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(54) Title: ZIKA VIRUS VACCINE

(57) Abstract: Compositions and methods useful for treating and/or preventing a Zika virus infection are provided.



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ZIKA VIRUS VACCINE

Related Applications

This application claims the benefit of priority to U.S. Provisional Application No. 62/410,165, filed October 19, 2016, the entire contents of which is hereby incorporated in its entirety.

Government Interest

This invention was made with Government support under National Institutes of Health Grant AI109740. The Government has certain rights in the invention.

Background

The ongoing Zika virus outbreak underscores a critical need for the development of candidate vaccines. Vesicular stomatitis virus (VSV), a rhabdovirus, has been successfully used as a vaccine vector, with the recent approval of a recombinant VSV-based Ebola virus vaccine (VSV-EBOV) demonstrating that such VSV based vaccines can be safe and effective. VSV grows robustly in cell culture, is not associated with disease in humans, and can be readily engineered to incorporate foreign antigens. However, to date there are no reports of the successful incorporation of functional flavivirus envelope proteins into VSV particles. Indeed, efforts to incorporate envelope proteins from the flavivirus Dengue into a VSV vector were unsuccessful (Buonocore, et.al. (2002) J. Virol. 76, 6865).

The viral envelope proteins of rhabdoviruses, such as VSV, are structurally very different from the envelope proteins of flaviviruses, such as Zika. Viral envelope proteins mediate attachment to cells and fusion between viral and cellular membranes to initiate the process of infection. Viral fusogens fall into 3 classes. The class I proteins - best exemplified by influenza HA and HIV gp160 - are trimeric, activated by cleavage of a precursor to leave an N-terminal fusion peptide and in response to specific triggers undergo conformational changes in which the fusion peptide inserts into a target membrane with subsequent refolding of the protein into the post-fusion trimer. The class II fusion proteins that are present on flaviviruses exist as dimers, have a hydrophobic fusion loop that inserts into the target membrane during conformational rearrangements of the dimer to a trimer. In the case of the class I and class II fusion proteins such conformational rearrangements are irreversible. The class III fusogens are best exemplified by VSV, here the protein exists as a trimer on the surface of the virus that can reversibly adopt pre and post fusion conformations. Fusion is accomplished by the insertion of two small hydrophobic loops into the target membrane. The

envelope proteins that have been successfully incorporated into VSV particles are predominantly class I and class III fusogens.

The presentation of the envelope proteins on the surface of flavivirus vs rhabdovirus particles is also markedly different. In immature flavivirus particles, the E protein forms a total of 60 heterodimers with prM, the precursor protein of M on the virion surface. This association prevents E from undergoing conformational changes that lead to fusion of viral and cellular membranes. As the virus matures through the trans-golgi network, prM is cleaved by the host endopeptidase, furin. In the mature flavivirus particle, the envelope proteins are arranged flat on the virion surface as a set of 90 homodimers. Under low pH conditions in the endosome upon entry into cells, the dimers of the E protein rearrange to a trimeric form. By contrast, VSV buds from the cell surface and it is at the plasma membrane where the trimers of VSV G are incorporated into viral particles. Thus both the assembly, and arrangement of the envelope proteins on the mature virions are markedly different.

The geometry of intact virus particles are also completely different. VSV has a bullet shaped geometry and is approximately 180 nm in length and 80 nm in diameter the surface of the virus is decorated by approximately 400 spikes – each corresponding to a trimer of the VSV G protein. By contrast, Zika virus particles are completely coated with 90 homodimers of the E protein and are spherical with a diameter of approximately 40 nm. Consequently, it was not known whether Zika E protein could be successfully incorporated into VSV particles, and whether such incorporated E protein would be functional.

Summary

Provided herein are methods and compositions useful in the treatment and/or prevention of a Zika virus infection. In one aspect, provided herein is a recombinant vesicular stomatitis virus (VSV) comprising in its genome a nucleic acid sequence encoding a Zika virus envelope (E) protein. In some embodiments, the recombinant VSV genome comprises the nucleic acid sequence encoding a Zika virus precursor membrane (prM) protein and/or a Zika virus capsid (C) protein. In some embodiments, the nucleic acid sequence encoding a Zika virus E protein substantially replaces the endogenous VSV viral glycoprotein (G) in the VSV genome.

In some aspects, provided herein is a recombinant VSV comprising a Zika virus envelope (E) protein or fragment thereof. In some embodiments, the recombinant VSV

further comprises a Zika virus precursor membrane (prM) protein and/or a Zika virus capsid (C) protein.

In certain aspects, provided herein is a pharmaceutical composition (*e.g.*, a Zika virus vaccine) comprising a recombinant VSV disclosed herein, and a pharmaceutically acceptable carrier. In certain embodiments, the pharmaceutical composition further comprises an adjuvant. In certain embodiments, the recombinant VSV is a live virus.

In certain aspects, provided herein is a method for inducing in a subject an immune response against Zika virus comprising administering to the subject a composition comprising a recombinant VSV disclosed herein. In some aspects, provided herein is a method for protecting a subject from Zika virus, comprising administering to the subject a recombinant VSV disclosed herein. In some aspects, provided herein is a method of treating a Zika virus infection, the method comprising administering a recombinant VSV disclosed herein, a pharmaceutical composition disclosed herein, and/or a vaccine disclosed herein, to a subject (*e.g.*, a subject in need thereof).

In certain aspects, provided herein is a nucleic acid encoding the recombinant VSV disclosed herein. In yet another aspect, provided herein is an expression vector comprising the nucleic acid encoding the recombinant VSV disclosed herein. In certain aspects, provided herein is a method of making virus-like particles (VLP) comprising infecting a cell with an expression vector disclosed herein; culturing the cell under conditions such that the cell produces a Zika virus VLP; and collecting the Zika virus VLP.

Brief Description of the Figures

Fig. 1A and Fig. 1B show exemplary schematic representations of VSV-Zika virus construction and rescue. Fig. 1A shows exemplary schematics of the VSV-Zika virus constructs containing prM-E or C-prM-E. Fig. 1B shows a schematic of an exemplary method of recombinant virus recovery following transfection.

Fig. 2A – Fig. 2D show infection of Vero cells with rVSVΔG-Zika-CprME. Fig. 2A and Fig. 2B demonstrate infection independent of VSV G. GFP was monitored as an indicator of infection

Fig. 3A – Fig. 3C show that VSVΔG-Zika recombinants express Zika E in infected cells. Fig. 3A is a gel showing metabolic labeling of viral proteins. Vero cells were infected with VSV-eGFP or rVSVΔG-Zika-prM-E at an MOI of 3. At 6 hours post infection, cells were starved in methionine-free DMEM for 30 minutes, followed by the addition of ³⁵S-

methionine for 30 minutes. Cells were lysed and analyzed by SDS-PAGE. Fig. 3B is an image of a Western blot of infected cell lysates and culture supernatants probed with a pan flavivirus antibody that reacts with ZIKV-E (4G2) or VSV-M. Fig. 3C shows the immunofluorescence of cells infected with VSV-eGFP or rVSVΔG-Zika-prM-E probed with the 4G2 antibody (red channel).

Fig. 4 show that Zika E protein is incorporated into VSV particles. A Coomassie stained SDS-PAGE of purified virus, following sedimentation through sucrose is shown. M: molecular weight markers. Lane 1: rVSVΔG-Zika-C-prM-E. Lane 2: rVSV. The Zika E band is identified.

Fig. 5 shows a plaque assay of rVSV-Zika-CprME on Vero cells. The numbers represent the dilutions of a typical virus stock which demonstrates the high titer of the stocks routinely attained.

Fig. 6 shows that Zika E protein is present together with sedimented VSV. SDS-PAGE analysis of recombinant viruses following concentration on sucrose cushions. Lane 1: rVSVΔG-Zika-CprME, Lane 2: r VSV-Zika-CprME, Lane 3: rVSV-EGFP.

Fig. 7A – Fig. 7D show the production of Zika VLPs and VSV-ZIKA-E coated particles from rVSVΔG-Zika-CprME (Fig. 7A and Fig. 7B) and rVSV-Zika-CprME (Fig. 7C and Fig. 7D). Cells were infected with the indicated recombinant VSV and the cell culture supernatants clarified by centrifugation, virus and VLPs collected by centrifugation through a sucrose cushion, resuspended in NTE and then separated by centrifugation through a linear 15-45% sucrose gradient by ultracentrifugation. Fractions were collected and analyzed by Coomassie stain (Fig. 7A and Fig. 7C) and by blotting to detect the presence of VSV M, G and Zika E proteins (Fig. 7B and Fig. 7D).

Fig. 8A – Fig. 8D show that the production of Zika VLPs and VSV-ZIKA-E coated particles from rVSVΔG-Zika-prME (Fig. 8A and Fig. 8B) and rVSV-Zika-prME (Fig. 8C and Fig. 8D). Cells were infected with the indicated recombinant VSV and the cell culture supernatants clarified by centrifugation, virus and VLPs collected by centrifugation through a sucrose cushion, resuspended in NTE and then separated by centrifugation through a linear 15-45% sucrose gradient by ultracentrifugation. Fractions were collected and analyzed by Coomassie stain (Fig. 8A and Fig. 8C) and by blotting to detect the presence of VSV M protein, and Zika E protein (Fig. 8B and Fig. 8D).

Fig. 9A and **Fig. 9B** show the electron micrographs of VLPs and VSV-Zika particles. Gradient fractions containing Zika VLPs (Fig. 9A) and VSV particles (Fig. 9B) were analyzed by negative-stain electron microscopy. Size bars are 100 nm and 500 nm respectively.

5 **Fig. 10A – Fig. 10D** show the composition and infectivity of VSV-ZIKV recombinants. Fig. 10A is a schematic diagram of recombinant VSV-ZIKV genomes. The VSV genes encoding N – nucleocapsid, P – phospho, M – matrix, G – glyco, L - large polymerase and the eGFP – enhanced green fluorescent protein reporter are shown flanked by the viral Le – leader and Tr – trailer regulatory sequences. The ZIKV precursor
10 membrane envelope (prME) together with the signal peptide portion of the capsid protein (C) are shown together with their position of insertion. Viral titers determined by plaque assay on Vero cells for viruses encoding VSV G are expressed as plaque forming units per milliliter (pfu ml⁻¹) and representative images shown. For viruses lacking VSV, G titers were determined by flow cytometry detection of the eGFP reporter and are expressed as infectious
15 florescence units per milliliter (ifu ml⁻¹) and representative images shown at 40X magnification. Fig. 10B is an image of an SDS-PAGE gel showing protein composition of purified virions. Equivalent protein amounts of VSV-eGFP, the VSV-ZIKV recombinants and wild type ZIKV (strain: MR766) were analyzed by SDS-PAGE and proteins visualized by Coomassie staining. The VSV N, P, M, G and L and the ZIKV E proteins are identified at
20 the side of this representative gel. Fig. 10C is an image of a Western blot showing glycoprotein composition of purified virions. VSV G and ZIKV E were detected by Western blot using antibodies that recognize the cytoplasmic tail of VSV G or flavivirus envelope proteins (4G2) respectively, together with VSV-M as control for virion composition. A 10X exposure of the 4G2 Western blot is also shown to visualize the relatively low levels of E
25 incorporated. Fig. 10D shows exemplary structural properties of purified viral particles. Sucrose gradient purified virions were visualized by negative stain (2% phosphotungstic acid) electron microscopy. Scale bar = 200 nm.

Fig. 11A and **Fig. 11B** show that VSV-ZIKV vectors express ZIKV E protein in infected cells. Fig. 11A is an image of an SDS-PAGE gel showing total protein synthesis in
30 infected cells. Vero cells were infected (MOI=3) with the indicated VSV recombinant and protein synthesis measured by metabolic incorporation of [³⁵S]-methionine from 5-6 h post infection. Protein synthesis in MR766 infected cells (MOI=10) was measured by metabolic

labeling for 1h at 40h post infection. Total cytoplasmic extracts were prepared, equivalent amounts analyzed by SDS-PAGE and proteins detected by phosphoimage analysis. The VSV proteins, together with the eGFP reporter are identified on the left side of the gel, and ZIKV E on the right. Fig. 11B shows the detection of viral proteins by immunofluorescence microscopy. Vero cells were infected as in Fig. 11A, fixed at 6h post infection (VSV recombinants) or 48h post infection (MR766) prior to protein detection using primary antibodies 4G2 for Zika E or IE2 for VSV G. Primary antibodies were detected using Alexa fluor 594 Goat α -mouse secondary antibody and images false colored red for Zika E and green for VSV G. Nuclei (blue) were visualized by NucBlue™.

Fig. 12 shows that the Zika envelope is functional on VSV particles. Immunofluorescence or eGFP epifluorescence of Vero cells infected with the indicated virus. Where indicated, viruses were pre-incubated for 30 minutes at 34°C with 0.1 mg ml⁻¹ of the VSV G neutralizing monoclonal antibody (IE2). Cells were fixed, permeabilized and Zika virus envelope detected using the flavivirus antibody (4G2) and a secondary Alexa fluor 594 Goat α -mouse at 6h p.i. for VSV recombinants and at 48h p.i. for ZIKV MR766 strain.

Fig. 13A – Fig. 13E show data regarding the purification of VSV-ZIKV and Zika VLPs. Fig. 13A is a schematic illustrating purification of VSV-Zika and Virus Like Particles (VLPs) from cell culture supernatants. Cell culture supernatants are collected and virions and VLPs recovered by centrifugation followed by sedimentation through a sucrose cushion and subsequent separation on a 15-45% sucrose gradient. Fractions (0.5 ml) were collected from the sucrose gradient and their protein constituents analyzed by SDS-PAGE or Western Blots (Fig. 13B – Fig. 13E). Each of the fractions were resolved on a 10% low bis gel and stained by Coomassie (top panels) or proteins detected using 4G2 antibody (Zika E), VSV-G tail antibody or VSV-M antibody. Fractions are shown on gels going from top (left) to bottom (right). Fig. 13B VSV- Δ G-prME, Fig. 13C VSV- Δ G-CprME, Fig. 13D VSV-prME and Fig. 13E VSV-CprME.

Fig. 14A – Fig. 14E show properties of Zika VLPs produced by VSV-prME and VSV-CprME infections. Fig. 14A shows the image of a Western blot after VLPs were collected from cell culture supernatants by precipitation using polyethylene glycol, resuspended and separated on a 15-45% sucrose gradient and the fractions analyzed by SDS-PAGE and probed by western blot for ZIKV E using the 4G2 antibody. Fig. 14B shows the

detection of the E protein in VSV-ΔG-CprME virions, VLPs from VSV-CprME and purified wt ZIKV MR766 virus using the ZIKV Mab (ZV-54). Fig. 14C and Fig. 14D show negative stain electron micrographs of purified VLPs. stained with 0.5% uranyl formate obtained from the VLP fractions of VSV-prME (Fig. 14C) or VSV-CprME (Fig. 14D) scale bars represent 100 nm. Fig. 14 E is a graph showing diameters (nm) of VLPs produced by VSV-prME (prME) and VSV-CprME (CprME).

Fig. 15A – Fig. 15C show that VSV-Zika are immunogenic in BALB/c mice. Fig. 15A is a schematic showing the immunization schedule for BALB/c mice (n=5 /group). Fig. 15B is a plot showing results of ELISA assay for E-specific antibody present in animals immunized with the indicated immunogen. Fig. 15C is plot showing Sera from the mice inoculated with the indicated immunogens was used to test the ability to neutralize the MR766 strain of Zika (n=3). Dilutions of serum that protect Vero cells from 100 TCID₅₀ of ZIKV MR766 virus infection are shown.

Detailed Description

In certain aspects, provided herein are methods and compositions related to the treatment and/or prevention of a Zika virus infection. In some embodiments, disclosed herein are recombinant vesicular stomatis viruses (VSV), proteins produced by these viruses (*e.g.*, variant polypeptides and fragments thereof), nucleic acids encoding the viruses, expression vectors comprising these nucleic acids, methods of making virus like particles from the recombinant VSV or nucleic acids encoding them, and methods for the use of recombinant VSV in various applications, such as methods for treating and/or vaccinating against a number of conditions including, but not limited to, Zika virus infections. While in no way intended to be limiting, exemplary recombinant VSV and methods for making and using any of the foregoing are described below.

Recombinant Vesicular Stomatis viruses

In certain aspects, provided herein are recombinant vesicular stomatis viruses (VSV). An exemplary nucleic acid sequence for a wild type VSV is as follows (SEQ ID NO: 1):

SEQ ID NO: 1	ACGAAGACAAACAAACCATTATTATCATTTAAAAGGCTCAGGAGAACTTTAACAGTAATCAAA ATGTCCTGTACAGTCAAGAGAATCATTTGACAACACAGTCATAGTTCCAAAACCTTCCTGCAAAT GAGGATCCAGTGGAAATACCCGGCAGATTACTTCAGAAAATCAAAGGAGATTCTCTTTACATC AATACTACAAAAAGTTTGTGATCTAAGAGGATATGTCTACCAAGGCCTCAAATCCGGAAAT GTATCAATCATACATGTCAACAGCTACTTGTATGGAGCATTAAGGACATCCGGGGTAAGTTG
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GATAAAGATTGGTCAAGTTTCGGAATAAACATCGGGAAAGCAGGGGATACAATCGGAATATTT GACCTTGTATCCTTGAAAGCCCTGGACGGCGTACTTCCAGATGGAGTATCGGATGCTTCCAGA ACCAGCGCAGATGACAAATGGTTGCCTTTGTATCTACTTGGCTTATACAGAGTGGGCAGAACA CAAATGCCTGAATACAGAAAAAGCTCATGGATGGGCTGACAAATCAATGCAAAATGATCAAT GAACAGTTTGAACCTCTTGTGCCAGAAGGTCGTGACATTTTTTGATGTGTGGGGAAATGACAGT AATTACACAAAAATTGTCGCTGCAGTGGACATGTTCTTCCACATGTTCAAAAAACATGAATGT GCCTCGTTCAGATACGGAACCTATTGTTTCCAGATTCAAAGATTGTGCTGCATTGGCAACATTT GGACACCTCTGCAAAATAACCGGAATGTCTACAGAAGATGTAACGACCTGGATCTTGAACCGA GAAGTTGCAGATGAAATGGTCCAAATGATGCTTCCAGGCCAAGAAATTGACAAGGCCGATTCA TACATGCCTTATTTGATCGACTTTGGATTGTCTTCTAAGTCTCCATATTCTTCCGTCAAAAAC CCTGCCTTCCACTTCTGGGGGCAATTGACAGCTCTTCTGCTCAGATCCACCAGAGCAAGGAAT GCCCCGACAGCCTGATGACATTGAGTATACATCTCTTACTACAGCAGGTTTGTGTACGCTTAT GCAGTAGGATCCTCTGCCGACTTGGCACAACAGTTTTGTGTTGGAGATAACAAATACACTCCA GATGATAGTACCGGAGGATTGACGACTAATGCACCGCCACAAGGCAGAGATGTGGTCAATGG CTCGGATGGTTTGAAGATCAAAACAGAAAACCGACTCCTGATATGATGCAGTATGCGAAAAGA GCAGTCATGTCACTGCAAGGCCTAAGAGAGAAGACAATTGGCAAGTATGCTAAGTCAGAAATTT GACAAATGACCTTATAATTCTCAGATCACCTATTATATATTATGCTACATATGAAAAAACTA ACAGATATCATGGATAATCTCACAAAAGTTCGTGAGTATCTCAAGTCCTATTCTCGTCTGGAT CAGGCGGTAGGAGAGATAGATGAGATCGAAGCACAAACGAGCTGAAAAGTCCAATTATGAGTTG TTCCAAGAGGATGGAGTGGAAGAGCATACTAAGCCCTCTTATTTTCAGGCAGCAGATGATTCT GACACAGAATCTGAACCAGAAATTGAAGACAATCAAGGTTTGTATGCACAGGATCCAGAAGCT GAGCAAGTTGAAGGCTTTATACAGGGGCCCTTTAGATGACTATGCAGATGAGGAAGTGGATGTT GTATTTACTTCGGACTGGAAACCACCTGAGCTTGAATCTGACGAGCATGGAAAGACCTTACGG TTGACATCGCCAGAGGGTTTAAGTGGAGAGCAGAAATCCCAGTGGCTTTTCGACGATTAAAGCA GTCGTGCAAAGTGCCAAATACTGGAATCTGGCAGAGTGCACATTTGAAGCATCGGGAGAAGGG GTCATTATGAAGGAGCGCCAGATAACTCCGGATGTATATAAGGTCCTCCAGTGATGAACACA CATCCGTCCCAATCAGAAGCAGTATCAGATGTTTGGTCTCTCTCAAAGACATCCATGACTTTC CAACCCAGAAAGCAAGTCTTCAGCCTCTCACCATATCCTTGGATGAATTGTTCTCATCTAGA GGAGAGTTCATCTCTGTGCGGAGGTGACGGACGAATGTCTCATAAAGAGGCCATCCTGCTCGGC CTGAGATACAAAAAGTTGTACAATCAGGCGAGAGTCAAATATTCTCTGTAGACTATGAAAAA AGTAACAGATATCACGATCTAAGTGTATCCCAATCCATTCATCATGAGTTCCTTAAAGAAGA TTCTCGGTCTGAAGGGGAAAGGTAAGAAATCTAAGAAATTAGGGATCGCACCACCCCTTATG AAGAGGACACTAGCATGGAGTATGCTCCGAGCGCTCCAATTGACAAATCCTATTTTGGAGTTG ACGAGATGGACACCTATGATCCGAATCAATTAAGATATGAGAAATTCTTCTTTACAGTGAAAA TGACGGTTAGATCTAATCGTCCGTTTCAAGACATACTCAGATGTGGCAGCCGCTGTATCCCATT GGGATCACATGTACATCGGAATGGCAGGGAAACGTCCCTTCTACAAAATCTTGGCTTTTTTGG GTTCTTCTAATCTAAAGGCCACTCCAGCGGTATTGGCAGATCAAGGTCAACCAGAGTATCACA CTCACTGCGAAGGCAGGGCTTATTTGCCACATAGGATGGGGAAGACCCCTCCCATGCTCAATG TACCAGAGCACTTCAGAAGACCATTCAATATAGGTCTTTACAAGGGAACGATTGAGCTCACAA
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TGACCATCTACGATGATGAGTCACTGGAAGCAGCTCCTATGATCTGGGATCATTTCAATTCTT CCAAATTTTCTGATTTCAAGAGAGAAGGCCTTAATGTTTGGCCTGATTGTGCGAGAAAAAGGCAT CTGGAGCGTGGGTCTTGGATTCTATCAGCCACTTCAAATGAGCTAGTCTAACTTCTAGCTTCT GAACAATCCCCGGTTTACTCAGTCTCTCCTAATTCAGCCTCTCGAACAATAATATCCTGTC TTTTCTATCCCTATGAAAAAACTAACAGAGATCGATCTGTTTCCTTGACACTATGAAGTGCC TTTTGTACTTAGCCTTTTATTCATTGGGGTGAATTGCAAGTTCACCATAGTTTTTCCACACA ACCAAAAAGGAACTGGAAAAATGTTCTTCTAATTACCATTATTGCCCGTCAAGCTCAGATT TAAATTGGCATAATGACTTAATAGGCACAGCCATACAAGTCAAATGCCCAAGAGTCACAAGG CTATTC AAGCAGACGGTTGGATGTGTCTGCTTCCAAATGGGTCACTACTTGTGATTTCCGCT GGTATGGACCGAAGTATATAACACAGTCCATCCGATCCTTCACTCCATCTGTAGAACAATGCA AGGAAAGCATTGAACAAACGAAACAAGGAACTTGGCTGAATCCAGGCTTCCCTCCTCAAAGTT GTGGATATGCAACTGTGACGGATGCCGAAGCAGTGATTGTCCAGGTGACTCCTCACCATGTGC TGGTTGATGAATACACAGGAGAATGGGTTGATTACAGTTCATCAACGGAAAATGCAGCAATT ACATATGCCCCACTGTCCATAACTCTACAACCTGGCATTCTGACTATAAGGTCAAAGGGCTAT GTGATTCTAACCTCATTTCCATGGACATCACCTTCTTCTCAGAGGACGGAGAGCTATCATCCC TGGGAAAAGGAGGGCACAGGGTTT CAGAAGTAACTACTTTGCTTATGAACTGGAGGCAAGGCCT GCAAAATGCAATACTGCAAGCATTGGGGAGTCAGACTCCCATCAGGTGTCTGGTTCGAGATGG CTGATAAGGATCTCTTTGCTGCAGCCAGATTCCCTGAATGCCCAGAAGGGTCAAGTATCTCTG CTCCATCTCAGACCTCAGTGGATGTAAGTCTAATT CAGGACGTTGAGAGGATCTTGGATTATT CCCTCTGCCAAGAAACCTGGAGCAAAATCAGAGCGGGTCTTCCAATCTCTCCAGTGGATCTCA GCTATCTTGCTCCTAAAAACCCAGGAACCGGTCTGCTTTCACCATAATCAATGGTACCCTAA AATACTTTGAGACCAGATACATCAGAGTCGATATTGCTGCTCCAATCCTCTCAAGAATGGTCG GAATGATCAGTGGAACCTACCACAGAAAGGGAACGTGGGGATGACTGGGCACCATATGAAGACG TGGAAATTGGACCCAATGGAGTTCTGAGGACCAGTTCAGGATATAAGTTTCTTTTATACATGA TTGGACATGGTATGTTGGACTCCGATCTTCATCTTAGCTCAAAGGCTCAGGTGTTTGAACATC CTCACATTCAAGACGCTGCTTCGCAACTTCCTGATGATGAGAGTTTATTTTTTGGTGATACTG GGCTATCCAAAAATCCAATCGAGCTTGTAGAAGGTTGGTTCAGTAGTTGGAAAAGCTCTATTG CCTCTTTTTTCTTTATCATAGGGTTAATCATTGGACTATTCTTGGTTCTCCGAGTTGGTATCC ATCTTTGCATTAAATTAAAGCACACCAAGAAAAGACAGATTTATACAGACATAGAGATGAACC GACTTGGAAAGTAACTCAAATCCTGCACAACAGATTCTTCATGTTTGGACCAAATCAACTTGT GATACCATGCTCAAAGAGGCCTCAATTATATTTGAGTTTTTAAATTTTTATGAAAAAACTAAC AGCAATCATGGAAGTCCACGATTTTGAGACCGACGAGTTCAATGATTTCAATGAAGATGACTA TGCCACAAGAGAATTCCTGAATCCCGATGAGCGCATGACGTACTTGAATCATGCTGATTACAA TTTGAATTCTCCTCTAATTAGTGATGATATTGACAATTTGATCAGGAAATTCAATTCTCTTCC GATTCCCTCGATGTGGGATAGTAAGAACTGGGATGGAGTTCTTGAGATGTTAACATCATGTCA AGCCAATCCCATCTCAACATCTCAGATGCATAAATGGATGGGAAGTTGGTTAATGTCTGATAA TCATGATGCCAGTCAAGGGTATAGTTTTTTTACATGAAGTGGACAAAGAGGCAGAAATAACATT TGACGTGGTGGAGACCTTCATCCGCGGTGGGGCAACAAACCAATTGAATACATCAAAAAGGA AAGATGGACTGACTCATTCAAAATTCTCGCTTATTTGTGTCAAAGTTTTTGGACTTACACAA
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GTTGACATTAATCTTAAATGCTGTCTCTGAGGTGGAATTGCTCAACTTGGCGAGGACTTTCAA AGGCCAAAGTCAGAAGAAGTTCTCATGGAACGAACATATGCAGGATTAGGGTTCCCAGCTTGGG TCCTACTTTTATTTTTCAGAAGGATGGGCTTACTTCAAGAACTTGATATTTCTAATGGACCGAAA CTTTCTGTTAATGGTCAAAGATGTGATTATAGGGAGGATGCAAACGGTGCTATCCATGGTATG TAGAATAGACAACCTGTTCTCAGAGCAAGACATCTTCTCCCTTCTAAATATCTACAGAATTGG AGATAAAATTGTGGAGAGGCAGGGAAATTTTTCTTATGACTTGATTAAAATGGTGGAACCGAT ATGCAACTTGAAGCTGATGAAATTAGCAAGAGAATCAAGGCCTTTAGTCCCACAATTCCTCA TTTTGAAAATCATATCAAGACTTCTGTTGATGAAGGGGCAAAAATTGACCGAGGTATAAGATT CCTCCATGATCAGATAATGAGTGTGAAAACAGTGGATCTCACACTGGTGATTTATGGATCGTT CAGACATTGGGGTCATCCTTTTATAGATTATTACACTGGACTAGAAAAATTACATTCCCAAGT AACCATGAAGAAAGATATTGATGTGTCATATGCAAAAGCACTTGCAAGTGATTTAGCTCGGAT TGTTCTATTTCAACAGTTCATGATCATAAAAAGTGGTTCGTGAATGGAGACTTGCTCCCTCA TGATCATCCCTTTAAAAGTCATGTTAAAGAAAATACATGGCCACAGCTGCTCAAGTTCAGA TTTTGGAGATAAATGGCATGAACTTCGCTGATTAAATGTTTTGAAATACCCGACTTACTAGA CCCATCGATAATATACTCTGACAAAAGTCATTCAATGAATAGGTGAGAGGTGTTGAAACATGT CCGAATGAATCCGAACACTCCTATCCCTAGTAAAAAGGTGTTGCAGACTATGTTGGACACAAA GGCTACCAATTGGAAAAGAATTTCTTAAAGAGATTGATGAGAAGGGCTTAGATGATGATGATCT AATTATTGGTCTTAAAGGAAAGGAGAGGGAACTGAAGTTGGCAGGTAGATTTTTCTCCCTAAT GTCTTGGAATTTGCGAGAATACTTTGTAATTACCGAATATTTGATAAAGACTCATTTCTGTCCT TATGTTTAAAGGCCTGACAATGGCGGACGATCTAACTGCAGTCATTAAAAAGATGTTAGATTCT CTCATCCGGCCAAGGATTGAAGTCATATGAGGCAATTTGCATAGCCAATCACATTGATTACGA AAAAATGGAATAACCACCAAAGGAAGTTATCAAACGGCCCAGTGTTCCGAGTTATGGGCCAGTT CTTAGGTTATCCATCCTTAATCGAGAGAACTCATGAATTTTTTGGAGAAAAGTCTTATATACTA CAATGGAAGACCAGACTTGATGCGTGTTCAACAACACACTGATCAATTCAACCTCCCAACG AGTTTGTTGGCAAGGACAAGAGGGTGGACTGGAAGGTCTACGGCAAAAAGGATGGACTATCCT CAATCTACTGGTTATTTCAAAGAGAGGCTAAAAATCAGAAACACTGCTGTCAAAGTCTTGGCACA AGGTGATAATCAAGTTATTTGCACACAGTATAAACGAAGAAATCGAGAAACGTTGTAGAATT ACAGGGTGCTCTCAATCAAAATGGTTTCTAATAATGAGAAAATTATGACTGCAATCAAAATAGG GACAGGGAAGTTAGGACTTTTGATAAATGACGATGAGACTATGCAATCTGCAGATTACTTGAA TTATGGAAAAATACCGATTTTCCGTGGAGTGATTAGAGGGTTAGAGACCAAGAGATGGTCACG AGTGACTTGTTGTCACCAATGACCAAATACCCACTTGTTGCTAATATAATGAGCTCAGTTTCCAC AAATGCTCTCACCGTAGCTCATTTTGCTGAGAACCCAATCAATGCCATGATACAGTACAATTA TTTTGGGACATTTGCTAGACTCTTGTTGATGATGCATGATCCTGCTCTTCGTCAATCATTGTA TGAAGTTCAAGATAAGATACCGGGCTTGACAGTTCTACTTTCAAATACGCCATGTTGTATTT GGACCTTCCATTGGAGGAGTGTCGGGCATGTCTTTGTCCAGGTTTTTGATTAGAGCCTTCCC AGATCCCGTAACAGAAAGTCTCTCATTTCTGGAGATTCATCCATGTACATGCTCGAAGTGAGCA TCTGAAGGAGATGAGTGCAGTATTTGGAAACCCCGAGATAGCCAAGTTTCGAATAACTCACAT AGACAAGCTAGTAGAAGATCCAACCTCTCTGAACATCGCTATGGGAATGAGTCCAGCGAAGTT GTTAAAGACTGAGGTTAAAAAATGCTTAATCGAATCAAGACAAACCATCAGGAACCAGGTGAT
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TAAGGATGCAACCATATATTTGTATCATGAAGAGGATCGGCTCAGAAGTTTCTTATGGTCAAT AAATCCTCTGTTCCCTAGATTTTAAAGTGAATTCAAATCAGGCACTTTTTTGGGAGTCGCAGA CGGGCTCATCAGTCTATTTCAAAATTCTCGTACTATTTCGGAACCTCTTTAAGAAAAAGTATCA TAGGGAATTGGATGATTTGATTGTGAGGAGTGAGGTATCCTCTTTGACACATTTAGGGAACT TCATTTGAGAAGGGGATCATGTAAATGTGGACATGTTTCAGCTACTCATGCTGACACATTAAG ATACAAATCCTGGGGCCGTACAGTTATTGGGACAACTGTACCCCATCCATTAGAAATGTTGGG TCCACAACATCGAAAAGAGACTCCTTGTGCACCATGTAACACATCAGGGTTCAATTATGTTTC TGTGCATTGTCCAGACGGGATCCATGACGTCTTTAGTTCACGGGGACCATTGCCTGCTTATCT AGGGTCTAAAACATCTGAATCTACATCTATTTTGCAGCCTTGGGAAAGGGAAAGCAAAGTCCC ACTGATTAAAAGAGCTACACGTCTTAGAGATGCTATCTCTTGGTTTGTGAACCCGACTCTAA ACTAGCAATGACTATACTTTCTAACATCCACTCTTTAACAGGCGAAGAATGGACCAAAGGCA GCATGGGTTCAAAAGAACAGGGTCTGCCCTTCATAGGTTTTTCGACATCTCGGATGAGCCATGG TGGGTTTCGCATCTCAGAGCACTGCAGCATTGACCAGGTTGATGGCAACTACAGACACCATGAG GGATCTGGGAGATCAGAATTTGACTTTTTTATTCCAAGCAACGTTGCTCTATGCTCAAATTAC CACCACTGTTGCAAGAGACGGATGGATCACCAGTTGTACAGATCATTATCATATTGCCTGTAA GTCCTGTTTGAGACCCATAGAAGAGATCACCTGGACTCAAGTATGGACTACACGCCCCCAGA TGTATCCCATGTGCTGAAGACATGGAGGAATGGGGAAGGTTTCGTGGGGACAAGAGATAAAACA GATCTATCCTTTAGAAGGGAATTGGAAGAATTTAGCACCTGCTGAGCAATCCTATCAAGTCGG CAGATGTATAGGTTTTCTATATGGAGACTTGGCGTATAGAAAATCTACTCATGCCGAGGACAG TTCTCTATTTCTCTATCTATACAAGTTCGTATTAGAGGTCGAGGTTTCTTAAAAGGGTTGCT AGACGGATTAATGAGAGCAAGTTGCTGCCAAGTAATACACCGGAGAAGTCTGGCTCATTTGAA GAGGCCGGCCAACGCAGTGTACGGAGGTTTGATTTACTTGATTGATAAATTGAGTGATCACC TCCATTCCCTTTCTCTTACTAGATCAGGACCTATTAGAGACGAATTAGAAACGATTCCCCACAA GATCCCAACCTCCTATCCGACAAGCAACCGTGATATGGGGTGATTGTGAGAAATTACTTCAA ATACCAATGCCGTCTAATTGAAAAGGGAAAATACAGATCACATTATTCACAATTATGGTTATT CTCAGATGTCTTATCCATAGACTTCATTGGACCATTCTCTATTTCCACCACCTCTTGCAAAT CCTATACAAGCCATTTTTATCTGGGAAAGATAAGAATGAGTTGAGAGAGCTGGCAAATCTTTC TTCATTGCTAAGATCAGGAGAGGGGTGGGAAGACATACATGTGAAATCTTCCACCAAGGACAT ATTATTGTGTCCAGAGGAAATCAGACATGCTTGCAAGTTCGGGATTGCTAAGGATAATAATAA AGACATGAGCTATCCCCCTTGGGGAAGGGAATCCAGAGGGACAATTACAACAATCCCTGTTTA TTATACGACCACCCCTTACCCAAAGATGCTAGAGATGCCTCCAAGAATCCAAAATCCCCTGCT GTCCGGAATCAGGTTGGGCAATTACCAACTGGCGCTCATTATAAAATTTCGGAGTATATTACA TGGAATGGGAATCCATTACAGGGACTTCTTGAGTTGTGGAGACGGCTCCGGAGGGATGACTGC TGCATTACTACGAGAAAAATGTGCATAGCAGAGGAATATTCAATAGTCTGTTAGAATTATCAGG GTCAGTCATGCGAGGCGCCTCTCCTGAGCCCCCAGTGCCCTAGAACTTTAGGAGGAGATAA ATCGAGATGTGTAATGGTGAAACATGTTGGGAATATCCATCTGACTTATGTGACCCAAGGAC TTGGGACTATTTCTCCGACTCAAAGCAGGCTTGGGGCTTCAAATTGATTTAATTGTAATGGA TATGGAAGTTCGGGATTCTTCTACTAGCCTGAAAATTGAGACGAATGTTAGAAATTATGTGCA CCGGATTTTGGATGAGCAAGGAGTTTTTAATCTACAAGACTTATGGAACATATATTTGTGAGAG

CGAAAAGAATGCAGTAACAATCCTTGGTCCCATGTTCAAGACGGTCGACTTAGTTCAAACAGA ATTTAGTAGTTCTCAAACGTCTGAAGTATATATGGTATGTAAAGGTTTGAAGAAATTAATCGA TGAACCCAATCCCGATTGGTCTTCCATCAATGAATCCTGGAAAAACCTGTACGCATTCCAGTC ATCAGAACAGGAATTTGCCAGAGCAAAGAAGGTTAGTACATACTTTACCTTGACAGGTATTCC CTCCCAATTCATTCTGATCCTTTTGTAAACATTGAGACTATGCTACAAATATTTCGGAGTACC CACGGGTGTGTCTCATGCGGCTGCCTTAAAATCATCTGATAGACCTGCAGATTTATTGACCAT TAGCCTTTTTTATATGGCGATTATATCGTATTATAACATCAATCATATCAGAGTAGGACCGAT ACCTCCGAACCCCCCATCAGATGGAATTGCACAAAATGTGGGGATCGCTATAACTGGTATAAG CTTTTGGCTGAGTTTGATGGAGAAAGACATTCCTACTATATCAACAGTGTTTAGCAGTTATCCA GCAATCATTCCCGATTAGGTGGGAGGCTGTTTCAGTAAAAGGAGGATACAAGCAGAAGTGGAG TACTAGAGGTGATGGGCTCCCAAAAGATACCCGAACCTTCAGACTCCTTGGCCCCAATCGGGAA CTGGATCAGATCTCTGGAATTGGTCCGAAACCAAGTTCGTCTAAATCCATTCAATGAGATCTT GTTCAATCAGCTATGTCTGACAGTGGATAATCATTTGAAATGGTCAAATTTGCGAAGAAACAC AGGAATGATTGAATGGATCAATAGACGAATTTCAAAGAAGACCGGTCTATACTGATGTTGAA GAGTGACCTACACGAGGAAAACTCTTGGAGAGATTAAAAAATCATGAGGAGACTCCAACTTT AAGTATGAAAAAACTTTGATCCTTAAGACCCCTCTTGTGGTTTTTATTTTTTATCTGGTTTTG TGGTCTTCGTGGGTCCGCATGGCATCTCCACCTCCTCGCGGTCCGACCTGGGCATCCGAAGGA GGACGTCTGCTCCACTCGGATGGCTAAGGGAGAGCTCGGATCCGGCTGCTAACAAAGCCCGAAAG GAAGCTGAGTTGGCTGCTGCCACCGCTGAGCAATAACTAGCATAACCCCTTGGGGCCTCTAAA CGGGTCTTGAGGGGTTTTTTGCTGAAAGGAGGAACTATATCCGGATCGAGATCCTCTAGAGTC GACCTGCAGGCATGCAAGCTTGTATTCTATAGTGTACCTAAATCGTATGTGTATGATACATA AGGTTATGTATTAATTGTAGCCGCGTTCTAACGACAATATGTACAAGCCTAATTGTGTAGCAT CTGGCTTACTGAAGCAGACCCTATCATCTCTCTCGTAAACTGCCGTCAGAGTCGGTTTGGTTG GACGAACCTTCTGAGTTTCTGGTAACGCCGTCCCGACCCGGAAATGGTCAGCGAACCAATCA GCAGGGTCATCGCTAGCCAGATCCTCTACGCCGACGCATCGTGGCCGGCATCACC GGCGCCA CAGGTGCGGTTGCTGGCGCTATATCGCCGACATCACCGATGGGGAAGATCGGGCTCGCCACT TCGGGCTCATGAGCGCTTGTTTTCGGCGTGGGTATGGTGGCAGGCCCGTGGCCGGGGACTGT TGGGCGCCATCTCCTTGACCATTCCTTGCGGCGGCGGTGCTCAACGGCCTCAACCTACTACT GGGCTGCTTCCTAATGCAGGAGTCGCATAAGGGAGAGCGTCAATGGTGCCTCTCAGTACAA TCTGCTCTGATGCCGCATAGTTAAGCCAGCCCCGACACCCGCCAACACCCGCTGACGCGCCCT GACGGGCTTGCTGCTCCCGGCATCCGCTTACAGACAAGCTGTGACCGTCTCCGGGAGCTGCA TGTGTCAGAGGTTTTACCGTCATCACCGAAACGCGCGAGACGAAAGGGCCTCGTGATACGCC TATTTTTATAGGTTAATGTCATGATAATAATGGTTTCTTAGACGTGAGGTGGCACTTTTCGGG GAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAAATACATTCAAATATGTATCCGCTCA TGAGACAATAACCTGATAAATGCTTCAATAATATTGAAAAAGGAAGAGTATGAGTATTCAAC ATTTCCGTGTCGCCCTTATTCCTTTTTTGCGGCATTTTGCCTTCCTGTTTTTGCTCACCCAG AAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCACGAGTGGGTTACATCGAAC TGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCCAATGATGA GCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACGCCGGGCAAGAGCAAC
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	TCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAAAAGC ATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACA CTGCGGCCAACTTACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACA ACATGGGGGATCATGTAACTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCATACCAA ACGACGAGCGTGACACCACGATGCCTGTAGCAATGGCAACAACGTTGCGCAAACCTATTAAGT GCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGGATGGAGGCGGATAAAGTTG CAGGACCACTTCTGCGCTCGGCCCTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCG GTGAGCGTGGGTCTCGCGGTATCATTCGAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCG TAGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGA TAGGTGCCTCACTGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGA TTGATTTAAAACTTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTTGATAATCTCA TGACCAAAATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCA AAGGATCTTCTTGAGATCCTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAACCAC CGCTACCAGCGGTGGTTTGTTTGCCGGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAAGT GCTTCAGCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTAGTTAGGCCACCACT TCAAGAACTCTGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTG CCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGC AGCGGTGCGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCG AACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGG ACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAA ACGCCTGGTATCTTTATAGTCCTGTGCGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGT GATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCCTTTTTACGGTTCC TGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGATA ACCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCGAGCCGAACGACCGAGCGCAGCG AGTCAGTGAGCGAGGAAGCGGAAGAGCGCCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGC CGATTTCATTAATGCAGGGGGATCTCGATCCCGCGAAATTAATACGACTCACTATAGG
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In some embodiments, the recombinant viruses further comprise in its genome a nucleic acid sequence encoding an enhanced Green Fluorescent Protein (eGFP) or fragment thereof. An exemplary nucleic acid sequence for wild type VSV with eGFP is as follows

5 (SEQ ID NO: 12):

SEQ ID NO: 12	ACGAAGACAAACAAACCATTTATTATCATTTAAAAGGCTCAGGAGAACTTTAACAGTAATCAGA ATTCTCGAGAAAGCCACCATGGTGAGCAAGGGCGAGGAGCTGTTACCGGGGTGGTGCCCATC CTGGTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGC GATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCACCGGAAGCTGCCCCGTGCC TGGCCACCCCTCGTGACCACCTGACCTACGGCGTGAGTGCTTCAGCCGCTACCCCGACCAC
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ATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCCCCAAGGCTACGTCCAGGAGCGCACCATC TTCTTCAAGGACGACGGCAACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTG GTGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAG CTGGAGTACAACACTACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATC AAGGTGAACTTCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTAC CAGCAGAACACCCCCATCGGCGACGGCCCCGTGCTGCTGCCCCACAACCACTACCTGAGCACC CAGTCCGCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTG ACCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAGTAATGGCCATATGAAAAAAC TAACAGTAATCAAAATGTCTGTTACAGTCAAGAGAATCATTGACAACACAGTCATAGTTCCAA AACTTCCTGCAAATGAGGATCCAGTGGAAATACCCGGCAGATTACTTCAGAAAATCAAAGGAGA TTCCTCTTTACATCAATACTACAAAAAGTTTGTGAGATCTAAGAGGATATGTCTACCAAGGCC TCAAATCCGGAATGTATCAATCATAACATGTCAACAGCTACTTGTATGGAGCATTAAGGACA TCCGGGGTAAGTTGGATAAAGATTGGTCAAGTTTCGGAATAAACATCGGGAAAGCAGGGGATA CAATCGGAATATTTGACCTTGTATCCTTGAAAGCCCTGGACGGCGTACTTCCAGATGGAGTAT CGGATGCTTCCAGAACCAGCGCAGATGACAAATGGTTGCCTTTGTATCTACTTGGCTTATACA GAGTGGGCAGAACACAAATGCCTGAATACAGAAAAAGCTCATGGATGGGCTGACAAATCAAT GCAAAATGATCAATGAACAGTTTGAACCTCTTGTGCCAGAAGGTCGTGACATTTTTGATGTGT GGGGAAATGACAGTAATTACACAAAAATTGTCGCTGCAGTGGACATGTTCTTCCACATGTTCA AAAACATGAATGTGCCTCGTTCAGATACGGAACATATTGTTTCCAGATTCAAAGATTGTGCTG CATTGGCAACATTTGGACACCTCTGCAAAATAACCGGAATGTCTACAGAAGATGTAACGACCT GGATCTTGAACCGAGAAGTTGCAGATGAAATGGTCCAAATGATGCTTCCAGGCCAAGAAATTG ACAAGGCCGATTTCATACATGCCTTATTTGATCGACTTTGGATTGTCTTCTAAGTCTCCATATT CTTCCGTCAAAAACCCTGCCTTCCACTTCTGGGGGCAATTGACAGCTCTTCTGCTCAGATCCA CCAGAGCAAGGAATGCCCCAGAGCCTGATGACATTGAGTATACATCTCTTACTACAGCAGGTT TGTTGTACGCTTATGCAGTAGGATCCTCTGCCGACTTGGCACAACAGTTTTGTGTTGGAGATA ACAAATACACTCCAGATGATAGTACCGGAGGATTGACGACTAATGCACCGCCACAAGGCAGAG ATGTGGTCGAATGGCTCGGATGGTTTGAAGATCAAAACAGAAAACCGACTCCTGATATGATGC AGTATGCGAAAAGAGCAGTCATGTCACTGCAAGGCCAAGAGAGAAGACAATTGGCAAGTATG CTAAGTCAGAATTTGACAAATGACCCCTATAATTCTCAGATCACCTATTATATATTATGCTACA TATGAAAAAACTAACAGATATCATGGATAATCTCACAAAAGTTTCGTGAGTATCTCAAGTCCT ATTCTCGTCTGGATCAGGCGGTAGGAGAGATAGATGAGATCGAAGCACAACGAGCTGAAAAGT CCAATTATGAGTTGTTCCAAGAGGATGGAGTGGAAGAGCATACTAAGCCCTCTTATTTTCAGG CAGCAGATGATTCTGACACAGAATCTGAACCAGAAAATTGAAGACAATCAAGGTTTGTATGCAC AGGATCCAGAAGCTGAGCAAGTTGAAGGCTTTATACAGGGGCCCTTTAGATGACTATGCAGATG AGGAAGTGGATGTTGTATTTACTTCGGACTGGAAACCACCTGAGCTTGAATCTGACGAGCATG GAAAGACCTTACGGTTGACATCGCCAGAGGGTTTAAAGTGGAGAGCAGAAATCCAGTGGCTTT CGACGATTAAAGCAGTCGTGCAAAGTGCCAAATACTGGAATCTGGCAGAGTGCACATTTGAAG CATCGGGAGAAGGGGTCAATTATGAAGGAGCGCCAGATAACTCCGGATGTATATAAGGTCCTC CAGTGATGAACACACATCCGTCCCAATCAGAAGCAGTATCAGATGTTTGGTCTCTCTCAAAGA

CATCCATGACTTTCCAACCCAAGAAAGCAAGTCTTCAGCCTCTCACCATATCCTTGGATGAAT TGTTCTCATCTAGAGGAGAGTTTCATCTCTGTCTGGAGGTGACGGACGAATGTCTCATAAAGAGG CCATCCTGCTCGGCCTGAGATACAAAAAGTTGTACAATCAGGCGAGAGTCAAATATTCTCTGT AGACTATGAAAAAAGTAACAGATATCACGATCTAAGTGTTATCCCAATCCATTCATCATGAG TTCCTTAAAGAAGATTCTCGGTCTGAAGGGGAAAGGTAAGAAATCTAAGAAATTAGGGATCGC ACCACCCCTTATGAAGAGGACACTAGCATGGAGTATGCTCCGAGCGCTCCAATTGACAAATC CTATTTTGGAGTTGACGAGATGGACACCTATGATCCGAATCAATTAAGATATGAGAAATTCCTT CTTTACAGTGAAAATGACGGTTAGATCTAATCGTCCGTTTCTAGAACATACTCAGATGTGGCAGC CGCTGTATCCCATTGGGATCACATGTACATCGGAATGGCAGGGAAACGTCCCTTCTACAAAAT CTTGGCTTTTTTGGGTTCTTCTAATCTAAAGGCCACTCCAGCGGTATTGGCAGATCAAGGTCA ACCAGAGTATCACACTCACTGCGAAGGCAGGGCTTATTTGCCACATAGGATGGGGAAGACCCC TCCCATGCTCAATGTACCAGAGCACTTCAGAAGACCATTCAATATAGGTCTTTACAAGGGAAC GATTGAGCTCACAATGACCATCTACGATGATGAGTCACTGGAAGCAGCTCCTATGATCTGGGA TCATTTCAATTCTTCCAAATTTTCTGATTTCTAGAGAGAAGGCCTTAATGTTTGGCCTGATTGT CGAGAAAAAGGCATCTGGAGCGTGGGTCTGGATTCTATCAGCCACTTCAAATGAGCTAGTCT AACTTCTAGCTTCTGAACAATCCCCGGTTTACTCAGTCTCTCCTAATTCAGCCTCTCGAACA ACTAATATCCTGTCTTTTCTATCCCTATGAAAAAACTAACAGAGATCGATCTGTTTCCTTGA CACTATGAAGTGCCTTTTGTACTTAGCCTTTTTTATTCATTGGGGTGAATTGCAAGTTCACCAT AGTTTTTCCACACAACCAAAAAGGAAACTGGAAAAATGTTCCCTTCTAATTACCATTATTGCC GTCAAGCTCAGATTTAAATTGGCATAATGACTTAATAGGCACAGCCATACAAGTCAAATGCC CAAGAGTCACAAGGCTATTCAAGCAGACGGTTGGATGTGTCTGCTTCCAAATGGGTCACTAC TTGTGATTTCCGCTGGTATGGACCGAAGTATATAACACAGTCCATCCGATCCTTCACTCCATC TGTAGAACAAATGCAAGGAAAGCATTGAACAAACGAAACAAGGAACCTGGCTGAATCCAGGCTT CCCTCCTCAAAGTTGTGGATATGCAACTGTGACGGATGCCGAAGCAGTGATTGTCCAGGTGAC TCCTCACCATGTGCTGGTTGATGAATACACAGGAGAATGGGTTGATTCACAGTTCATCAACGG AAAATGCAGCAATTACATATGCCCCACTGTCCATAACTCTACAACCTGGCATTCTGACTATAA GGTCAAAGGGCTATGTGATTCTAACCTCATTTCCATGGACATCACCTTCTTCTCAGAGGACGG AGAGCTATCATCCCTGGGAAAAGGAGGGCACAGGGTTCAGAAGTAACTACTTTGCTTATGAAAC TGGAGGCAAGGCCTGCAAAATGCAATACTGCAAGCATTGGGGAGTCAGACTCCCATCAGGTGT CTGGTTCGAGATGGCTGATAAGGATCTCTTTGCTGCAGCCAGATTCCCTGAATGCCGAGAAGG GTCAAGTATCTCTGCTCCATCTCAGACCTCAGTGGATGTAAGTCTAATTCAGGACGTTGAGAG GATCTTGGATTATTCCCTCTGCCAAGAAACCTGGAGCAAAATCAGAGCGGGTCTTCCAATCTC TCCAGTGGATCTCAGCTATCTTGCTCCTAAAAACCCAGGAACCGGTCTGCTTTCACCATAAT CAATGGTACCCTAAAAATACTTTGAGACCAGATACATCAGAGTCGATATTGCTGCTCCAATCCT CTCAAGAATGGTCGGAATGATCAGTGGAACTACCACAGAAAGGGAACGTGGGGATGACTGGGC ACCATATGAAGACGTGGAAATGGACCCAATGGAGTTCTGAGGACCAGTTCAGGATATAAGTT TCCTTTATACATGATTGGACATGGTATGTTGGACTCCGATCTTCATCTTAGCTCAAAGGCTCA GGTGTTTCGAACATCCTCACATTCAGACGCTGCTTCGCAACTTCCTGATGATGAGAGTTTATT TTTTGGTGATACTGGGCTATCCAAAAATCCAATCGAGCTTGTTAGAAGGTTGGTTCAGTAGTTG
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	GAAAAGCTCTATTGCCTCTTTTTCTTTATCATAGGGTTAATCATTGGACTATTCTTGGTTCT CCGAGTTGGTATCCATCTTGCATTAAATTAAAGCACACCAAGAAAAGACAGATTTATACAGA CATAGAGATGAACCGACTTGGAAAGTAACTCAAATCCTGCACAACAGATTCTTCATGTTTGGA CCAAATCAACTTGTGATACCATGCTCAAAGAGGCCTCAATTATATTTGAGTTTTTAATTTTTA TGAAAAAACTAACAGCAATCATGGAAGTCCACGATTTTGAGACCGACGAGTTCAATGATTTTC AATGAAGATGACTATGCCACAAGAGAATTCTGAATCCCGATGAGCGCATGACGTACTTGAAT CATGCTGATTACAATTTGAATTCTCCTCTAATTAGTGATGATATTGACAATTTGATCAGGAAA TTCAATTCTCTTCCGATTCCCTCGATGTGGGATAGTAAGAACTGGGATGGAGTTCTTGAGATG TTAACATCATGTCAAGCCAATCCCATCTCAACATCTCAGATGCATAAATGGATGGGAAGTTGG TTAATGTCTGATAATCATGATGCCAGTCAAGGGTATAGTTTTTTTACATGAAGTGGACAAAGAG GCAGAAATAACATTTGACGTGGTGGAGACCTTCATCCGCGGCTGGGGCAACAAACCAATTGAA TACATCAAAAAGGAAAGATGGACTGACTCATTCAAATTTCTCGCTTATTTGTGTCAAAAGTTT TTGGACTTACACAAGTTGACATTAATCTTAAATGCTGTCTCTGAGGTGGAATTGCTCAACTTG GCGAGGACTTTCAAAGGCAAAGTCAGAAGAAGTTCTCATGGAACGAACATATGCAGGATTAGG GTTCCCAGCTTGGGTCTACTTTTTATTTTCAAGAGGATGGGCTTACTTCAAGAACTTGATATT CTAATGGACCGAAACTTTCTGTTAATGGTCAAAGATGTGATTATAGGGAGGATGCAAACGGTG CTATCCATGGTATGTAGAATAGACAACCTGTTCTCAGAGCAAGACATCTTCTCCCTTCTAAAT ATCTACAGAATTGGAGATAAAATTGTGGAGAGGCAGGGAAATTTTTCTTATGACTTGATTAAA ATGGTGGAACCGATATGCAACTTGAAGCTGATGAAATTAGCAAGAGAATCAAGGCCTTTAGTC CCACAATTCCCTCATTTTGAAAATCATATCAAGACTTCTGTTGATGAAGGGGCAAAAATTGAC CGAGGTATAAGATTCCCTCCATGATCAGATAATGAGTGTGAAAACAGTGGATCTCACACTGGTG ATTTATGGATCGTTCAGACATTGGGGTCATCCTTTTATAGATTATTACACTGGACTAGAAAAA TTACATTCCCAAGTAACCATGAAGAAAGATATTGATGTGTATATGCAAAAGCACTTGCAAGT GATTTAGCTCGGATTGTTCTATTTCAACAGTTCAATGATCATAAAAAGTGGTTCGTGAATGGA GACTTGCTCCCTCATGATCATCCCTTTAAAAGTCATGTTAAAGAAAATACATGGCCACAGCT GCTCAAGTTCAAGATTTTGGAGATAAATGGCATGAACTTCCGCTGATTAAATGTTTTGAAATA CCCGACTTACTAGACCCATCGATAATATACTCTGACAAAAGTCATTCAATGAATAGGTCAGAG GTGTTGAAACATGTCCGAATGAATCCGAACACTCCTATCCCTAGTAAAAAGGTGTTGCAGACT ATGTTGGACACAAAGGCTACCAATTGGAAAGAATTTCTTAAAGAGATTGATGAGAAGGGCTTA GATGATGATGATCTAATTATTGGTCTTAAAGGAAAGGAGAGGGAAGTGAAGTTGGCAGGTAGA TTTTTCTCCCTAATGTCTTGGAATTTGCGAGAATACTTTGTAATTACCGAATATTTGATAAAG ACTCATTTCTGTCCTATGTTTAAAGGCCTGACAATGGCGGACGATCTAACTGCAGTCATTAAA AAGATGTTAGATTCCCTCATCCGGCCAAGGATTGAAGTCATATGAGGCAATTTGCATAGCCAAT CACATTGATTACGAAAAATGGAATAACCACCAAAGGAAGTTATCAAACGGCCCAGTGTTCGGA GTTATGGGCCAGTTCTTAGGTTATCCATCCTTAATCGAGAGAACTCATGAATTTTTTGAGAAA AGTCTTATATACTACAATGGAAGACCAGACTTGATGCGTGTTTACAACAACACACTGATCAAT TCAACCTCCCAACGAGTTTGTGTTGGCAAGGACAAGAGGGTGGACTGGAAGGTCTACGGCAAAAA GGATGGACTATCCTCAATCTACTGGTTATTCAAAGAGAGGCTAAAATCAGAAACACTGCTGTC AAAGTCTTGGCACAAAGGTGATAATCAAGTTATTTGCACACAGTATAAAACGAAGAAATCGAGA
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AACGTTGTAGAATTACAGGGTGCTCTCAATCAAATGGTTTCTAATAATGAGAAAATTATGACT GCAATCAAAATAGGGACAGGGAAGTTAGGACTTTTTGATAAATGACGATGAGACTATGCAATCT GCAGATTACTTGAATTATGGAAAAATACCGATTTTCCGTGGAGTGATTAGAGGGTTAGAGACC AAGAGATGGTCACGAGTGACTTGTGTACCAATGACCAAATACCCACTTGTGCTAATATAATG AGCTCAGTTTCCACAAATGCTCTCACCCTAGCTCATTTTGGCTGAGAACCCCAATCAATGCCATG ATACAGTACAATTATTTTGGGACATTTGCTAGACTCTTGTGATGATGCATGATCCTGCTCTT CGTCAATCATTGTATGAAGTTCAAGATAAGATACCGGGCTTGCACAGTTCTACTTTCAAATAC GCCATGTTGTATTTGGACCCTTCCATTGGAGGAGTGTGCGGCATGTCTTTGTCCAGGTTTTTG ATTAGAGCCTTCCCAGATCCCGTAACAGAAAAGTCTCTCATTCTGGAGATTCATCCATGTACAT GCTCGAAGTGAGCATCTGAAGGAGATGAGTGCAGTATTTGGAAACCCCGAGATAGCCAAGTTT CGAATAACTCACATAGACAAGCTAGTAGAAGATCCAACCTCTCTGAACATCGCTATGGGAATG AGTCCAGCGAACTTGTTAAAGACTGAGGTTAAAAAATGCTTAATCGAATCAAGACAAACCATC AGGAACCAGGTGATTAAGGATGCAACCATATATTTGTATCATGAAGAGGATCGGCTCAGAAGT TTCTTATGGTCAATAAATCCTCTGTTCCCTAGATTTTTAAGTGAATTCAAATCAGGCACTTTTT TTGGGAGTCGCAGACGGGCTCATCAGTCTATTTCAAATCTCTGTAATTCGGAACCTCCTTT AAGAAAAAGTATCATAGGGAATTGGATGATTTGATTGTGAGGAGTGAGGTATCCTCTTTGACA CATTTAGGGAACTTCATTTGAGAAGGGGATCATGTAAAATGTGGACATGTTGAGCTACTCAT GCTGACACATTAAGATACAAATCCTGGGGCCGTACAGTTATTGGGACAACTGTACCCCATCCA TTAGAAATGTTGGGTCCACAACATCGAAAAGAGACTCCTTGTGCACCATGTAACACATCAGGG TTCAATTATGTTTCTGTGCATTGTCCAGACGGGATCCATGACGTCTTTAGTTACGGGGACCA TTGCTTCTTATCTAGGGTCTAAAACATCTGAATCTACATCTATTTTGCAGCCTTGGGAAAGG GAAAGCAAAGTCCCACTGATTAAAAGAGCTACACGTCTTAGAGATGCTATCTCTTGGTTTGT GAACCCGACTCTAAACTAGCAATGACTATACTTTCTAACATCCACTCTTTAACAGGCGAAGAA TGGACCAAAAGGCAGCATGGGTTCAAAGAAGAGGGTCTGCCCTTCATAGGTTTTTCGACATCT CGGATGAGCCATGGTGGGTTCGCATCTCAGAGCACTGCAGCATTGACCAGGTTGATGGCAACT ACAGACACCATGAGGGATCTGGGAGATCAGAATTTGACTTTTTTATTTCCAAGCAACGTTGCTC TATGCTCAAATTACCACCACTGTTGCAAGAGACGGATGGATCACCAGTTGTACAGATCATTAT CATATTGCCTGTAAGTCCTGTTTGGAGCCCATAGAAGAGATCACCTGGACTCAAGTATGGAC TACACGCCCCCAGATGTATCCCATGTGCTGAAGACATGGAGGAATGGGGAAGGTTTCGTGGGGA CAAGAGATAAAACAGATCTATCCTTTAGAAGGGAATTGGAAGAATTTAGCACCTGCTGAGCAA TCCTATCAAGTCGGCAGATGTATAGGTTTTCTATATGGAGACTTGGCGTATAGAAAATCTACT CATGCCGAGGACAGTTCTCTATTTCTCTATCTATACAAGGTCGTATTAGAGGTCGAGGTTTC TTAAAAGGGTTGCTAGACGGATTAAATGAGAGCAAGTTGCTGCCAAGTAATACCCGGAGAAGT CTGGCTCATTTGAAGAGGCCGGCCAACGCAGTGTACGGAGGTTTGATTTACTTGATTGATAAA TTGAGTGTATCACCTCCATTCCTTTCTCTTACTAGATCAGGACCTATTAGAGACGAATTAGAA ACGATTTCCCAAGATCCCAACCTCCTATCCGACAAGCAACCGTGATATGGGGGTGATTGTC AGAAATTACTTCAAATACCAATGCCGTCTAATTGAAAAGGGAAAATACAGATCACATTATTCA CAATTATGGTTATTCTCAGATGTCTTATCCATAGACTTCATTGGACCATTCCTCTATTTCCACC ACCCTCTTGCAAATCCTATACAAGCCATTTTTTATCTGGGAAAGATAAGAATGAGTTGAGAGAG

CTGGCAAATCTTCTTCATTGCTAAGATCAGGAGAGGGGTGGGAAGACATACATGTGAAATTC TTCACCAAGGACATATTATTGTGTCCAGAGGAAATCAGACATGCTTGCAAGTTCGGGATTGCT AAGGATAATAATAAAGACATGAGCTATCCCCCTTGGGGAAGGGAATCCAGAGGGACAATTACA ACAATCCCTGTTTATTATACGACCACCCCTTACCCAAAGATGCTAGAGATGCCTCCAAGAATC CAAAATCCCCTGCTGTCCGGAATCAGGTTGGGCCAATTACCAACTGGCGCTCATTATAAAATT CGGAGTATATTACATGGAATGGGAATCCATTACAGGGACTTCTTGAGTTGTGGAGACGGCTCC GGAGGGATGACTGCTGCATTACTACGAGAAAATGTGCATAGCAGAGGAATATTCAATAGTCTG TTAGAATTATCAGGGTCAGTCATGCGAGGCGCCTCTCCTGAGCCCCCAGTGCCCTAGAACT TTAGGAGGAGATAAATCGAGATGTGTAAATGGTGAAACATGTTGGGAATATCCATCTGACTTA TGTGACCCCAAGGACTTGGGACTATTTCTCCGACTCAAAGCAGGCTTGGGGCTTCAAATTGAT TTAATTGTAATGGATATGGAAGTTCGGGATTCTTCTACTAGCCTGAAAATTGAGACGAATGTT AGAAATTATGTGCACCGGATTTTGGATGAGCAAGGAGTTTAACTTACAAGACTTATGGAACA TATATTTGTGAGAGCGAAAAGAATGCAGTAACAATCCTTGGTCCCATGTTCAAGACGGTCGAC TTAGTTCAAACAGAATTTAGTAGTTCTCAAACGTCTGAAGTATATATGGTATGTAAAGGTTTG AAGAAATTAATCGATGAACCCAATCCCGATTGGTCTTCCATCAATGAATCCTGGAAAAACCTG TACGCATTCCAGTCATCAGAACAGGAATTTGCCAGAGCAAAGAAGGTTAGTACATACTTTACC TTGACAGGTATTCCCTCCCAATTCATTCCCTGATCCTTTTGTAACATTGAGACTATGCTACAA ATATTCGGAGTACCCACGGGTGTGTCTCATGCGGCTGCCTTAAAATCATCTGATAGACCTGCA GATTTATTGACCATTAGCCTTTTTTATATGGCGATTATATCGTATTATAACATCAATCATATC AGAGTAGGACCGATACCTCCGAACCCCCCATCAGATGGAATTGCACAAAATGTGGGGATCGCT ATAACTGGTATAAGCTTTTGGCTGAGTTTGATGGAGAAAGACATTCACCTATATCAACAGTGT TTAGCAGTTATCCAGCAATCATTCCCGATTAGGTGGGAGGCTGTTTCAGTAAAAGGAGGATAC AAGCAGAAGTGGAGTACTAGAGGTGATGGGCTCCCAAAGATAACCCGAACCTCAGACTCCTTG GCCCCAATCGGGAACCTGGATCAGATCTCTGGAATTGGTCCGAAACCAAGTTCGTCTAAATCCA TTCAATGAGATCTTGTTCAATCAGCTATGTCGTACAGTGGATAATCATTTGAAATGGTCAAAT TTGCGAAGAAACACAGGAATGATTGAATGGATCAATAGACGAATTTCAAAGAAGACCGGTCT ATACTGATGTTGAAGAGTGACCTACACGAGGAAAACCTCTTGAGAGATTAAAAAATCATGAGG AGACTCCAAACTTTAAGTATGAAAAAACTTTGATCCTTAAGACCCTCTTGTTGGTTTTTATTT TTTATCTGGTTTTGTGGTCTTCGTGGGTGCGCATGGCATCTCCACCTCCTCGCGGTCCGACCT GGGCATCCGAAGGAGGACGTCTGTCCTCGGATGGCTAAGGGAGAGCTCGGATCCGGCTGCTA ACAAAGCCCGAAAGGAAGCTGAGTTGGCTGCTGCCACCGCTGAGCAATAACTAGCATAACCCC TTGGGGCCTCTAAACGGGTCTTGAGGGGTTTTTTGCTGAAAGGAGGAACATATCCGGATCGA GATCCTCTAGAGTCGACCTGCAGGCATGCAAGCTTGATTCTATAGTGTACCTAAATCGTAT GTGTATGATACATAAGGTTATGTATTAATTGTAGCCGCGTTCTAACGACAATATGTACAAGCC TAATTGTGTAGCATCTGGCTTACTGAAGCAGACCCTATCATCTCTCTCGTAACTGCCGTGAG AGTCGGTTTTGGTTGGACGAACCTTCTGAGTTTCTGGTAACGCCGTCCCGACCCGGAAATGGT CAGCGAACCAATCAGCAGGGTCATCGCTAGCCAGATCCTCTACGCCGACGCATCGTGGCCGG CATCACCGGCGCCACAGGTGCGGTTGCTGGCGCCTATATCGCCGACATCACCGATGGGGAAGA TCGGGCTCGCCACTTCGGGCTCATGAGCGCTTGTTTCGGCGTGGGTATGGTGGCAGGCCCCGT
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GGCCGGGGGACTGTTGGGCGCCATCTCCTTGCAACCATTCCTTGCGGCGGCGGTGCTCAACGGC CTCAACCTACTACTGGGCTGCTTCCTAATGCAGGAGTCGCATAAGGGAGAGCGTCGAATGGTG CACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCCAGCCCCGACACCCGCCAACACC CGCTGACGCGCCCTGACGGGCTTGTCTGCTCCCGGCATCCGCTTACAGACAAGCTGTGACCGT CTCCGGGAGCTGCATGTGTCAGAGGTTTTACCGTCATCACCGAAACGCGCGAGACGAAAGGG CCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAATGGTTTCTTAGACGTCAGG TGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTTATTTTTCTAAATACATTCAA TATGTATCCGCTCATGAGACAATAACCCTGATAAATGCTTCAATAATATTGAAAAAGGAAGAG TATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCTTTTTTGCGGCATTTTGCCTTCCTGT TTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCACGAGT GGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACG TTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACGC CGGGCAAGAGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACC AGTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATAAC CATGAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGGAGGACCGAAGGAGCTAAC CGCTTTTTTGCACAACATGGGGGATCATGTAACCTCGCCTTGATCGTTGGGAACCGGAGCTGAA TGAAGCCATACCAAACGACGAGCGTGACACCACGATGCCTGTAGCAATGGCAACAACGTTGCG CAAACCTATTAAGTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGGATGGA GGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGA TAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTCAGCACTGGGGCCAGATGGTAA GCCCTCCCGTATCGTAGTTATCTACACGACGGGAGTCAGGCAACTATGGATGAACGAAATAG ACAGATCGCTGAGATAGGTGCCTCACTGATTAAGCATTTGGTAACTGTCAGACCAAGTTTACTC ATATATACTTTAGATTGATTTAAACCTTCATTTTTTAATTTAAAGGATCTAGGTGAAGATCCT TTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTTCGTTCCACTGAGCGTCAGACCC CGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCA AACAAAAAACACCCTACCAGCGGTGGTTTGTTCGCGGATCAAGAGCTACCAACTCTTTT TCCGAAGGTAACCTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTA GTTAGGCCACCACTTCAAGAACTCTGTAGCACCAGCTACATACCTCGCTCTGCTAATCCTGTT ACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGCTTACCGGGTTGGACTCAAGACGATAGTT ACCGGATAAGGCGCAGCGGTGCGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCG AACGACCTACACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCAGCTTCCCGA AGGGAGAAAAGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGA GCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTGCGGTTTTCGCCACCTCTGACTTGA GCGTCGATTTTTGTGATGCTCGTCAGGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGC CTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCTGCGTTATCCCC TGATTCTGTGGATAACCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCGAGCCGAAC GACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCCAATACGCAAACCGCCTCT CCCCGCGCGTTGGCCGATTCAATTAATGCAGGGGGATCTCGATCCCGCGAAATTAATACGACTC ACTATAGG
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In some embodiments, the recombinant viruses comprise in its genome a nucleic acid sequence encoding a Zika virus envelope protein or fragment thereof. An exemplary nucleic acid sequence for a wild type Zika virus envelope protein is as follows (SEQ ID NO: 2):

SEQ ID NO: 2	ATCCGGTGTATCGGCGTGTCCAACCGGGACTTCGTGGAAGGCATGAGCGGCGGCACATGGGTG GACGTGGTGCTGGAACATGGCGGCTGCGTGACAGTGATGGCTCAGGACAAGCCCACCGTGGAC ATCGAGCTCGTGACCACCACCGTGTCCAATATGGCCGAAGTGCGGAGCTACTGCTACGAGGCC AGCATCAGCGACATGGCAAGCGACAGCAGATGCCCTACACAGGGCGAGGCCCTACCTGGACAAG CAGTCCGACACCCAGTACGTGTGCAAGCGGACCCCTGGTGGATAGAGGCTGGGGCAATGGCTGC GGCCTGTTTGGCAAGGGCAGCCTCGTGACCTGCGCCAAGTTCGCCTGCAGCAAGAAGATGACC GGCAAGAGCATCCAGCCCGAGAACCTGGAATACCGGATCATGCTGAGCGTGCACGGCAGCCAG CACTCCGGCATGATCGTGAACGACACCGGCCACGAGACAGACGAGAACC GGCCCAAGGTGGAA ATCACCCCCAACAGCCCTAGAGCCGAGGCCACACTGGGCGGCTTTGGATCTCTGGGCCTGGAC TGCGAGCCTAGAACCGGCTGGATTT CAGCGACCTGTACTACCTGACCATGAACAACAAGCAC TGGCTGGTGCACAAAGAGTGGTTCCACGACATCCCCCTGCCCTGGCATGCCGGCGCTGATACA GGCACACCCCCACTGGAACAACAAGAGGCTCTGGTGAATTCAAGGACGCCCACGCCAAGCGG CAGACCGTGGTGGTGCTGGGATCTCAGGAAGGCGCCGTGCATACAGCTCTGGCTGGCGCCCTG GAAGCCGAAATGGATGGCGCCAAAGGCAGACTGTCCAGCGGCCACCTGAAGTGCCGGCTGAAG ATGGACAAGCTGCGGCTGAAGGGCGTGTCTACAGCCTGTGTACCGCCGCTTCACCTTCACC AAGATCCCCGCCGAGACACTGCACGGCACCGTGACTGTGGAAGTGCAGTACGCCGGCACCGAC GGCCCTTGTAAGTGCTGCTCAGATGGCCGTGGATATGCAGACCCTGACCCCCGTGGGCAGA CTGATCACCGCCAACCCTGTGATCACCGAGAGCACCGAGAACAGCAAGATGATGCTGGAAGT GACCCCCCTTCGGCGACTCCTACATCGTGATCGGCGTGGGAGAGAAGAAGATCACCCACCAC TGGCACAGAAGCGGCAGCACCATCGGCAAGGCCCTTTGAGGCTACAGTGCGGGGAGCCAAGAGA ATGGCCGTGCTGGGAGATACCGCCTGGGACTTTGGCTCTGTGGGCGGAGCCCTGAACTCTCTG GGCAAGGGAATCCACCAGATCTTCGGAGCCGCCCTTAAAGAGCCTGTTCCGGCGGCATGAGCTGG TTCAGCCAGATCCTGATCGGCACCCTGCTGATGTGGCTGGGCCTGAACGCCAAGAACGGCAGC ATCTCCCTGATGTGCCTGGCTCTGGGAGGCGTGCTGATCTTCCTGAGCACAGCCGTGTCTGCC
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In some embodiments, the recombinant viruses further comprise in its genome a nucleic acid sequence encoding a Zika virus precursor membrane (prM) protein or fragment thereof. An exemplary nucleic acid sequence for a prM protein is as follows (SEQ ID NO: 3):

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SEQ ID NO: 3	AGAAGAGGCAGCGCCTACTACATGTACCTGGACCGGAACGATGCCGGCGAGGCCATCAGCTTT CCAACCACCCTGGGCATGAACAAGTGCTACATCCAGATCATGGACCTGGGCCACACCTGTGAC GCCACCATGAGCTACGAGTGCCCCATGCTGGACGAGGGCGTGGAACCCGACGATGTGGACTGC TGGTGCAACACCACCAGCACCTGGGTGGTGTACGGCACCTGTCACCACAAGAAGGGCGAAGCC AGACGGTCCAGACGGGCCGTGACACTGCCTAGCCACAGCACCAGAAAGCTGCAGACCCGGTCC CAGACCTGGCTGGAAAGCAGAGAGTACACCAAGCACCTGATCCGGGTGGAAACTGGATCTTC CGGAACCCCGGCTTTGCCCTGGCCGCTGCTGCTATTGCTTGGCTGCTGGGCAGCAGCACCTCC CAGAAAGTGATCTACCTCGTGATGATCCTGCTGATCGCCCCCTGCCTACAGC
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In some embodiments, the recombinant viruses further comprise in its genome a nucleic acid sequence encoding Zika virus capsid (C) protein or fragment thereof. An exemplary nucleic acid sequence for a portion of the C protein (codon optimized) is as follows (SEQ ID NO: 4):

SEQ ID NO: 4	ACCAGCGTGGGCATCGTGGGCCTGCTGCTGACCACCGCCATGGCCGCCGAGGTGACC
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In some embodiments, the recombinant VSV comprises a nucleic acid sequence that is at least 80 (*e.g.*, at least 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99) % identical to: (i) the nucleic acid of SEQ ID NO:2; (ii) the nucleic acid of SEQ ID NO:3; or (iii) the nucleic acid of SEQ ID NO:4. In some embodiments, the recombinant VSV comprises a nucleic acid sequence that is identical to: (i) the nucleic acid of SEQ ID NO:2; (ii) the nucleic acid of SEQ ID NO:3; or (iii) the nucleic acid of SEQ ID NO:4.

In some embodiments, the nucleic acid sequence encoding a Zika virus E protein substantially replaces the endogenous VSV viral glycoprotein (G) in the VSV genome. Exemplary sequences where the Zika coding sequences were cloned into the VSV genome, replacing the endogenous VSV viral glycoprotein (G), include the sequences of rVSVΔGZika-prME (SEQ ID NO:5) and rVSVΔGZika-CprME (SEQ ID NO:6).

SEQ ID NO:5	ACGAAGACAAACAAACCATTATTATCATTTAAAGGCTCAGGAGAACTTTAACAGTAATCAGA ATTCTCGAGAAAGCCACCATGGTGAGCAAGGGCGAGGAGCTGTTACCGGGGTGGTGCCCATC CTGGTCTGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGC GATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCACCGCAAGCTGCCCCGTGCCC TGGCCACCCCTCGTGACCACCCTGACCTACGGCGTGAGTGCTTCAGCCGCTACCCCGACCAC
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ATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCCCCAAGGCTACGTCCAGGAGCGCACCATC TTCTTCAAGGACGACGGCAACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTG GTGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAG CTGGAGTACAACACTACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATC AAGGTGAACTTCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTAC CAGCAGAACACCCCCATCGGCGACGGCCCCGTGCTGCTGCCCCACAACCACTACCTGAGCACC CAGTCCGCCCTGAGCAAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTG ACCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAGTAATGGCCATATGAAAAAAC TAACAGTAATCAAAATGTCTGTTACAGTCAAGAGAATCATTGACAACACAGTCATAGTTCCAA AACTTCCTGCAAATGAGGATCCAGTGGAAATACCCGGCAGATTACTTCAGAAAATCAAAGGAGA TTCCTCTTTACATCAATACTACAAAAAGTTTGTGATCTAAGAGGATATGTCTACCAAGGCC TCAAATCCGGAATGTATCAATCATAATGTCAACAGCTACTTGTATGGAGCATTAAGGACA TCCGGGGTAAGTTGGATAAAGATTGGTCAAGTTTCGGAATAAACATCGGGAAAGCAGGGGATA CAATCGGAATATTTGACCTTGTATCCTTGAAAGCCCTGGACGGCGTACTTCCAGATGGAGTAT CGGATGCTTCCAGAACCAGCGCAGATGACAAATGGTTGCCTTTGTATCTACTTGGCTTATACA GAGTGGGCAGAACACAAATGCCTGAATACAGAAAAAGCTCATGGATGGGCTGACAAATCAAT GCAAAATGATCAATGAACAGTTTGAACCTCTTGTGCCAGAAGGTCGTGACATTTTTGATGTGT GGGGAAATGACAGTAATTACACAAAAATTGTGCTGCAGTGGACATGTTCTCCACATGTTCA AAAAACATGAATGTGCCTCGTTCAGATACGGAACATATTGTTTCCAGATTCAAAGATTGTGCTG CATTGGCAACATTTGGACACCTCTGCAAAATAACCGGAATGTCTACAGAAGATGTAACGACCT GGATCTTGAACCGAGAAGTTGCAGATGAAATGGTCCAAATGATGCTTCCAGGCCAAGAAATTG ACAAGGCCGATTACATACATGCCTTATTTGATCGACTTTGGATTGTCTTCTAAGTCTCCATATT CTTCCGTCAAAAACCCTGCCTTCCACTTCTGGGGGCAATTGACAGCTCTTCTGCTCAGATCCA CCAGAGCAAGGAATGCCCCAGAGCCTGATGACATTGAGTATACATCTCTTACTACAGCAGGTT TGTTGTACGCTTATGCAGTAGGATCCTCTGCCGACTTGGCACAACAGTTTTGTGTTGGAGATA ACAAATACACTCCAGATGATAGTACCGGAGGATTGACGACTAATGCACCGCCACAAGGCAGAG ATGTGGTCGAATGGCTCGGATGGTTTGAAGATCAAAACAGAAAACCGACTCCTGATATGATGC AGTATGCGAAAAGAGCAGTCATGTCACTGCAAGGCCTAAGAGAGAAGACAATTGGCAAGTATG CTAAGTCAGAATTTGACAAATGACCCCTATAATTCTCAGATCACCTATTATATATTATGCTACA TATGAAAAAACTAACAGATATCATGGATAATCTCACAAAAGTTTCGTGAGTATCTCAAGTCCT ATTCTCGTCTGGATCAGGCGGTAGGAGAGATAGATGAGATCGAAGCACAACGAGCTGAAAAGT CCAATTATGAGTTGTTCCAAGAGGATGGAGTGGAAGAGCATACTAAGCCCTCTTATTTTCAGG CAGCAGATGATTCTGACACAGAATCTGAACCAGAAATTGAAGACAATCAAGGTTTGTATGCAC AGGATCCAGAAGCTGAGCAAGTTGAAGGCTTTATACAGGGGCCCTTTAGATGACTATGCAGATG AGGAAGTGGATGTTGTATTTACTTCGGACTGGAAACCACCTGAGCTTGAATCTGACGAGCATG GAAAGACCTTACGGTTGACATCGCCAGAGGGTTTAAAGTGGAGAGCAGAAATCCAGTGGCTTT CGACGATTAAAGCAGTCGTGCAAAGTGCCAAATACTGGAATCTGGCAGAGTGCACATTTGAAG CATCGGGAGAAGGGGTCAATTATGAAGGAGCGCCAGATAACTCCGGATGTATATAAGGTCCTC CAGTGATGAACACACATCCGTCCCAATCAGAAGCAGTATCAGATGTTTGGTCTCTCTCAAAGA
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	CATCCATGACTTTCCAACCCAAGAAAGCAAGTCTTCAGCCTCTCACCATATCCTTGGATGAAT TGTTCTCATCTAGAGGAGAGTTTCATCTCTGTGCGGAGGTGACGGACGAATGTCTCATAAAGAGG CCATCCTGCTCGGCCTGAGATACAAAAAGTTGTACAATCAGGCGAGAGTCAAATATTCTCTGT AGACTATGAAAAAAGTAACAGATATCACGATCTAAGTGTTATCCCAATCCATTCATCATGAG TTCCTTAAAGAAGATTCTCGGTCTGAAGGGGAAAGGTAAGAAATCTAAGAAATTAGGGATCGC ACCACCCCTTATGAAGAGGACACTAGCATGGAGTATGCTCCGAGCGCTCCAATTGACAAATC CTATTTTGGAGTTGACGAGATGGACACCTATGATCCGAATCAATTAAGATATGAGAAATTCCTT CTTTACAGTGAAAATGACGGTTAGATCTAATCGTCCGTTTCAAGACATACTCAGATGTGGCAGC CGCTGTATCCCATTGGGATCACATGTACATCGGAATGGCAGGGAAACGTCCCTTCTACAAAAT CTTGGCTTTTTTGGGTTCTTCTAATCTAAAGGCCACTCCAGCGGTATTGGCAGATCAAGGTCA ACCAGAGTATCACACTCACTGCGAAGGCAGGGCTTATTTGCCACATAGGATGGGGAAGACCCC TCCCATGCTCAATGTACCAGAGCACTTCAGAAGACCATTCAATATAGGTCTTTACAAGGGAAC GATTGAGCTCACAATGACCATCTACGATGATGAGTCACTGGAAGCAGCTCCTATGATCTGGGA TCATTTCAATTCTTCCAAATTTTCTGATTTTCAGAGAGAAGGCCTTAATGTTTGGCCTGATTGT CGAGAAAAAGGCATCTGGAGCGTGGGTCTGGATTCTATCAGCCACTTCAAATGAGCTAGTCT AACTTCTAGCTTCTGAACAATCCCCGGTTTACTCAGTCTCTCCTAATTCAGCCTCTCGAACA ACTAATATCCTGTCTTTTCTATCCCTATGAAAAAACTAACAGAGATCGATCTGTTTCCTTGA CACGCGTACCATGAGAAGAGGCAGCGCCTACTACATGTACCTGGACCGGAACGATGCCGGCGA GGCCATCAGCTTTCCAACCACCCTGGGCATGAACAAGTGCTACATCCAGATCATGGACCTGGG CCACACCTGTGACGCCACCATGAGCTACGAGTGCCCCATGCTGGACGAGGGCGTGGAACCCGA CGATGTGGACTGCTGGTGCAACACCACCAGCACCTGGGTGGTGTACGGCACCTGTCACCACAA GAAGGGCGAAGCCAGACGGTCCAGACGGGCGGTGACACTGCCTAGCCACAGCACCAGAAAGCT GCAGACCCGGTCCCAGACCTGGCTGGAAAGCAGAGAGTACACCAAGCACCTGATCCGGGTGGA AACTGGATCTTCCGGAACCCCGGCTTTGCCCTGGCCGCTGCTGCTATTGCTTGGCTGCTGGG CAGCAGCACCTCCCAGAAAGTGATCTACCTCGTGATGATCCTGCTGATCGCCCCGCTACAG CATCCGGTGATATCGGCGTGTCGAACCGGGACTTCGTGGAAGGCATGAGCGGCGGCACATGGGT GGACGTGGTGCTGGAACATGGCGGCTGCGTGACAGTGATGGCTCAGGACAAGCCACCGTGGA CATCGAGCTCGTGACCACCACCGTGTCGAATATGGCCGAAGTGCGGAGCTACTGCTACGAGGC CAGCATCAGCGACATGGCCAGCGACAGCAGATGCCCTACACAGGGCGAGGCCTACCTGGACAA GCAGTCCGACACCCAGTACGTGTGCAAGCGGACCCTGGTGGATAGAGGCTGGGGCAATGGCTG CGGCCTGTTTGGCAAGGGCAGCCTCGTGACCTGCGCCAAGTTCGCCTGCAGCAAGAAGATGAC CGGCAAGAGCATCCAGCCCAGAACCTGGAATACCGGATCATGCTGAGCGTGCACGGCAGCCA GCACTCCGGCATGATCGTGAACGACACCGGCCACGAGACAGACGAGAACCGGGCCAAGGTGGA AATCACCCCCAACAGCCCTAGAGCCGAGGCCACACTGGGCGGCTTTGGATCTCTGGGCCTGGA CTGCGAGCCTAGAACCGGCCTGGATTTTCAGCGACCTGTACTACCTGACCATGAACAACAAGCA CTGGCTGGTGACAAAAGAGTGGTTCACGACATCCCCCTGCCCTGGCATGCCGGCGCTGATAC AGGCACACCCCACTGGAACAACAAGAGGCTCTGGTGGAAATTCAGGACGCCCACGCCAAGCG GCAGACCGTGGTGGTGCTGGGATCTCAGGAAGGCGCCGTGCATACAGCTCTGGCTGGCGCCCT GGAAGCCGAAATGGATGGCGCCAAAGGCAGACTGTCCAGCGGCCACCTGAAGTGCCGGCTGAA
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	GATGGACAAGCTGCGGCTGAAGGGCGTGTCTACAGCCTGTGTACCGCCGCCTTCACCTTCAC CAAGATCCCCGCCGAGACACTGCACGGCACCGTGACTGTGGAAGTGCAGTACGCCGGCACCGA CGGCCCTTGTAAGTGCCTGCTCAGATGGCCGTGGATATGCAGACCCTGACCCCCGTGGGCAG ACTGATCACCGCCAACCCTGTGATCACCGAGAGCACCGAGAACAGCAAGATGATGCTGGAAC GGACCCCCCTTCGGCGACTCCTACATCGTGATCGGCGTGGGAGAGAAGAAGATCACCCACCA CTGGCACAGAAGCGGCAGCACCATCGGCAAGGCCTTTGAGGCTACAGTGCGGGGAGCCAAGAG AATGGCCGTGCTGGGAGATACCGCCTGGGACTTTGGCTCTGTGGGCGGAGCCCTGAACCTCTCT GGGCAAGGGAATCCACCAGATCTTCGGAGCCGCCTTTAAGAGCCTGTTTCGGCGGCATGAGCTG GTTTCAGCCAGATCCTGATCGGCACCCTGCTGATGTGGCTGGGCCTGAACGCCAAGAACGGCAG CATCTCCCTGATGTGCCTGGCTCTGGGAGGCGTGCTGATCTTCCTGAGCACAGCCGTGTCTGC CTAAGCGGCCGCCCTGCACAACAGATTCTTCATGTTTTGGACCAAATCAACTTGTGATACCATG CTCAAAGAGGCCCTCAATTATATTTGAGTTTTTAATTTTTATGAAAAAACTAACAGCAATCAT GGAAGTCCACGATTTTGAGACCGACGAGTTCAATGATTTCAATGAAGATGACTATGCCACAAG AGAATTCCTGAATCCCGATGAGCGCATGACGTACTTGAATCATGCTGATTACAATTTGAATTC TCCTCTAATTAGTGATGATATTGACAATTTGATCAGGAAATTCATTTCTCTCCGATTCCCTC GATGTGGGATAGTAAGAACTGGGATGGAGTTCTTGAGATGTTAACATCATGTCAAGCCAATCC CATCTCAACATCTCAGATGCATAAATGGATGGGAAGTTGGTTAATGTCTGATAATCATGATGC CAGTCAAGGGTATAGTTTTTTACATGAAGTGGACAAAAGAGGCAGAAATAACATTTGACGTGGT GGAGACCTTCATCCGCGGCTGGGGCAACAAACCAATTGAATACATCAAAAAGGAAAGATGGAC TGACTCATTCAAAATTTCTCGCTTATTTGTGTCAAAAGTTTTTGGACTTACACAAGTTGACATT AATCTTAAATGCTGTCTCTGAGGTGGAATTGCTCAACTTGGCGAGGACTTTCAAAGGCAAAGT CAGAAGAAGTTCTCATGGAACGAACATATGCAGGATTAGGGTTCCAGCTTGGGTCTACTTT TATTTCAGAAGGATGGGCTTACTTCAAGAACTTGATATTCTAATGGACCGAACTTTCTGTT AATGGTCAAAGATGTGATTATAGGGAGGATGCAAACGGTGCTATCCATGGTATGTAGAATAGA CAACCTGTTCTCAGAGCAAGACATCTTCTCCCTTCTAAATATCTACAGAATTGGAGATAAAAT TGTGGAGAGGCAGGGAAATTTTTCTTATGACTTGATTAAAATGGTGGAACCGATATGCAACTT GAAGCTGATGAAATTAGCAAGAGAATCAAGGCCTTTAGTCCCACAATTCCTCATTTTTGAAAA TCATATCAAGACTTCTGTTGATGAAGGGGCAAAATTGACCGAGGTATAAGATTCTCCATGA TCAGATAATGAGTGTGAAAACAGTGGATCTCACACTGGTGATTTATGGATCGTTCAGACATTG GGGTATCCTTTTATAGATTATTACACTGGACTAGAAAAATTACATTCCCAAGTAACCATGAA GAAAGATATTGATGTGCATATGCAAAAGCACTTGCAAGTGATTTAGCTCGGATTGTTCTATT TCAACAGTTCAATGATCATAAAAAGTGGTTCGTGAATGGAGACTTGCTCCCTCATGATCATCC CTTTAAAAGTCATGTTAAAGAAAATACATGGCCACAGCTGCTCAAGTTCAAGATTTTGGAGA TAAATGGCATGAACTTCCGCTGATTAAATGTTTTGAAATACCCGACTTACTAGACCCATCGAT AATATACTCTGACAAAAGTCATTCAATGAATAGGTCAGAGGTGTTGAAACATGTCCGAATGAA TCCGAACACTCCTATCCCTAGTAAAAAGGTGTTGCAGACTATGTTGGACACAAAGGCTACCAA TTGGAAAGAATTTCTTAAAGAGATTGATGAGAAGGGCTTAGATGATGATGATCTAATTATTGG TCTTAAAGGAAAGGAGAGGGAAGTGAAGTTGGCAGGTAGATTTTTCTCCCTAATGTCTTGGA ATTGCGAGAATACTTTGTAATTACCGAATATTTGATAAAGACTCATTTTCGTCCCTATGTTTAA
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	CGGTAAGCGGCAGGGTTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGT ATCTTTATAGTCCTGTGCGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGT CAGGGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTT GCTGGCCTTTTGCTCACATGTTCTTTCTGCGTTATCCCCTGATTCTGTGGATAACCGTATTA CCGCCTTTGAGTGAGCTGATAACGCTCGCCGAGCCGAACGACCGAGCGCAGCGAGTCAGTGA GCGAGGAAGCGGAAGAGCGCCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCAAT AATGCAGGGGGATCTCGATCCCGCGAAATTAATACGACTCACTATAGG
SEQ ID NO:6	ACGAAGACAAACAAACCATTATTATCATTTAAAGGGCTCAGGAGAAACTTTAACAGTAATCAGA ATTCTCGAGAAAGCCACCATGGTGAGCAAGGGCGAGGAGCTGTTACCCGGGGTGGTGCCCATC CTGGTCGAGCTGGACGGCGACGTAAACGGCCACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGC GATGCCACCTACGGCAAGCTGACCCTGAAGTTCATCTGCACCACCGGCAAGCTGCCCCGTGCC TGGCCCCACCTCGTGACCACCTGACCTACGGCGTGCAGTGCTTCAGCCGCTACCCCCGACCAC ATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCCCGAAGGCTACGTCCAGGAGCGCACCATC TTCTTCAAGGACGACGGCAACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGGCGACACCCTG GTGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCACAAG CTGGAGTACAACACTACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATC AAGGTGAACCTTCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCCTAC CAGCAGAACACCCCCATCGGCGACGGCCCCGTGCTGCTGCCGACAACCCTACCTGAGCACC CAGTCCGCCCTGAGCAAGACCCCCAACGAGAAGCGCGATCACATGGTCTGCTGGAGTTCGTG ACCGCCGCCGGGATCACTCTCGGCATGGACGAGCTGTACAAGTAATGGCCATATGAAAAAAC TAACAGTAATCAAAATGTCTGTTACAGTCAAGAGAATCATTGACAACACAGTCATAGTTCCAA AACTTCTGCAAATGAGGATCCAGTGGAATACCCGGCAGATTACTTCAGAAAATCAAAGGAGA TTCCTCTTTACATCAATACTACAAAAAGTTTGTGATCTAAGAGGATATGTCTACCAAGGCC TCAAATCCGGAAATGTATCAATCATACATGTCAACAGCTACTTGTATGGAGCATTAAGGACA TCCGGGGTAAGTTGGATAAAGATTGGTCAAGTTTCGGAATAAACATCGGGAAAGCAGGGGATA CAATCGGAATATTTGACCTTGTATCCTTGAAAGCCCTGGACGGCGTACTTCCAGATGGAGTAT CGGATGCTTCCAGAACCAGCGCAGATGACAAATGGTTGCCCTTGTATCTACTTGGCTTATACA GAGTGGGCAGAACACAAATGCCTGAATACAGAAAAAGCTCATGGATGGGCTGACAAATCAAT GCAAAATGATCAATGAACAGTTTGAACCTCTTGTGCCAGAAGGTGTCGATTTTTGATGTGT GGGGAAATGACAGTAATTACACAAAAATTTGTCGCTGCAGTGGACATGTTCTTCCACATGTTCA AAAAACATGAATGTGCCTCGTTCAGATACGGAACCTATTGTTTCCAGATTCAAAGATTGTGCTG CATTGGCAACATTTGGACACCTCTGCAAAATAACCGGAATGTCTACAGAAGATGTAACGACCT GGATCTTGAACCGAGAAGTTGCAGATGAAATGGTCCAAATGATGCTTCCAGGCCAAGAAATTG ACAAGGCCGATTATACATGCCTTATTTGATCGACTTTGGATTGTCTTCTAAGTCTCCATATT CTTCCGTCAAAAACCTTGCCTTCCACTTCTGGGGGCAATTGACAGCTCTTCTGCTCAGATCCA CCAGAGCAAGGAATGCCCCGACAGCCTGATGACATTGAGTATACATCTCTTACTACAGCAGGTT TGTTGTACGCTTATGCAGTAGGATCCTCTGCCGACTTGGCACAACAGTTTTGTGTTGGAGATA ACAAATACACTCCAGATGATAGTACCGGAGGATTGACGACTAATGCACCGCCACAAGGCAGAG

ATGTGGTCGAATGGCTCGGATGGTTTGAAGATCAAAACAGAAAACCGACTCCTGATATGATGC AGTATGCGAAAAGAGCAGTCATGTCACTGCAAGGCCAAGAGAGAAGACAATTGGCAAGTATG CTAAGTCAGAATTTGACAAATGACCCTATAATTCTCAGATCACCTATTATATATTATGCTACA TATGAAAAAACTAACAGATATCATGGATAATCTCACAAAAGTTCGTGAGTATCTCAAGTCCT ATTCTCGTCTGGATCAGGCGGTAGGAGAGATAGATGAGATCGAAGCACAAACGAGCTGAAAAGT CCAATTATGAGTTGTTCCAAGAGGATGGAGTGGAAGAGCATACTAAGCCCTCTTATTTTCAGG CAGCAGATGATTCTGACACAGAATCTGAACCAGAAATTGAAGACAATCAAGGTTTGTATGCAC AGGATCCAGAAGCTGAGCAAGTTGAAGGCTTTATACAGGGGCCCTTTAGATGACTATGCAGATG AGGAAGTGGATGTTGTATTTACTTTCGGACTGGAAACCACCTGAGCTTGAATCTGACGAGCATG GAAAGACCTTACGGTTGACATCGCCAGAGGGTTTAAGTGGAGAGCAGAAATCCCAGTGGCTTT CGACGATTAAAGCAGTCGTGCAAAGTGCCAAATACTGGAATCTGGCAGAGTGCACATTTGAAG CATCGGGAGAAGGGGTCAATTATGAAGGAGCGCCAGATAACTCCGGATGTATATAAGGTCACCTC CAGTGATGAACACACATCCGTCCCAATCAGAAGCAGTATCAGATGTTTGGTCTCTCTCAAAGA CATCCATGACTTTCCAACCCAAGAAAGCAAGTCTTCAGCCTCTCACCATATCCTTGGATGAAT TGTTCTCATCTAGAGGAGAGTTCATCTCTGTCTGGAGGTGACGGACGAATGTCTCATAAAGAGG CCATCCTGCTCGGCCTGAGATACAAAAAGTTGTACAATCAGGCGAGAGTCAAATATTCTCTGT AGACTATGAAAAAAAGTAACAGATATCACGATCTAAGTGTTATCCCAATCCATTCATCATGAG TTCCTTAAAGAAGATTCTCGGTCTGAAGGGGAAAGGTAAGAAATCTAAGAAATTAGGGATCGC ACCACCCCTTATGAAGAGGACACTAGCATGGAGTATGCTCCGAGCGCTCCAATTGACAAATC CTATTTTGGAGTTGACGAGATGGACACCTATGATCCGAATCAATTAAGATATGAGAAATTCTT CTTTACAGTGAAAAATGACGGTTAGATCTAATCGTCCGTTGAGAACATACTCAGATGTGGCAGC CGCTGTATCCCATTGGGATCACATGTACATCGGAATGGCAGGGAAACGTCCCTTCTACAAAT CTTGGCTTTTTTGGGTTCTTCTAATCTAAAGGCCACTCCAGCGGTATTGGCAGATCAAGGTCA ACCAGAGTATCACACTCACTGCGAAGGCAGGGCTTATTTGCCACATAGGATGGGGAAGACCCC TCCCATGCTCAATGTACCAGAGCACTTCAGAAGACCATTCAATATAGGTCTTTACAAGGGAAC GATTGAGCTCACAATGACCATCTACGATGATGAGTCACTGGAAGCAGCTCCTATGATCTGGGA TCATTTCAATTCTTCCAAATTTTCTGATTTGAGAGAGAAGGCCTTAATGTTTGGCCTGATTGT CGAGAAAAAGGCATCTGGAGCGTGGGTCTGGATTCTATCAGCCACTTCAAATGAGCTAGTCT AACTTCTAGCTTCTGAACAATCCCCGGTTTACTCAGTCTCTCCTAATTCAGCCTCTCGAACA ACTAATATCCTGTCTTTTCTATCCCTATGAAAAAACTAACAGAGATCGATCTGTTTCCTTGA CACGCGTGCCACCATGACCAGCGTGGGCATCGTGGGCCTGCTGCTGACCACCGCCATGGCCGC CGAGGTGACCAGAAGAGGCAGCGCCTACTACATGTACCTGGACCGGAACGATGCCGGCGAGGC CATCAGCTTTCCAACCACCCTGGGCATGAACAAGTGCTACATCCAGATCATGGACCTGGGCCA CACCTGTGACGCCACCATGAGCTACGAGTGCCCCATGCTGGACGAGGGCGTGAACCCGACGA TGTGGACTGCTGGTGCAACACCACCAGCACCTGGGTGGTGTACGGCACCTGTCACCACAAGAA GGGCGAAGCCAGACGGTCCAGACGGGCCGTGACACTGCCTAGCCACAGCACCAGAAAGCTGCA GACCCGGTCCCAGACCTGGCTGGAAAGCAGAGAGTACACCAAGCACCTGATCCGGGTGAAAA CTGGATCTTCCGGAACCCCGGCTTTGCCCTGGCCGCTGCTGCTATTGCTTGGCTGCTGGGCAG CAGCACCTCCCAGAAAGTGATCTACCTCGTGATGATCCTGCTGATCGCCCCTGCCTACAGCAT
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CCGGTGTATCGGCGTGTCCAACCGGGACTTCGTGGAAGGCATGAGCGGCGGCACATGGGTGGA CGTGGTGCTGGAACATGGCGGCTGCGTGACAGTGATGGCTCAGGACAAGCCACCGTGGACAT CGAGCTCGTGACCACCACCGTGTCCAATATGGCCGAAGTGCGGAGCTACTGCTACGAGGCCAG CATCAGCGACATGGCCAGCGACAGCAGATGCCCTACACAGGGCGAGGCCCTACCTGGACAAGCA GTCCGACACCCAGTACGTGTGCAAGCGGACCCCTGGTGGATAGAGGCTGGGGCAATGGCTGCGG CCTGTTTGGCAAGGGCAGCCTCGTGACCTGCGCCAAGTTCGCCTGCAGCAAGAAGATGACCGG CAAGAGCATCCAGCCCGAGAACCTGGAATACCGGATCATGCTGAGCGTGACGGCAGCCAGCA CTCCGGCATGATCGTGAACGACACCGGCCACGAGACAGACGAGAACCGGGCCAAGGTGGAAT CACCCCCAACAGCCCTAGAGCCGAGGCCACACTGGGCGGCTTTGGATCTCTGGGCCTGGACTG CGAGCCTAGAACC GGCCCTGGATTT CAGCGACCTGTACTACCTGACCATGAACAACAAGCACTG GCTGGTGCACAAAGAGTGGTTCCACGACATCCCCCTGCCCTGGCATGCCGGCGCTGATACAGG CACACCCCACTGGAACAACAAGAGGCTCTGGTGGAAATTCAGGACGCCCACGCCAAGCGGCA GACCGTGGTGGTGTCTGGGATCTCAGGAAGGCGCCGTGCATACAGCTCTGGCTGGCGCCCTGGA AGCCGAAATGGATGGCGCCAAAGGCAGACTGTCCAGCGGCCACCTGAAGTGCCGGCTGAAGAT GGACAAGCTGCGGCTGAAGGGCGTGTCTACAGCCTGTGTACCGCCGCCTTCACCTTCACCAA GATCCCCGCCGAGACACTGCACGGCACCCTGACTGTGGAAGTGAGTACGCCGGCACCAGCGG CCCTTGTAAGTGCCTGCTCAGATGGCCGTGGATATGCAGACCCCTGACCCCGTGGGCAGACT GATCACCGCCAACCCTGTGATCACCGAGAGCACCGAGAACAGCAAGATGATGCTGGAATGGA CCCCCCTTCGGCGACTCCTACATCGTGATCGGCGTGGGAGAGAAGAAGATCACCCACCACTG GCACAGAAGCGGCAGCACCATCGGCAAGGCCTTTGAGGCTACAGTGCGGGGAGCCAAGAGAAT GGCCGTGCTGGGAGATACCGCCTGGGACTTTGGCTCTGTGGGCGGAGCCCTGAACCTCTCTGGG CAAGGGAATCCACCAGATCTTCGGAGCCGCCTTTAAGAGCCTGTTGCGCGGCATGAGCTGGTT CAGCCAGATCCTGATCGGCACCCTGCTGATGTGGCTGGGCCTGAACGCCAAGAACGGCAGCAT CTCCCTGATGTGCCTGGCTCTGGGAGGCGTGCTGATCTTCCTGAGCACAGCCGTGTCTGCCTg agcggccgcCCTGCACAACAGATTCTTCATGTTTGGACCAAATCAACTTGTGATACCATGCTC AAAGAGGCCTCAATTATATTTGAGTTTTTAAATTTTTATGAAAAAACTAACAGCAATCATGGA AGTCCACGATTTTGGAGACCGACGAGTTCAATGATTTCAATGAAGATGACTATGCCACAAGAGA ATTCTGAATCCCGATGAGCGCATGACGTAATTGAATCATGCTGATTACAATTTGAATTTCTCC TCTAATTAGTGATGATATTGACAATTTGATCAGGAAATTCATTTCTCTTCCGATTCCTCGAT GTGGGATAGTAAGAACTGGGATGGAGTTCTTGAGATGTTAACATCATGTCAAGCCAATCCCAT CTCAACATCTCAGATGCATAAATGGATGGGAAGTTGGTTAATGTCTGATAATCATGATGCCAG TCAAGGGTATAGTTTTTTTACATGAAGTGGACAAAGAGGCAGAAATAACATTTGACGTGGTGGA GACCTTCATCCGCGGCTGGGGCAACAAACCAATTGAATACATCAAAAAGGAAAGATGGACTGA CTCATTCAAAATTCTCGCTTATTTGTGTCAAAAGTTTTTGGACTTACACAAGTTGACATTAAT CTTAAATGCTGTCTCTGAGGTGGAATTGCTCAACTTGGCGAGGACTTTCAAAGGCAAAGTCAG AAGAAGTTCTCATGGAACGAACATATGCAGGATTAGGGTTCCCAGCTTGGGTCTACTTTTAT TTCAGAAGGATGGGCTTACTTCAAGAACTTGATATTCTAATGGACCGAAACTTTCTGTTAAT GGTCAAAGATGTGATTATAGGGAGGATGCAAACGGTGCTATCCATGGTATGTAGAATAGACAA CCTGTTCTCAGAGCAAGACATCTTCTCCCTTCTAAATATCTACAGAATTGGAGATAAAATTGT
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GGAGAGGCAGGGAAATTTTTCTTATGACTTGATTAAAATGGTGGAACCGATATGCAACTTGAA GCTGATGAAATTAGCAAGAGAATCAAGGCCTTTAGTCCCACAATTCCCTCATTTTGAAAATCA TATCAAGACTTCTGTTGATGAAGGGGCAAAAATTGACCGAGGTATAAGATTCCCTCCATGATCA GATAATGAGTGTGAAAACAGTGGATCTCACACTGGTGATTTATGGATCGTTCAGACATTGGGG TCATCCTTTTATAGATTATTACACTGGACTAGAAAAATTACATTCCCAAGTAACCATGAAGAA AGATATTGATGTGTCATATGCAAAAGCACTTGCAAGTGATTTAGCTCGGATTGTTCTATTTCA ACAGTTCAATGATCATAAAAAGTGGTTCGTGAATGGAGACTTGCTCCCTCATGATCATCCCTT TAAAAGTCATGTTAAAGAAAAATACATGGCCACAGCTGCTCAAGTTCAAGATTTTGGAGATAA ATGGCATGAACTTCCGCTGATTAAATGTTTTGAAATACCCGACTTACTAGACCCATCGATAAT ATACTCTGACAAAAGTCATTCAATGAATAGGTCAGAGGTGTTGAAACATGTCCGAATGAATCC GAACACTCCTATCCCTAGTAAAAAGGTGTTGCAGACTATGTTGGACACAAAGGCTACCAATTG GAAAGAATTTCTTAAAGAGATTGATGAGAAGGGCTTAGATGATGATGATCTAATTATTGGTCT TAAAGGAAAGGAGAGGGAACTGAAGTTGGCAGGTAGATTTTTCTCCCTAATGTCTTGGAATTT GCGAGAATACTTTGTAATTACCGAATATTTGATAAAGACTCATTTTCGTCCCTATGTTTAAAGG CCTGACAATGGCGGACGATCTAACTGCAGTCATTAAAAAGATGTTAGATTCCCTCATCCGGCCA AGGATTGAAGTCATATGAGGCAATTTGCATAGCCAATCACATTGATTACGAAAAATGGAATAA CCACCAAAGGAAGTTATCAAACGGCCCGAGTGTTCGAGTTATGGGCCAGTTCTTAGGTTATCC ATCCTTAATCGAGAGAACTCATGAATTTTTTGAGAAAAGTCTTATATACTACAATGGAAGACC AGACTTGATGCGTGTTCAACAACACACTGATCAATTCAACCTCCCAACGAGTTTGTGGCA AGGACAAGAGGGTGGACTGGAAGGTCTACGGCAAAAAGGATGGACTATCCTCAATCTACTGGT TATTCAAAGAGAGGCTAAAAATCAGAAACACTGCTGTCAAAGTCTTGGCACAAGGTGATAATCA AGTTATTTGCACACAGTATAAAACGAAGAAATCGAGAAACGTTGTAGAATTACAGGGTGCTCT CAATCAAATGGTTTCTAATAATGAGAAAATTATGACTGCAATCAAATAGGGACAGGGAAGTT AGGACTTTTGATAAATGACGATGAGACTATGCAATCTGCAGATTACTTGAATTATGGAAAAAT ACCGATTTTCCGTGGAGTGATTAGAGGGTTAGAGACCAAGAGATGGTCACGAGTGACTTGTGT CACCAATGACCAAATACCCACTTGTGCTAATATAATGAGCTCAGTTTCCACAAATGCTCTCAC CGTAGCTCATTTTGCTGAGAACCCAATCAATGCCATGATACAGTACAATTATTTGGGACATT TGCTAGACTCTTGTTGATGATGCATGATCCTGCTCTTCGTCAATCATTGTATGAAGTTCAAGA TAAGATACCGGGCTTGACACAGTTCTACTTTCAAATACGCCATGTTGTATTTGGACCCCTCCAT TGGAGGAGTGTCGGGCATGTCTTTGTCCAGGTTTTTTGATTAGAGCCTTCCCAGATCCCCTAAC AGAAAGTCTCTCATTCTGGAGATTCATCCATGTACATGCTCGAAGTGAGCATCTGAAGGAGAT GAGTGCAGTATTTGGAAACCCCGAGATAGCCAAGTTTTCGAATAACTCACATAGACAAGCTAGT AGAAGATCCAACCTCTCTGAACATCGCTATGGGAATGAGTCCAGCGAAGTTGTTAAAGACTGA GGTTAAAAAATGCTTAATCGAATCAAGACAAACCATCAGGAACCAGGTGATTAAGGATGCAAC CATATATTTGTATCATGAAGAGGATCGGCTCAGAAGTTTCTTATGGTCAATAAATCCTCTGTT CCCTAGATTTTAAAGTGAATCAAATCAGGCACTTTTTTGGGAGTCGCAGACGGGCTCATCAG TCTATTTCAAAATCTCGTACTATTTCGGAACCTTTTAAAGAAAAAGTATCATAGGGAATTGGA TGATTTGATTGTGAGGAGTGAGGTATCCTCTTTGACACATTTAGGGAACTTCATTTGAGAAG GGGATCATGTAAAAATGTGGACATGTTTCAGCTACTCATGCTGACACATTAAGATACAAATCCTG
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GGGCCGTACAGTTATTGGGACAACGTACCCCATCCATTAGAAATGTTGGGTCCACAACATCG AAAAGAGACTCCTTGTGCACCATGTAACACATCAGGGTCAATTATGTTTCTGTGCATTGTCC AGACGGGATCCATGACGTCTTTAGTTACGCGGGACCATTGCCTGCTTATCTAGGGTCTAAAAC ATCTGAATCTACATCTATTTTGCAGCCTTGGGAAAGGGAAAGCAAAGTCCCAGTATTAAAAG AGCTACACGTCTTAGAGATGCTATCTCTTGGTTTGTGAACCCGACTCTAACTAGCAATGAC TATACTTTCTAACATCCACTCTTTAACAGGCGAAGAATGGACCAAAGGCAGCATGGGTTCAA AAGAACAGGGTCTGCCCTTCATAGGTTTTCGACATCTCGGATGAGCCATGGTGGGTTCGCATC TCAGAGCACTGCAGCATTGACCAGGTTGATGGCAACTACAGACACCATGAGGGATCTGGGAGA TCAGAATTTGACTTTTTTATTCCAAGCAACGTTGCTCTATGCTCAAATTACCACCACTGTTGC AAGAGACGGATGGATCACCAGTTGTACAGATCATTATCATATTGCCTGTAAGTCCTGTTTGAG ACCCATAGAAGAGATCACCTGGACTCAAGTATGGACTACACGCCCCCAGATGTATCCCATGT GCTGAAGACATGGAGGAATGGGGAAGGTTTCGTGGGGACAAGAGATAAAACAGATCTATCCTTT AGAAGGGAATTGGAAGAATTTAGCACCTGCTGAGCAATCCTATCAAGTCGGCAGATGTATAGG TTTTCTATATGGAGACTTGGCGTATAGAAAATCTACTCATGCCGAGGACAGTTCTCTATTTCC TCTATCTATACAAGGTCGTATTAGAGGTCGAGGTTTCTTAAAAGGGTTGCTAGACGGATTAAT GAGAGCAAGTTGCTGCCAAGTAATACACCGGAGAAGTCTGGCTCATTTGAAGAGGCCGGCCAA CGCAGTGACGGAGGTTTGATTTACTTGATTGATAAATTGAGTGTATCACCTCCATTCCTTTC TCTTACTAGATCAGGACCTATTAGAGACGAATTAGAAACGATTCCCCACAAGATCCCAACCTC CTATCCGACAAGCAACCGTGATATGGGGTGATTGTCAGAAATTACTTCAAATACCAATGCCG TCTAATTGAAAAGGGAAAATACAGATCACATTATTCACAATTATGGTTATTCTCAGATGTCTT ATCCATAGACTTCATTGGACCATTCTCTATTTCCACCACCCTCTTGCAAATCCTATACAAGCC ATTTTTATCTGGGAAAAGATAAGAATGAGTTGAGAGAGCTGGCAAATCTTCTTCATTGCTAAG ATCAGGAGAGGGGTGGGAAGACATACATGTGAAATTCTTCACCAAGGACATATTATTGTGTCC AGAGGAAATCAGACATGCTTGCAAGTTCGGGATTGCTAAGGATAATAATAAGACATGAGCTA TCCCCCTTGGGGAAGGGAATCCAGAGGGACAATTACAACAATCCCTGTTTATTATACGACCAC CCCTTACCCAAAGATGCTAGAGATGCCTCCAAGAATCCAAAATCCCTGCTGTCCGGAATCAG GTTGGGCCAATTACCAACTGGCGCTCATTATAAAATTGCGAGTATATTACATGGAATGGGAAT CCATTACAGGGACTTCTTGAGTTGTGGAGACGGCTCCGGAGGGATGACTGCTGCATTACTACG AGAAAATGTGCATAGCAGAGGAATATTCAATAGTCTGTTAGAATTATCAGGGTCAGTCATGCG AGGCGCCTCTCCTGAGCCCCCAGTGCCCTAGAACTTTAGGAGGAGATAAATCGAGATGTGT AAATGGTGAAACATGTTGGGAATATCCATCTGACTTATGTGACCCAAGGACTTGGGACTATTT CCTCCGACTCAAAGCAGGCTTGGGGCTTCAAATTGATTTAATTGTAATGGATATGGAAGTTCG GGATTCTTCTACTAGCCTGAAAATTGAGACGAATGTTAGAAATTATGTGCACCGGATTTTGGA TGAGCAAGGAGTTTTAATCTACAAGACTTATGGAACATATATTTGTGAGAGCGAAAAGAATGC AGTAACAATCCTTGGTCCCATGTTCAAGACGGTCGACTTAGTTCAAACAGAATTTAGTAGTTC TCAAACGTCTGAAGTATATATGGTATGTAAAGGTTTGAAGAAATTAATCGATGAACCCAATCC CGATTGGTCTTCCATCAATGAATCCTGGAAAAACCTGTACGCATTCCAGTCATCAGAACAGGA ATTTGCCAGAGCAAAGAAGGTTAGTACATACTTTACCTTGACAGGTATTCCTCCCAATTCAT TCCTGATCCTTTTGTAACATTGAGACTATGCTACAAATATTGCGAGTACCCACGGGTGTGTC

TCATGCGGCTGCCTTAAAAATCATCTGATAGACCTGCAGATTTATTGACCATTAGCCTTTTTTA TATGGCGATTATATCGTATTATAACATCAATCATATCAGAGTAGGACCGATACCTCCGAACCC CCCATCAGATGGAATTGCACAAAATGTGGGGATCGCTATAACTGGTATAAGCTTTTGGCTGAG TTTGATGGAGAAAAGACATTCCACTATATCAACAGTGTTTAGCAGTTATCCAGCAATCATTTCC GATTAGGTGGGAGGCTGTTTCAGTAAAAGGAGGATACAAGCAGAAGTGGAGTACTAGAGGTGA TGGGCTCCCAAAAGATACCCGAACTTCAGACTCCTTGGCCCCAATCGGGAACCTGGATCAGATC TCTGGAATTGGTCCGAAACCAAGTTCGTCTAAATCCATTCAATGAGATCTTGTTCATCAGCT ATGTCGTACAGTGGATAATCATTTGAAATGGTCAAATTTGCGAAGAAACACAGGAATGATTGA ATGGATCAATAGACGAATTTCAAAGAAGACCGGTCTATACTGATGTTGAAGAGTGACCTACA CGAGGAAAACTCTTGGAGAGATTAAAAATCATGAGGAGACTCCAACTTTAAGTATGAAAA AACTTTGATCCTTAAGACCCCTCTTGTGGTTTTTTATTTTTTATCTGGTTTTGTGGTCTTCGTGG GTGCGCATGGCATCTCCACCTCCTCGCGGTCCGACCTGGGCATCCGAAGGAGGACGTGCTCCA CTCGGATGGCTAAGGGAGAGCTCGGATCCGGCTGCTAACAAAGCCCCGAAAGGAAGCTGAGTTG GCTGCTGCCACCGCTGAGCAATAACTAGCATAACCCCTTGGGGCCTCTAAACGGGTCTTGAGG GGTTTTTTGCTGAAAGGAGGAACTATATCCGGATCGAGATCCTCTAGAGTCGACCTGCAGGCA TGCAAGCTTGATTCTATAGTGTACCTAAATCGTATGTGTATGATACATAAGGTTATGTATT AATTGTAGCCGCTTCTAACGACAATATGTACAAGCCTAATTGTGTAGCATCTGGCTTACTGA AGCAGACCCCTATCATCTCTCTCGTAAACTGCCGTGAGAGTCGGTTTTGGTTGGACGAACCTTCT GAGTTTCTGGTAACGCCGTCCCGCACCCGGAATGGTCAGCGAACCAATCAGCAGGGTCATCG CTAGCCAGATCCTCTACGCCGACGCATCGTGGCCGGCATCACCGCGCCACAGGTGCGGTTG CTGGCGCCTATATCGCCGACATCACCGATGGGGAAGATCGGGCTCGCCACTTCGGGCTCATGA GCGCTTGTTTCGGCGTGGGTATGGTGGCAGGCCCGTGGCCGGGGGACTGTTGGGCGCCATCT CCTTGACCATTCCTTGCGGCGGCGGTGCTCAACGGCCTCAACCTACTACTGGGCTGCTTCCT AATGCAGGAGTCGCATAAGGGAGAGCGTCGAATGGTGCACCTCTCAGTACAATCTGCTCTGATG CCGCATAGTTAAGCCAGCCCCGACACCCGCCAACACCCGCTGACGCGCCCTGACGGGCTTGTC TGCTCCCGCATCCGCTTACAGACAAGCTGTGACCGTCTCCGGGAGCTGCATGTGTGAGAGGT TTTCACCGTCATCACCGAAACGCGCGAGACGAAAGGGCCTCGTGATACGCCTATTTTTATAGG TTAATGTCATGATAATAATGGTTTCTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCG GAACCCCTATTTGTTTATTTTTCTAAATACATTCAAATATGTATCCGCTCATGAGACAATAAC CCTGATAAATGCTTCAATAATATTGAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTGTG CCCTTATTCCTTTTTTGCGGCATTTTGCCTTCCTGTTTTTGCTCACCCAGAAACGCTGGTGA AAGTAAAAGATGCTGAAGATCAGTTGGGTGCACGAGTGGGTACATCGAACTGGATCTCAACA GCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCCAATGATGAGCACTTTTAAAG TTCTGCTATGTGGCGCGGTATTATCCCGTATTGACGCCGGGCAAGAGCAACTCGGTGCGCGCA TACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAAAAGCATCTTACGGATG GCATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAAACTGCGGCCAACT TACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGACAACATGGGGGATC ATGTAACCTGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCATACCAAACGACGAGCGTG ACACCACGATGCCTGTAGCAATGGCAACAACGTTGCGCAAACCTATTAACCTGGCGAACTACTTA
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	CTCTAGCTTCCCGGCAACAATTAATAGACTGGATGGAGGCGGATAAAAGTTGCAGGACCACTTC TGC GCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGTGGGT CTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGTAGTTATCTACA CGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAGGTGCCTCAC TGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAAAC TTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTTGATAATCTCATGACCAAAATCC CTTAACGTGAGTTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTT GAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAACACCGCTACCAGCGG TGGTTTGTGGCCGGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAAGTGGCTTCAGCAGAG CGCAGATACCAAAATACTGTCCTTCTAGTGCTAGCCGTAGTTAGGCCACCACTTCAAGAAGTCTG TAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATA AGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCCGGCT GAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACC TACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGG TAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGAAACGCCTGGTATC TTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAG GGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCCTTTTTACGGTTCCTGGCCTTTTGCT GGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGATAACCGTATTACCG CCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCG AGGAAGCGGAAGAGCGCCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCAATTAAT GCAGGGGGATCTCGATCCCGCGAAATTAATACGACTCACTATAGG
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In some embodiments, the nucleic acid sequence encoding a Zika virus prM protein is adjacent in the VSV genome to the nucleic acid sequence encoding a Zika virus E protein.

In some embodiments, the nucleic acid sequence encoding a Zika virus prM protein is

5 adjacent in the VSV genome to the nucleic acid sequence encoding a Zika virus C protein.

Exemplary sequences include rVSV-Zika-prME (SEQ ID NO:7) and rVSV-Zika-CprME (SEQ ID NO:8)

SEQ ID NO:7	ACGAAGACAAACAAACCATTATTATCATTTAAAAGGCTCAGGAGAACTTTAACAGTAATCAGA ATTCTCGAGAAAGCCACCATGAGAAGAGGCAGCGCCTACTACATGTACCTGGACCGGAACGAT GCCGGCGAGGCCATCAGCTTTCCAACCACCCTGGGCATGAACAAGTGCTACATCCAGATCATG GACCTGGGCCACACCTGTGACGCCACCATGAGCTACGAGTGCCCCATGCTGGACGAGGGCGTG GAACCCGACGATGTGGACTGCTGGTGCAACACCACCAGCACCTGGGTGGTGTACGGCACCTGT CACCACAAGAAGGGCGAAGCCAGACGGTCCAGACGGGCCGTGACACTGCCTAGCCACAGCACC AGAAAGCTGCAGACCCGGTCCCAGACCTGGCTGGAAAGCAGAGAGTACACCAAGCACCTGATC
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CGGGTGGAAACTGGATCTTCCGGAACCCCGGCTTTGCCCTGGCCGCTGCTGCTATTGCTTGG CTGCTGGGCAGCAGCACCTCCCAGAAAGTGATCTACCTCGTGATGATCCTGCTGATCGCCCCT GCCTACAGCATCCGGTGTATCGGCGTGTCCAACCGGGACTTCGTGGAAGGCATGAGCGGCGGC ACATGGGTGGACGTGGTGCTGGAACATGGCGGCTGCGTGACAGTGATGGCTCAGGACAAGCCC ACCGTGGACATCGAGCTCGTGACCACCACCGTGTCCAATATGGCCGAAGTGCGGAGCTACTGC TACGAGGCCAGCATCAGCGACATGGCCAGCGACAGCAGATGCCCTACACAGGGCGAGGCCTAC CTGGACAAGCAGTCCGACACCCAGTACGTGTGCAAGCGGACCCCTGGTGGATAGAGGCTGGGGC AATGGCTGCGGCCTGTTTGGCAAGGGCAGCCTCGTGACCTGCGCCAAGTTCGCCTGCAGCAAG AAGATGACCGGCAAGAGCATCCAGCCCGAGAACCTGGAATACCGGATCATGCTGAGCGTGAC GGCAGCCAGCACTCCGGCATGATCGTGAACGACACCGGCCACGAGACAGACGAGAACCGGGCC AAGGTGGAAATCACCCCCAACAGCCCTAGAGCCGAGGCCACACTGGGCGGCTTTGGATCTCTG GGCCTGGACTGCGAGCCTAGAACCGGCCTGGATTTTACGCGACCTGTACTACCTGACCATGAAC AACAAAGCACTGGCTGGTGCACAAAGAGTGGTTCACGACATCCCCCTGCCCTGGCATGCCGGC GCTGATACAGGCACACCCCACTGGAACAACAAAGAGGCTCTGGTGGAAATTCAGGACGCCCAC GCCAAGCGGCAGACCGTGGTGGTGTGGGATCTCAGGAAGCGCCGTGCATACAGCTCTGGCT GGCGCCCTGGAAGCCGAAATGGATGGCGCCAAAGGCAGACTGTCCAGCGGCCACCTGAAGTGC CGGCTGAAGATGGACAAGCTGCGGCTGAAGGGCGTGTCTACAGCCTGTGTACCGCCGCCTTC ACCTTCACCAAGATCCCCGCCGAGACACTGCACGGCACCGTGAAGTGTGGAAGTGCAGTACGCC GGCACCGACGGCCCTTGTAAGTGCCTGCTCAGATGGCCGTGGATATGCAGACCCCTGACCCCC GTGGGCAGACTGATCACCGCCAACCCTGTGATCACCGAGAGCACCGAGAACAGCAAGATGATG CTGGAAGTGGACCCCCCTTCGGCGACTCCTACATCGTGATCGGCGTGGGAGAGAAGAAGATC ACCCACCACTGGCACAGAAAGCGGCAGCACCATCGGCAAGGCCTTTGAGGCTACAGTGCGGGGA GCCAAGAGAATGGCCGTGCTGGGAGATACCGCCTGGGACTTTGGCTCTGTGGGCGGAGCCCTG AACTCTCTGGGCAAGGGAATCCACCAGATCTTCGGAGCCGCCTTTAAGAGCCTGTTTCGGCGGC ATGAGCTGGTTCAGCCAGATCCTGATCGGCACCCTGCTGATGTGGCTGGGCCGTAACGCCAAG AACGGCAGCATCTCCCTGATGTGCCTGGCTCTGGGAGGCGTGCTGATCTTCCTGAGCACAGCC GTGTCTGCCTAAATGGCCATATGAAAAAACTAACAGTAATCAAAATGTCTGTTACAGTCAAG AGAATCATTGACAACACAGTCATAGTTCCAAAACCTTCCTGCAAATGAGGATCCAGTGAATAC CCGGCAGATTACTTCAGAAAAATCAAAGGAGATTCTCTTTTACATCAATACTACAAAAAGTTTG TCAGATCTAAGAGGATATGTCTACCAAGGCCTCAAATCCGGAAATGTATCAATCATACATGTC AACAGCTACTTGTATGGAGCATTAAGGACATCCGGGGTAAGTTGGATAAAGATTGGTCAAGT TTCGGAATAAACATCGGGAAAGCAGGGGATACAATCGGAATATTTGACCTTGTATCCTTGAAA GCCCTGGACGGCGTACTTCCAGATGGAGTATCGGATGCTTCCAGAACCAGCGCAGATGACAAA TGGTTGCCTTTGTATCTACTTGGCTTATACAGAGTGGGCAGAACACAAATGCCTGAATACAGA AAAAAGCTCATGGATGGGCTGACAAATCAATGCAAAATGATCAATGAACAGTTTGAACCTCTT GTGCCAGAAGGTCTGACATTTTTGATGTGTGGGGAAATGACAGTAATTACACAAAAATTGTC GCTGCAGTGGACATGTTCTTCCACATGTTCAAAAAACATGAATGTGCCCTCGTTTACAGATACGGA ACTATTGTTTCCAGATTCAAAGATTGTGCTGCATTGGCAACATTTGGACACCTCTGCAAAATA ACCGGAATGTCTACAGAAGATGTAACGACCTGGATCTTGAACCGAGAAGTTGCAGATGAAATG

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	GATAATGAGTGTGAAAACAGTGGATCTCACACTGGTGATTTATGGATCGTTCAGACATTGGGG TCATCCTTTTATAGATTATTACACTGGACTAGAAAAATTACATTCCCAAGTAACCATGAAGAA AGATATTGATGTGTCATATGCAAAAGCACTTGCAAGTGATTTAGCTCGGATTGTTCTATTTCA ACAGTTCAATGATCATAAAAAGTGGTTCGTGAATGGAGACTTGCTCCCTCATGATCATCCCTT TAAAAGTCATGTTAAAAGAAAATACATGGCCACAGCTGCTCAAGTTCAAGATTTTGGAGATAA ATGGCATGAACTTCCGCTGATTAAATGTTTTGAAATACCCGACTTACTAGACCCATCGATAAT ATACTCTGACAAAAGTCATTCAATGAATAGGTCAGAGGTGTTGAAACATGTCCGAATGAATCC GAACACTCCTATCCCTAGTAAAAAGGTGTTGCAGACTATGTTGGACACAAAGGCTACCAATTG GAAAGAATTTCTTAAAGAGATTGATGAGAAGGGCTTAGATGATGATGATCTAATTATTTGGTCT TAAAGGAAAAGGAGAGGGAACTGAAGTTGGCAGGTAGATTTTTCTCCCTAATGTCTTGAAATT GCGAGAATACTTTGTAATTACCGAATATTTGATAAAGACTCATTTTCGTCCCTATGTTTAAAGG CCTGACAATGGCGGACGATCTAACTGCAGTCATTAAAAAGATGTTAGATTCCCTCATCCGGCCA AGGATTGAAGTCATATGAGGCAATTTGCATAGCCAATCACATTGATTACGAAAAATGGAATAA CCACCAAAGGAAGTTATCAAACGGCCCAGTGTTCCGAGTTATGGGCCAGTTCTTAGGTTATCC ATCCTTAATCGAGAGAACTCATGAATTTTTTGGAGAAAAGTCTTATATACTACAATGGAAGACC AGACTTGATGCGTGTTCAACAACACACTGATCAATTC AACCTCCCAACGAGTTTGTGGCA AGGACAAGAGGGTGGACTGGAAGGTCTACGGCAAAAAGGATGGACTATCCTCAATCTACTGGT TATTCAAAGAGAGGCTAAAAATCAGAAACACTGCTGTCAAAGTCTTGGCACAAGGTGATAATCA AGTTATTTGCACACAGTATAAACGAAGAAATCGAGAAACGTTGTAGAATTACAGGGTGCTCT CAATCAAATGTTTTCTAATAATGAGAAAATTATGACTGCAATCAAATAGGGACAGGGAAGTT AGGACTTTTGATAAATGACGATGAGACTATGCAATCTGCAGATTACTTGAATTATGGAAAAAT ACCGATTTTCCGTGGAGTGATTAGAGGGTTAGAGACCAAGAGATGGTCACGAGTGACTTGTGT CACCAATGACCAAATACCCACTTGTGCTAATATAATGAGCTCAGTTTCCACAAATGCTCTCAC CGTAGCTCATTTTGCTGAGAACCCAATCAATGCCATGATACAGTACAATTATTTTGGGACATT TGCTAGACTCTTGTGATGATGCATGATCCTGCTCTTCGTCAATCATTGTATGAAGTTCAAGA TAAGATACCGGGCTTGACAGTTCTACTTTCAAATACGCCATGTTGTATTTGGACCTTCCAT TGGAGGAGTGTCGGGCATGTCTTTGTCCAGGTTTTTTGATTAGAGCCTTCCCAGATCCCGTAAC AGAAAGTCTCTCATTCTGGAGATT CATCCATGTACATGCTCGAAGTGAGCATCTGAAGGAGAT GAGTGCAGTATTTGGAAAACCCCGAGATAGCCAAGTTTTCGAATAACTCACATAGACAAGCTAGT AGAAGATCCAACCTCTCTGAACATCGCTATGGGAATGAGTCCAGCGAACTTGTAAAGACTGA GGTTAAAAAATGCTTAATCGAATCAAGACAAACCATCAGGAACCAGGTGATTAAGGATGCAAC CATATATTTGTATCATGAAGAGGATCGGCTCAGAAGTTTTCTTATGGTCAATAAATCCTCTGTT CCCTAGATTTTTTAAGTGAATTCAAATCAGGCACCTTTTTTGGGAGTCGCAGACGGGCTCATCAG TCTATTTCAAATTTCTCGTACTATTTCGGAACTCCTTTAAGAAAAAGTATCATAGGGAATTGGA TGATTTGATTGTGAGGAGTGAGGTATCCTCTTTGACACATTTAGGGAACTTCATTTGAGAAG GGGATCATGTAAAAATGTGGACATGTT CAGCTACTCATGCTGACACATTAAGATACAAATCCTG GGGCCGTACAGTTATTGGGACAACTGTACCCCATCCATTAGAAATGTTGGGTCCACAACATCG AAAAGAGACTCCTTGTGCACCATGTAACACATCAGGGTCAATTATGTTTCTGTGCATTGTCC AGACGGGATCCATGACGTCTTTAGTT CACGGGGACCATTGCCTGCTTATCTAGGGTCTAAAAAC
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	CGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAGGTGCCTCAC TGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAAC TTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTTGATAATCTCATGACCAAATCC CTTAACGTGAGTTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTT GAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAACACCAGCTACCAGCGG TGGTTTGTTTGCCGGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAAGTGGCTTCAGCAGAG CGCAGATACCAAATACTGTCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTG TAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATA AGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTGGGCT GAACGGGGGGTTTCGTGCACACAGCCCAGCTTGAGCGAACGACCTACACCGAACTGAGATACC TACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGG TAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATC TTTATAGTCCTGTGCGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAG GGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCCTTTTTACGGTTTCTGGCCTTTTGCT GGCCTTTTGCTCACATGTTCTTCTGCGTTATCCCCTGATTCTGTGGATAACCGTATTACCG CCTTTGAGTGAGCTGATACCGCTCGCCGAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCG AGGAAGCGGAAGAGCGCCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCAATTAAT GCAGGGGGATCTCGATCCCGCGAAATTAATACGACTCACTATAGG
SEQ ID NO:8	ACGAAGACAAACAAACCATTATTATCATTAAGGCTCAGGAGAACTTTAACAGTAATCAGA ATTCGCCACCATGACCAGCGTGGGCATCGTGGGCCTGCTGCTGACCACCGCCATGGCCGCCGA GGTGACCAGAAGAGGCGAGCGCTACTACATGTACCTGGACCGGAACGATGCCGGCGAGGCCAT CAGCTTTCCAACCACCTGGGCATGAACAAGTGCTACATCCAGATCATGGACCTGGGCCACAC CTGTGACGCCACCATGAGCTACGAGTGCCCCATGCTGGACGAGGGCGTGGAACCCGACGATGT GGACTGCTGGTGCAACACCACCAGCACCTGGGTGGTGTACGGCACCTGTCACCACAAGAAGGG CGAAGCCAGACGGTCCAGACGGGCGGTGACACTGCCCTAGCCACAGCACCAGAAAGCTGCAGAC CCGGTCCCAGACCTGGCTGGAAGCAGAGAGTACACCAAGCACCTGATCCGGGTGGAAGAACTG GATCTTCCGGAACCCCGGCTTTGCCCTGGCCGCTGCTGCTATTGCTTGGCTGCTGGGCAGCAG CACCTCCCAGAAAGTGATCTACCTCGTGATGATCCTGCTGATCGCCCCCTGCCCTACAGCATCCG GTGTATCGGCGTGTTCAACCGGGACTTCGTGGAAGGCATGAGCGGCGGCACATGGGTGGACGT GGTGCTGGAACATGGCGGCTGCGTGACAGTGATGGCTCAGGACAAGCCACCGTGGACATCGA GCTCGTGACCACCACCGTGTTCAATATGGCCGAAGTGCGGAGCTACTGCTACGAGGCCAGCAT CAGCGACATGGCAAGCGACAGCAGATGCCCTACACAGGGCGAGGCCCTACCTGGACAAGCAGTC CGACACCCAGTACGTGTGCAAGCGGACCTGGTGGATAGAGGCTGGGGCAATGGCTGCGGCCT GTTTGGCAAGGGCAGCCTCGTGACCTGCGCCAAGTTCGCCTGCAGCAAGAAGATGACCGGCAA GAGCATCCAGCCCGAGAACCTGGAATACCGGATCATGCTGAGCGTGACGGCAGCCAGCACTC CGGCATGATCGTGAACGACACCGGCCACGAGACAGACGAGAACCGGGCCAAGGTGGAATCAC CCCCAACAGCCCTAGAGCCGAGGCCACACTGGGCGGCTTTGGATCTCTGGGCCTGGACTGCGA GCCTAGAACCGGCTGGATTTACGCGACCTGTACTACCTGACCATGAACAACAAGCACTGGCT

GGTGCACAAAGAGTGGTTCCACGACATCCCCCTGCCCTGGCATGCCGGCGCTGATACAGGCAC ACCCCACTGGAACAACAAAGAGGCTCTGGTGGAAATCAAGGACGCCACGCCAAGCGGCAGAC CGTGGTGGTGCTGGGATCTCAGGAAGGCGCCGTGCATACAGCTCTGGCTGGCGCCCTGGAAGC CGAAATGGATGGCGCCAAAGGCAGACTGTCCAGCGGCCACCTGAAGTGCCGGCTGAAGATGGA CAAGCTGCGGCTGAAGGGCGTGTCTACAGCCTGTGTACCGCCGCCTTCACCTTCACCAAGAT CCCCGCCGAGACACTGCACGGCACCGTGACTGTGGAAGTGCAGTACGCCGGCACCGACGGCCC TTGTAAAGTGCTGCTCAGATGGCCGTGGATATGCAGACCCTGACCCCGTGGGCAGACTGAT CACCGCCAACCCCTGTGATCACCGAGAGCACCGAGAACAGCAAGATGATGCTGGAACCTGGACCC CCCCCTTCGGCGACTCCTACATCGTGATCGGCGTGGGAGAGAAGAAGATCACCCACCCTGGCA CAGAAGCGGCAGCACCATCGGCAAGGCCCTTGGAGGCTACAGTGCGGGGAGCCAAGAGAATGGC CGTGCTGGGAGATACCGCCTGGGACTTTGGCTCTGTGGGCGGAGCCCTGAACTCTCTGGGCAA GGGAATCCACCAGATCTTCGGAGCCGCCCTTAAGAGCCTGTTTCGGCGGCATGAGCTGGTTTCAG CCAGATCCTGATCGGCACCCCTGCTGATGTGGCTGGGCCTGAACGCCAAGAACGGCAGCATCTC CCTGATGTGCCTGGCTCTGGGAGGCGTGCTGATCTTCCTGAGCACAGCCGTGTCTGCCTGATG GCCATATGAAAAAACTAACAGTAATCAAAATGTCTGTTACAGTCAAGAGAATCATTGACAAC ACAGTCATAGTTCCAAAACCTTCCTGCAAATGAGGATCCAGTGGAAATACCCGGCAGATTACTTC AGAAAAACAAAGGAGATTCTCTTTACATCAATACTACAAAAAGTTTGTGATCTAAGAGGA TATGTCTACCAAGGCCTCAAATCCGGAAATGTATCAATCATACATGTCAACAGCTACTTGTAT GGAGCATTAAGGACATCCGGGGTAAGTTGGATAAAGATTGGTCAAGTTTCGGAATAAACATC GGGAAAGCAGGGGATACAATCGGAATATTTGACCTTGTATCCTTGAAAGCCCTGGACGGCGTA CTTCCAGATGGAGTATCGGATGCTTCCAGAACCAGCGCAGATGACAAATGGTTGCCTTTGTAT CTACTTGGCTTATACAGAGTGGGCAGAACACAAATGCCTGAATACAGAAAAAGCTCATGGAT GGGCTGACAAATCAATGCAAAATGATCAATGAACAGTTTGAACCTCTTGTGCCAGAAGGTCGT GACATTTTTGATGTGTGGGAAATGACAGTAATTACACAAAAATTTGTCGCTGCAGTGGACATG TTCTTCCACATGTTCAAAAAACATGAATGTGCCTCGTTCAGATACGGAACATTTGTTTCCAGA TTCAAAGATTGTGCTGCATTGGCAACATTTGGACACCTCTGCAAAATAACCGGAATGTCTACA GAAGATGTAACGACCTGGATCTTGAACCGAGAAGTTGCAGATGAAATGGTCCAAATGATGCTT CCAGGCCAAGAAATTGACAAGGCCGATTTCATACATGCCTTATTTGATCGACTTTGGATTGTCT TCTAAGTCTCCATATTCTTCCGTCAAAAACCCCTGCCTTCCACTTCTGGGGGCAATTGACAGCT CTTCTGCTCAGATCCACCAGAGCAAGGAATGCCCCGACAGCCTGATGACATTGAGTATACATCT CTTACTACAGCAGGTTTGTGTACGCTTATGCAGTAGGATCCTCTGCCGACTTGGCACAACAG TTTTGTGTTGGAGATAACAAATACACTCCAGATGATAGTACCGGAGGATTGACGACTAATGCA CCGCCACAAGGCAGAGATGTGGTCGAATGGCTCGGATGGTTTGAAGATCAAAACAGAAAACCG ACTCCTGATATGATGCAGTATGCGAAAAGAGCAGTCATGTCACTGCAAGGCCTAAGAGAGAAG ACAATTGGCAAGTATGCTAAGTCAGAATTTGACAAATGACCCTATAATTCTCAGATCACCTAT TATATATTATGCTACATATGAAAAAACTAACAGATATCATGGATAATCTCACAAAAGTTTCGT GAGTATCTCAAGTCCTATTCTCGTCTGGATCAGGCGGTAGGAGAGATAGATGAGATCGAAGCA CAACGAGCTGAAAAGTCCAATTATGAGTTGTTCCAAGAGGATGGAGTGGAAGAGCATACTAAG CCCTCTTATTTTCAGGCAGCAGATGATTCTGACACAGAATCTGAACCAGAAATTGAAGACAAT
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CAAGGTTTGTATGCACAGGATCCAGAAGCTGAGCAAGTTGAAGGCTTTATACAGGGGCCTTTA GATGACTATGCAGATGAGGAAGTGGATGTTGTATTTACTTCGGACTGGAAACCACCTGAGCTT GAATCTGACGAGCATGGAAAGACCTTACGGTTGACATCGCCAGAGGGTTTAAAGTGGAGAGCAG AAATCCCAGTGGCTTTTCGACGATTAAAGCAGTCGTGCAAAGTGCCAAATACTGGAATCTGGCA GAGTGCACATTTGAAGCATCGGGAGAAGGGGTCAATTATGAAGGAGCGCCAGATAACTCCGGAT GTATATAAGGTCCTCCAGTGATGAACACACATCCGTCCCAATCAGAAGCAGTATCAGATGTT TGGTCTCTCTCAAAGACATCCATGACTTTCCAACCCAAGAAAGCAAGTCTTCAGCCTCTCACC ATATCCTTGGATGAATTGTTCTCATCTAGAGGAGAGTTCATCTCTGTCTGGAGGTGACGGACGA ATGTCTCATAAAGAGGCCATCCTGCTCGGCCTGAGATACAAAAAGTTGTACAATCAGGCGAGA GTCAAATATTCTCTGTAGACTATGAAAAAAGTAACAGATATCACGATCTAAGTGTTATCCCA ATCCATTTCATCATGAGTTCCTTAAAGAAGATTCTCGGTCTGAAGGGGAAAGGTAAGAAATCTA AGAAATTAGGGATCGCACCACCCCTTATGAAGAGGACACTAGCATGGAGTATGCTCCGAGCG CTCCAATTGACAAATCCTATTTTGGAGTTGACGAGATGGACACCTATGATCCGAATCAATTAA GATATGAGAAATCTTCTTTACAGTGAAAATGACGGTTAGATCTAATCGTCCGTTTCAGAACAT ACTCAGATGTGGCAGCCGCTGTATCCCATTTGGGATCACATGTACATCGGAATGGCAGGGAAAC GTCCCTTCTACAAAATCTTGGCTTTTTTGGGTTCTTCTAATCTAAAGGCCACTCCAGCGGTAT TGGCAGATCAAGGTCAACCAGAGTATCACACTCACTGCGAAGGCAGGGCTTATTTGCCACATA GGATGGGGAAGACCCCTCCCATGCTCAATGTACCAGAGCACTTCAGAAGACCATTCAATATAG GTCTTTACAAGGGAACGATTGAGCTCACAATGACCATCTACGATGATGAGTCACTGGAAGCAG CTCCTATGATCTGGGATCATTTCAATTCTTCCAAATTTTCTGATTTTCAGAGAGAAGGCCTTAA TGTTTTGGCCTGATTGTCTGAGAAAAAGGCATCTGGAGCGTGGGTCTGGATTCTATCAGCCACT TCAAATGAGCTAGTCTAACTTCTAGCTTCTGAACAATCCCGGTTTTACTCAGTCTCTCCTAAT TCCAGCCTCTCGAACAACTAATATCCTGTCTTTTCTATCCCTATGAAAAAACTAACAGAGAT CGATCTGTTTCTTGACACTATGAAGTGCCTTTTTGTACTTAGCCTTTTTTATTCAATTGGGGTGA ATTGCAAGTTCACCATAGTTTTTCCACACAACCAAAAAGGAAACTGGAAAAATGTTCTTCTA ATTACCATTATTGCCCGTCAAGCTCAGATTTAAATTGGCATAATGACTTAATAGGCACAGCCA TACAAGTCAAAATGCCCCAAGAGTCACAAGGCTATTCAAGCAGACGGTTGGATGTGTCATGCTT CCAAATGGGTCACTACTTGTGATTTCCGCTGGTATGGACCGAAGTATATAACACAGTCCATCC GATCCTTCACTCCATCTGTAGAACAATGCAAGGAAAGCATTGAACAAACGAAACAAGGAACCTT GGCTGAATCCAGGCTTCCCTCCTCAAAGTTGTGGATATGCAACTGTGACGGATGCCGAAGCAG TGATTGTCCAGGTGACTCCTCACCATGTGCTGGTTGATGAATACACAGGAGAATGGGTTGATT CACAGTTCATCAACGGAAAAATGCAGCAATTACATATGCCCCACTGTCCATAACTCTACAACCT GGCATTCTGACTATAAGGTCAAAGGGCTATGTGATTCTAACCTCATTTCCATGGACATCACCT TCTTCTCAGAGGACGGAGAGCTATCATCCCTGGGAAAGGAGGGCACAGGGTTCAGAAGTAACT ACTTTGCTTATGAAACTGGAGGCAAGGCCTGCAAAATGCAATACTGCAAGCATTTGGGGAGTCA GACTCCCATCAGGTGTCTGGTTCGAGATGGCTGATAAGGATCTCTTTGCTGCAGCCAGATTCC CTGAATGCCCAGAAGGGTCAAGTATCTCTGCTCCATCTCAGACCTCAGTGGATGTAAGTCTAA TTCAGGACGTTGAGAGGATCTTGGATTATTCCTCTGCCAAGAAACCTGGAGCAAAATCAGAG CGGGTCTTCCAATCTCTCCAGTGGATCTCAGCTATCTTGCTCCTAAAAACCCAGGAACCGGTC
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CTGCTTTCACCATAATCAATGGTACCCTAAAATACTTTGAGACCAGATACATCAGAGTCGATA TTGCTGCTCCAATCCTCTCAAGAATGGTCGGAATGATCAGTGGAACCTACCACAGAAAGGGAAC TGTGGGATGACTGGGCACCATATGAAGACGTGGAAATTGGACCCAATGGAGTTCCTGAGGACCA GTTTACGGATATAAGTTTCCTTTATACATGATTGGACATGGTATGTTGGACTCCGATCTTCATC TTAGCTCAAAGGCTCAGGTGTTTGAACATCCTCACATTCAAGACGCTGCTTCGCAACTTCCTG ATGATGAGAGTTTATTTTTTGGTGATACTGGGCTATCCAAAAATCCAATCGAGCTTGTAGAAG GTTGGTTCAGTAGTTGGAAAAGCTCTATTGCCTCTTTTTTCTTTATCATAGGGTTAATCATTG GACTATTCTTGTTCTCCGAGTTGGTATCCATCTTTGCATTAAATTAAAGCACACCAAGAAAA GACAGATTTATACAGACATAGAGATGAACCGACTTGGAAAGTAACTCAAATCCTGCACAACAG ATTCTTCATGTTTGGACCAAATCAACTTGTGATACCATGCTCAAAGAGGCCTCAATTATATTT GAGTTTTTAATTTTTATGAAAAAACTAACAGCAATCATGGAAGTCCACGATTTTGAGACCGA CGAGTTCAATGATTTCAATGAAGATGACTATGCCACAAGAGAATTCCTGAATCCCGATGAGCG CATGACGTACTTGAATCATGCTGATTACAATTTGAATTCTCCTCTAATTAGTGATGATATTGA CAATTTGATCAGGAAATCAATTCTCTTCCGATTCCCTCGATGTGGGATAGTAAGAAGTGGGA TGGAGTTCTTGAGATGTTAACATCATGTCAAGCCAATCCCATCTCAACATCTCAGATGCATAA ATGGATGGGAAGTTGGTTAATGTCTGATAATCATGATGCCAGTCAAGGGTATAGTTTTTTACA TGAAGTGGACAAAGAGGCAGAAATAACATTTGACGTGGTGGAGACCTTCATCCGCGGCTGGGG CAACAAACCAATTGAATACATCAAAAAGGAAAGATGGACTGACTCATTCAAATTTCTCGCTTA TTTGTGTCAAAAGTTTTTGGACTTACACAAGTTGACATTAATCTTAAATGCTGTCTCTGAGGT GGAATTGCTCAACTTGGCGAGGACTTTCAAAGGCAAAGTCAGAAGAAGTTCTCATGGAACGAA CATATGCAGGATTAGGGTTCCCAGCTTGGGTCTTACTTTTTATTTTCAAGAGGATGGGCTTACTT CAAGAACTTGATATTCTAATGGACCGAACTTTCTGTTAATGGTCAAAGATGTGATTATAGG GAGGATGCAAACGGTGCTATCCATGGTATGTAGAATAGACAACCTGTTCTCAGAGCAAGACAT CTTCTCCCTTCTAAATATCTACAGAATTGGAGATAAAATTGTGGAGAGGCAGGGAAATTTTTTC TTATGACTTGATTAAAATGGTGGAAACCGATATGCAACTTGAAGCTGATGAAATTAGCAAGAGA ATCAAGGCCTTTAGTCCCACAATTCCCTCATTTTGAAAATCATATCAAGACTTCTGTTGATGA AGGGGCAAAAATTGACCGAGGTATAAGATTCCCTCATGATCAGATAATGAGTGTGAAAACAGT GGATCTCACACTGGTGATTTATGGATCGTTTCAAGACATTGGGGTCATCCTTTTATAGATTATTA CACTGGACTAGAAAAATTACATTCCCAAGTAACCATGAAGAAAGATATTGATGTGTCATATGC AAAAGCACTTGCAAGTGATTTAGCTCGGATTGTTCTATTTCAACAGTTCAATGATCATAAAAA GTGGTTCGTGAATGGAGACTTGCTCCCTCATGATCATCCCTTTAAAGTCATGTTAAAGAAAA TACATGGCCACAGCTGCTCAAGTTCAAGATTTTGGAGATAAATGGCATGAACCTCCGCTGAT TAAATGTTTTGAAATACCCGACTTACTAGACCCATCGATAATATACTCTGACAAAAGTCATTC AATGAATAGGTGAGAGGTGTTGAAACATGTCCGAATGAATCCGAACACTCCTATCCCTAGTAA AAAGGTGTTGCAGACTATGTTGGACACAAAGGCTACCAATTGGAAAGAATTTCTTAAAGAGAT TGATGAGAAGGGCTTAGATGATGATGATCTAATTATTGGTCTTAAAGGAAAGGAGAGGGAACT GAAGTTGGCAGGTAGATTTTTCTCCCTAATGTCTTGGAAATTGCGAGAATACTTTGTAATTAC CGAATATTTGATAAAGACTCATTTTCTCCCTATGTTTAAAGGCCTGACAATGGCGGACGATCT AACTGCAGTCATTAAAAAGATGTTAGATTCCCTCATCCGGCCAAGGATTGAAGTCATATGAGGC

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AATACACCGGAGAAGTCTGGCTCATTTGAAGAGGCCGGCCAACGCAGTGTACGGAGGTTTGAT TTACTTGATTGATAAATTGAGTGTATCACCTCCATTCCCTTCTCTTACTAGATCAGGACCTAT TAGAGACGAATTAGAAACGATTCCCCACAAGATCCCAACCTCCTATCCGACAAGCAACCGTGA TATGGGGGTGATTGTGAGAAATTACTTCAAATACCAATGCCGTCTAATTGAAAAGGGAAAATA CAGATCACATTATTACAATTATGGTTATTCTCAGATGTCTTATCCATAGACTTCATTGGACC ATTCTCTATTTCCACCACCCTCTTGCAAATCCTATACAAGCCATTTTTATCTGGGAAAGATAA GAATGAGTTGAGAGAGCTGGCAAATCTTCTCTCATTGCTAAGATCAGGAGAGGGGTGGGAAGA CATACATGTGAAATTCTTCACCAAGGACATATTATTGTGTCCAGAGGAAATCAGACATGCTTG CAAGTTCGGGATTGCTAAGGATAATAATAAAGACATGAGCTATCCCCCTTGGGGAAGGGAATC CAGAGGGACAATTACAACAATCCCTGTTTATTATACGACCACCCCTTACCCAAAGATGCTAGA GATGCCTCCAAGAATCCAAAATCCCCCTGCTGTCCGGAATCAGGTTGGGCCAATTACCAACTGG CGCTCATTATAAAATTCTGGAGTATATTACATGGAATGGGAATCCATTACAGGGACTTCTTGAG TTGTGGAGACGGCTCCGGAGGGATGACTGCTGCATTACTACGAGAAAATGTGCATAGCAGAGG AATATTCAATAGTCTGTTAGAATTATCAGGGTCAGTCATGCGAGGCGCCTCTCCTGAGCCCCC CAGTGCCCTAGAACTTTAGGAGGAGATAAATCGAGATGTGTAAATGGTGAAACATGTTGGGA ATATCCATCTGACTTATGTGACCCAAGGACTTGGGACTATTTCTCCGACTCAAAGCAGGCTT GGGGCTTCAAATTGATTTAATTGTAATGGATATGGAAGTTCGGGATTCTTCTACTAGCCTGAA AATTGAGACGAATGTTAGAAATTATGTGCACCGGATTTTGGATGAGCAAGGAGTTTAACTCA CAAGACTTATGGAACATATATTTGTGAGAGCGAAAAGAATGCAGTAACAATCCTTGGTCCCAT GTTCAAGACGGTCGACTTAGTTCAAACAGAATTTAGTAGTTCTCAAACGTCTGAAGTATATAT GGTATGTAAAGGTTTGAAGAAATTAATCGATGAACCCAATCCCGATTGGTCTTCCATCAATGA ATCCTGGAAAAACCTGTACGCATTCCAGTCATCAGAACAGGAATTTGCCAGAGCAAAGAAGGT TAGTACATACTTTACCTTGACAGGTATTCCCTCCCAATTCATTCTGATCCTTTTGTAACAT TGAGACTATGCTACAAATATTCTGGAGTACCCACGGGTGTGTCTCATGCGGCTGCCTTAAATC ATCTGATAGACCTGCAGATTTATTGACCATTAGCCTTTTTTATATGGCGATTATATCGTATTA TAACATCAATCATATCAGAGTAGGACCGATACCTCCGAACCCCCCATCAGATGGAATTGCACA AAATGTGGGGATCGCTATAACTGGTATAAGCTTTTGGCTGAGTTTGATGGAGAAAGACATTCC ACTATATCAACAGTGTTTAGCAGTTATCCAGCAATCATTCCCGATTAGGTGGGAGGCTGTTTC AGTAAAAGGAGGATACAAGCAGAAGTGGAGTACTAGAGGTGATGGGCTCCCAAAGATACCCG AACTTCAGACTCCTTGGCCCCAATCGGGAAGTGGATCAGATCTCTGGAATTGGTCCGAAACCA AGTTCGTCTAAATCCATTCAATGAGATCTTGTTCATCAGCTATGTCTGACAGTGGATAATCA TTTGAAATGGTCAAATTTGCGAAGAAACACAGGAATGATTGAATGGATCAATAGACGAATTTTC AAAAGAAGACCGGTCTATACTGATGTTGAAGAGTGACCTACACGAGGAAAACCTCTGGAGAGA TTAAAAAATCATGAGGAGACTCCAAACTTTAAGTATGAAAAAACTTTGATCCTTAAGACCCT CTTGTGGTTTTTATTTTTTATCTGGTTTTGTGGTCTTCGTGGGTCCGCATGGCATCTCCACCT CCTCGGGTCCGACCTGGGCATCCGAAGGAGGACGTCGTCCACTCGGATGGCTAAGGGAGAGC TCGGATCCGGCTGCTAACAAAGCCCCGAAAGGAAGCTGAGTTGGCTGCTGCCACCGCTGAGCAA TAACTAGCATAACCCCTTGGGGCTCTAAACGGGTCTTGAGGGTTTTTTGCTGAAAGGAGGA ACTATATCCGGATCGAGATCCTCTAGAGTCGACCTGCAGGCATGCAAGCTTGATTCTATAGT

GTCACCTAAATCGTATGTGTATGATACATAAGGTTATGTATTAATTGTAGCCGCGTTCTAACG ACAATATGTACAAGCCTAATTGTGTAGCATCTGGCTTACTGAAGCAGACCCCTATCATCTCTCT CGTAAACTGCCGTCAGAGTCGGTTTGGTTGGACGAACCTTCTGAGTTTCTGGTAACGCCGTcC CGCACCCGGAAATGGTCAGCGAACCAATCAGCAGGGTCATCGCTAGCCAGATCCTCTACGCCG GACGCATCGTGGCCGGCATCACCGGCGCCACAGGTGCGGTTGCTGGCGCCTATATCGCCGACA TCACCGATGGGGAAGATCGGGCTCGCCACTTCGGGCTCATGAGCGCTTGTTTCGGCGTGGGTA TGGTGGCAGGCCCCGTGGCCGGGGGACTGTTGGGCGCCATCTCCTTGACCATTCCTTGCGGC GGCGGTGCTCAACGGCCTCAACCTACTACTGGGCTGCTTCCTAATGCAGGAGTCGCATAAGGG AGAGCGTCGAATGGTGCACCTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCCAGCCCC GACACCCGCCAACACCCGCTGACGCGCCCTGACGGGCTTGCTGCTCCCGGCATCCGCTTACA GACAAGCTGTGACCGTCTCCGGGAGCTGCATGTGTGAGAGGTTTTACCGTCATCACCGAAAC GCGCGAGACGAAAGGGCCTCGTGATACGCCTATTTTTATAGGTTAATGTCATGATAATAATGG TTTCTTAGACGTCAGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTT TCTAAATACATTCAAATATGTATCCGCTCATGAGACAATAACCCGTATAAATGCTTCAATAAT ATTGAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCTTTTTTTCGGG CATTTTGCTTCCTGTTTTTGGCTCACCCAGAAACGCTGGTGAAAGTAAAGATGCTGAAGATC AGTTGGGTGCACGAGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTT TTCGCCCCGAAGAACGTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTAT TATCCCGTATTGACGCCGGGCAAGAGCAACTCGGTGCGCGCATACACTATTCTCAGAATGACT TGGTTGAGTACTCACCACTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTAT GCAGTGCTGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGGAG GACCGAAGGAGCTAACCCTTTTTTGCACAACATGGGGGATCATGTAACCTCGCCTTGATCGTT GGGAACCGGAGCTGAATGAAGCCATACCAAACGACGAGCGTGACACCACGATGCCTGTAGCAA TGGCAACAACGTTGCGCAAACTATTAACCTGGCGAACTACTTACTCTAGCTTCCCGGCAACAAT TAATAGACTGGATGGAGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTG GCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTCAGCAC TGGGGCCAGATGGTAAGCCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTA TGGATGAACGAAATAGACAGATCGCTGAGATAGGTGCCTCACTGATTAAGCATTGGTAACGTG CAGACCAAGTTTACTCATATATACTTTAGATTGATTTAAAACCTTCATTTTTTAATTTAAAAGGA TCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTCTGTTCC ACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCG TAATCTGCTGCTTGCAAACAAAAAACACCGCTACCAGCGGTGGTTTGTGTTGCCGGATCAAG AGCTACCAACTCTTTTTCCGAAGGTAACCTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCC TTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTCG CTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGG ACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTGCGGCTGAACGGGGGGTTCTGTGCACAC AGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAA GCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAG GAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTGCGGTTTT
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	GCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAA ACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCT TTCCTGCGTTATCCCCCTGATTCTGTGGATAACCGTATTACCGCCTTTGAGTGAGCTGATACCG CTCGCCGAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCCAA TACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATGCAGGGGGATCTCGATCCCGC GAAATTAATACGACTCACTATAGG
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In some embodiments, the recombinant VSV comprises a nucleic acid sequence that is at least 80 (*e.g.*, at least 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99) % identical to: (i) the nucleic acid of SEQ ID NO:5; (ii) the nucleic acid of SEQ ID NO:6; (iii) the nucleic acid of SEQ ID NO:7; or (iv) the nucleic acid of SEQ ID NO:8. In some embodiments, the recombinant VSV comprises a nucleic acid sequence that is identical to: (i) the nucleic acid of SEQ ID NO:5; (ii) the nucleic acid of SEQ ID NO:6; (iii) the nucleic acid of SEQ ID NO:7; or (iv) the nucleic acid of SEQ ID NO:8.

Nucleic acid molecules provided herein can be obtained using standard molecular biology techniques. For example, nucleic acid molecules described herein can be cloned using standard PCR techniques or chemically synthesized.

In certain embodiments, provided herein are vectors that contain the isolated nucleic acid molecules described herein. As used herein, the term “vector,” refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of vector is a “plasmid”, which refers to a circular double stranded DNA loop into which additional DNA segments may be ligated. Another type of vector is a viral vector, wherein additional DNA segments may be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) can be integrated into the genome of a host cell upon introduction into the host cell, and thereby be replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes. Such vectors are referred to herein as “recombinant expression vectors” (or simply, “expression vectors”).

In another aspect, disclosed herein are recombinant VSV comprising a Zika virus envelope (E) protein or fragment thereof. An exemplary amino acid sequence for a wild type Zika virus envelope protein is as follows (SEQ ID NO: 9):

SEQ ID NO: 9	IRCI GVS NRDFVEGMSGGTWVDVVLEHGGCVTVMAQDKPTVDIELVTTTVSNMAEIRSYCYEA SISDMASDSRCPTQGEAYLDKQSDTQYVCKRTLVD RGWNGCGLFGKGS LVTCAKFACSKKMT GKSIQPENLEYRIMLSVHGSQHSGMIVNDTGHETDENRAKVEITPNSPRAEATLGGFGSLGLD CEPRTGLDFSDLYYLTMNNKHVLVHKEWFHDIPLPWHAGADTGT PHWNNKEALVEFKDAHAKR QTVVVLGSQEGAVHTALAGALEAEMDGAKGRLSSGHLKCRLKMDKLRLKGVSYSLCTAAFTFT KIPAETLHGTVTVEVQYAGTDGPCKVPAQMAVDMQTLTPVGRLITANPVITESTENSKMMLEL DPPFGDSYIVIGVGEKKITHHWRSGSTIGKA FEATVRGAKRMAVLGDTAWDFGSVGGALNSL GKGIHQIFGA AFKSLFGGMSWFSQILIGTLLMWLGLNTKNGSISLMCLALGGVLI FLSTAVSA
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In some embodiments, the recombinant viruses further comprise a Zika virus precursor membrane (prM) protein or fragment thereof. An exemplary amino acid sequence for a wild type Zika virus prM protein is as follows (SEQ ID NO: 10):

SEQ ID NO: 10	RRGSAYMYLDRNDAGEAISFP TTLGMNKCYIQIMDLGHMCDATMSYEC PMLDEGVEPDDVDC WCNTTSTWVVG TCHHKKGEARRSRRAVTLPSHSTRKLQTRSQTWLESREYTKHLIRVENWIF RNPGFALAAAAIAWLLGSSTSQKVIYLV MILLIAPAYS
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In some embodiments, the recombinant viruses further comprise a Zika virus capsid (C) protein or fragment thereof. An exemplary amino acid sequence for a wild type Zika virus capsid protein is as follows (SEQ ID NO: 11):

SEQ ID NO: 11	MKNPKKKSGGFRIVNMLKRGVARVSPFGGLKRLPAGLLLGHGP I RMVLAILAFLRFTA I KPSL GLINRWGSGVGKKEAMEI I KKFKKDLAAMLRI INARKEKKRRGADTSVGIVGLLLT TAMAAEVT
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In some embodiments, a protein described herein, or a fragment thereof, has an amino acid sequence that is at least 80 (*e.g.*, at least 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99) % identical to: (i) the amino acid of SEQ ID NO:9; (ii) the amino acid of SEQ ID NO:10; or (iii) the amino acid of SEQ ID NO:11. In some embodiments, a protein described herein, or a fragment thereof, has an amino acid sequence

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that is identical to: (i) the amino acid of SEQ ID NO:9; (ii) the amino acid of SEQ ID NO:10; or (iii) the amino acid of SEQ ID NO:11.

Percent amino acid sequence identity is defined as the percentage of amino acids in a candidate sequence that are identical to the amino acids in a reference sequence, after
5 aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software, such as BLAST software or ClustalW2. Appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal
10 alignment over the full-length of the sequences being compared can be determined by known methods.

Suitable cell lines for propagating a recombinant VSV or producing virus like particles include mammalian cells, such as BSRT7 cells, Vero cells, AGMK cells, BHK-21 cells, COS-I or COS-7 cells, MDCK cells, CV-1 cells, LLC-MK2 cells, primary cell lines
15 such as fetal Rhesus lung (FRhL-2) cells, BSC-1 cells, and MRC-5 cells, or human diploid fibroblasts, as well as avian cells, chicken or duck embryo derived cell lines, *e.g.*, AGEL cells, and primary, chicken embryo fibroblasts, and insect cell lines, such as C6/36 or Sf9 or Sf21. To propagate virus in cell culture, a recombinant vesicular stomatitis virus is used to infect the host cell (for example, selected from among the suitable cell types listed above).
20 After virus adsorption, the cultures are fed with medium capable of supporting growth of the cells. The host cells are maintained in culture until the desired virus titer is achieved.

To recover virus, the virus is harvested by common methods known in the art including slow-speed centrifugation, or by filtration through a filter of pore size of 0.45 μ m. Methods for concentrating recovered virus or VLPs are within the scope of a person with
25 ordinary skill in the art and include, for example, ultrafiltration (*e.g.*, with a membrane of no greater than 300 kDa pore size), or precipitation with polyethylene glycol (PEG) 8000. Methods for purifying viruses are known to a person with ordinary skill in the art and include continuous or multi-step sucrose gradients, purification by column chromatography using size exclusion, ion exchange, adsorption, or affinity columns, or purification by
30 partitioning in polymer two-phase or multi-phase systems, and any combination thereof. Methods for assaying for virus positive fractions include plaque assay, hemagglutination (HA) assay, and/or antigen assays such as immunoassays.

Pharmaceutical Compositions and Vaccines

In certain aspects, provided herein are pharmaceutical compositions and/or vaccines comprising a recombinant VSV described herein.

5 In some embodiments, the pharmaceutical compositions and/or vaccines described herein include a recombinant VSV comprising a Zika virus envelope (E) protein together with one or more excipients and/or adjuvants. In some embodiments, the recombinant VSV further comprises a Zika virus precursor membrane (prM) protein and/or a Zika virus capsid (C) protein or fragment thereof.

10 In some embodiments, the pharmaceutical composition and/or vaccine described herein comprises a recombinant VSV viral genome and/or a gene encoding a Zika virus envelope (E) protein. In some embodiments, the pharmaceutical composition and/or vaccine described herein comprises a gene encoding a Zika virus precursor membrane (prM) protein and/or a Zika virus capsid (C) protein or fragment thereof. The pharmaceutical composition
15 and/or vaccine can contain genetic material expressing a Zika virus envelope (E), a Zika virus precursor membrane (prM) protein and/or a Zika virus capsid (C) protein or fragment thereof. In such a case, the a Zika virus envelope (E), a Zika virus precursor membrane (prM) protein and/or a Zika virus capsid (C) protein can be expressed in cells of a susceptible species immunized with the vaccine containing a recombinant VSV. The cells
20 infected with these viruses release Zika virus like particles. The viruses, and the virus like particles can be isolated, purified and used as source of antigen for vaccine purposes. Immunity against wild type Zika virus can thereby be conferred in a species and/or tissue normally susceptible to a Zika virus infection.

In some embodiments, the pharmaceutical composition and/or vaccine may further
25 comprise an adjuvant that can augment the immune response by increasing delivery of antigen, stimulating cytokine production, and/or stimulating antigen presenting cells. In some embodiments, the adjuvant can be administered concurrently with the pharmaceutical composition and/or vaccine composition disclosed herein, *e.g.*, in the same composition or in separate compositions. For example, an adjuvant can be administered prior or subsequent to
30 the pharmaceutical composition and/or vaccine composition disclosed herein. Such adjuvants include, but are not limited to: aluminum salts, non-toxic bacterial fragments, cholera toxin (and detoxified fractions thereof), chitosan, homologous heat-labile of *E. coli*

(and detoxified fractions thereof), lactide/glycolide homo and copolymers (PLA/GA), polyanhydride *e.g.* trimellitylimido-L-tyrosine, DEAE-dextran, saponins complexed to membrane protein antigens (immune stimulating complexes—ISCOMS), bacterial products such as lipopolysaccharide (LPS) and muramyl dipeptide, (MDP), liposomes, cochelates, proteinoids, cytokines (interleukins, interferons), genetically engineered live microbial vectors, non-infectious pertussis mutant toxin, neurimidase/galactose oxidase, and attenuated bacterial and viral toxins derived from mutant strains.

In some embodiments, the recombinant VSV is able to induce an immune response in a subject against the Zika virus.

In certain embodiments, the pharmaceutical composition, vaccine and/or adjuvant can be administered to a subject, *e.g.*, a human subject, using a variety of methods that depend, in part, on the route of administration. The route can be, *e.g.*, intravenous injection or infusion (IV), subcutaneous injection (SC), intraperitoneal (IP) injection, or intramuscular injection (IM).

Therapeutic Methods

In certain aspects, provided herein is a method for inducing an immune response against Zika virus in a subject comprising administering to the subject a composition (*e.g.*, a vaccine composition) disclosed herein. In some embodiments, provided herein is a method for protecting a subject from Zika virus, comprising administering to the subject a composition disclosed herein. In some embodiments, provided herein is a method of treating a subject for a Zika virus infection comprising administering to the subject a composition disclosed herein.

A “subject,” as used herein, can be any mammal. For example, a subject can be a human, a non-human primate (*e.g.*, monkey, baboon, or chimpanzee), a horse, a cow, a pig, a sheep, a goat, a dog, a cat, a rabbit, a guinea pig, a gerbil, a hamster, a rat, or a mouse. In some embodiments, the subject is an infant (*e.g.*, a human infant). In some embodiments, the subject is female (*e.g.*, a human female). For example, a subject can be a human female of child-bearing age or a human female who is pregnant.

In certain embodiments, the subject is exposed to Zika virus due to the subject’s exposure to a mosquito comprising the Zika virus. The subject may be exposed to a *Aedes* mosquitoes, particularly *A. aegypti*. Such a subject may be at risk of developing a Zika virus infection and disease states related to or caused by such an infection. In certain

embodiments, the subject was exposed to Zika virus or a mosquito, within the last 6 month, within the last month, within the last two weeks, within the last week, within the last 72 hours, within the last 48 hours, within the last 24 hours, within the last 12 hours, within the last 6 hours, within the last 4 hours, within the last 2 hours, or within the last hour.

5 In certain embodiments, the subject does not have, but is at risk of developing a Zika virus infection. A subject "at risk" may or may not have detectable disease, and may or may not have displayed detectable disease prior to the treatment methods described herein. "At risk" denotes that an individual who is determined to be more likely to develop a symptom based on conventional risk assessment methods or has one or more risk factors that correlate
10 with development of a particular condition. An individual having one or more of these risk factors has a higher probability of developing a condition than an individual without these risk factors. Examples (i.e., categories) of risk groups are well known in the art and discussed herein, such as those subjects who are traveling to a region of the world where Zika virus is prevalent. For example, in some embodiments the region is in the United States,
15 Anguilla, Antigua, Argentina, Aruba, Barbados, Barbuda, Belize, Bolivia, Bonaire, Brazil, Cayman Islands, Colombia, Commonwealth of Puerto Rico, Costa Rica, Cuba, Curacao, Dominica, Dominican Republic, Ecuador, El Salvador, French Guiana, Grenada, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Jamaica, Martinique, Mexico, Nicaragua, Panama, Paraguay, Peru, Saba, Saint Barthélemy, Saint Lucia, Saint Martin, Saint Vincent
20 and the Grenadines, Sint Eustatius, Sint Maarten, Suriname, Trinidad and Tobago, Turks and Caicos, U.S. Virgin Islands, American Samoa, Fiji, Kosrae, Federated States of Micronesia, Marshall Islands, New Caledonia, Papua New Guinea, Samoa, Tonga, Venezuela, and Cape Verde.

Examples

25 The invention now being generally described will be more readily understood by reference to the following examples which are included merely for purposes of illustration of certain aspects and embodiments of the present invention, and are not intended to limit the invention in any way.

Example 1 - Construction and recovery of recombinant VSV expressing ZIKV envelope

30 As a first step to develop recombinant VSV expressing Zika virus envelope protein, or producing Zika virus VLPs, a fragment of the Zika virus spanning the prM (membrane), and E (envelope) proteins was chemically synthesized which generated four different

recombinant VSV. Two variants of Zika fragment were selected that differ in their N-terminus. In one case, the sequence that spans prM-E (prM-E) was included. In the second variant, the N-terminus of prM was extended into the capsid sequence of Zika because this region is predicted to be a transmembrane region that may help with the proper processing and folding of prM, (CprM-E). Those two different Zika fragments, prM-E and C-prM-E were each cloned into two different VSV vectors. In one VSV vector, the Zika coding sequences were cloned into the VSV genome, replacing the endogenous VSV viral glycoprotein (G), to yield rVSVΔGZika-prME and rVSVΔGZika-CprME (see schematic in Fig. 1A). The second vector was designed to maximally express the Zika virus antigens and therefore the Zika sequences were cloned into wild type VSV in front of the N gene of the virus to yield rVSV-Zika-prME and rVSV-Zika-CprME.

Example 2 - Rescue of recombinant virus with Zika envelope replacing VSV envelope: rVSVΔG-Zika-CprME and rVSVΔG-Zika-prME

rVSVΔG-Zika-CprME and rVSVΔG-Zika-prME infectious viruses were recovered by transfection of BSRT7 cells with each of the corresponding constructs together with the necessary VSV expression plasmids N, P, L and G. (as a tool to monitor infection of cells in culture eGFP was included in the VSV genome.) Fig. 1A illustrates the arrangement of coding sequences for the constructs and the method for transfection and recovery of virus.

Following subsequent amplification of each virus in BSRT7 cells by complementation with VSV G expressed in trans, rVSVΔG-Zika-prME and rVSVΔG-Zika-C-prME yielded 1.2×10^8 and 1×10^7 infectious units per ml respectively as determined by eGFP expression (Fig. 2A – Fig. 2D). By contrast, when virus was propagated in cells that lack VSV G expressed by transfection of plasmid, infectivity of both rVSVΔG-Zika-prME and rVSVΔG-Zika-CprME was reduced approximately 2 logs. It is important to note, however, that infection of the recombinant viruses propagated in the absence of VSV G indicating that infection is mediated by the Zika envelope protein and demonstrating that it is functionally incorporated into infectious particles.

The complete sequence of the recovered viruses was determined by RT-PCR and shown to contain no additional mutations.

Example 3 - Expression of Zika E in cells infected with VSVΔG variants.

Next, the VSV recombinants were confirmed to express the Zika envelope protein. To this end, cells were infected with VSV or the rVSVΔG-Zika variants and were monitored for expression of Zika proteins by metabolic incorporation of ^{35}S -methionine (Fig. 3A). Recombinant virus expresses a unique protein not seen in VSV infected cells of the

molecular weight expected for Zika envelope, together with the expected VSV proteins N, P, L and M.

When analyzed by Western blot using the anti- Dengue envelope monoclonal antibody 4G2 that cross reacts with Zika envelope (Fig. 3B), ZIKV envelope could be detected in extracts from infected cells (Fig. 3B, lanes 4 and 5). Note that the recombinant virus containing sequences of the Zika capsid protein (rVSVΔG-ZikaCprME) produce more envelope protein than the recombinant lacking C (rVSVΔG-Zika-prME). Zika envelope was also present in the cell culture supernatants of infected cells (Fig. 3B, lane 3) and infectious virus stocks (Fig. 3B, lane 6) suggesting that the ZIKV envelope incorporated into VSV particles or that Zika virus like particles were produced from the infected cells. As a control for the western blot, purified Zika virus, MR766 strain (lane 2) was included which confirms that the antibody recognizes E and confirming its mobility. As shown in Fig. 3C, monoclonal antibody 4G2 also uniquely labels cells infected with recombinant virus, but not wild type VSV.

Example 4 - Zika envelope is incorporated into VSVΔG particles.

To determine whether the recombinant VSVΔG-Zika incorporate Zika E into virions, cell culture supernatants were collected and purified by centrifugation. The sedimented particles were analyzed for their protein composition by SDS-PAGE and compared them to rVSV-eGFP. This result (Fig. 4) demonstrates that rVSVΔG-ZikaCprME incorporates Zika E into the virions further substantiating that the infectivity of these particles is mediated by E.

Example 5 - Recovery and growth of recombinant VSV containing both VSV G and Zika E: rVSV-Zika-prME and rVSV-Zika-CprME

rVSV- Zika-prME and rVSV-Zika-CprME were assembled and virus recovered by the schematic of Fig. 1A. Note from the sequence that the Zika encoding sequences were cloned into wild type VSV in front of the N gene, and the wild type VSV G remains in the genome, so that these viruses have the genetic structure 3'-Le-ZIKA-N-P-M-G-L-Tr-5'. Note also that these viruses did not contain GFP as a tool to monitor infection. Infectious virus were recovered from both constructs and a representative plaque assay is shown (Fig. 5) demonstrating routine titers of 1.5×10^8 pfu/ml.

Example 6 - VSV-Zika particles incorporate Zika E

To determine whether the VSV-Zika particles incorporate Zika E, infectious virus were purified through a sucrose cushion and analyzed those particles by SDS-PAGE (Fig. 6). Both VSV-G and Zika E envelope proteins are present in the purified material - despite the presence of the cognate VSV-G protein. This result suggests that either E was incorporated into the VSV particles or Zika like VLPs were generated.

Example 7 - All VSV-Zika recombinants incorporate E and produce Zika VLPs to different extents.

To determine whether the different viruses produce Zika VLPs and incorporate Zika E into the VSV particles, the products of infection were analyzed by sucrose gradient centrifugation. Briefly, Vero cells were infected with the indicated virus (Fig. 7A – 7D and Fig. 8A – 8D) and the cell culture fluids collected at 48h post infection. The cell culture fluids were clarified by low speed centrifugation to eliminate cellular debris and the resultant supernatant subjected to further centrifugation through a sucrose cushion to collect the viral particles and VLPs. The pellet fraction was resuspended in NTE and laid over a preformed linear 15-45% sucrose gradient. Following centrifugation to separate the different particles based on their density, fractions were collected using a gradient fractionator and analyzed for the presence of protein by SDS-PAGE and detection with Coomassie stain and by Western blot with the indicated antibodies (Fig. 7A – 7D and Fig. 8A – 8D). Each of the recombinant viruses generate both VLPs and VSV particles that contained Zika virus E. In addition, the recombinants rVSV-Zika-prME and rVSV-Zika-CprME showed the presence of VSV G in the VSV fractions (Fig. 7A – 7D and Fig. 8A – 8D) reflecting the presence of G in the viral genome and its expression during infection. Note the absence of VSV G in the corresponding fractions of rVSVΔG-Zika-prME and rVSVΔG-Zika-CprME (Fig. 7A – 7D and Fig. 8A – 8D). By comparing the levels of E incorporated into various VSV fractions, it appears that Zika E is most efficiently incorporated by rVSVΔG-Zika-prME. Although all the viruses produce Zika VLPs we note that the rVSV-Zika-CprME appears to be most efficient (compare Fig. 7A – 7D and Fig. 8A – 8D).

To confirm that the fractions correspond to VLPs and VSV particles, the fractions were analyzed by negative-stain electron microscopy. As shown (Fig. 9A and Fig. 9B) the VLP fraction have the spherical appearance of flavivirus VLPs and their dimensions (40nm diameter) are also consistent with this. The VSV-recombinants retain their bullet shape and

are approximately 200 nm by 80 nm. Collectively, these data (EM and gradient fractions) confirm that the recombinants generate Zika VLPs and VSV with Zika envelope. These data also demonstrate that the viruses that express VSV G from their genome also yield particles that incorporate VSV G.

5 While the present disclosure has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the disclosure. In addition, many modifications may be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective,
10 spirit and scope of the present disclosure. All such modifications are intended to be within the scope of the disclosure.

 All publications, patents, patent applications and sequence accession numbers mentioned herein are hereby incorporated by reference in their entirety as if each individual publication, patent or patent application was specifically and individually indicated to be
15 incorporated by reference. In case of conflict, the present application, including any definitions herein, will control.

What is claimed is:

1. A recombinant vesicular stomatitis virus (VSV) comprising in its genome a nucleic acid sequence encoding a Zika virus envelope (E) protein or fragment thereof.
2. The recombinant VSV of claim 1, further comprising in its genome a nucleic acid sequence encoding a Zika virus precursor membrane (prM) protein or fragment thereof.
3. The recombinant VSV of claim 2, further comprising in its genome a nucleic acid sequence encoding Zika virus capsid (C) protein or fragment thereof.
4. The recombinant VSV of claim 2 or 3, wherein the nucleic acid sequence encoding a Zika virus prM protein is adjacent in the VSV genome to the nucleic acid sequence encoding a Zika virus E protein.
5. The recombinant VSV of claim 3, wherein the nucleic acid sequence encoding a Zika virus prM protein is adjacent in the VSV genome to the nucleic acid sequence encoding a Zika virus C protein.
6. The recombinant VSV of any preceding claim, wherein the nucleic acid sequence encoding a Zika virus E protein substantially replaces the endogenous VSV viral glycoprotein (G) in the VSV genome.
7. The recombinant VSV of any preceding claim, wherein the nucleic acid encoding the Zika virus E protein has a sequence 90% identical to SEQ ID NO:2.
8. The recombinant VSV of claim 7, wherein the nucleic acid encoding Zika virus E protein has a sequence that is identical to SEQ ID NO: 2.
9. The recombinant VSV of any one of claims 2 to 8, wherein the nucleic acid encoding Zika virus prM has a sequence 90% identical to SEQ ID NO: 3.
10. The recombinant VSV of claim 9, wherein the Zika virus prM protein has a nucleic acid sequence that is identical to SEQ ID NO: 3.
11. The recombinant VSV of any one of claims 3 to 8, wherein the nucleic acid encoding Zika virus capsid (C) protein has a sequence 90% identical to SEQ ID NO:4.
12. The recombinant VSV of claim 11, wherein the nucleic acid encoding Zika virus capsid (C) has a sequence that is identical to SEQ ID NO: 4.
13. The recombinant VSV of any one of claim 1, 2, 4, 6 and 7-10, wherein the genome of the recombinant VSV has a nucleic acid sequence 90% identical to SEQ ID NO:5.

14. The recombinant VSV of claim 13, wherein the nucleic acid sequence is identical to SEQ ID NO:5.
15. The recombinant VSV of one of claims 1-12, wherein the genome of the recombinant VSV has a nucleic acid sequence 90% identical to SEQ ID NO:6.
16. The recombinant VSV of claim 15, wherein the nucleic acid sequence is identical to SEQ ID NO:6.
17. The recombinant VSV of any one of claims 1, 2, 4, and 7-10, wherein the genome of the recombinant VSV has a nucleic acid sequence 90% identical to SEQ ID NO:7.
18. The recombinant VSV of claim 17, wherein the nucleic acid sequence is identical to SEQ ID NO:7.
19. The recombinant VSV of any one of claims 1-5 and 7-10, wherein the genome of the recombinant VSV has a nucleic acid sequence 90% identical to SEQ ID NO:8.
20. The recombinant VSV of claim 19, wherein the nucleic acid sequence is identical to SEQ ID NO:8.
21. A recombinant VSV comprising a Zika virus envelope (E) protein or fragment thereof.
22. The recombinant VSV of claim 21, wherein the Zika virus envelope (E) protein or fragment thereof comprises an amino acid sequence that is at least 90% identical to SEQ ID No 9.
23. The recombinant VSV of claim 22, wherein the amino acid sequence is identical to SEQ ID No 9.
24. The recombinant VSV of claim 21, further comprising a Zika virus precursor membrane (prM) protein or fragment thereof.
25. The recombinant VSV of claim 24, wherein the Zika virus precursor membrane (prM) or fragment thereof comprises an amino acid sequence that is at least 90% identical to SEQ ID No 10.
26. The recombinant VSV of claim 25, wherein the amino acid sequence is identical to SEQ ID No 10.
27. The recombinant VSV of claim 21, further comprising a Zika virus capsid (C) protein or fragment thereof.

28. The recombinant VSV of claim 27, wherein the a Zika virus capsid (C) protein or fragment thereof comprises an amino acid sequence that is at least 90% identical to SEQ ID No 11.
29. The recombinant VSV of claim 28, wherein the amino acid sequence is identical to SEQ ID No 11.
30. A pharmaceutical composition comprising the recombinant VSV of any preceding claim, and a pharmaceutically acceptable carrier.
31. The pharmaceutical composition of claim 30, further comprising an adjuvant.
32. A Zika virus vaccine comprising the recombinant VSV of any one of claims 1-29.
33. The vaccine of claim 32, wherein the recombinant virus is live.
34. A nucleic acid encoding the recombinant VSV according to any one of claims 1-29.
35. The nucleic acid of claim 34, wherein the nucleic acid has a sequence that is at least 90% identical to SEQ ID No 9.
36. The nucleic acid of claim 35, wherein the sequence is 90% identical to SEQ ID No 9.
37. An expression vector comprising the nucleic acid of any one of claims 34-36.
38. A cell comprising the nucleic acid according to any one of claims 34-36 or the expression vector according to claim 37.
39. A method for inducing an immune response against Zika virus in a subject, the method comprising administering to the subject a composition comprising the recombinant virus of any one of claims 1-29.
40. The method of claim 39, wherein the subject is a human.
41. The method of claim 41, wherein the subject is female.
42. The method of claim 42, wherein the subject is of child-bearing age.
43. The method of claim 42, wherein the subject is pregnant.
44. The method of any one of claims 39-43, wherein the subject has been exposed to Zika virus.
45. The method of any one of claims 39-44, wherein the subject has been exposed to a mosquito comprising or suspected of comprising the Zika virus.
46. The method of any one of claims 39-45, wherein the subject does not have, but is at risk of developing a Zika virus infection.
47. The method of any one of claims 39-46, wherein the subject is traveling to a region where the Zika virus is prevalent.

48. The method of claim 47, wherein the region is in the United States, Anguilla, Antigua, Argentina, Aruba, Barbados, Barbuda, Belize, Bolivia, Bonaire, Brazil, Cayman Islands, Colombia, Commonwealth of Puerto Rico, Costa Rica, Cuba, Curacao, Dominica, Dominican Republic, Ecuador, El Salvador, French Guiana, Grenada, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Jamaica, Martinique, Mexico, Nicaragua, Panama, Paraguay, Peru, Saba, Saint Barthélemy, Saint Lucia, Saint Martin, Saint Vincent and the Grenadines, Sint Eustatius, Sint Maarten, Suriname, Trinidad and Tobago, Turks and Caicos, U.S. Virgin Islands, American Samoa, Fiji, Kosrae, Federated States of Micronesia, Marshall Islands, New Caledonia, Papua New Guinea, Samoa, Tonga, Venezuela, and Cape Verde.
49. A method for protecting a subject from Zika virus, comprising administering to the subject the recombinant virus of any one of claims 1-29.
50. The method of claims 49, wherein the subject is a human.
51. The method of claim 50, wherein the subject is female.
52. The method of claim 51, wherein the subject is of child-bearing age.
53. The method of claim 51, wherein the subject is pregnant.
54. The method of any one of claims 49-53, wherein the subject is exposed to Zika virus.
55. The method of any one of claims 49-54, wherein the subject is exposed to a mosquito comprising the Zika virus.
56. The method of any one of claims 49-55, wherein the subject does not have, but is at risk of developing a Zika virus infection.
57. The method of any one of claims 49-56, wherein the subject is traveling to a region where the Zika virus is prevalent.
58. The method of claim 57, wherein the region is in the United States, Anguilla, Antigua, Argentina, Aruba, Barbados, Barbuda, Belize, Bolivia, Bonaire, Brazil, Cayman Islands, Colombia, Commonwealth of Puerto Rico, Costa Rica, Cuba, Curacao, Dominica, Dominican Republic, Ecuador, El Salvador, French Guiana, Grenada, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Jamaica, Martinique, Mexico, Nicaragua, Panama, Paraguay, Peru, Saba, Saint Barthélemy, Saint Lucia, Saint Martin, Saint Vincent and the Grenadines, Sint Eustatius, Sint Maarten, Suriname, Trinidad and Tobago, Turks and Caicos, U.S. Virgin Islands, American Samoa, Fiji, Kosrae, Federated States of Micronesia, Marshall Islands, New Caledonia, Papua New Guinea, Samoa, Tonga, Venezuela, and Cape Verde.

59. A method of treating a Zika virus infection in a subject, the method comprising administering to the subject a composition comprising the recombinant virus of any one of claims 1-29.
60. The method of claim 59, wherein the subject is a human.
61. The method of claim 60, wherein the subject is female.
62. The method of claim 61, wherein the subject is of child-bearing age.
63. The method of claim 61, wherein the subject is pregnant.
64. A method of making virus-like particles (VLP) comprising :
transfecting a cell with the expression vector of claim 37;
culturing the cell under conditions such that the cell produces a Zika virus VLP; and
collecting the Zika virus VLP.
65. The method of claim 64, wherein the cells are BSRT7 cells

Fig. 1A

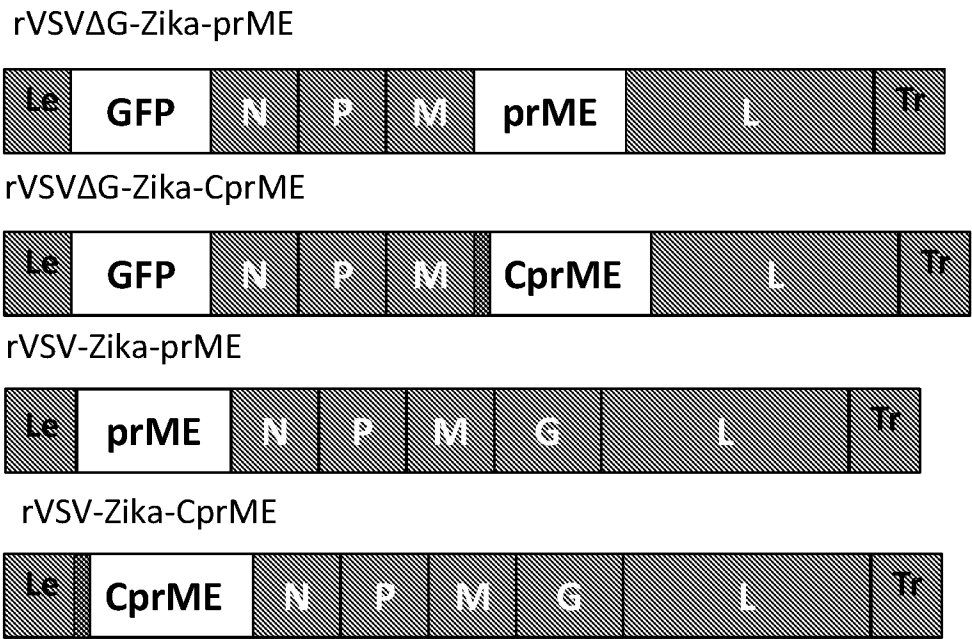


Fig. 1B

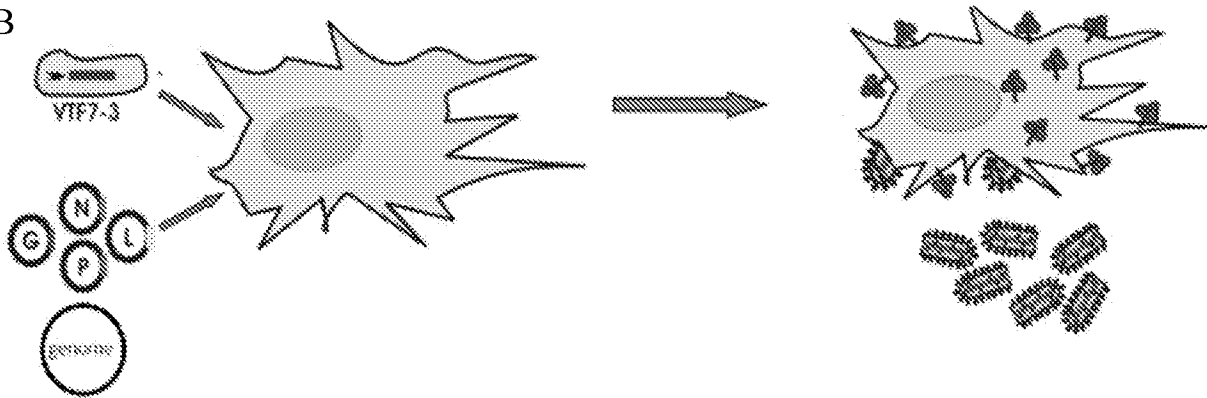


Fig. 2A

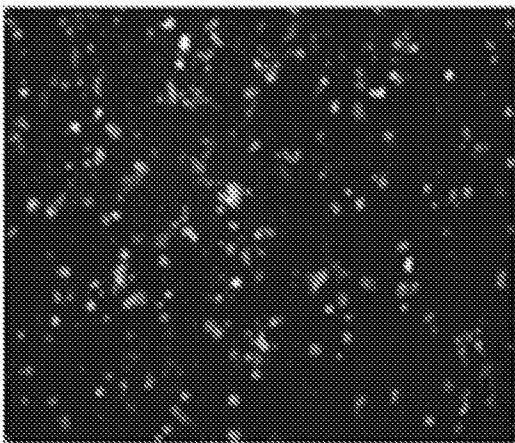


Fig. 2C

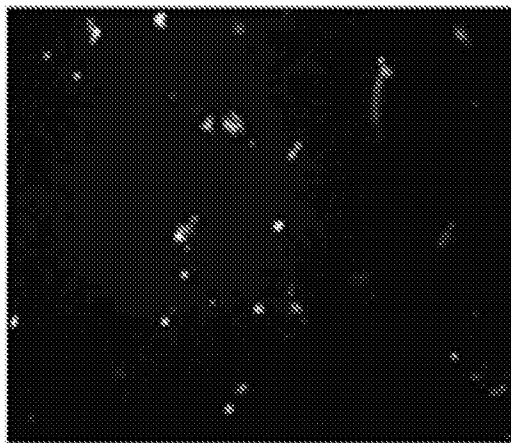


Fig. 2B

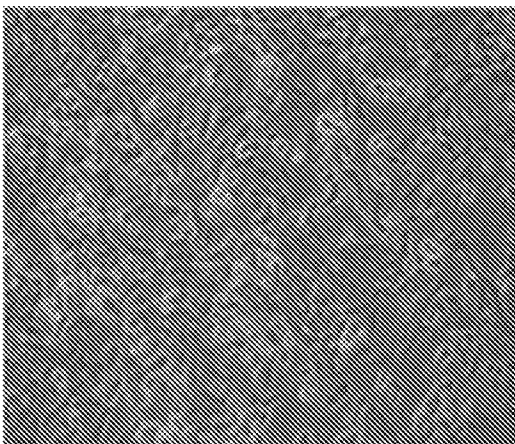


Fig. 2D

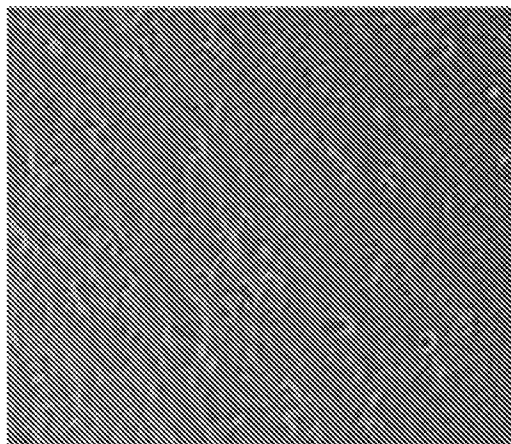


Fig. 3A

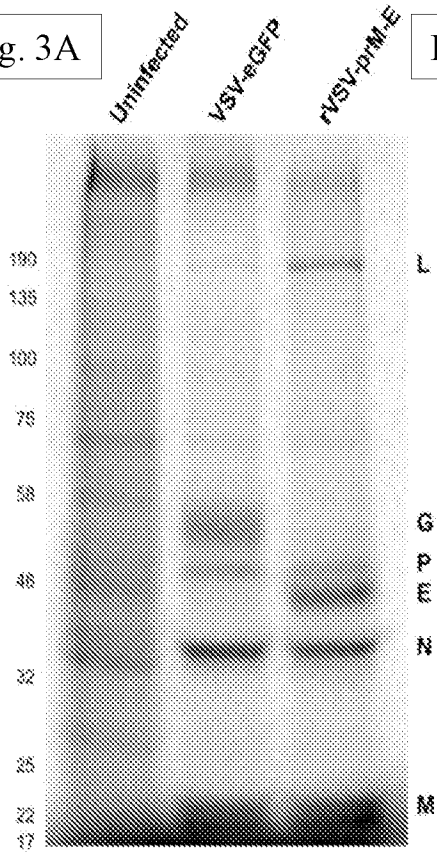


Fig. 3B

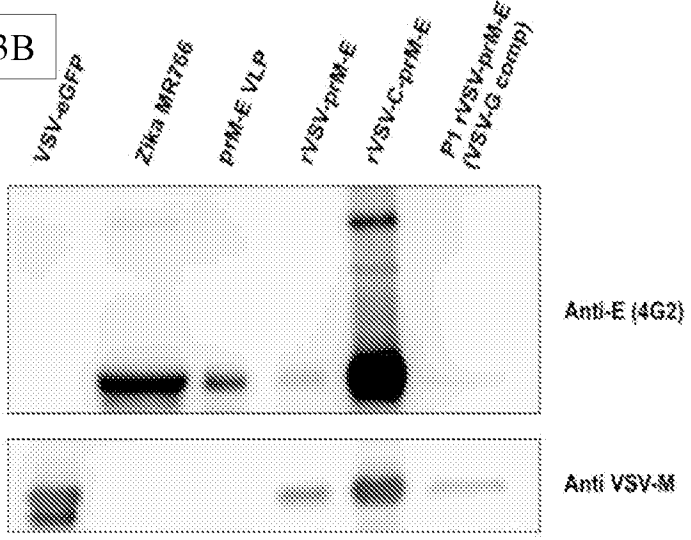


Fig. 3C

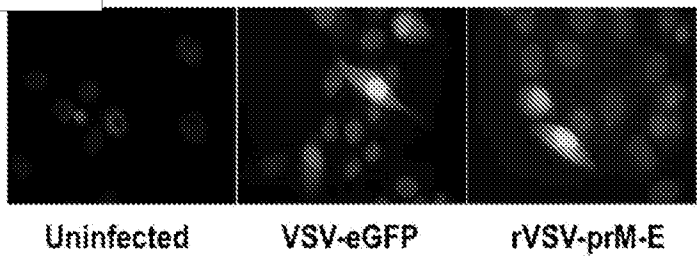


Fig. 4

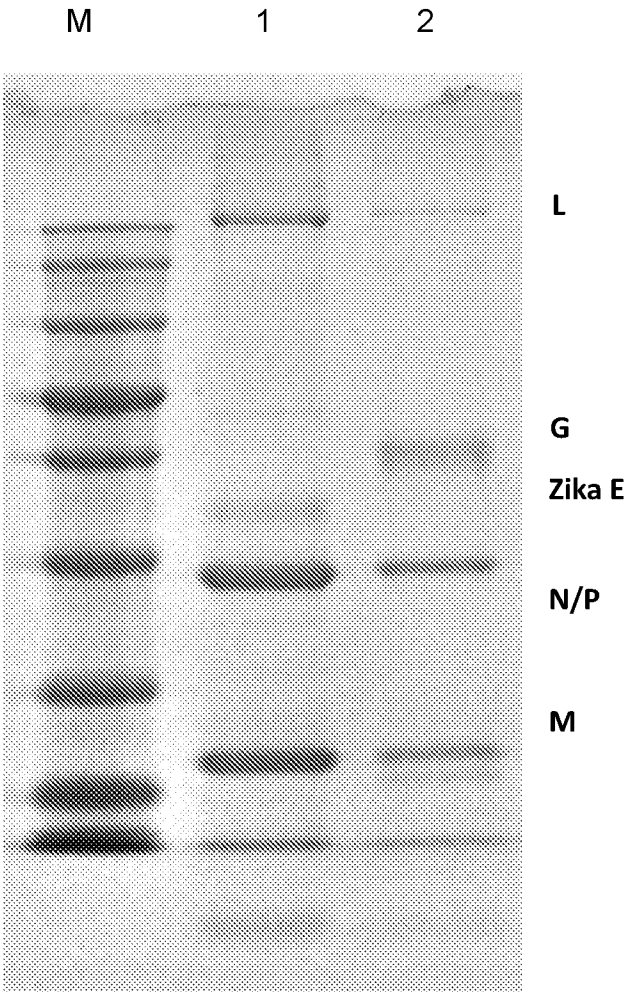


Fig. 5

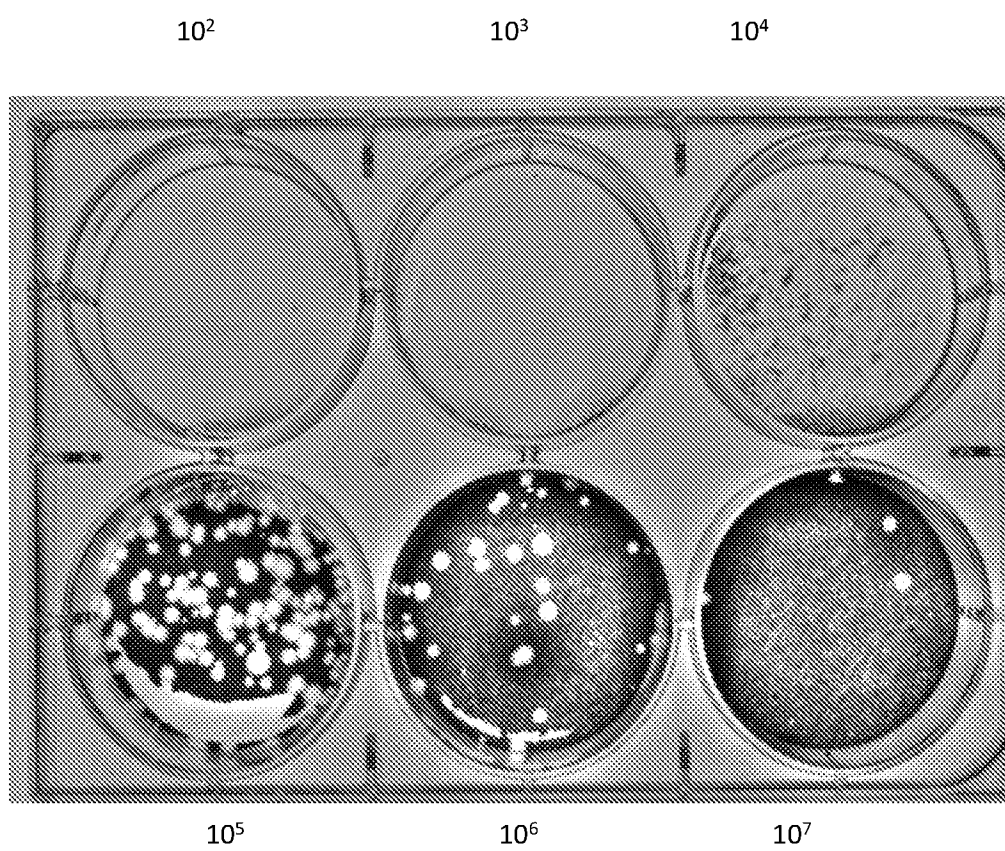


Fig. 6

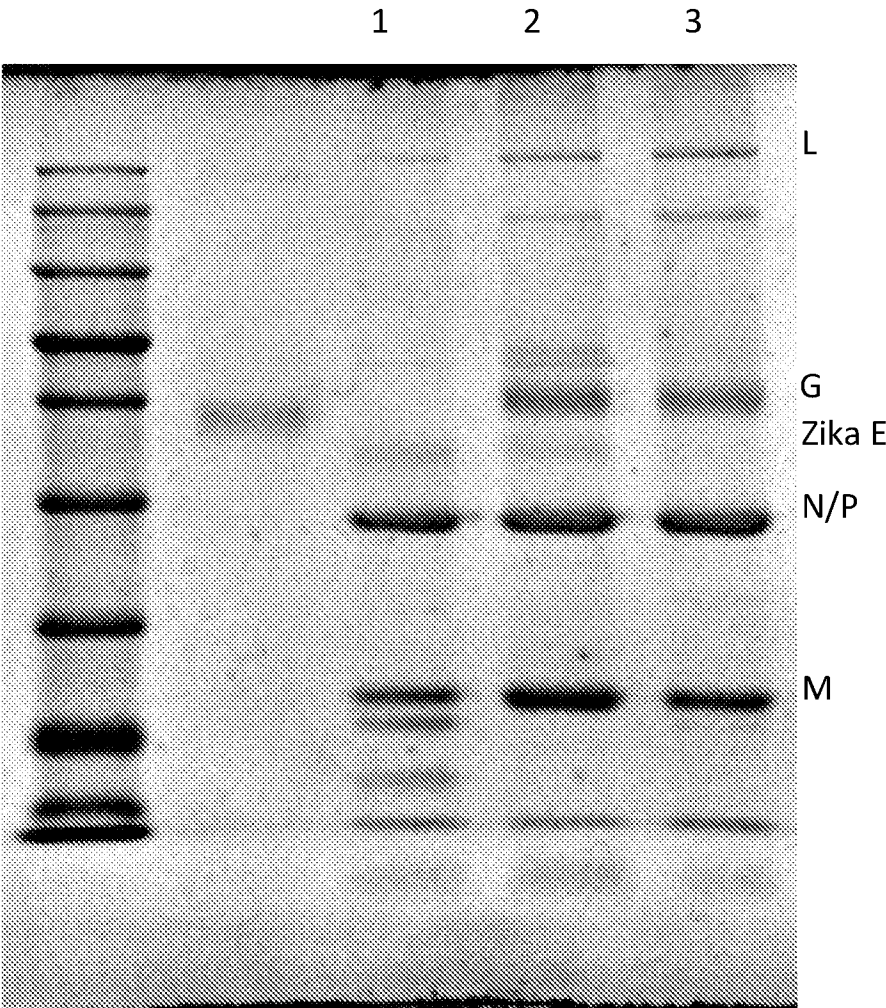


Fig. 7A

rVSVΔG-Zika-CprME

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22

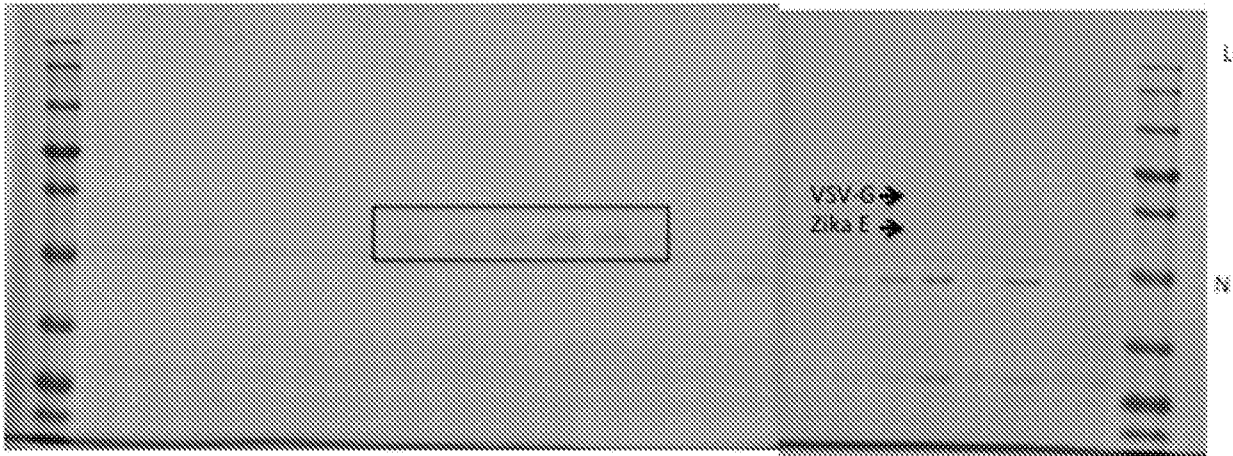


Fig. 7B

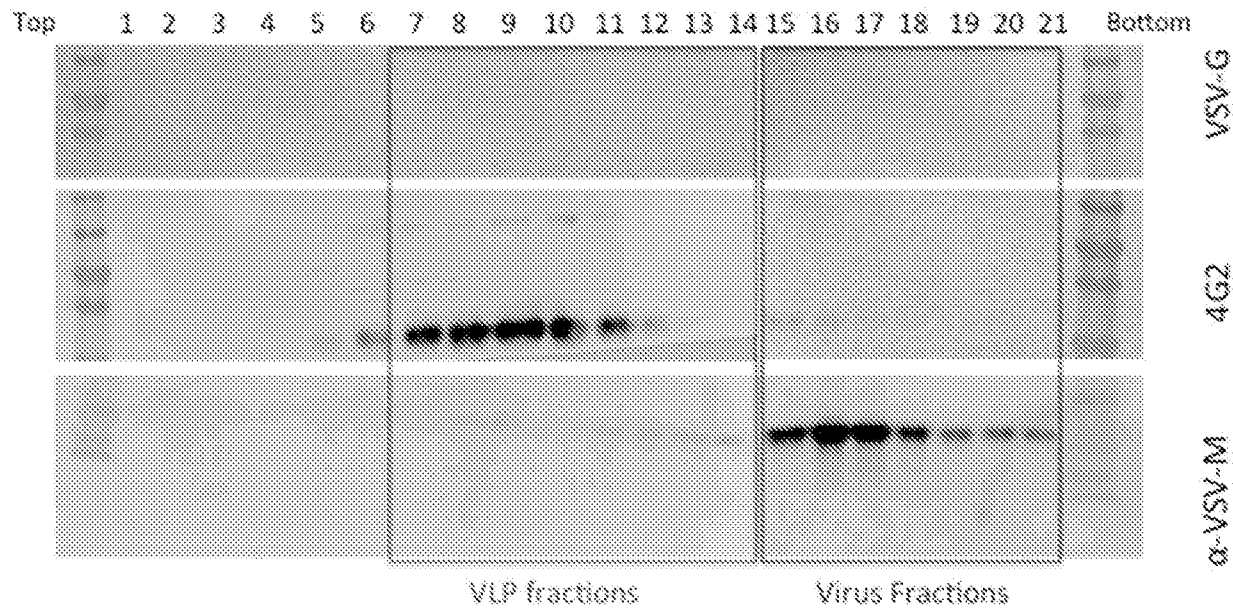


Fig. 7C

rVSV-Zika-CprME

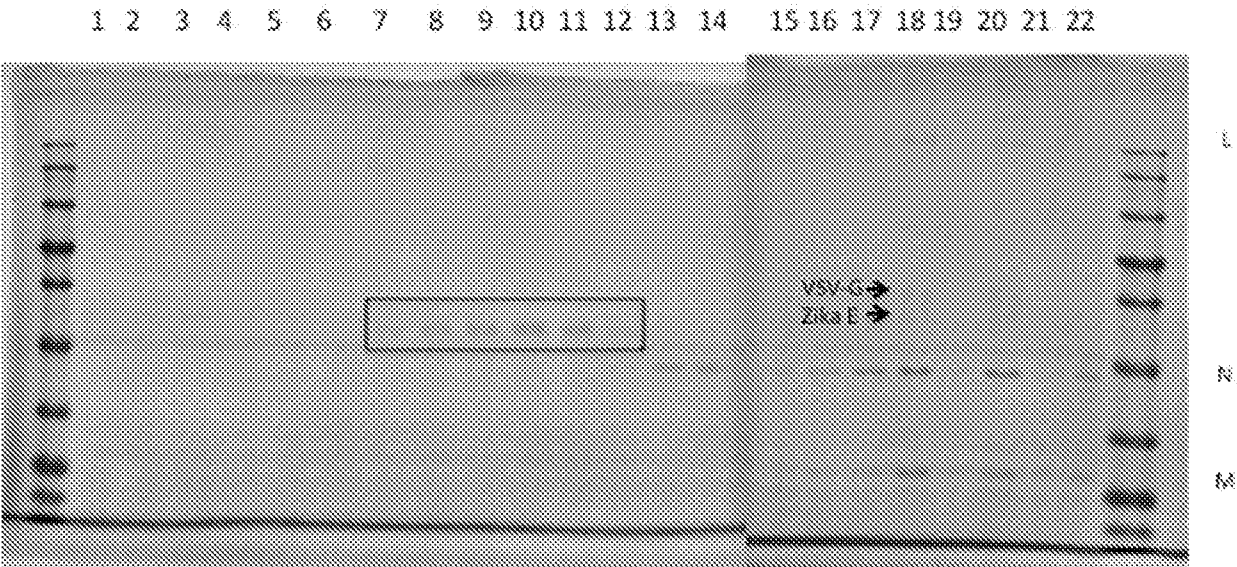
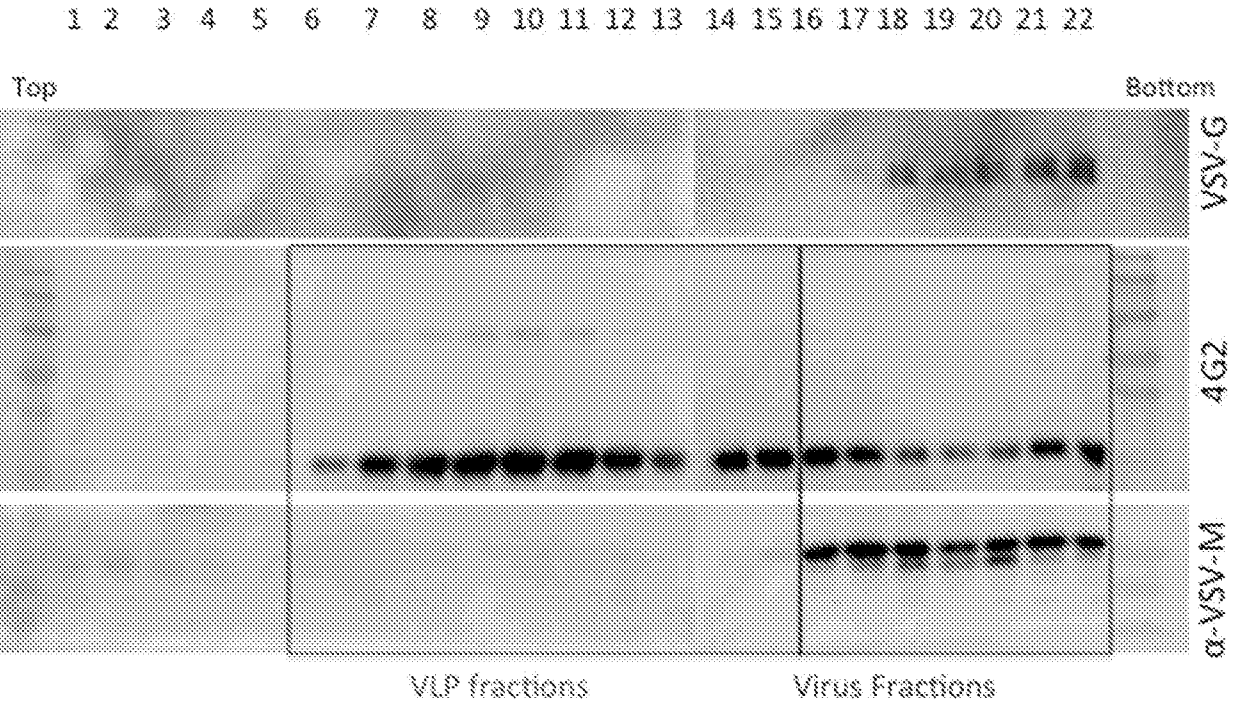


Fig. 7D



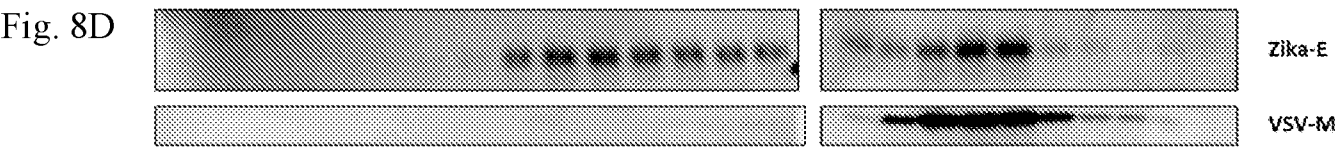
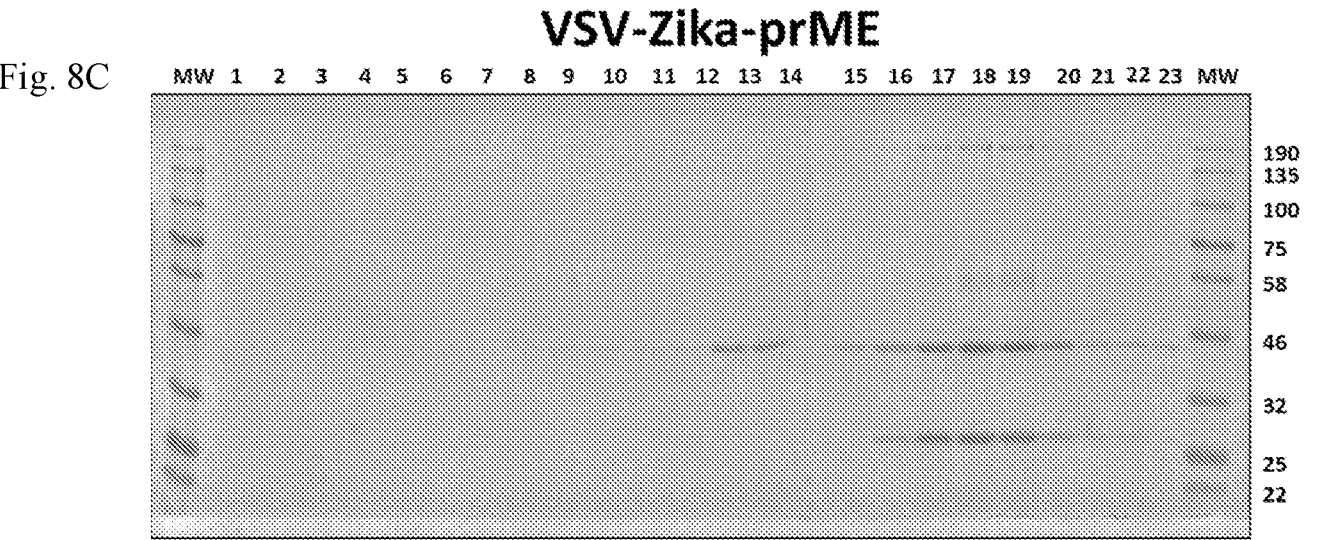
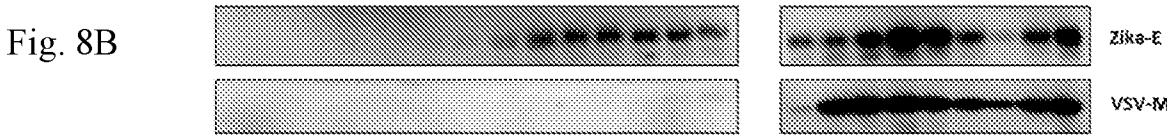
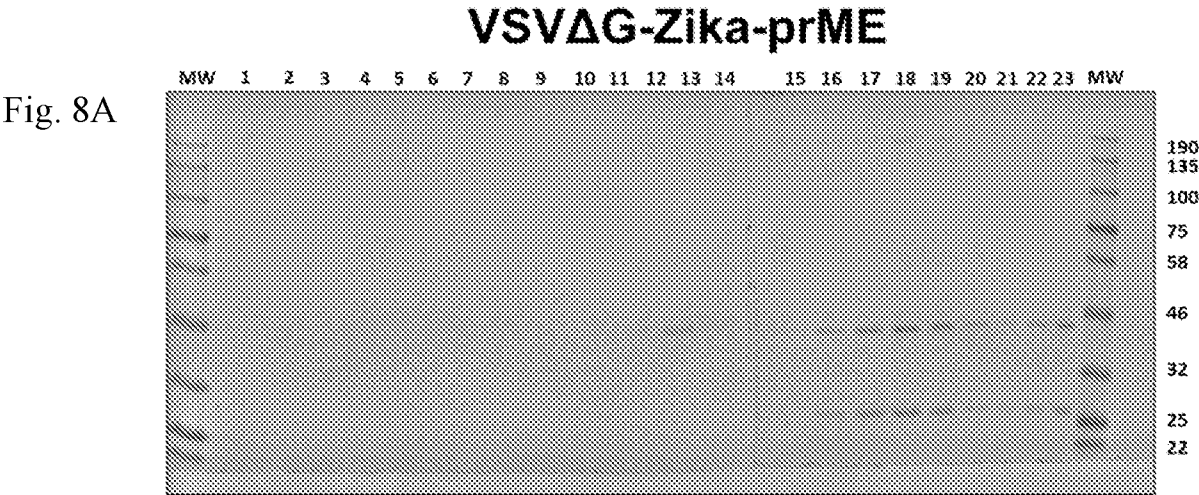


Fig. 9A

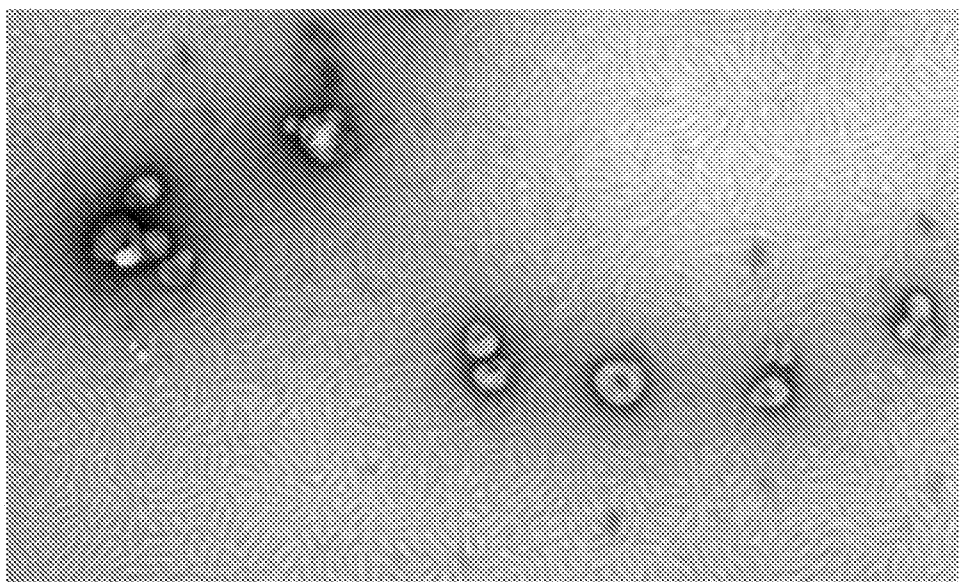


Fig. 9B

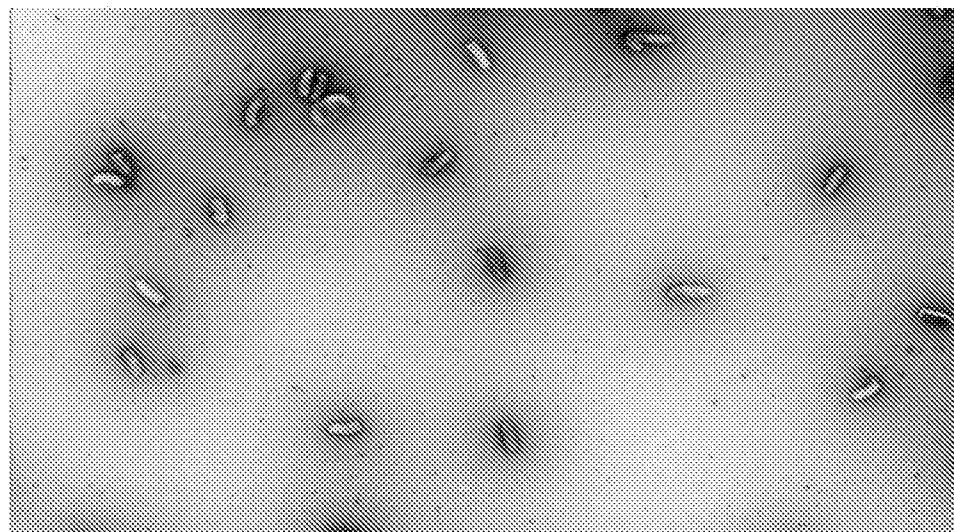


Fig. 10A

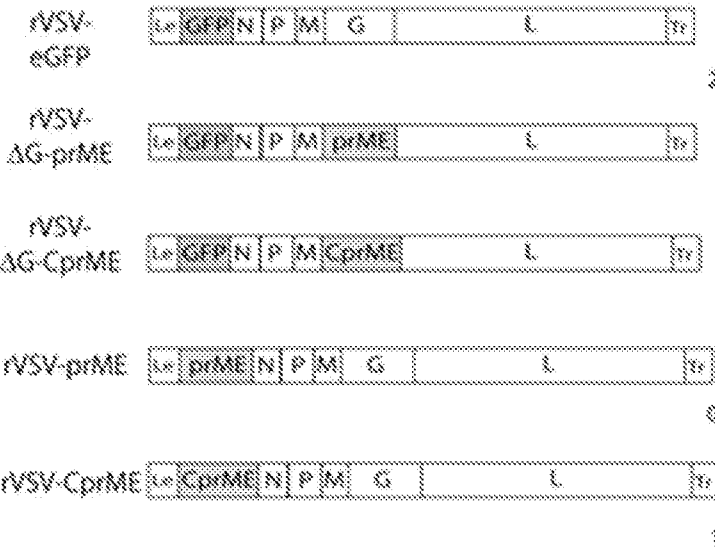


Fig. 10B

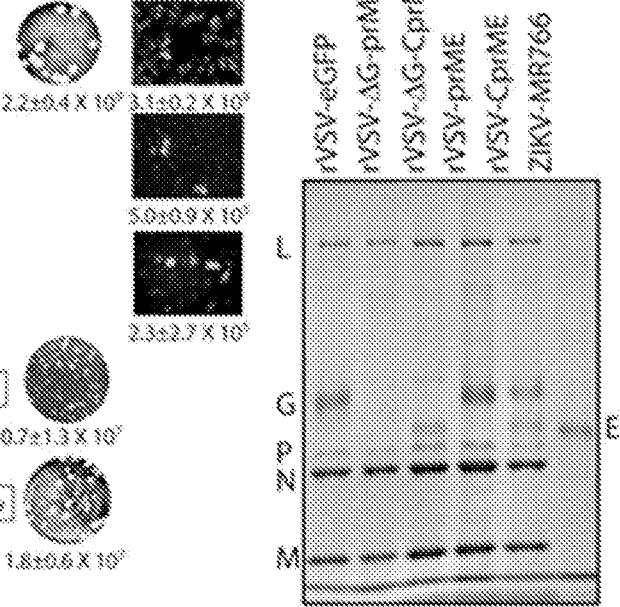


Fig. 10C

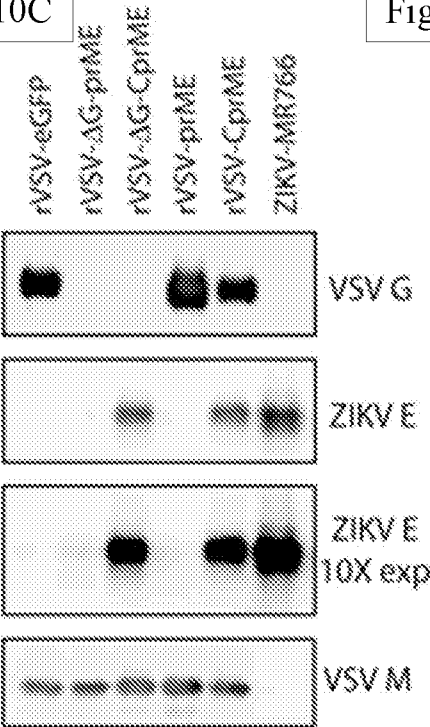


Fig. 10D

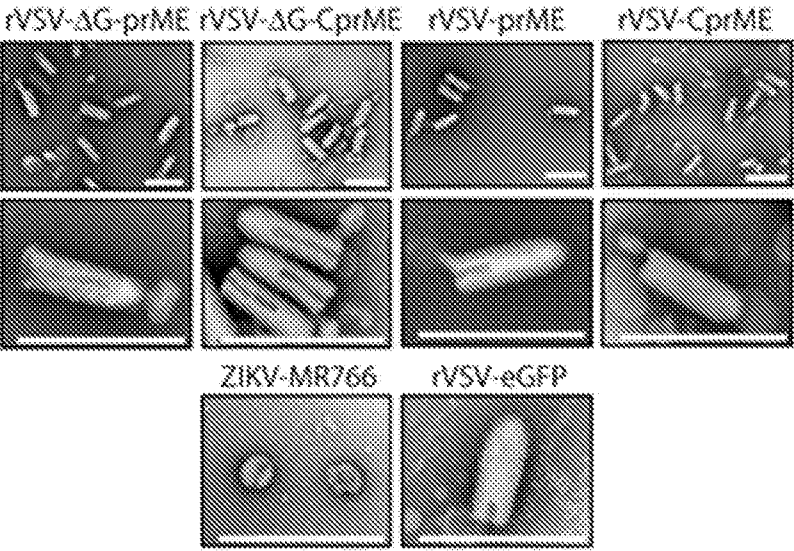


Fig. 11A

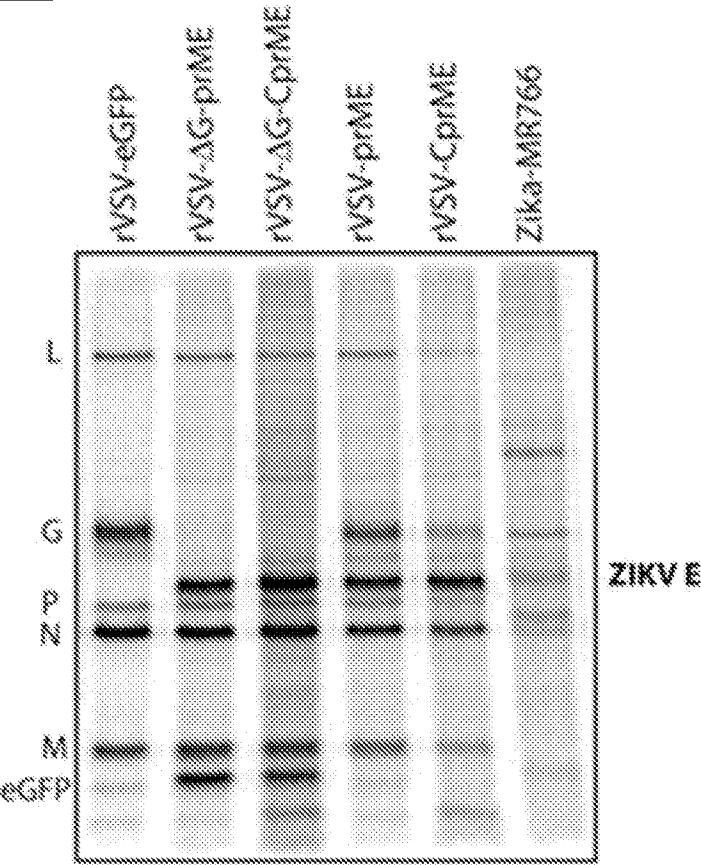


Fig. 11B

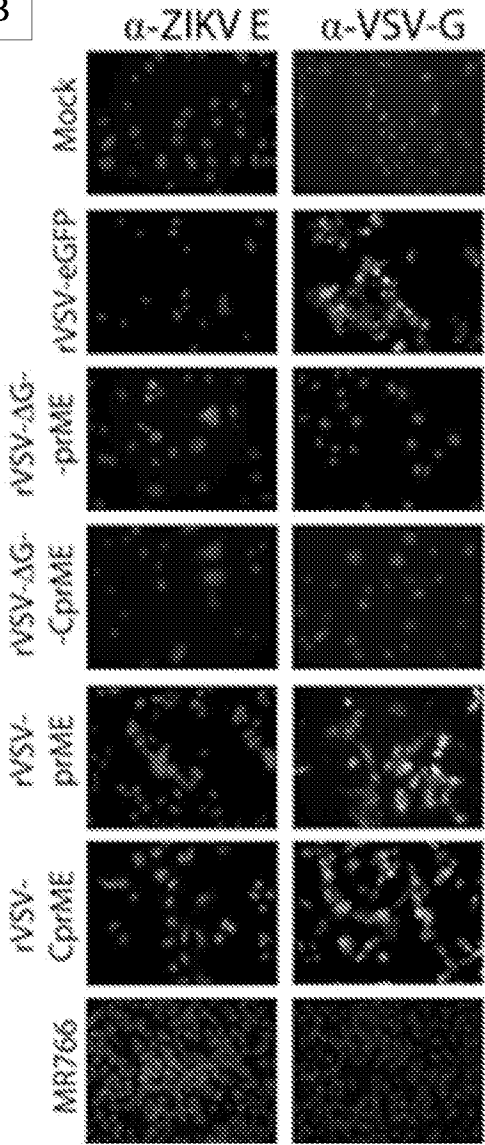


Fig. 12

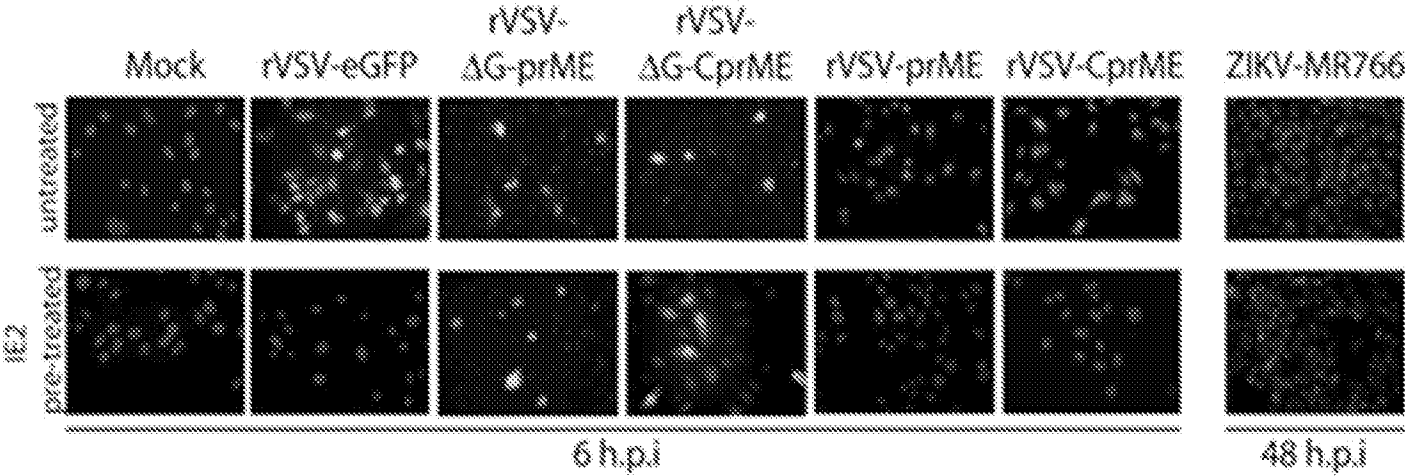


Fig. 13A

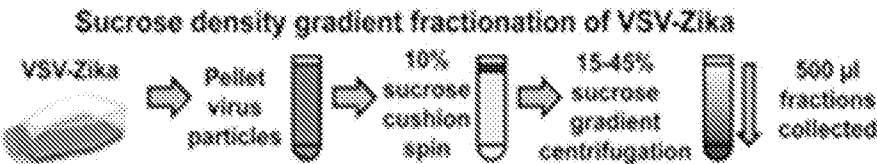


Fig. 13B

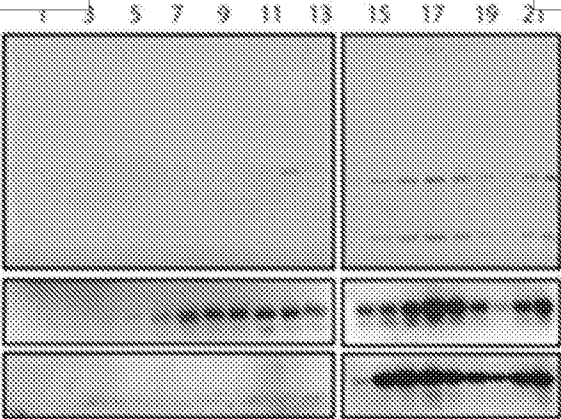


Fig. 13C

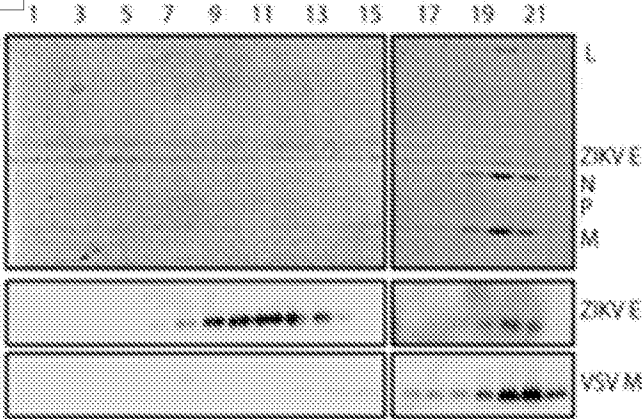


Fig. 13D

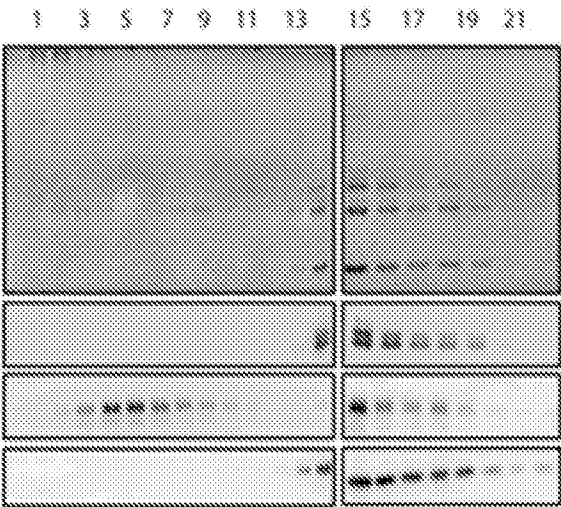


Fig. 13E

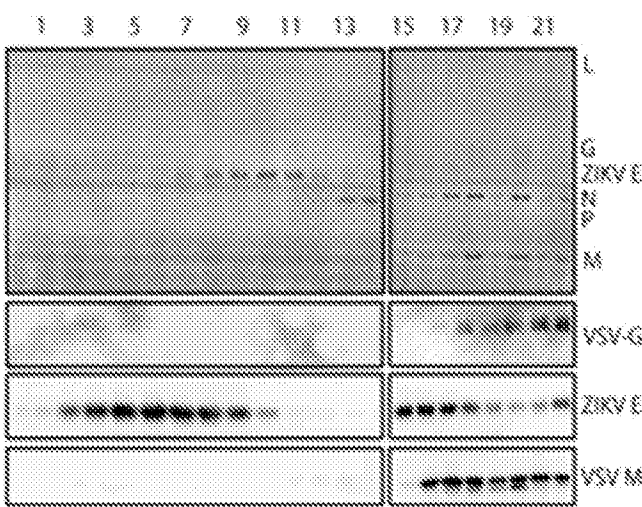


Fig. 14A

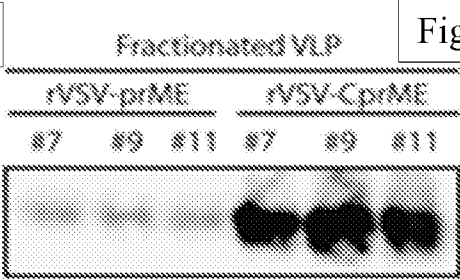


Fig. 14B

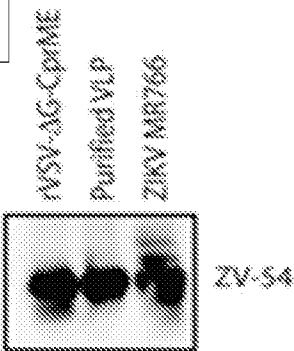


Fig. 14C

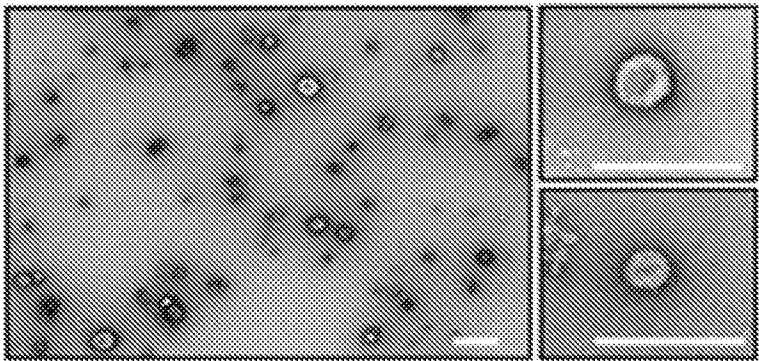


Fig. 14D

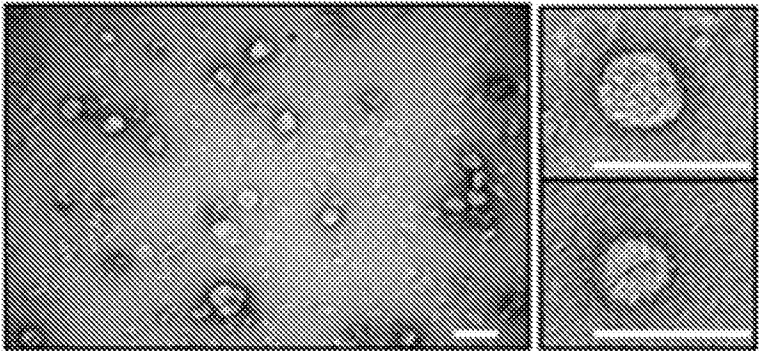


Fig. 14E

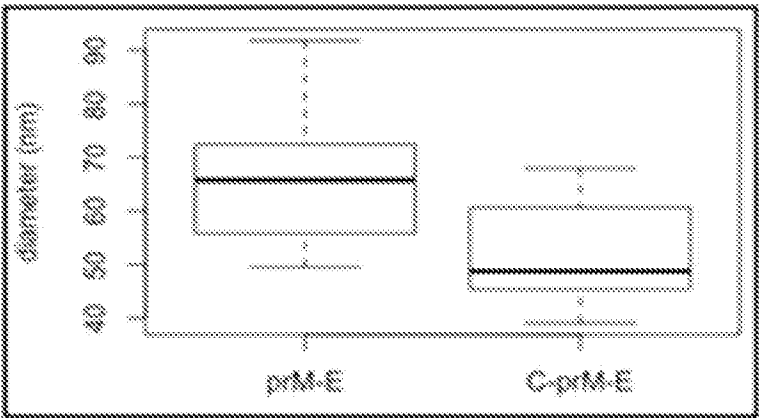


Fig. 15A

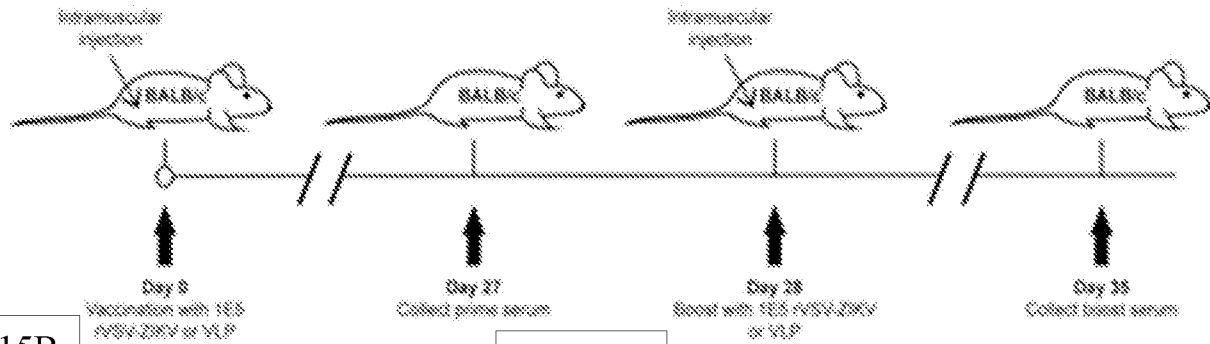


Fig. 15B

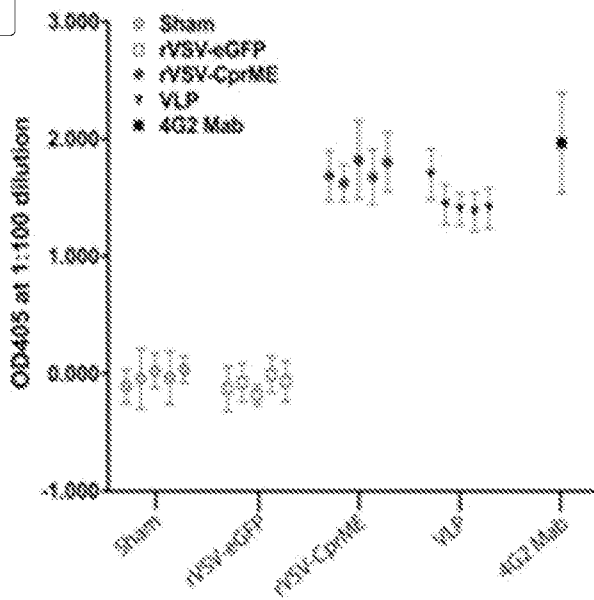
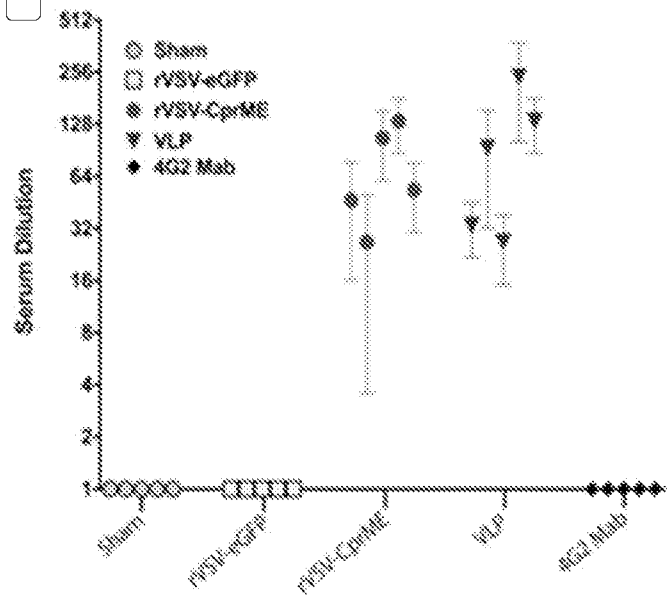


Fig. 15C



INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/057361

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K39/12
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EUN KIM ET AL: "Preventative Vaccines for Zika Virus Outbreak: Preliminary Evaluation", EBIOMEDICINE, vol. 13, 3 October 2016 (2016-10-03), pages 315-320, XP055443543, ISSN: 2352-3964, DOI: 10.1016/j.ebiom.2016.09.028 abstract page 319, left-hand column, paragraph 4 - right-hand column, paragraph 1 ----- -/--	1-6,21, 24,27, 30-34, 37-65



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

24 January 2018

Date of mailing of the international search report

19/02/2018

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
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Fax: (+31-70) 340-3016

Authorized officer

Malamoussi, A

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2017/057361

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	P. ABBINK ET AL: "Protective efficacy of multiple vaccine platforms against Zika virus challenge in rhesus monkeys", SCIENCE, vol. 353, no. 6304, 9 September 2016 (2016-09-09), pages 1129-1132, XP055314484, ISSN: 0036-8075, DOI: 10.1126/science.aah6157 abstract -----	1-6,21, 24,27, 30-34, 37-65
Y	RAFAEL A. LAROCCA ET AL: "Vaccine protection against Zika virus from Brazil", NATURE, vol. 536, no. 7617, 26 June 2016 (2016-06-26), pages 474-478, XP055314483, ISSN: 0028-0836, DOI: 10.1038/nature18952 abstract page 474, right-hand column, paragraph 1 -----	1-6,21, 24,27, 30-34, 37-65
Y	K. A. DOWD ET AL: "Rapid development of a DNA vaccine for Zika virus", SCIENCE, vol. 354, no. 6309, 14 October 2016 (2016-10-14), pages 237-240, XP055428976, ISSN: 0036-8075, DOI: 10.1126/science.aai9137 page 237, right-hand column, paragraph 1 page 240; figures 3,4 -----	1-6,21, 24,27, 30-34, 37-65
Y	Anonymous: "Zika Virus: The Hunt for a Vaccine", 2 July 2016 (2016-07-02), pages 1-19, XP055444026, Retrieved from the Internet: URL: http://immunitytales.com/zika-virus-the-hunt-for-a-vaccine/ [retrieved on 2018-01-24] page 1 -----	1-6,21, 24,27, 30-34, 37-65
Y	SITA AWASTHI: "Zika Virus: Prospects for the Development of Vaccine and Antiviral Agents", JOURNAL OF ANTIVIRALS & ANTIRETROVIRALS, vol. 08, no. 01, 1 January 2016 (2016-01-01), XP055443605, DOI: 10.4172/jaa.1000e130 page 1, right-hand column, paragraph 2 ----- -/--	1-6,21, 24,27, 30-34, 37-65

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2017/057361

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	FLAVIO LAURETTI ET AL: "Recombinant vesicular stomatitis virus-based dengue-2 vaccine candidate induces humoral response and protects mice against lethal infection", HUMAN VACCINES AND IMMUNOTHERAPEUTICS, vol. 12, no. 9, 16 May 2016 (2016-05-16), pages 2327-2333, XP055444029, US ISSN: 2164-5515, DOI: 10.1080/21645515.2016.1183857 abstract	1-6,21, 24,27, 30-34, 37-65
A	----- Lianpan Dai ET AL: "Structures of the Zika Virus Envelope Protein and Its Complex with a Flavivirus Broadly Protective Antibody", Cell Host & Microbe, 11 May 2016 (2016-05-11), pages 696-704, XP055444032, United States DOI: 10.1016/j.chom.2016.04.013 Retrieved from the Internet: URL:http://www.cell.com/cms/attachment/2067899602/2067180398/mmc1.pdf [retrieved on 2018-01-24] figure S2	1-6,21, 24,27, 30-34, 37-65
E	----- WO 2017/192856 A1 (UNIV MIAMI [US]) 9 November 2017 (2017-11-09) page 40, paragraph 0155	1,2,21, 24,30, 32,34, 37-65
X,P	----- DILLON BETANCOURT ET AL: "Cutting Edge: Innate Immune Augmenting Vesicular Stomatitis Virus Expressing Zika Virus Proteins Confers Protective Immunity", THE JOURNAL OF IMMUNOLOGY, vol. 198, no. 8, 3 April 2017 (2017-04-03) , pages 3023-3028, XP055439172, US ISSN: 0022-1767, DOI: 10.4049/jimmunol.1602180 abstract ----- -/--	1,2,21, 24,30, 32,34, 37-65

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2017/057361

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LIANPAN DAI ET AL: "Structures of the Zika Virus Envelope Protein and Its Complex with a Flavivirus Broadly Protective Antibody", CELL HOST & MICROBE, vol. 19, no. 5, 1 May 2016 (2016-05-01), pages 696-704, XP055352074, NL ISSN: 1931-3128, DOI: 10.1016/j.chom.2016.04.013 the whole document -----	1-6,21, 24,27, 30-34, 37-65

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/057361

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 7-20, 22, 23, 25, 26, 28, 29, 35, 36
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 7-20, 22, 23, 25, 26, 28, 29, 35, 36

The specific sequences of claims 7-20, 22-23, 25-26, 28-29, and 35-36 have, according to Rule 13ter.1(d) PCT, not been searched since the sequence disclosed in the application does not comply with WIPO standard ST.25 as prescribed under Rule 5.2 PCT. A Standard-compliant sequence listing has not been furnished in text (TXT) format and the applicant has not remedied the deficiencies within the time limit fixed in the invitation pursuant to Rule 13ter.1(a) PCT (see Guidelines for Search and Examination at the EPO as PCT Authority, B-VIII, 3.2).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guidelines C-IV, 7.2), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2017/057361

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2017192856	A1	09-11-2017	NONE
