STAR METHODS

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EXPERIMENTAL MODEL AND SUBJECT DETAILS

Ethics statement. This study was carried out in strict accordance with the recommendations in the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health. The protocols were approved by the Institutional Animal Care and Use Committee (IACUC) at the Washington University School of Medicine (Assurance Number: A3381-01), the IACUC at the La Jolla Institute for Allergy & Immunology under protocol # AP028-SS1-0615, and the IACUC at Utah State University under protocol 2598. Dissections and footpad injections were performed under anesthesia that was induced and maintained with ketamine hydrochloride and xylazine, and all efforts were made to minimize suffering.

Mouse experiments. BALB/c and C57BL/6 mice were purchased from The Jackson Laboratory, and AG129 mice were bred in the animal facilities at Utah State University, Washington University, or the La Jolla Institute for Allergy and Immunology. All mice were housed in pathogen-free mouse facilities. For immunizations, mice were inoculated via an intramuscular route with 50 μl of the indicated vaccine LNP constructs. For challenge studies, mice were inoculated subcutaneously with 10^4 PFU of ZIKV P6-740 or 10^6 FFU of mouse-adapted ZIKV Dakar 41519 in 50 μl of HBSS + 0.1% FBS. For ZIKV challenge studies in BALB/c and C57BL/6 mice, 2 mg of anti-IFNAR1 blocking antibody (MAR1-5A3 (Sheehan et al., 2006)) was administered via intraperitoneal injection 24 hours prior to viral infection. For DENV challenge studies in AG129 mice, animals were passively transferred pooled vaccine immune sera or PBS one day prior to infection with ~10^5 FFU of DENV-2 S221. Animals were monitored

for mortality and clinical score (1 = heathy; 2 = slightly ruffled fur; 3 = very ruffled fur; 4 = mild lethargy, decreased scurrying activity; 5 = very sick, slow to no movement; 6 = very sick, euthanize (in distress); 7 = deceased) as described previously (Tang et al., 2016).

METHOD DETAILS

Viruses and cells. ZIKV strain Dakar 41519 (Senegal, 1984) and P6-740 (Malaysia, 1966) were provided by the World Reference Center for Emerging Viruses and Arboviruses (R. Tesh and S. Weaver, University of Texas Medical Branch). To create a mouse-adapted more pathogenic variant of ZIKV Dakar 41519, it was passaged twice in *Rag1*$^{-/-}$ mice (Sapparapu et al., 2016; Zhao et al., 2016). ZIKV strain Paraiba 2015 (Brazil) was provided by S. Whitehead (NIH, Bethesda, MD) (Tsetsarkin et al., 2016). DENV-2 strain S221 is a mouse-adapted strain that has been described previously (Yauch et al., 2009). Virus stocks were propagated in mycoplasma-free Vero cells and titrated by focus-forming assay (FFA), as described previously (Lazear et al., 2016). Experiments with ZIKV and DENV were conducted under biosafety level 2 (BSL2) containment at Washington University School of Medicine or under BSL3 containment at Utah State University with Institutional Biosafety Committee approval.

Generation of modified mRNA and LNP The mRNA was synthesized *in vitro* using T7 polymerase-mediated DNA-dependent RNA transcription where the UTP was substituted with 1-methylpseudoUTP, using a linearized DNA template, which incorporates 5' and 3' untranslated regions (UTRs) and includes a poly-A tail (5'-UTR: TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACTCACTATAGGGAAATAAGAGAGAA AAGAAGAGTAAGAAGAAATATAAGAGCCACC; and 3'-UTR: TGATAATAGGCTGGAGCCTCGGTGGCCATGCTTCTTGCCCCTTGGGCCTCCCCCCAGCCC CTCCTCCCCTTCCTGCACCCGTACCCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGC).

A donor methyl group S-adenosylmethionine (SAM) was added to the methylated capped RNA

(cap 0), resulting in a cap 1 structure to increase mRNA translation efficiency. The modified mRNAs encoded the signal sequences from human IgE (MDWTWILFLVAAATRVHS) or JEV prM (MWLVSLAIVTACAGA) and the prM and E genes from an Asian ZIKV strain (Micronesia 2007, GenBank accession number EU545988 (Lanciotti et al., 2008)), which is >99% identical to circulating American strains.

LNP formulations were prepared using a modified procedure of a method described for siRNA (Chen et al., 2016). Briefly, lipids were dissolved in ethanol at molar ratios of 50:10:38.5:1.5 (ionizable lipid: DSPC: cholesterol: PEG-lipid). The lipid mixture was combined with a 50 mm citrate buffer (pH 4.0) containing mRNA at a ratio of 3:1 (aqueous:ethanol) using a microfluidic mixer (Precision Nanosystems, Vancouver, BC). Formulations were dialyzed against PBS (pH 7.4) in dialysis cassettes for at least 18 h. Formulations were concentrated using Amicon Ultra Centrifugal Filters (EMD Millipore, Billerica, MA), passed through a 0.22-µm filter and stored at 4˚C until use. All formulations were tested for particle size, RNA encapsulation, and endotoxin and were found to be between 80 to 100 nm in size, with greater than 90% encapsulation and <1 EU/ml of endotoxin.

Viral protein analysis. SVPs were floated on a 10-50% sucrose gradient (50 mM MES pH 5.5, 120 mM NaCl) and ultracentrifuged at 32,000 rpm at 4℃ for 4 h in a Beckman SW55 rotor. Fractions (1 ml) were collected and pelleted by a second ultracentrifugation step over a 20% sucrose cushion at 32,000 rpm at 4℃ for 2 h. P rotein concentration of SVPs was measured using a spectrophotometer (280 nm wavelength). Western blotting was performed using NuPAGE MES Western blot system (Thermo Fisher) reagents as per the manufacturer's instructions. Samples were boiled at 100^{o}C for 10 min in the absence of reducing agent. Samples (100 or 500 ng total protein) were loaded on 4-12% NuPAGE gradient gel and electrophoresed. Proteins were transferred onto nitrocellulose membranes using iBlot 2 gel transfer system. Membranes were washed three times with deionized water and blocked in PBS with 5% Blotto (Thermo Fisher) overnight at 4^{o}C. Primary mAbs (WNV E60 (Oliphant et al.,

2006) or mouse anti-ZIKV E (Biofront, BF-1176-86)) were added at 1 μg/ml in PBS supplemented with 5% Blotto and 0.2% (v/v) Tween 20 (Sigma) and incubated for 2 h at room temperature with agitation. Membranes were washed three times with PBS supplemented with 0.2% Tween 20. Secondary antibody (horseradish peroxidase conjugated goat anti-mouse IgG (Ab97023, Abcam)) was added at 0.25 μg/ml in PBS supplemented with 5% Blotto and 0.2% Tween 20 for 2 h at room temperature with agitation. After final washing, blots were developed using Amersham ECL prime solution (GE Healthcare Life Sciences) for 2 min and imaged. SeeBlue plus 2 pre-stained protein ladders were included for molecular weight references.

To compare expression of SVPs from different mRNA vaccine constructs, HeLa cells were transfected with 1.25 μg of mRNA constructs using Lipofectamine 2000 (Thermo Fisher), and cells were harvested 24 h later. Cell lysates were prepared in RIPA lysis buffer (Thermo Fisher) with phosphatase and protease inhibitors (Millipore) added.

Electron microscopy of SVPs. The SVPs were imaged by electron microscopy and negative staining using a fee-for-service facility (University of California, Los Angeles). Briefly, purified SVPs (2.5 μl) were applied to a Glow-discharge carbon-coated grid (Ted Pella Inc.). Staining (2% uranyl acetate) was added in a drop-wise manner for 60 sec. After blotting of excess liquid and drying, the images were collected on a FEI Tecnai TF20 transmission electron microscope at an accelerating voltage of 200 kV using TVIPS EM-Menu program. The nominal magnifications used were 50,000, 29,000 and 14,500 with 2 binning.

Measurement of viral burden. At specified time points after ZIKV challenge, blood was collected and organs were recovered. Organs were weighed and homogenized using a bead-beater apparatus (MagNA Lyser, Roche), and serum was prepared after coagulation and centrifugation. Tissue samples and serum from ZIKV-infected mice were extracted with the RNeasy Mini Kit (Qiagen). ZIKV RNA levels were determined by TaqMan one-step quantitative reverse transcriptase PCR (qRT-PCR) on an ABI 7500 Fast Instrument using standard cycling

conditions. Viral burden is expressed on a $\log_{10}$ scale as viral RNA equivalents per gram or per milliliter after comparison with a standard curve produced using serial 5-fold dilutions of ZIKV RNA from known quantities of infectious virus. For ZIKV, the following primer sets were used: 1183F: 5′-CCACCAATGTTCTCTTGCAGACATATTG-3′; 1268R: 5′-TTCGGACAGCCGTTGTCCAACACAAG-3′; and probes (1213F): 5′-56-FAM/AGCCTACCT TGACAAGCAGTC/3IABkFQ-3′.

Neutralization assays. (a) PRNT or FRNT assays. Serial dilutions of heat-inactivated sera obtained from AG129 or C57BL/6 mice were incubated with 50 to 100 FFU of ZIKV (Paraiba, Brazil 2015) for 1 h at 37 ℃. The serum Ab-virus complexes were added to Vero cell monolayers in 96-well plates for 60 min at 37℃. Plaque assays were performed as described previously (Brien et al., 2013; Lazear et al., 2016) For FRNT assays, cells were overlaid with 1% (w/v) methylcellulose in MEM supplemented with 4% heat-inactivated FBS. Plates were fixed 40 h later with 1% PFA in PBS for 1 h at room temperature. The plates were incubated sequentially with 500 ng/ml of humanized anti-WNV E60 (Oliphant et al) and horseradish-peroxidase-conjugated goat anti-human IgG in PBS supplemented with 0.1% (w/v) saponin (Sigma) and 0.1% BSA. ZIKV-infected cell foci were visualized using TrueBlue peroxidase substrate (KPL) and quantitated on an ImmunoSpot 5.0.37 macroanalyzer (Cellular Technologies). (b) RVP assays. RVPs incorporating the structural proteins of ZIKV or DENV were produced by complementation of a previously described sub-genomic GFP-expressing replicon derived from a lineage II strain of WNV (Dowd et al., 2016a; Dowd et al., 2015). Serial dilutions of heat-inactivated sera obtained from BALB/c mice were mixed with ZIKV (strain H/PF/2013; French Polynesia, 2013) or DENV-2 (strain 16681) reporter viral particles (RVPs) and incubated for 1 h at 37℃. Immune complexes were added in duplicate technical replicates to pre-plated Vero cells in a 96-well plate and incubated for two days. Cells were trypsinized, resuspended in 4% PFA in PBS, and RVP infection scored as a function of GFP expression by flow cytometry. All neutralization data were analyzed by non-linear regression to determine the

dilution of sera required to inhibit 50% (EC50) and 90% (EC90) of infection. RVP studies were performed starting at an initial serum dilution of 1:100 (based on the final volume of cells, virus, and sera per well), which was designated as the limit of detection.

ADE assays. Serial dilutions of heat-inactivated sera obtained from BALB/c mice were mixed with DENV-1 RVPs (Western Pacific-74 strain) and incubated for 1 h at 37℃. Immune complexes were added in duplicate technical replicates to K562 cells that express the Fc-γ receptor CD32A and incubated for two days. Due to limited volumes of sera, a small number of samples (four) could not be performed in duplicate. Cells were fixed with 2% PFA, and RVP infection was scored as a function of GFP expression by flow cytometry. To normalize the magnitude of enhancement across independent experiments, results are displayed relative to the maximum infectivity observed with a control cross-reactive WNV mAb E60 (Oliphant et al., 2006) run in parallel. ADE studies were performed starting at an initial serum dilution of 1:60 (based on the final volume of cells, virus, and sera per well), which was designated as the limit of detection. For calculations of peak enhancing titer, samples for which no enhancement (infectivity) was observed are reported as a titer of 30 (one half the limit of detection).

QUANTIFICATION AND STATISTICAL ANALYSIS. All data were analyzed with GraphPad Prism software. Kaplan-Meier survival curves were analyzed by the log rank test, and weight losses were compared using two-way ANOVA. For neutralization antibody titers and viral burden analysis, the log titers and levels of viral RNA were analyzed by a Kruskal-Wallis 2-way ANOVA with a multiple comparisons correction. A P value of < 0.05 indicated statistically significant differences.

DATA AND SOFTWARE AVAILABILITY. All data is available upon request to the lead contact author. No proprietary software was used in the data analysis.

ADDITIONAL RESOURCES. mRNA LNP vaccines are available from Valera/Moderna upon request and completion of appropriate Material Transfer Agreements.

SUPPLEMENTAL TITLES AND LEGENDS

SUPPLEMENTAL FIGURE LEGENDS

Figure S1. Production of LNPs for vaccination, Related to Figure 1. A. Schematic representation of the process to encapsulate mRNA into LNPs. **B**. A representative cryo-electron microscopy image of an LNP solution, following mRNA encapsulation.

Figure S2. Serum neutralization curves from IgE_{sig}-prM-E vaccinated AG129 mice, Related to Figure 1. Ten AG129 mice in each group (combined from two independent experiments) were immunized with 10 (Groups 1 and 2, *panels* **A-B**) or 2 (Groups 3 and 4, panels **C-D**) μgs of IgE_{sig} prM-E mRNA LNPs. Some of the mice (Groups 1 and 3) were boosted with an equivalent dose 21 days later. Serum was collected at 6 weeks (day 42) post initial vaccination and analyzed for ZIKV neutralization activity by PRNT. Each line represents the neutralization curve from an individual mouse.

Figure S3. Serum neutralization curves from IgE_{sig} prM-E vaccinated C57BL/6 mice, Related to Figure 2. Ten C57BL/6 mice in each group (combined from two independent experiments) were immunized with 10 μg of IgE_{sig}-prM-E mRNA LNPs and boosted with an equivalent dose four weeks later. Serum was collected at 4 (**B**), 8 (**C**), and 18 (**D**) weeks post initial vaccination and analyzed for ZIKV neutralization

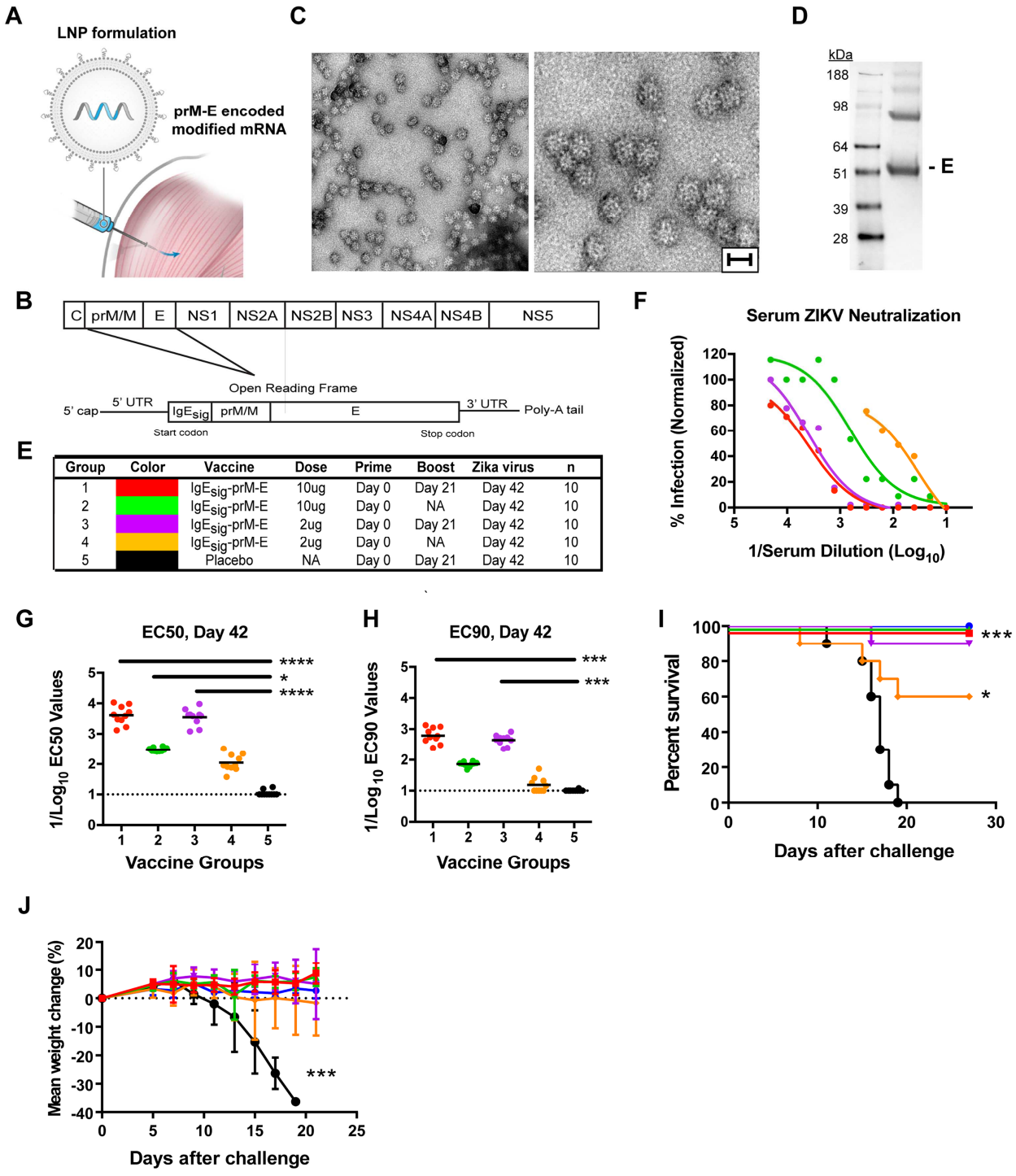
activity by FRNT. Serum from mice immunized with placebo mRNA LNPs also were analyzed (**A**) Each line represents the neutralization curve from an individual mouse. Error bars indicate the standard deviation (SD) of triplicate technical replicates.

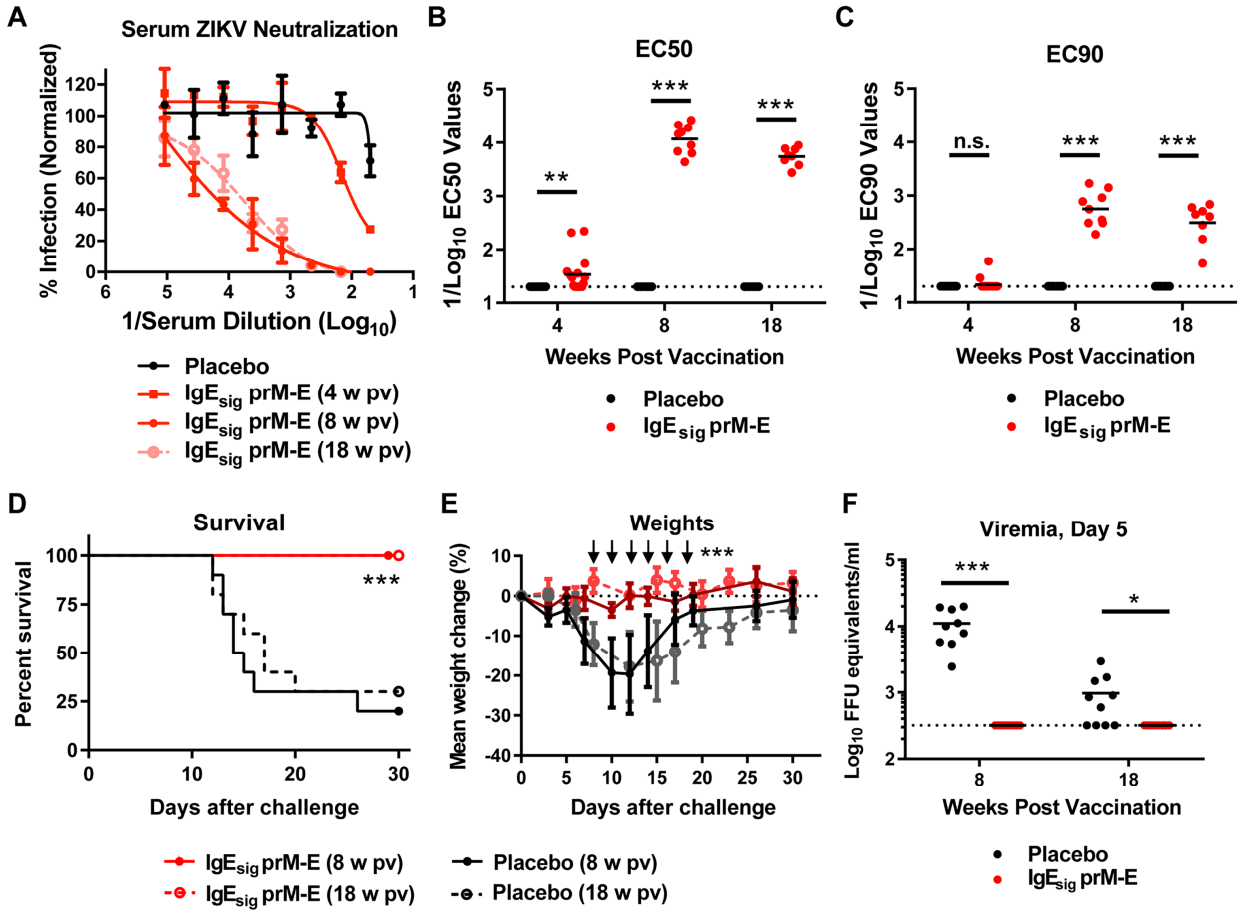
Figure S4. Serum neutralization curves from LNP vaccines containing WT or mutant FL sequences, Related to Figure 3. Ten BALB/c mice in each group (combined from two independent experiments) were immunized with 2 or 10 μg of prM-E mRNA LNP vaccines containing IgE or JEV signal sequences and WT or mutant fusion loop (FL) sequences or placebo mRNA LNPs (Groups 1-9, **A-I**). Animals were boosted with the equivalent dose of the same vaccine 4 weeks later. At week 8, serum was harvested and analyzed for ZIKV neutralization capacity by incubating serial dilutions of serum with GFP-expressing ZIKV RVPs, followed by infection of Vero cells. Infected cells were quantified 2 days later by flow cytometry. Each curve represents the data from an individual mouse analyzed by non-linear regression analysis. Error bars indicate the range of duplicate technical replicates.

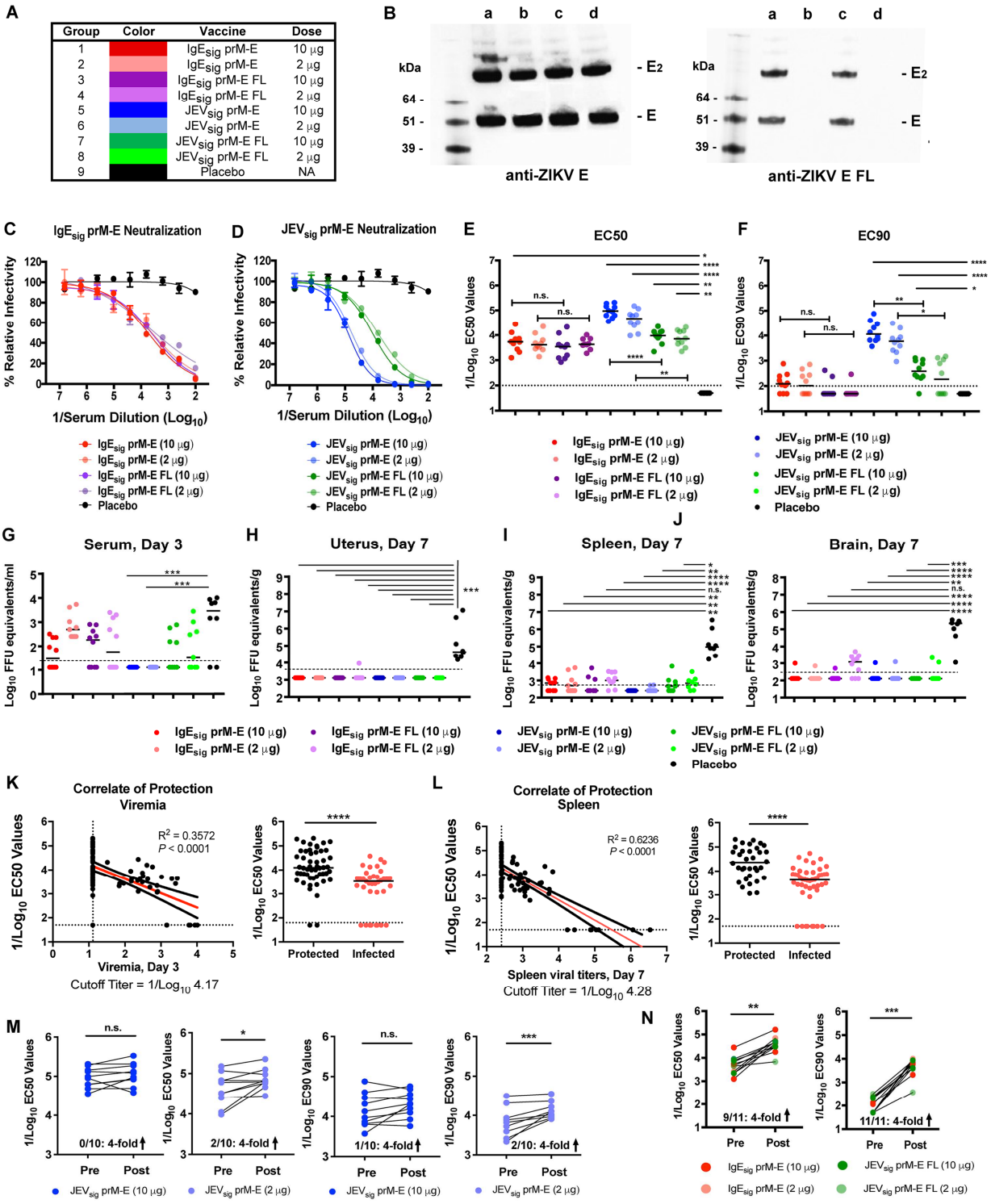
Figure S5. ADE curves from LNP vaccines containing WT or FL mutant sequences, Related to Figure 4. Ten BALB/c mice in each group (combined from two independent experiments) were immunized with 2 or 10 μg of prM-E mRNA LNP vaccines containing IgE or JEV signal sequences and WT or mutant FL sequences or placebo mRNA LNPs (Groups 1-9, **A-I**). Animals were boosted with the equivalent dose of the same vaccine 4 weeks later. At week 8, serum was harvested from vaccinated mice. Serial dilutions of sera were mixed with GFP-expressing DENV-1 (strain West-Pac 74) RVPs and incubated with FcγR-expressing K562 cells. Infected cells were quantified by flow cytometry. In each experiment, the cross-reactive FL-specific mAb

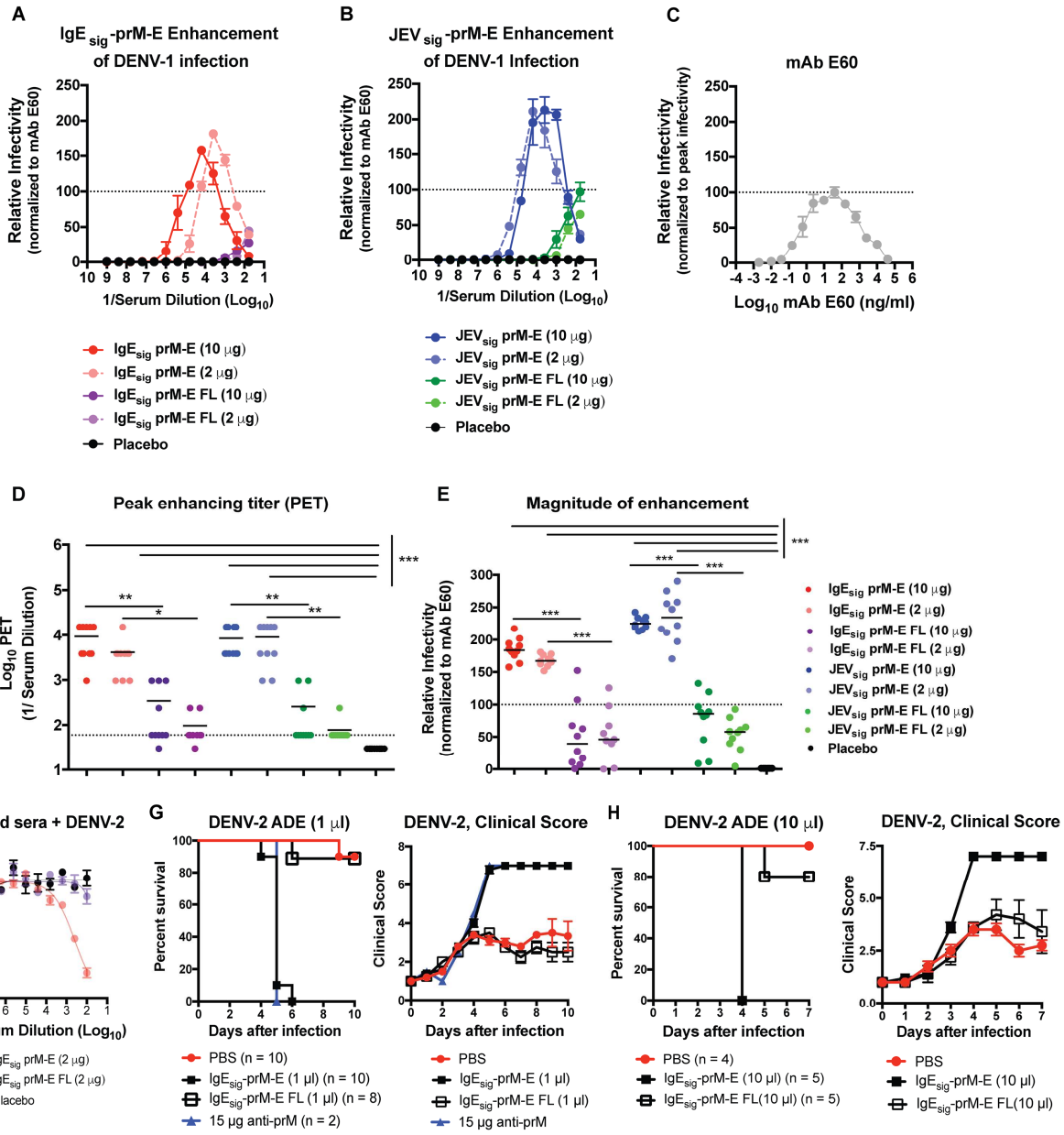
E60 was included as a control (**J**). To normalize the magnitude of enhancement across independent experiments, results are displayed relative to the maximum infectivity observed with mAb E60 run in parallel (designated by the dotted line at 100). Each line represents the enhancement curve from an individual mouse. Error bars indicate the range of duplicate technical replicates.

Figure S6. **ZIKV mRNA LNP vaccines containing mutant FL sequences showed reduced ADE against DENV in AG129 mice, Related to Figure 4. A**. Neutralization of DENV-2 RVPs by sera pooled from placebo or JEV_{sig}-prM-E (2 μg dose of WT or FL mutant) vaccinated mice. Error bars indicate the range of duplicate technical replicates. **B.** Enhancing effects of ZIKV immune serum on DENV-2 infection in AG129 mice. Recipient AG129 mice were passively transferred PBS or 10 μl of pooled serum from BALB/c mice vaccinated with WT or FL mutant JEV_{sig}-prM E LNPs. One day later, animals were challenged with 10^4 FFU of DENV-2 (strain S220) and followed for mortality. Results are pooled from two independent challenge experiments (numbers of animals indicated beneath graph). Survival curves between serum transfers from JEV_{sig}-prM-E (WT and FL mutant LNPs) vaccinated mice were statistically different (***, $P < 0.001$, log-rank test).


A
LNP formulation
prM-E encoded
modified mRNA
C
D
kDa
188
98
64
51
39
28
- E
B
C
prM/M
E
NS1
NS2A
NS2B
NS3
NS4A
NS4B
NS5
Open Reading Frame
5' cap
5' UTR
IgE$_{sig}$
prM/M
E
3' UTR
Poly-A tail
Start codon
Stop codon
E
Group | Color | Vaccine | Dose | Prime | Boost | Zika virus | n
1 | IgE$_{sig}$-prM-E | 10ug | Day 0 | Day 21 | Day 42 | 10
2 | IgE$_{sig}$-prM-E | 10ug | Day 0 | NA | Day 42 | 10
3 | IgE$_{sig}$-prM-E | 2ug | Day 0 | Day 21 | Day 42 | 10
4 | IgE$_{sig}$-prM-E | 2ug | Day 0 | NA | Day 42 | 10
5 | Placebo | NA | Day 0 | Day 21 | Day 42 | 10
F
Serum ZIKV Neutralization
% Infection (Normalized)
1/Serum Dilution (Log$_{10}$)
G
EC50, Day 42
1/Log$_{10}$ EC50 Values
Vaccine Groups
****
*
****
H
EC90, Day 42
1/Log$_{10}$ EC90 Values
Vaccine Groups
***
***
I
Percent survival
Days after challenge
***
*
J
Mean weight change (%)
Days after challenge
***


A
Serum ZIKV Neutralization
% Infection (Normalized)
1/Serum Dilution (Log10)
Placebo
IgEsig prM-E (4 w pv)
IgEsig prM-E (8 w pv)
IgEsig prM-E (18 w pv)
B
EC50
1/Log10 EC50 Values
Weeks Post Vaccination
Placebo
IgEsig prM-E
C
EC90
1/Log10 EC90 Values
n.s.
Weeks Post Vaccination
Placebo
IgEsig prM-E
D
Survival
Percent survival
Days after challenge
IgEsig prM-E (8 w pv)
IgEsig prM-E (18 w pv)
E
Weights
Mean weight change (%)
Days after challenge
Placebo (8 w pv)
Placebo (18 w pv)
F
Viremia, Day 5
Log10 FFU equivalents/ml
Weeks Post Vaccination
Placebo
IgEsig prM-E


A
Group | Color | Vaccine | Dose
1 | IgE$_{sig}$ prM-E | 10 μg
2 | IgE$_{sig}$ prM-E | 2 μg
3 | IgE$_{sig}$ prM-E FL | 10 μg
4 | IgE$_{sig}$ prM-E FL | 2 μg
5 | JEV$_{sig}$ prM-E | 10 μg
6 | JEV$_{sig}$ prM-E | 2 μg
7 | JEV$_{sig}$ prM-E FL | 10 μg
8 | JEV$_{sig}$ prM-E FL | 2 μg
9 | Placebo | NA
B
a b c d
kDa
64 -
51 -
39 -
- E2
- E
anti-ZIKV E
anti-ZIKV E FL
C
IgE$_{sig}$ prM-E Neutralization
% Relative Infectivity
1/Serum Dilution (Log$_{10}$)
IgE$_{sig}$ prM-E (10 μg)
IgE$_{sig}$ prM-E (2 μg)
IgE$_{sig}$ prM-E FL (10 μg)
IgE$_{sig}$ prM-E FL (2 μg)
Placebo
D
JEV$_{sig}$ prM-E Neutralization
% Relative Infectivity
1/Serum Dilution (Log$_{10}$)
JEV$_{sig}$ prM-E (10 μg)
JEV$_{sig}$ prM-E (2 μg)
JEV$_{sig}$ prM-E FL (10 μg)
JEV$_{sig}$ prM-E FL (2 μg)
Placebo
E
EC50
1/Log$_{10}$ EC50 Values
n.s.
IgE$_{sig}$ prM-E (10 μg)
IgE$_{sig}$ prM-E (2 μg)
IgE$_{sig}$ prM-E FL (10 μg)
IgE$_{sig}$ prM-E FL (2 μg)
F
EC90
1/Log$_{10}$ EC90 Values
n.s.
JEV$_{sig}$ prM-E (10 μg)
JEV$_{sig}$ prM-E (2 μg)
JEV$_{sig}$ prM-E FL (10 μg)
JEV$_{sig}$ prM-E FL (2 μg)
Placebo
G
Serum, Day 3
Log$_{10}$ FFU equivalents/ml
H
Uterus, Day 7
Log$_{10}$ FFU equivalents/g
I
Spleen, Day 7
Log$_{10}$ FFU equivalents/g
J
Brain, Day 7
Log$_{10}$ FFU equivalents/g
IgE$_{sig}$ prM-E (10 μg)
IgE$_{sig}$ prM-E (2 μg)
IgE$_{sig}$ prM-E FL (10 μg)
IgE$_{sig}$ prM-E FL (2 μg)
JEV$_{sig}$ prM-E (10 μg)
JEV$_{sig}$ prM-E (2 μg)
JEV$_{sig}$ prM-E FL (10 μg)
JEV$_{sig}$ prM-E FL (2 μg)
Placebo
K
Correlate of Protection
Viremia
1/Log$_{10}$ EC50 Values
R^2 = 0.3572
P < 0.0001
Viremia, Day 3
Cutoff Titer = 1/Log$_{10}$ 4.17
Protected
Infected
L
Correlate of Protection
Spleen
1/Log$_{10}$ EC50 Values
R^2 = 0.6236
P < 0.0001
Spleen viral titers, Day 7
Cutoff Titer = 1/Log$_{10}$ 4.28
Protected
Infected
M
1/Log$_{10}$ EC50 Values
0/10: 4-fold
2/10: 4-fold
1/Log$_{10}$ EC90 Values
1/10: 4-fold
2/10: 4-fold
Pre
Post
JEV$_{sig}$ prM-E (10 μg)
JEV$_{sig}$ prM-E (2 μg)
N
1/Log$_{10}$ EC50 Values
9/11: 4-fold
1/Log$_{10}$ EC90 Values
11/11: 4-fold
Pre
Post
IgE$_{sig}$ prM-E (10 μg)
IgE$_{sig}$ prM-E (2 μg)
JEV$_{sig}$ prM-E FL (10 μg)
JEV$_{sig}$ prM-E FL (2 μg)


A
IgE sig -prM-E Enhancement of DENV-1 infection
Relative Infectivity (normalized to mAb E60)
1/Serum Dilution (Log10)
IgEsig prM-E (10 μg)
IgEsig prM-E (2 μg)
IgEsig prM-E FL (10 μg)
IgEsig prM-E FL (2 μg)
Placebo
B
JEV sig -prM-E Enhancement of DENV-1 Infection
Relative Infectivity (normalized to mAb E60)
1/Serum Dilution (Log10)
JEVsig prM-E (10 μg)
JEVsig prM-E (2 μg)
JEVsig prM-E FL (10 μg)
JEVsig prM-E FL (2 μg)
Placebo
C
mAb E60
Relative Infectivity (normalized to peak infectivity)
Log10 mAb E60 (ng/ml)
D
Peak enhancing titer (PET)
Log10 PET (1/ Serum Dilution)
E
Magnitude of enhancement
Relative Infectivity (normalized to mAb E60)
IgEsig prM-E (10 μg)
IgEsig prM-E (2 μg)
IgEsig prM-E FL (10 μg)
IgEsig prM-E FL (2 μg)
JEVsig prM-E (10 μg)
JEVsig prM-E (2 μg)
JEVsig prM-E FL (10 μg)
JEVsig prM-E FL (2 μg)
Placebo
F
Pooled sera + DENV-2
% Relative Infectivity
1/Serum Dilution (Log10)
IgEsig prM-E (2 μg)
IgEsig prM-E FL (2 μg)
Placebo
G
DENV-2 ADE (1 μl)
Percent survival
Days after infection
PBS (n = 10)
IgEsig-prM-E (1 μl) (n = 10)
IgEsig-prM-E FL (1 μl) (n = 8)
15 μg anti-prM (n = 2)
DENV-2, Clinical Score
Clinical Score
Days after infection
PBS
IgEsig-prM-E (1 μl)
IgEsig-prM-E FL (1 μl)
15 μg anti-prM
H
DENV-2 ADE (10 μl)
Percent survival
Days after infection
PBS (n = 4)
IgEsig-prM-E (10 μl) (n = 5)
IgEsig-prM-E FL(10 μl) (n = 5)
DENV-2, Clinical Score
Clinical Score
Days after infection
PBS
IgEsig-prM-E (10 μl)
IgEsig-prM-E FL(10 μl)