

Prior Exposure to Zika Virus Significantly Enhances Dengue-2 Viremia in Rhesus Macaques

Jeffy George^{1#}, William G. Valiant^{1#}, Mary J. Mattapallil², Michelle Walker³, Yan-Jang S. Huang⁴, Dana L. Vanlandingham⁴, John Misamore³, Jack Greenhouse³, Deborah E. Weiss³, Daniela Verthelyi⁵, Stephen Higgs⁴, Hanne Andersen³, Mark G. Lewis³, & Joseph J. Mattapallil^{1*}

¹Uniformed Services University of the Health Sciences, Bethesda, MD 20814; ²National Eye Institute, National Institutes of Health, Bethesda, MD; ³Bioqual, Rockville, MD; ⁴Biosecurity Research Institute, Department of Diagnostic Medicine/Pathobiology, College of Veterinary Medicine, Kansas State University, Manhattan, Kansas; ⁵Food and Drug Administration, Silver Spring, MD;

Fig. S1. Plasma cytokine Levels. Kinetics of IL-1 β , G-CSF, IL-10, IL-6, IL-12, IL-17, MIP-1 α , GM-CSF, MIP-1 β , IL-15, HGF, VEGF, IFN γ , IL-1RA, TNF α , MIG, IL-4, RANTES, IL-5, and IL-2 in plasma that were collected longitudinally from ZIKV naïve (Group A; n = 4) and ZIKV immune (Group B; n = 5) rhesus macaques after DENV-2 challenge. No significant differences were observed between the groups. Differences between groups were determined using One-way ANOVA and differences between time points were determined by post-hoc analysis using Tukey's multiple comparisons test. A $p < 0.05$ was considered significant. Error bars represent standard error and * indicates $p < 0.05$.

Fig. S2. Gating strategy used to discriminate monocyte/macrophage subsets in peripheral blood. Peripheral blood mononuclear cells (PBMC) were stained with a panel of markers to discriminate CD3⁻CD8⁻VIVID⁻HLA-DR⁺CD20⁻CD11c/CD123⁻CD14 and CD16 subsets.

Fig. S3. Titration of DENV - 1, 2, 3 and 4 Reporter viral particles (RVP) using K562 cells. The concentration of DENV RVP to be used in the antibody dependent enhancement of infection in K562 cells was determined using ZIKV positive serum. Heat inactivated serum was incubated with different concentrations of RVP and then cultured with K562 cells for 48 hours. The frequency of GFP expressing cells was determined by flow cytometry.

Fig. S4. Changes in body temperature during DENV-2 infection. Body temperatures were measured in ZIKV naïve and ZIKV immune animals after DENV-2 infection. Raw values are shown.

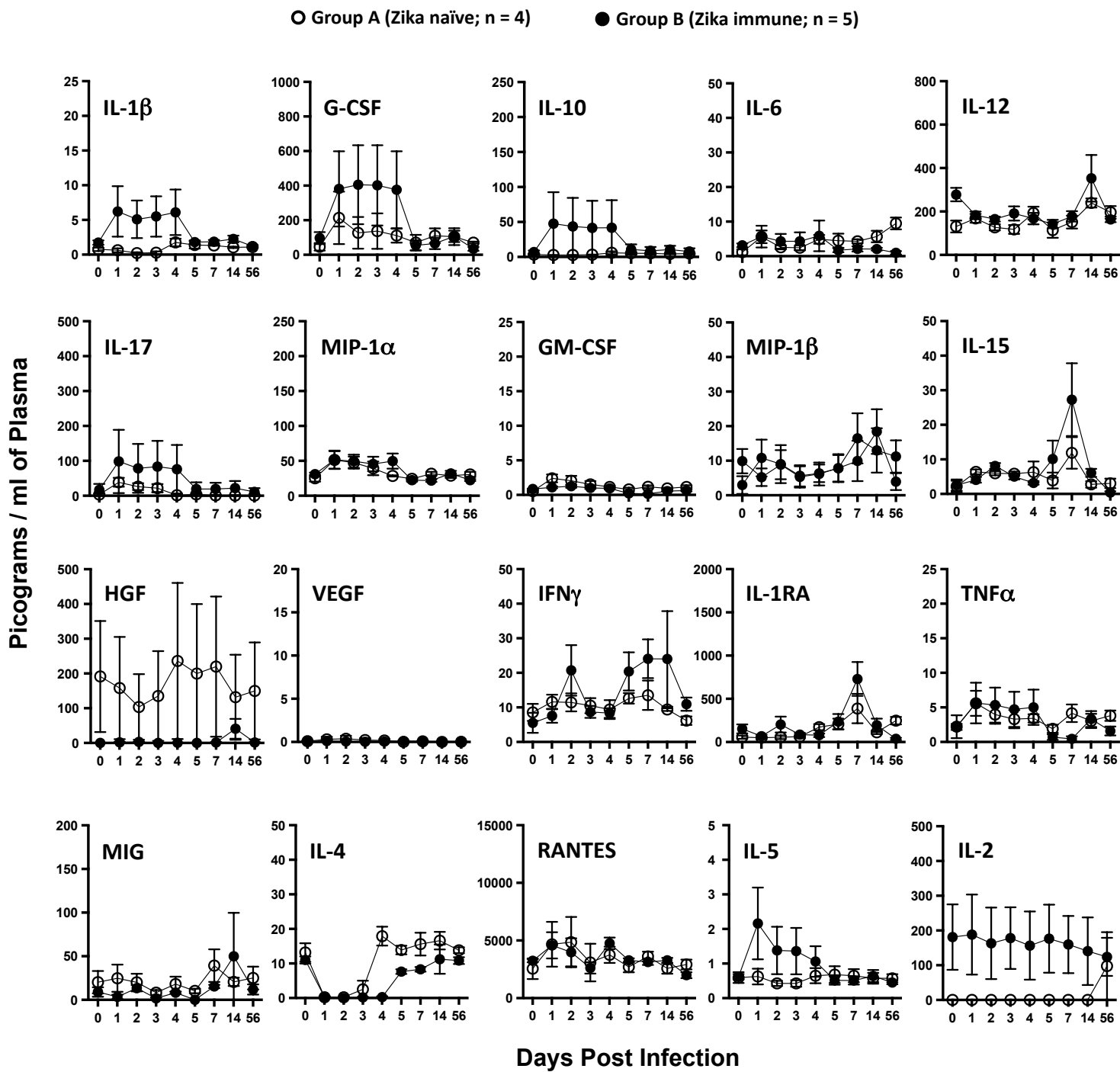


Fig. S1

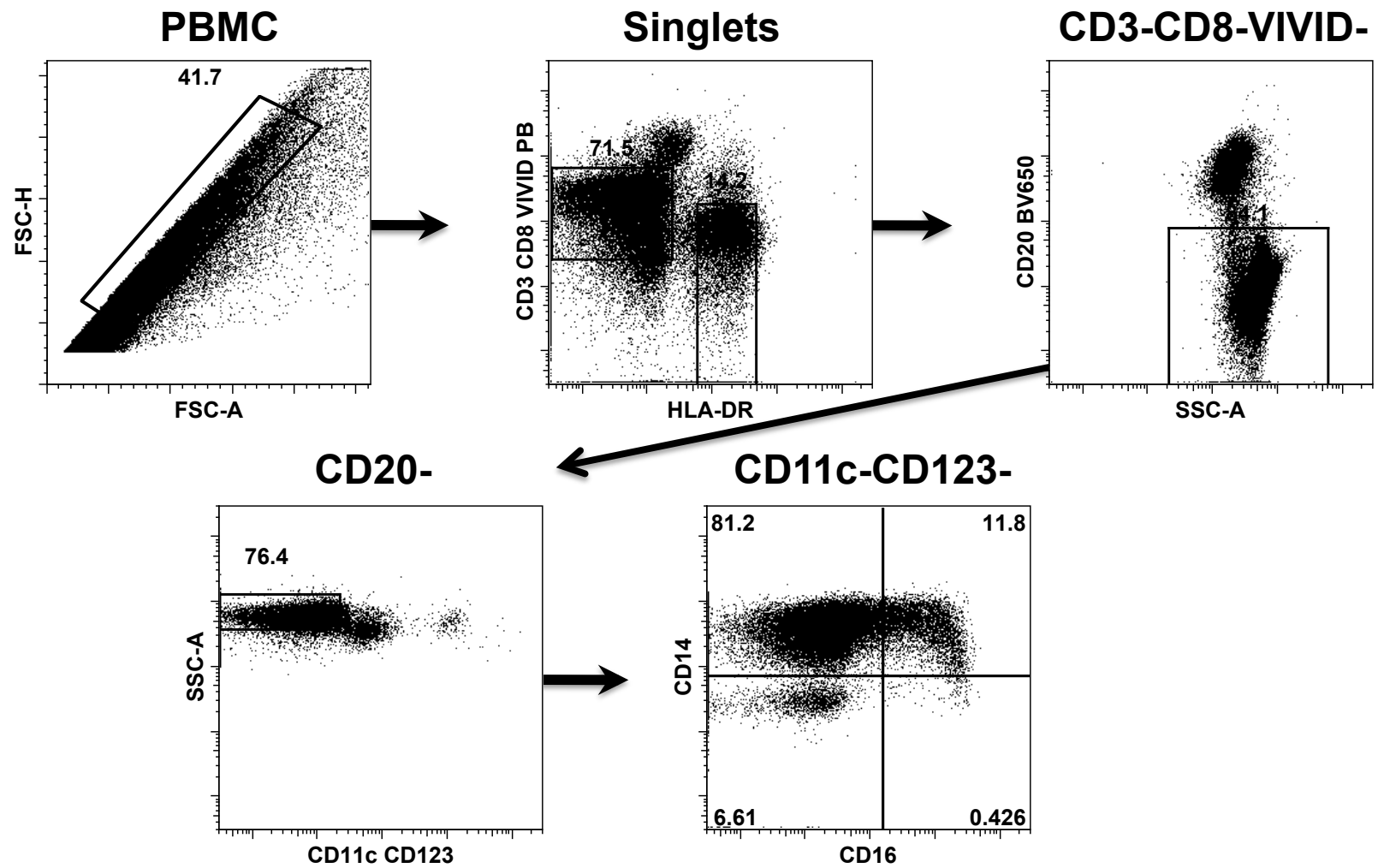


Fig. S2

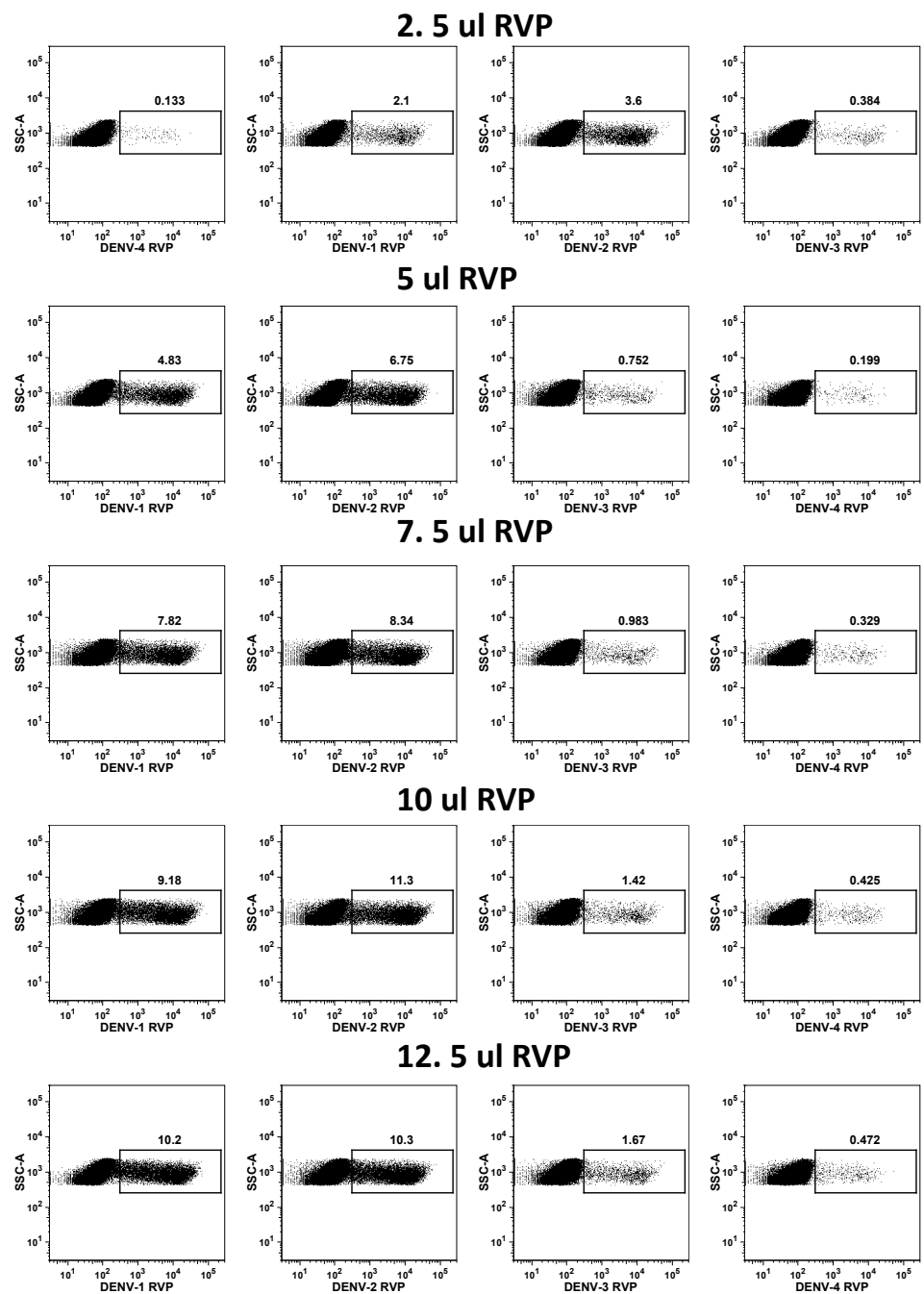


Fig. S3

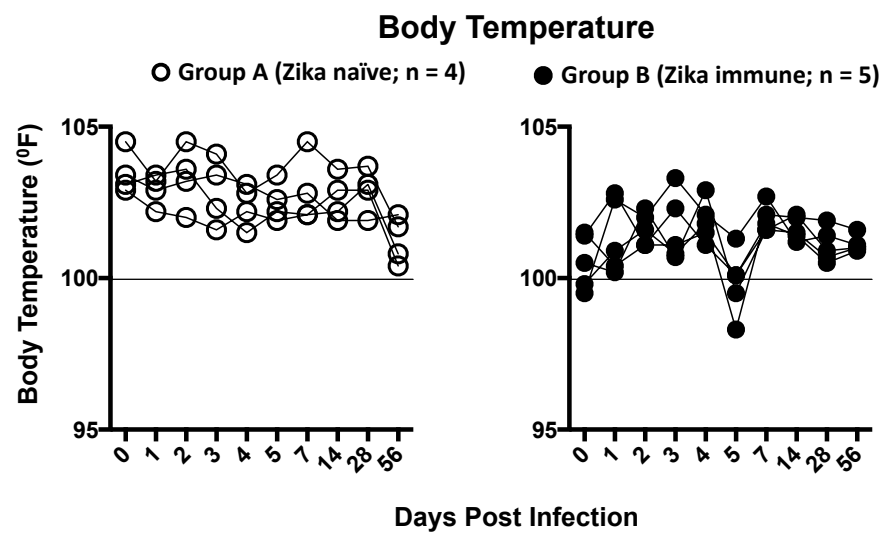


Fig. S4