> Artificial Sequence

<220>
<223> Dengue virus serotype 1, WVS

<220>
<221> misc_feature
<222> (763)..(763)
<223> Xaa is either alanine or glycine

<400> 33

Met Asn Asn Gln Arg Lys Lys Ala Lys Asn Thr Pro Phe Asn Met Leu
1 5 10 15

Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
20 25 30

Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
50 55 60

Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
65 70 75 80

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Leu Arg Gly Phe Arg₈₅ Lys Glu Ile Gly Arg₉₀ Met Leu Asn Ile Leu Asn₉₅
 Arg Arg Arg Arg₁₀₀ Ser Ala Gly Met Ile₁₀₅ Ile Met Leu Ile Pro₁₁₀ Thr Val
 Met Ala Phe₁₁₅ His Leu Thr Thr Arg₁₂₀ Gly Gly Glu Pro His₁₂₅ Met Ile Val
 Ser Lys₁₃₀ Gln Glu Arg Gly Lys₁₃₅ Ser Leu Leu Phe Lys₁₄₀ Thr Ser Ala Gly
 Val₁₄₅ Asn Met Cys Thr Leu₁₅₀ Ile Ala Met Asp Leu₁₅₅ Gly Glu Leu Cys Glu₁₆₀
 Asp Thr Met Thr Tyr₁₆₅ Lys Cys Pro Arg Ile₁₇₀ Thr Glu Ala Glu Pro₁₇₅ Asp
 Asp Val Asp Cys₁₈₀ Trp Cys Asn Ala Thr₁₈₅ Asp Thr Trp Val Thr₁₉₀ Tyr Gly
 Thr Cys Ser₁₉₅ Gln Thr Gly Glu His₂₀₀ Arg Arg Asp Lys Arg₂₀₅ Ser Val Ala
 Leu Ala₂₁₀ Pro His Val Gly Leu₂₁₅ Gly Leu Glu Thr Arg₂₂₀ Ala Glu Thr Trp
 Met Ser Ser Glu Gly Ala₂₃₀ Trp Lys Gln Ile Gln₂₃₅ Lys Val Glu Thr Trp₂₄₀
 Ala Leu Arg His Pro₂₄₅ Gly Phe Thr Val Ile₂₅₀ Ala Leu Phe Leu Ala₂₅₅ His
 Ala Ile Gly Thr₂₆₀ Ser Ile Thr Gln Lys₂₆₅ Gly Ile Ile Phe Ile₂₇₀ Leu Leu
 Met Leu Val₂₇₅ Thr Pro Ser Met Ala₂₈₀ Met Arg Cys Val Gly₂₈₅ Ile Gly Asn
 Arg Asp Phe Val Glu Gly Leu₂₉₅ Ser Gly Ala Thr Trp₃₀₀ Val Asp Val Val
 Leu Glu His Gly Ser Cys₃₁₀ Val Thr Thr Met Ala₃₁₅ Lys Asn Lys Pro Thr₃₂₀
 Leu Asp Ile Glu Leu₃₂₅ Leu Lys Thr Glu Val₃₃₀ Thr Asn Pro Ala Val₃₃₅ Leu
 Arg Lys Leu Cys₃₄₀ Ile Glu Ala Lys Ile₃₄₅ Ser Asn Thr Thr Thr₃₅₀ Asp Ser

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Arg Cys Pro Thr Gln Gly Glu Ala Thr Leu Val Glu Glu Gln Asp Ala
 355 360 365
 Asn Phe Val Cys Arg Arg Thr Phe Val Asp Arg Gly Trp Gly Asn Gly
 370 375 380
 Cys Gly Leu Phe Gly Lys Gly Ser Leu Ile Thr Cys Ala Lys Phe Lys
 385 390 395 400
 Cys Val Thr Lys Leu Glu Gly Lys Ile Val Gln Tyr Glu Asn Leu Lys
 405 410 415
 Tyr Ser Val Ile Val Thr Val His Thr Gly Asp Gln His Gln Val Gly
 420 425 430
 Asn Glu Thr Thr Glu His Gly Thr Thr Ala Thr Ile Thr Pro Gln Ala
 435 440 445
 Pro Thr Ser Glu Ile Gln Leu Thr Asp Tyr Gly Thr Leu Thr Leu Asp
 450 455 460
 Cys Ser Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Val Leu Leu Thr
 465 470 475 480
 Met Lys Glu Arg Ser Trp Leu Val His Lys Gln Trp Phe Leu Asp Leu
 485 490 495
 Pro Leu Pro Trp Thr Ser Gly Ala Ser Thr Ser Gln Glu Thr Trp Asn
 500 505 510
 Arg Gln Asp Leu Leu Val Thr Phe Lys Thr Ala His Ala Lys Lys Gln
 515 520 525
 Glu Val Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu
 530 535 540
 Thr Gly Ala Thr Glu Ile Gln Thr Ser Gly Thr Thr Thr Ile Phe Ala
 545 550 555 560
 Gly His Leu Lys Cys Arg Leu Lys Met Asp Lys Leu Thr Leu Lys Gly
 565 570 575
 Met Ser Tyr Val Met Cys Thr Gly Ser Phe Lys Leu Glu Lys Glu Val
 580 585 590
 Ala Glu Thr Gln His Gly Thr Val Leu Val Gln Val Lys Tyr Glu Gly
 595 600 605
 Thr Asp Ala Pro Cys Lys Ile Pro Phe Ser Thr Gln Asp Glu Lys Gly
 610 615 620

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Ala Thr Gln Asn Gly Arg Leu Ile Thr Ala Asn Pro Ile Val Thr Asp
625 630 635 640

Lys Glu Lys Pro Val Asn Ile Glu Ala Glu Pro Pro Phe Gly Glu Ser
645 650 655

Tyr Ile Val Val Gly Ala Gly Glu Lys Ala Leu Lys Leu Ser Trp Phe
660 665 670

Lys Lys Gly Ser Ser Ile Gly Lys Met Phe Glu Ala Thr Ala Arg Gly
675 680 685

Ala Arg Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser
690 695 700

Ile Gly Gly Val Phe Thr Ser Met Gly Lys Leu Val His Gln Val Phe
705 710 715 720

Gly Thr Ala Tyr Gly Val Leu Phe Ser Gly Val Ser Trp Thr Met Lys
725 730 735

Ile Gly Ile Gly Ile Leu Leu Thr Trp Leu Gly Leu Asn Ser Arg Asn
740 745 750

Thr Ser Leu Ser Met Met Cys Ile Ala Ala Xaa Ile Val Thr Leu Tyr
755 760 765

Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
770 775 780

Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
785 790 795 800

His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
805 810 815

Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
820 825 830

Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
835 840 845

Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
850 855 860

Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
865 870 875 880

Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
885 890 895

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Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
 900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
 915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
 930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
 945 950 955 960

Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
 965 970 975

Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
 980 985 990

Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
 995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
 1010 1015 1020

Gly Pro Val Ser Gln His Asn Tyr Arg Pro Gly Tyr His Thr Gln
 1025 1030 1035

Ile Thr Gly Pro Trp His Leu Gly Lys Leu Glu Met Asp Phe Asp
 1040 1045 1050

Phe Cys Asp Gly Thr Thr Val Val Val Thr Glu Asp Cys Gly Asn
 1055 1060 1065

Arg Gly Pro Ser Leu Arg Thr Thr Thr Ala Ser Gly Lys Leu Ile
 1070 1075 1080

Thr Glu Trp Cys Cys Arg Ser Cys Thr Leu Pro Pro Leu Arg Tyr
 1085 1090 1095

Arg Gly Glu Asp Gly Cys Trp Tyr Gly Met Glu Ile Arg Pro Leu
 1100 1105 1110

Lys Glu Lys Glu Glu Asn Leu Val Asn Ser Leu Val Thr Ala Gly
 1115 1120 1125

His Gly Gln Val Asp Asn Phe Ser Leu Gly Val Leu Gly Met Ala
 1130 1135 1140

Leu Phe Leu Glu Glu Met Leu Arg Thr Arg Val Gly Thr Lys His
 1145 1150 1155

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Ala	Ile	Leu	Leu	Val	Ala	Val	Ser	Phe	Val	Thr	Leu	Ile	Thr	Gly
	1160					1165					1170			
Asn	Met	Ser	Phe	Arg	Asp	Leu	Gly	Arg	Val	Met	Val	Met	Val	Gly
	1175					1180					1185			
Ala	Thr	Met	Thr	Asp	Asp	Ile	Gly	Met	Gly	Val	Thr	Tyr	Leu	Ala
	1190					1195					1200			
Leu	Leu	Ala	Ala	Phe	Lys	Val	Arg	Pro	Thr	Phe	Ala	Ala	Gly	Leu
	1205					1210					1215			
Leu	Leu	Arg	Lys	Leu	Thr	Ser	Lys	Glu	Leu	Met	Met	Thr	Thr	Ile
	1220					1225					1230			
Gly	Ile	Val	Leu	Leu	Ser	Gln	Ser	Thr	Leu	Pro	Glu	Thr	Ile	Leu
	1235					1240					1245			
Glu	Leu	Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met
	1250					1255					1260			
Val	Arg	Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala
	1265					1270					1275			
Ile	Leu	Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys
	1280					1285					1290			
Val	Ser	Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe
	1295					1300					1305			
Leu	Thr	Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu
	1310					1315					1320			
Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
	1325					1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
	1340					1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
	1355					1360					1365			
Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
	1370					1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
	1385					1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
	1400					1405					1410			

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Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
	1415					1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Asp	Gln	Thr	Leu	Thr	Ile	Leu
	1430					1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
	1445					1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
	1460					1465					1470			
Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
	1475					1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
	1490					1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
	1505					1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
	1520					1525					1530			
Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
	1535					1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
	1550					1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
	1565					1570					1575			
Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
	1580					1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
	1595					1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
	1610					1615					1620			
Leu	Tyr	Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser
	1625					1630					1635			
Ala	Ile	Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile
	1640					1645					1650			
Glu	Asp	Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu
	1655					1660					1665			

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His	Pro 1670	Gly	Ala	Gly	Lys	Thr 1675	Lys	Arg	Tyr	Leu	Pro 1680	Ala	Ile	Val
Arg	Glu 1685	Ala	Ile	Lys	Arg	Gly 1690	Leu	Arg	Thr	Leu	Ile 1695	Leu	Ala	Pro
Thr	Arg 1700	Val	Val	Ala	Ala	Glu 1705	Met	Glu	Glu	Ala	Leu 1710	Arg	Gly	Leu
Pro	Ile 1715	Arg	Tyr	Gln	Thr	Pro 1720	Ala	Ile	Arg	Ala	Val 1725	His	Thr	Gly
Arg	Glu 1730	Ile	Val	Asp	Leu	Met 1735	Cys	His	Ala	Thr	Phe 1740	Thr	Met	Arg
Leu	Leu 1745	Ser	Pro	Val	Arg	Val 1750	Pro	Asn	Tyr	Asn	Leu 1755	Ile	Ile	Met
Asp	Glu 1760	Ala	His	Phe	Thr	Asp 1765	Pro	Ala	Ser	Ile	Ala 1770	Ala	Arg	Gly
Tyr	Ile 1775	Ser	Thr	Arg	Val	Glu 1780	Met	Gly	Glu	Ala	Ala 1785	Gly	Ile	Phe
Met	Thr 1790	Ala	Thr	Pro	Pro	Gly 1795	Ser	Arg	Asp	Pro	Phe 1800	Pro	Gln	Ser
Asn	Ala 1805	Pro	Ile	Ile	Asp	Glu 1810	Glu	Arg	Glu	Ile	Pro 1815	Glu	Arg	Ser
Trp	Asn 1820	Ser	Gly	His	Glu	Trp 1825	Val	Thr	Asp	Phe	Lys 1830	Gly	Lys	Thr
Val	Trp 1835	Phe	Val	Pro	Ser	Ile 1840	Lys	Ala	Gly	Asn	Asp 1845	Ile	Ala	Ala
Cys	Leu 1850	Arg	Lys	Asn	Gly	Lys 1855	Lys	Val	Ile	Gln	Leu 1860	Ser	Arg	Lys
Thr	Phe 1865	Asp	Ser	Glu	Tyr	Val 1870	Lys	Thr	Arg	Thr	Asn 1875	Asp	Trp	Asp
Phe	Val 1880	Val	Thr	Thr	Asp	Ile 1885	Ser	Glu	Met	Gly	Ala 1890	Asn	Phe	Lys
Ala	Glu 1895	Arg	Val	Ile	Asp	Pro 1900	Arg	Arg	Cys	Met	Lys 1905	Pro	Val	Ile
Leu	Thr 1910	Asp	Gly	Glu	Glu	Arg 1915	Val	Ile	Leu	Ala	Gly 1920	Pro	Met	Pro

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Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
	1925					1930					1935			
Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
	1940					1945					1950			
Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
	1955					1960					1965			
Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
	1970					1975					1980			
Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
	1985					1990					1995			
Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
	2000					2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
	2015					2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
	2030					2035					2040			
Asn	Asn	Gln	Ile	Leu	Glu	Glu	Asn	Val	Glu	Val	Glu	Ile	Trp	Thr
	2045					2050					2055			
Lys	Glu	Gly	Glu	Arg	Lys	Lys	Leu	Lys	Pro	Arg	Trp	Leu	Asp	Ala
	2060					2065					2070			
Arg	Ile	Tyr	Ser	Asp	Pro	Leu	Ala	Leu	Lys	Glu	Phe	Lys	Glu	Phe
	2075					2080					2085			
Ala	Ala	Gly	Arg	Lys	Ser	Leu	Thr	Leu	Asn	Leu	Ile	Thr	Glu	Met
	2090					2095					2100			
Gly	Arg	Leu	Pro	Thr	Phe	Met	Thr	Gln	Lys	Ala	Arg	Asp	Ala	Leu
	2105					2110					2115			
Asp	Asn	Leu	Ala	Val	Leu	His	Thr	Ala	Glu	Ala	Gly	Gly	Arg	Ala
	2120					2125					2130			
Tyr	Asn	His	Ala	Leu	Ser	Glu	Leu	Pro	Glu	Thr	Leu	Glu	Thr	Leu
	2135					2140					2145			
Leu	Leu	Leu	Thr	Leu	Leu	Ala	Thr	Val	Thr	Gly	Gly	Ile	Phe	Leu
	2150					2155					2160			
Phe	Leu	Met	Ser	Ala	Arg	Gly	Ile	Gly	Lys	Met	Thr	Leu	Gly	Met
	2165					2170					2175			

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Cys	Cys	Ile	Ile	Thr	Ala	Ser	Ile	Leu	Leu	Trp	Tyr	Ala	Gln	Ile
	2180					2185					2190			
Gln	Pro	His	Trp	Ile	Ala	Ala	Ser	Ile	Ile	Leu	Glu	Phe	Phe	Leu
	2195					2200					2205			
Ile	Val	Leu	Leu	Ile	Pro	Glu	Pro	Glu	Lys	Gln	Arg	Thr	Pro	Gln
	2210					2215					2220			
Asp	Asn	Gln	Leu	Thr	Tyr	Val	Val	Ile	Ala	Ile	Leu	Thr	Val	Val
	2225					2230					2235			
Ala	Ala	Thr	Met	Ala	Asn	Glu	Met	Gly	Phe	Leu	Glu	Lys	Thr	Lys
	2240					2245					2250			
Lys	Asp	Leu	Gly	Leu	Gly	Ser	Ile	Ala	Thr	Gln	Gln	Pro	Glu	Ser
	2255					2260					2265			
Asn	Ile	Leu	Asp	Ile	Asp	Leu	Arg	Pro	Ala	Ser	Ala	Trp	Thr	Leu
	2270					2275					2280			
Tyr	Ala	Val	Ala	Thr	Thr	Phe	Val	Thr	Pro	Met	Leu	Arg	His	Ser
	2285					2290					2295			
Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
	2300					2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
	2315					2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
	2330					2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Ile	Ala	Ala	Leu	Phe	Leu	Leu	Val
	2345					2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
	2360					2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
	2375					2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
	2390					2395					2400			
Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
	2405					2410					2415			
Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
	2420					2425					2430			

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Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
	2435					2440					2445			
Glu	Gly	Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser
	2450					2455					2460			
Met	Ala	Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu
	2465					2470					2475			
Leu	Phe	Ser	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr
	2480					2485					2490			
Gly	Asn	Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu
	2495					2500					2505			
Asn	Ala	Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly
	2510					2515					2520			
Ile	Gln	Glu	Val	Asp	Arg	Thr	Leu	Ala	Lys	Glu	Gly	Ile	Lys	Arg
	2525					2530					2535			
Gly	Glu	Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu
	2540					2545					2550			
Arg	Trp	Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val
	2555					2560					2565			
Val	Asp	Leu	Gly	Cys	Gly	Arg	Gly	Gly	Trp	Ser	Tyr	Tyr	Cys	Gly
	2570					2575					2580			
Gly	Leu	Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly
	2585					2590					2595			
Pro	Gly	His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn
	2600					2605					2610			
Leu	Val	Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro
	2615					2620					2625			
Glu	Lys	Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro
	2630					2635					2640			
Asn	Pro	Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu
	2645					2650					2655			
Val	Glu	Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val
	2660					2665					2670			
Leu	Asn	Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu
	2675					2680					2685			

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Gln	Arg	Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg
	2690					2695					2700			
Asn	Ser	Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn
	2705					2710					2715			
Ile	Val	Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg
	2720					2725					2730			
Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
	2735					2740					2745			
Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
	2750					2755					2760			
Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
	2765					2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
	2780					2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
	2795					2800					2805			
Ser	Ser	Met	Val	Asn	Gly	Val	Val	Arg	Leu	Leu	Thr	Lys	Pro	Trp
	2810					2815					2820			
Asp	Val	Val	Pro	Met	Val	Thr	Gln	Met	Ala	Met	Thr	Asp	Thr	Thr
	2825					2830					2835			
Pro	Phe	Gly	Gln	Gln	Arg	Val	Phe	Lys	Glu	Lys	Val	Asp	Thr	Arg
	2840					2845					2850			
Thr	Gln	Glu	Pro	Lys	Glu	Gly	Thr	Lys	Lys	Leu	Met	Lys	Ile	Thr
	2855					2860					2865			
Ala	Glu	Trp	Leu	Trp	Lys	Glu	Leu	Gly	Lys	Lys	Lys	Thr	Pro	Arg
	2870					2875					2880			
Met	Cys	Thr	Arg	Glu	Glu	Phe	Thr	Arg	Lys	Val	Arg	Ser	Asn	Ala
	2885					2890					2895			
Ala	Leu	Gly	Ala	Ile	Phe	Thr	Asp	Glu	Asn	Lys	Trp	Lys	Ser	Ala
	2900					2905					2910			
Arg	Glu	Ala	Val	Glu	Asp	Ser	Arg	Phe	Trp	Glu	Leu	Val	Asp	Lys
	2915					2920					2925			
Glu	Arg	Asn	Leu	His	Leu	Glu	Gly	Lys	Cys	Glu	Thr	Cys	Val	Tyr
	2930					2935					2940			

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Asn	Met	Met	Gly	Lys	Arg	Glu	Lys	Lys	Leu	Gly	Glu	Phe	Gly	Lys
	2945					2950					2955			
Ala	Lys	Gly	Ser	Arg	Ala	Ile	Trp	Tyr	Met	Trp	Leu	Gly	Ala	Arg
	2960					2965					2970			
Phe	Leu	Glu	Phe	Glu	Ala	Leu	Gly	Phe	Leu	Asn	Glu	Asp	His	Trp
	2975					2980					2985			
Phe	Ser	Arg	Glu	Asn	Ser	Leu	Ser	Gly	Val	Glu	Gly	Glu	Gly	Leu
	2990					2995					3000			
His	Lys	Leu	Gly	Tyr	Ile	Leu	Arg	Asp	Val	Ser	Lys	Lys	Glu	Gly
	3005					3010					3015			
Gly	Ala	Met	Tyr	Ala	Asp	Asp	Thr	Ala	Gly	Trp	Asp	Thr	Arg	Ile
	3020					3025					3030			
Thr	Leu	Glu	Asp	Leu	Lys	Asn	Glu	Glu	Met	Val	Thr	Asn	His	Met
	3035					3040					3045			
Glu	Gly	Glu	His	Lys	Lys	Leu	Ala	Glu	Ala	Ile	Phe	Lys	Leu	Thr
	3050					3055					3060			
Tyr	Gln	Asn	Lys	Val	Val	Arg	Val	Gln	Arg	Pro	Thr	Pro	Arg	Gly
	3065					3070					3075			
Thr	Val	Met	Asp	Ile	Ile	Ser	Arg	Arg	Asp	Gln	Arg	Gly	Ser	Gly
	3080					3085					3090			
Gln	Val	Gly	Thr	Tyr	Gly	Leu	Asn	Thr	Phe	Thr	Asn	Met	Glu	Ala
	3095					3100					3105			
Gln	Leu	Ile	Arg	Gln	Met	Glu	Gly	Glu	Gly	Val	Phe	Lys	Ser	Ile
	3110					3115					3120			
Gln	His	Leu	Thr	Ile	Thr	Glu	Glu	Ile	Ala	Val	Gln	Asn	Trp	Leu
	3125					3130					3135			
Ala	Arg	Val	Gly	Arg	Glu	Arg	Leu	Ser	Arg	Met	Ala	Ile	Ser	Gly
	3140					3145					3150			
Asp	Asp	Cys	Val	Val	Lys	Pro	Leu	Asp	Asp	Arg	Phe	Ala	Ser	Ala
	3155					3160					3165			
Leu	Thr	Ala	Leu	Asn	Asp	Met	Gly	Lys	Ile	Arg	Lys	Asp	Ile	Gln
	3170					3175					3180			
Gln	Trp	Glu	Pro	Ser	Arg	Gly	Trp	Asn	Asp	Trp	Thr	Gln	Val	Pro
	3185					3190					3195			

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Phe	Cys 3200	Ser	His	His	Phe	His 3205	Glu	Leu	Ile	Met	Lys 3210	Asp	Gly	Arg
Val	Leu 3215	Val	Val	Pro	Cys	Arg 3220	Asn	Gln	Asp	Glu	Leu 3225	Ile	Gly	Arg
Ala	Arg 3230	Ile	Ser	Gln	Gly	Ala 3235	Gly	Trp	Ser	Leu	Arg 3240	Glu	Thr	Ala
Cys	Leu 3245	Gly	Lys	Ser	Tyr	Ala 3250	Gln	Met	Trp	Ser	Leu 3255	Met	Tyr	Phe
His	Arg 3260	Arg	Asp	Leu	Arg	Leu 3265	Ala	Ala	Asn	Ala	Ile 3270	Cys	Ser	Ala
Val	Pro 3275	Ser	His	Trp	Val	Pro 3280	Thr	Ser	Arg	Thr	Thr 3285	Trp	Ser	Ile
His	Ala 3290	Lys	His	Glu	Trp	Met 3295	Thr	Thr	Glu	Asp	Met 3300	Leu	Thr	Val
Trp	Asn 3305	Arg	Val	Trp	Ile	Gln 3310	Glu	Asn	Pro	Trp	Met 3315	Glu	Asp	Lys
Thr	Pro 3320	Val	Glu	Ser	Trp	Glu 3325	Glu	Ile	Pro	Tyr	Leu 3330	Gly	Lys	Arg
Glu	Asp 3335	Gln	Trp	Cys	Gly	Ser 3340	Leu	Ile	Gly	Leu	Thr 3345	Ser	Arg	Ala
Thr	Trp 3350	Ala	Lys	Asn	Ile	Gln 3355	Ala	Ala	Ile	Asn	Gln 3360	Val	Arg	Ser
Leu	Ile 3365	Gly	Asn	Glu	Glu	Tyr 3370	Thr	Asp	Tyr	Met	Pro 3375	Ser	Met	Lys
Arg	Phe 3380	Arg	Arg	Glu	Glu	Glu 3385	Glu	Ala	Gly	Val	Leu 3390	Trp	Lys	Ala
Lys	Leu 3395	Thr	Asn	Lys	Ala	Arg 3400	Ser	Gln	Val	Gly	Leu 3405	Ser	His	Ser
Thr	Glu 3410	Lys	Thr	Met	Leu	Pro 3415	Val	Ser	Pro	Val	Gln 3420	Gly	Arg	Lys
Lys	Ser 3425	Gly	His	His	Lys	Cys 3430	His	Ser	Leu	Ser	Lys 3435	Leu	Cys	Ser
Leu	Leu 3440	His	Leu	Arg	Arg	Cys 3445	Lys	Lys	Ser	Gly	Arg 3450	Pro	Gln	Thr

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Met Glu Ala Val Arg Met Ala Trp Thr Ser Gly
 3455 3460

<210> 34
 <211> 3464
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Dengue virus sertype 1, BVS

<400> 34

Met Asn Asn Gln Arg Lys Lys Ala Lys Asn Thr Pro Phe Asn Met Leu
 1 5 10 15

Lys Arg Glu Arg Asn Arg Val Ser Thr Val Gln Gln Leu Thr Lys Arg
 20 25 30

Phe Ser Leu Gly Met Leu Gln Gly Arg Gly Pro Leu Lys Leu Phe Met
 35 40 45

Ala Leu Val Ala Phe Leu Arg Phe Leu Thr Ile Pro Pro Thr Ala Gly
 50 55 60

Ile Leu Lys Arg Trp Gly Thr Ile Lys Lys Ser Lys Ala Ile Asn Val
 65 70 75 80

Leu Arg Gly Phe Arg Lys Glu Ile Gly Arg Met Leu Asn Ile Leu Asn
 85 90 95

Arg Arg Arg Arg Ser Ala Gly Met Ile Ile Met Leu Ile Pro Thr Val
 100 105 110

Met Ala Phe His Leu Thr Thr Arg Gly Gly Glu Pro His Met Ile Val
 115 120 125

Ser Lys Gln Glu Arg Gly Lys Ser Leu Leu Phe Lys Thr Ser Ala Gly
 130 135 140

Val Asn Met Cys Thr Leu Ile Ala Met Asp Leu Gly Glu Leu Cys Glu
 145 150 155 160

Asp Thr Met Thr Tyr Lys Cys Pro Arg Ile Thr Glu Ala Glu Pro Asp
 165 170 175

Asp Val Asp Cys Trp Cys Asn Ala Thr Asp Thr Trp Val Thr Tyr Gly
 180 185 190

Thr Cys Ser Gln Thr Gly Glu His Arg Arg Asp Lys Arg Ser Val Ala
 195 200 205

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```

Leu Ala Pro His Val Gly Leu Gly Leu Glu Thr Arg Ala Glu Thr Trp
 210                215                220

Met Ser Ser Glu Gly Ala Trp Lys Gln Ile Gln Lys Val Glu Thr Trp
 225                230                235                240

Ala Leu Arg His Pro Gly Phe Thr Val Ile Ala Leu Phe Leu Ala His
                245                250                255

Ala Ile Gly Thr Ser Ile Thr Gln Lys Gly Ile Ile Phe Ile Leu Leu
                260                265                270

Met Leu Val Thr Pro Ser Met Ala Met Arg Cys Val Gly Ile Gly Asn
 275                280                285

Arg Asp Phe Val Glu Gly Leu Ser Gly Ala Thr Trp Val Asp Val Val
 290                295                300

Leu Glu His Gly Ser Cys Val Thr Thr Met Ala Lys Asn Lys Pro Thr
 305                310                315                320

Leu Asp Ile Glu Leu Leu Lys Thr Glu Val Thr Asn Pro Ala Val Leu
                325                330                335

Arg Lys Leu Cys Ile Glu Ala Lys Ile Ser Asn Thr Thr Thr Asp Ser
                340                345                350

Arg Cys Pro Thr Gln Gly Glu Ala Thr Leu Val Glu Glu Gln Asp Ala
                355                360                365

Asn Phe Val Cys Arg Arg Thr Phe Val Asp Arg Gly Trp Gly Asn Gly
 370                375                380

Cys Gly Leu Phe Gly Lys Gly Ser Leu Ile Thr Cys Ala Lys Phe Lys
 385                390                395                400

Cys Val Thr Lys Leu Glu Gly Lys Ile Val Gln Tyr Glu Asn Leu Lys
                405                410                415

Tyr Ser Val Ile Val Thr Val His Thr Gly Asp Gln His Gln Val Gly
                420                425                430

Asn Glu Thr Thr Glu His Gly Thr Thr Ala Thr Ile Thr Pro Gln Ala
 435                440                445

Pro Thr Ser Glu Ile Gln Leu Thr Asp Tyr Gly Thr Leu Thr Leu Asp
 450                455                460

Cys Ser Pro Arg Thr Gly Leu Asp Phe Asn Glu Met Val Leu Leu Thr
 465                470                475                480

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Met Lys Glu Arg Ser Trp Leu Val His Lys Gln Trp Phe Leu Asp Leu
      485                      490                      495

Pro Leu Pro Trp Thr Ser Gly Ala Ser Thr Ser Gln Glu Thr Trp Asn
      500                      505                      510

Arg Gln Asp Leu Leu Val Thr Phe Lys Thr Ala His Ala Lys Lys Gln
      515                      520                      525

Glu Val Val Val Leu Gly Ser Gln Glu Gly Ala Met His Thr Ala Leu
      530                      535                      540

Thr Gly Ala Thr Glu Ile Gln Thr Ser Gly Thr Thr Thr Ile Phe Ala
      545                      550                      555                      560

Gly His Leu Lys Cys Arg Leu Lys Met Asp Lys Leu Thr Leu Lys Gly
      565                      570                      575

Met Ser Tyr Val Met Cys Thr Gly Ser Phe Lys Leu Glu Lys Glu Val
      580                      585                      590

Ala Glu Thr Gln His Gly Thr Val Leu Val Gln Val Lys Tyr Glu Gly
      595                      600                      605

Thr Asp Ala Pro Cys Lys Ile Pro Phe Ser Thr Gln Asp Glu Lys Gly
      610                      615                      620

Ala Thr Gln Asn Gly Arg Leu Ile Thr Ala Asn Pro Ile Val Thr Asp
      625                      630                      635                      640

Lys Glu Lys Pro Val Asn Ile Glu Ala Glu Pro Pro Phe Gly Glu Ser
      645                      650                      655

Tyr Ile Val Val Gly Ala Gly Glu Lys Ala Leu Lys Leu Ser Trp Phe
      660                      665                      670

Lys Lys Gly Ser Ser Ile Gly Lys Met Phe Glu Ala Thr Ala Arg Gly
      675                      680                      685

Ala Arg Arg Met Ala Ile Leu Gly Asp Thr Ala Trp Asp Phe Gly Ser
      690                      695                      700

Ile Gly Gly Val Phe Thr Ser Met Gly Lys Leu Val His Gln Val Phe
      705                      710                      715                      720

Gly Thr Ala Tyr Gly Val Leu Phe Ser Gly Val Ser Trp Thr Met Lys
      725                      730                      735

Ile Gly Ile Gly Ile Leu Leu Thr Trp Leu Gly Leu Asn Ser Arg Asn
      740                      745                      750

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Thr Ser Leu Ser Met Met Cys Ile Ala Ala Ala Ile Val Thr Leu Tyr
755 760 765

Leu Gly Val Met Val Gln Ala Asp Ser Gly Cys Val Val Ser Trp Lys
770 775 780

Asn Lys Glu Leu Lys Cys Gly Ser Gly Ile Phe Ile Thr Asp Asn Val
785 790 795 800

His Thr Trp Thr Glu Gln Tyr Lys Phe Gln Pro Glu Ser Pro Ser Lys
805 810 815

Leu Ala Ser Ala Ile Gln Lys Ala His Glu Glu Asp Ile Cys Gly Ile
820 825 830

Arg Ser Val Thr Arg Leu Glu Asn Leu Met Trp Lys Gln Ile Thr Pro
835 840 845

Glu Leu Asn His Ile Leu Ser Glu Asn Glu Val Lys Leu Thr Ile Met
850 855 860

Thr Gly Asp Ile Lys Gly Ile Met Gln Ala Gly Lys Arg Ser Leu Arg
865 870 875 880

Pro Gln Pro Thr Glu Leu Lys Tyr Ser Trp Lys Thr Trp Gly Lys Ala
885 890 895

Lys Met Leu Ser Thr Glu Ser His Asn Gln Thr Phe Leu Ile Asp Gly
900 905 910

Pro Glu Thr Ala Glu Cys Pro Asn Thr Asn Arg Ala Trp Asn Ser Leu
915 920 925

Glu Val Glu Asp Tyr Gly Phe Gly Val Phe Thr Thr Asn Ile Trp Leu
930 935 940

Lys Leu Lys Glu Lys Gln Asp Val Phe Cys Asp Ser Lys Leu Met Ser
945 950 955 960

Ala Ala Ile Lys Asp Asn Arg Ala Val His Ala Asp Met Gly Tyr Trp
965 970 975

Ile Glu Ser Ala Leu Asn Asp Thr Trp Lys Ile Glu Lys Ala Ser Phe
980 985 990

Ile Glu Val Lys Asn Cys His Trp Pro Lys Ser His Thr Leu Trp Ser
995 1000 1005

Asn Gly Val Leu Glu Ser Glu Met Ile Ile Pro Lys Asn Leu Ala
1010 1015 1020

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Gly	Pro	Val	Ser	Gln	His	Asn	Tyr	Arg	Pro	Gly	Tyr	His	Thr	Gln
1025						1030					1035			
Ile	Thr	Gly	Pro	Trp	His	Leu	Gly	Lys	Leu	Glu	Met	Asp	Phe	Asp
1040						1045					1050			
Phe	Cys	Asp	Gly	Thr	Thr	Val	Val	Val	Thr	Glu	Asp	Cys	Gly	Asn
1055						1060					1065			
Arg	Gly	Pro	Ser	Leu	Arg	Thr	Thr	Thr	Ala	Ser	Gly	Lys	Leu	Ile
1070						1075					1080			
Thr	Glu	Trp	Cys	Cys	Arg	Ser	Cys	Thr	Leu	Pro	Pro	Leu	Arg	Tyr
1085						1090					1095			
Arg	Gly	Glu	Asp	Gly	Cys	Trp	Tyr	Gly	Met	Glu	Ile	Arg	Pro	Leu
1100						1105					1110			
Lys	Glu	Lys	Glu	Glu	Asn	Leu	Val	Asn	Ser	Leu	Val	Thr	Ala	Gly
1115						1120					1125			
His	Gly	Gln	Val	Asp	Asn	Phe	Ser	Leu	Gly	Val	Leu	Gly	Met	Ala
1130						1135					1140			
Leu	Phe	Leu	Glu	Glu	Met	Leu	Arg	Thr	Arg	Val	Gly	Thr	Lys	His
1145						1150					1155			
Ala	Ile	Leu	Leu	Val	Ala	Val	Ser	Phe	Val	Thr	Leu	Ile	Thr	Gly
1160						1165					1170			
Asn	Met	Ser	Phe	Arg	Asp	Leu	Gly	Arg	Val	Met	Val	Met	Val	Gly
1175						1180					1185			
Ala	Thr	Met	Thr	Asp	Asp	Ile	Gly	Met	Gly	Val	Thr	Tyr	Leu	Ala
1190						1195					1200			
Leu	Leu	Ala	Ala	Phe	Lys	Val	Arg	Pro	Thr	Phe	Ala	Ala	Gly	Leu
1205						1210					1215			
Leu	Leu	Arg	Lys	Leu	Thr	Ser	Lys	Glu	Leu	Met	Met	Thr	Thr	Ile
1220						1225					1230			
Gly	Ile	Val	Leu	Leu	Ser	Gln	Ser	Thr	Leu	Pro	Glu	Thr	Ile	Leu
1235						1240					1245			
Glu	Leu	Thr	Asp	Ala	Leu	Ala	Leu	Gly	Met	Met	Val	Leu	Lys	Met
1250						1255					1260			
Val	Arg	Asn	Met	Glu	Lys	Tyr	Gln	Leu	Ala	Val	Thr	Ile	Met	Ala
1265						1270					1275			

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Ile	Leu	Cys	Val	Pro	Asn	Ala	Val	Ile	Leu	Gln	Asn	Ala	Trp	Lys
1280						1285					1290			
Val	Ser	Cys	Thr	Ile	Leu	Ala	Val	Val	Ser	Val	Ser	Pro	Leu	Phe
1295						1300					1305			
Leu	Thr	Ser	Ser	Gln	Gln	Lys	Thr	Asp	Trp	Ile	Pro	Leu	Ala	Leu
1310						1315					1320			
Thr	Ile	Lys	Gly	Leu	Asn	Pro	Thr	Ala	Ile	Phe	Leu	Thr	Thr	Leu
1325						1330					1335			
Ser	Arg	Thr	Ser	Lys	Lys	Arg	Ser	Trp	Pro	Leu	Asn	Glu	Ala	Ile
1340						1345					1350			
Met	Ala	Val	Gly	Met	Val	Ser	Ile	Leu	Ala	Ser	Ser	Leu	Leu	Lys
1355						1360					1365			
Asn	Asp	Ile	Pro	Met	Thr	Gly	Pro	Leu	Val	Ala	Gly	Gly	Leu	Leu
1370						1375					1380			
Thr	Val	Cys	Tyr	Val	Leu	Thr	Gly	Arg	Ser	Ala	Asp	Leu	Glu	Leu
1385						1390					1395			
Glu	Arg	Ala	Ala	Asp	Val	Lys	Trp	Glu	Asp	Gln	Ala	Glu	Ile	Ser
1400						1405					1410			
Gly	Ser	Ser	Pro	Ile	Leu	Ser	Ile	Thr	Ile	Ser	Glu	Asp	Gly	Ser
1415						1420					1425			
Met	Ser	Ile	Lys	Asn	Glu	Glu	Glu	Asp	Gln	Thr	Leu	Thr	Ile	Leu
1430						1435					1440			
Ile	Arg	Thr	Gly	Leu	Leu	Val	Ile	Ser	Gly	Leu	Phe	Pro	Val	Ser
1445						1450					1455			
Ile	Pro	Ile	Thr	Ala	Ala	Ala	Trp	Tyr	Leu	Trp	Glu	Val	Lys	Lys
1460						1465					1470			
Gln	Arg	Ala	Gly	Val	Leu	Trp	Asp	Val	Pro	Ser	Pro	Pro	Pro	Met
1475						1480					1485			
Gly	Lys	Ala	Glu	Leu	Glu	Asp	Gly	Ala	Tyr	Arg	Ile	Lys	Gln	Lys
1490						1495					1500			
Gly	Ile	Leu	Gly	Tyr	Ser	Gln	Ile	Gly	Ala	Gly	Val	Tyr	Lys	Glu
1505						1510					1515			
Gly	Thr	Phe	His	Thr	Met	Trp	His	Val	Thr	Arg	Gly	Ala	Val	Leu
1520						1525					1530			

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Met	His	Lys	Gly	Lys	Arg	Ile	Glu	Pro	Ser	Trp	Ala	Asp	Val	Lys
	1535					1540					1545			
Lys	Asp	Leu	Ile	Ser	Tyr	Gly	Gly	Gly	Trp	Lys	Leu	Glu	Gly	Glu
	1550					1555					1560			
Trp	Lys	Glu	Gly	Glu	Glu	Val	Gln	Val	Leu	Ala	Leu	Glu	Pro	Gly
	1565					1570					1575			
Lys	Asn	Pro	Arg	Ala	Val	Gln	Thr	Lys	Pro	Gly	Leu	Phe	Lys	Thr
	1580					1585					1590			
Asn	Ala	Gly	Thr	Ile	Gly	Ala	Val	Ser	Leu	Asp	Phe	Ser	Pro	Gly
	1595					1600					1605			
Thr	Ser	Gly	Ser	Pro	Ile	Ile	Asp	Lys	Lys	Gly	Lys	Val	Val	Gly
	1610					1615					1620			
Leu	Tyr	Gly	Asn	Gly	Val	Val	Thr	Arg	Ser	Gly	Ala	Tyr	Val	Ser
	1625					1630					1635			
Ala	Ile	Ala	Gln	Thr	Glu	Lys	Ser	Ile	Glu	Asp	Asn	Pro	Glu	Ile
	1640					1645					1650			
Glu	Asp	Asp	Ile	Phe	Arg	Lys	Arg	Arg	Leu	Thr	Ile	Met	Asp	Leu
	1655					1660					1665			
His	Pro	Gly	Ala	Gly	Lys	Thr	Lys	Arg	Tyr	Leu	Pro	Ala	Ile	Val
	1670					1675					1680			
Arg	Glu	Ala	Ile	Lys	Arg	Gly	Leu	Arg	Thr	Leu	Ile	Leu	Ala	Pro
	1685					1690					1695			
Thr	Arg	Val	Val	Ala	Ala	Glu	Met	Glu	Glu	Ala	Leu	Arg	Gly	Leu
	1700					1705					1710			
Pro	Ile	Arg	Tyr	Gln	Thr	Pro	Ala	Ile	Arg	Ala	Val	His	Thr	Gly
	1715					1720					1725			
Arg	Glu	Ile	Val	Asp	Leu	Met	Cys	His	Ala	Thr	Phe	Thr	Met	Arg
	1730					1735					1740			
Leu	Leu	Ser	Pro	Val	Arg	Val	Pro	Asn	Tyr	Asn	Leu	Ile	Ile	Met
	1745					1750					1755			
Asp	Glu	Ala	His	Phe	Thr	Asp	Pro	Ala	Ser	Ile	Ala	Ala	Arg	Gly
	1760					1765					1770			
Tyr	Ile	Ser	Thr	Arg	Val	Glu	Met	Gly	Glu	Ala	Ala	Gly	Ile	Phe
	1775					1780					1785			

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Met	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Arg	Asp	Pro	Phe	Pro	Gln	Ser
1790						1795					1800			
Asn	Ala	Pro	Ile	Ile	Asp	Glu	Glu	Arg	Glu	Ile	Pro	Glu	Arg	Ser
1805						1810					1815			
Trp	Asn	Ser	Gly	His	Glu	Trp	Val	Thr	Asp	Phe	Lys	Gly	Lys	Thr
1820						1825					1830			
Val	Trp	Phe	Val	Pro	Ser	Ile	Lys	Ala	Gly	Asn	Asp	Ile	Ala	Ala
1835						1840					1845			
Cys	Leu	Arg	Lys	Asn	Gly	Lys	Lys	Val	Ile	Gln	Leu	Ser	Arg	Lys
1850						1855					1860			
Thr	Phe	Asp	Ser	Glu	Tyr	Val	Lys	Thr	Arg	Thr	Asn	Asp	Trp	Asp
1865						1870					1875			
Phe	Val	Val	Thr	Thr	Asp	Ile	Ser	Glu	Met	Gly	Ala	Asn	Phe	Lys
1880						1885					1890			
Ala	Glu	Arg	Val	Ile	Asp	Pro	Arg	Arg	Cys	Met	Lys	Pro	Val	Ile
1895						1900					1905			
Leu	Thr	Asp	Gly	Glu	Glu	Arg	Val	Ile	Leu	Ala	Gly	Pro	Met	Pro
1910						1915					1920			
Val	Thr	His	Ser	Ser	Ala	Ala	Gln	Arg	Arg	Gly	Arg	Ile	Gly	Arg
1925						1930					1935			
Asn	Pro	Lys	Asn	Glu	Asn	Asp	Gln	Tyr	Ile	Tyr	Met	Gly	Glu	Pro
1940						1945					1950			
Leu	Glu	Asn	Asp	Glu	Asp	Cys	Ala	His	Trp	Lys	Glu	Ala	Lys	Met
1955						1960					1965			
Leu	Leu	Asp	Asn	Ile	Asn	Thr	Pro	Glu	Gly	Ile	Ile	Pro	Ser	Met
1970						1975					1980			
Phe	Glu	Pro	Glu	Arg	Glu	Lys	Val	Asp	Ala	Ile	Asp	Gly	Glu	Tyr
1985						1990					1995			
Arg	Leu	Arg	Gly	Glu	Ala	Arg	Lys	Thr	Phe	Val	Asp	Leu	Met	Arg
2000						2005					2010			
Arg	Gly	Asp	Leu	Pro	Val	Trp	Leu	Ala	Tyr	Arg	Val	Ala	Ala	Glu
2015						2020					2025			
Gly	Ile	Asn	Tyr	Ala	Asp	Arg	Arg	Trp	Cys	Phe	Asp	Gly	Val	Lys
2030						2035					2040			

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Asn 2045	Asn	Gln	Ile	Leu	Glu	Glu 2050	Asn	Val	Glu	Val	Glu 2055	Ile	Trp	Thr
Lys	Glu 2060	Gly	Glu	Arg	Lys	Lys 2065	Leu	Lys	Pro	Arg	Trp 2070	Leu	Asp	Ala
Arg	Ile 2075	Tyr	Ser	Asp	Pro	Leu 2080	Ala	Leu	Lys	Glu	Phe 2085	Lys	Glu	Phe
Ala	Ala 2090	Gly	Arg	Lys	Ser	Leu 2095	Thr	Leu	Asn	Leu	Ile 2100	Thr	Glu	Met
Gly	Arg 2105	Leu	Pro	Thr	Phe	Met 2110	Thr	Gln	Lys	Ala	Arg 2115	Asp	Ala	Leu
Asp	Asn 2120	Leu	Ala	Val	Leu	His 2125	Thr	Ala	Glu	Ala	Gly 2130	Gly	Arg	Ala
Tyr	Asn 2135	His	Ala	Leu	Ser	Glu 2140	Leu	Pro	Glu	Thr	Leu 2145	Glu	Thr	Leu
Leu	Leu 2150	Leu	Thr	Leu	Leu	Ala 2155	Thr	Val	Thr	Gly	Gly 2160	Ile	Phe	Leu
Phe	Leu 2165	Met	Ser	Ala	Arg	Gly 2170	Ile	Gly	Lys	Met	Thr 2175	Leu	Gly	Met
Cys	Cys 2180	Ile	Ile	Thr	Ala	Ser 2185	Ile	Leu	Leu	Trp	Tyr 2190	Ala	Gln	Ile
Gln	Pro 2195	His	Trp	Ile	Ala	Ala 2200	Ser	Ile	Ile	Leu	Glu 2205	Phe	Phe	Leu
Ile	Val 2210	Leu	Leu	Ile	Pro	Glu 2215	Pro	Glu	Lys	Gln	Arg 2220	Thr	Pro	Gln
Asp	Asn 2225	Gln	Leu	Thr	Tyr	Val 2230	Val	Ile	Ala	Ile	Leu 2235	Thr	Val	Val
Ala	Ala 2240	Thr	Met	Ala	Asn	Glu 2245	Met	Gly	Phe	Leu	Glu 2250	Lys	Thr	Lys
Lys	Asp 2255	Leu	Gly	Leu	Gly	Ser 2260	Ile	Ala	Thr	Gln	Gln 2265	Pro	Glu	Ser
Asn	Ile 2270	Leu	Asp	Ile	Asp	Leu 2275	Arg	Pro	Ala	Ser	Ala 2280	Trp	Thr	Leu
Tyr	Ala 2285	Val	Ala	Thr	Thr	Phe 2290	Val	Thr	Pro	Met	Leu 2295	Arg	His	Ser

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Ile	Glu	Asn	Ser	Ser	Val	Asn	Val	Ser	Leu	Thr	Ala	Ile	Ala	Asn
	2300					2305					2310			
Gln	Ala	Thr	Val	Leu	Met	Gly	Leu	Gly	Lys	Gly	Trp	Pro	Leu	Ser
	2315					2320					2325			
Lys	Met	Asp	Ile	Gly	Val	Pro	Leu	Leu	Ala	Ile	Gly	Cys	Tyr	Ser
	2330					2335					2340			
Gln	Val	Asn	Pro	Ile	Thr	Leu	Ile	Ala	Ala	Leu	Phe	Leu	Leu	Val
	2345					2350					2355			
Ala	His	Tyr	Ala	Ile	Ile	Gly	Pro	Gly	Leu	Gln	Ala	Lys	Ala	Thr
	2360					2365					2370			
Arg	Glu	Ala	Gln	Lys	Arg	Ala	Ala	Ala	Gly	Ile	Met	Lys	Asn	Pro
	2375					2380					2385			
Thr	Val	Asp	Gly	Ile	Thr	Val	Ile	Asp	Leu	Asp	Pro	Ile	Pro	Tyr
	2390					2395					2400			
Asp	Pro	Lys	Phe	Glu	Lys	Gln	Leu	Gly	Gln	Val	Met	Leu	Leu	Val
	2405					2410					2415			
Leu	Cys	Val	Thr	Gln	Val	Leu	Met	Met	Arg	Thr	Thr	Trp	Ala	Leu
	2420					2425					2430			
Cys	Glu	Ala	Leu	Thr	Leu	Ala	Thr	Gly	Pro	Ile	Ser	Thr	Leu	Trp
	2435					2440					2445			
Glu	Gly	Asn	Pro	Gly	Arg	Phe	Trp	Asn	Thr	Thr	Ile	Ala	Val	Ser
	2450					2455					2460			
Met	Ala	Asn	Ile	Phe	Arg	Gly	Ser	Tyr	Leu	Ala	Gly	Ala	Gly	Leu
	2465					2470					2475			
Leu	Phe	Ser	Ile	Met	Lys	Asn	Thr	Thr	Asn	Thr	Arg	Arg	Gly	Thr
	2480					2485					2490			
Gly	Asn	Ile	Gly	Glu	Thr	Leu	Gly	Glu	Lys	Trp	Lys	Ser	Arg	Leu
	2495					2500					2505			
Asn	Ala	Leu	Gly	Lys	Ser	Glu	Phe	Gln	Ile	Tyr	Lys	Lys	Ser	Gly
	2510					2515					2520			
Ile	Gln	Glu	Val	Asp	Arg	Thr	Leu	Ala	Lys	Glu	Gly	Ile	Lys	Arg
	2525					2530					2535			
Gly	Glu	Thr	Asp	His	His	Ala	Val	Ser	Arg	Gly	Ser	Ala	Lys	Leu
	2540					2545					2550			

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Arg	Trp	Phe	Val	Glu	Arg	Asn	Met	Val	Thr	Pro	Glu	Gly	Lys	Val
2555						2560					2565			
Val	Asp	Leu	Gly	Cys	Gly	Arg	Gly	Gly	Trp	Ser	Tyr	Tyr	Cys	Gly
2570						2575					2580			
Gly	Leu	Lys	Asn	Val	Arg	Glu	Val	Lys	Gly	Leu	Thr	Lys	Gly	Gly
2585						2590					2595			
Pro	Gly	His	Glu	Glu	Pro	Ile	Pro	Met	Ser	Thr	Tyr	Gly	Trp	Asn
2600						2605					2610			
Leu	Val	Arg	Leu	Gln	Ser	Gly	Val	Asp	Val	Phe	Phe	Ile	Pro	Pro
2615						2620					2625			
Glu	Lys	Cys	Asp	Thr	Leu	Leu	Cys	Asp	Ile	Gly	Glu	Ser	Ser	Pro
2630						2635					2640			
Asn	Pro	Thr	Val	Glu	Ala	Gly	Arg	Thr	Leu	Arg	Val	Leu	Asn	Leu
2645						2650					2655			
Val	Glu	Asn	Trp	Leu	Asn	Asn	Asn	Thr	Gln	Phe	Cys	Ile	Lys	Val
2660						2665					2670			
Leu	Asn	Pro	Tyr	Met	Pro	Ser	Val	Ile	Glu	Lys	Met	Glu	Ala	Leu
2675						2680					2685			
Gln	Arg	Lys	Tyr	Gly	Gly	Ala	Leu	Val	Arg	Asn	Pro	Leu	Ser	Arg
2690						2695					2700			
Asn	Ser	Thr	His	Glu	Met	Tyr	Trp	Val	Ser	Asn	Ala	Ser	Gly	Asn
2705						2710					2715			
Ile	Val	Ser	Ser	Val	Asn	Met	Ile	Ser	Arg	Met	Leu	Ile	Asn	Arg
2720						2725					2730			
Phe	Thr	Met	Arg	Tyr	Lys	Lys	Ala	Thr	Tyr	Glu	Pro	Asp	Val	Asp
2735						2740					2745			
Leu	Gly	Ser	Gly	Thr	Arg	Asn	Ile	Gly	Ile	Glu	Ser	Glu	Ile	Pro
2750						2755					2760			
Asn	Leu	Asp	Ile	Ile	Gly	Lys	Arg	Ile	Glu	Lys	Ile	Lys	Gln	Glu
2765						2770					2775			
His	Glu	Thr	Ser	Trp	His	Tyr	Asp	Gln	Asp	His	Pro	Tyr	Lys	Thr
2780						2785					2790			
Trp	Ala	Tyr	His	Gly	Ser	Tyr	Glu	Thr	Lys	Gln	Thr	Gly	Ser	Ala
2795						2800					2805			

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 Ser Ser Met Val Asn Gly Val Val Arg Leu Leu Thr Lys Pro Trp
 2810 2815 2820

Asp Val Val Pro Met Val Thr Gln Met Ala Met Thr Asp Thr Thr
 2825 2830 2835

Pro Phe Gly Gln Gln Arg Val Phe Lys Glu Lys Val Asp Thr Arg
 2840 2845 2850

Thr Gln Glu Pro Lys Glu Gly Thr Lys Lys Leu Met Lys Ile Thr
 2855 2860 2865

Ala Glu Trp Leu Trp Lys Glu Leu Gly Lys Lys Lys Thr Pro Arg
 2870 2875 2880

Met Cys Thr Arg Glu Glu Phe Thr Arg Lys Val Arg Ser Asn Ala
 2885 2890 2895

Ala Leu Gly Ala Ile Phe Thr Asp Glu Asn Lys Trp Lys Ser Ala
 2900 2905 2910

Arg Glu Ala Val Glu Asp Ser Arg Phe Trp Glu Leu Val Asp Lys
 2915 2920 2925

Glu Arg Asn Leu His Leu Glu Gly Lys Cys Glu Thr Cys Val Tyr
 2930 2935 2940

Asn Met Met Gly Lys Arg Glu Lys Lys Leu Gly Glu Phe Gly Lys
 2945 2950 2955

Ala Lys Gly Ser Arg Ala Ile Trp Tyr Met Trp Leu Gly Ala Arg
 2960 2965 2970

Phe Leu Glu Phe Glu Ala Leu Gly Phe Leu Asn Glu Asp His Trp
 2975 2980 2985

Phe Ser Arg Glu Asn Ser Leu Ser Gly Val Glu Gly Glu Gly Leu
 2990 2995 3000

His Lys Leu Gly Tyr Ile Leu Arg Asp Val Ser Lys Lys Glu Gly
 3005 3010 3015

Gly Ala Met Tyr Ala Asp Asp Thr Ala Gly Trp Asp Thr Arg Ile
 3020 3025 3030

Thr Leu Glu Asp Leu Lys Asn Glu Glu Met Val Thr Asn His Met
 3035 3040 3045

Glu Gly Glu His Lys Lys Leu Ala Glu Ala Ile Phe Lys Leu Thr
 3050 3055 3060

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Tyr	Gln	Asn	Lys	Val	Val	Arg	Val	Gln	Arg	Pro	Thr	Pro	Arg	Gly
3065						3070					3075			
Thr	Val	Met	Asp	Ile	Ile	Ser	Arg	Arg	Asp	Gln	Arg	Gly	Ser	Gly
3080						3085					3090			
Gln	Val	Gly	Thr	Tyr	Gly	Leu	Asn	Thr	Phe	Thr	Asn	Met	Glu	Ala
3095						3100					3105			
Gln	Leu	Ile	Arg	Gln	Met	Glu	Gly	Glu	Gly	Val	Phe	Lys	Ser	Ile
3110						3115					3120			
Gln	His	Leu	Thr	Ile	Thr	Glu	Glu	Ile	Ala	Val	Gln	Asn	Trp	Leu
3125						3130					3135			
Ala	Arg	Val	Gly	Arg	Glu	Arg	Leu	Ser	Arg	Met	Ala	Ile	Ser	Gly
3140						3145					3150			
Asp	Asp	Cys	Val	Val	Lys	Pro	Leu	Asp	Asp	Arg	Phe	Ala	Ser	Ala
3155						3160					3165			
Leu	Thr	Ala	Leu	Asn	Asp	Met	Gly	Lys	Ile	Arg	Lys	Asp	Ile	Gln
3170						3175					3180			
Gln	Trp	Glu	Pro	Ser	Arg	Gly	Trp	Asn	Asp	Trp	Thr	Gln	Val	Pro
3185						3190					3195			
Phe	Cys	Ser	His	His	Phe	His	Glu	Leu	Ile	Met	Lys	Asp	Gly	Arg
3200						3205					3210			
Val	Leu	Val	Val	Pro	Cys	Arg	Asn	Gln	Asp	Glu	Leu	Ile	Gly	Arg
3215						3220					3225			
Ala	Arg	Ile	Ser	Gln	Gly	Ala	Gly	Trp	Ser	Leu	Arg	Glu	Thr	Ala
3230						3235					3240			
Cys	Leu	Gly	Lys	Ser	Tyr	Ala	Gln	Met	Trp	Ser	Leu	Met	Tyr	Phe
3245						3250					3255			
His	Arg	Arg	Asp	Leu	Arg	Leu	Ala	Ala	Asn	Ala	Ile	Cys	Ser	Ala
3260						3265					3270			
Val	Pro	Ser	His	Trp	Val	Pro	Thr	Ser	Arg	Thr	Thr	Trp	Ser	Ile
3275						3280					3285			
His	Ala	Lys	His	Glu	Trp	Met	Thr	Thr	Glu	Asp	Met	Leu	Thr	Val
3290						3295					3300			
Trp	Asn	Arg	Val	Trp	Ile	Gln	Glu	Asn	Pro	Trp	Met	Glu	Asp	Lys
3305						3310					3315			

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Thr	Pro	Val	Glu	Ser	Trp	Glu	Glu	Ile	Pro	Tyr	Leu	Gly	Lys	Arg
	3320					3325					3330			
Glu	Asp	Gln	Trp	Cys	Gly	Ser	Leu	Ile	Gly	Leu	Thr	Ser	Arg	Ala
	3335					3340					3345			
Thr	Trp	Ala	Lys	Asn	Ile	Gln	Ala	Ala	Ile	Asn	Gln	Val	Arg	Ser
	3350					3355					3360			
Leu	Ile	Gly	Asn	Glu	Glu	Tyr	Thr	Asp	Tyr	Met	Pro	Ser	Met	Lys
	3365					3370					3375			
Arg	Phe	Arg	Arg	Glu	Glu	Glu	Glu	Ala	Gly	Val	Leu	Trp	Lys	Ala
	3380					3385					3390			
Lys	Leu	Thr	Asn	Lys	Ala	Arg	Ser	Gln	Val	Gly	Leu	Ser	His	Ser
	3395					3400					3405			
Thr	Glu	Lys	Thr	Met	Leu	Pro	Val	Ser	Pro	Val	Gln	Gly	Arg	Lys
	3410					3415					3420			
Lys	Ser	Gly	His	His	Lys	Cys	His	Ser	Leu	Ser	Lys	Leu	Cys	Ser
	3425					3430					3435			
Leu	Leu	His	Leu	Arg	Arg	Cys	Lys	Lys	Ser	Gly	Arg	Pro	Gln	Thr
	3440					3445					3450			
Met	Glu	Ala	Val	Arg	Met	Ala	Trp	Thr	Ser	Gly				
	3455					3460								