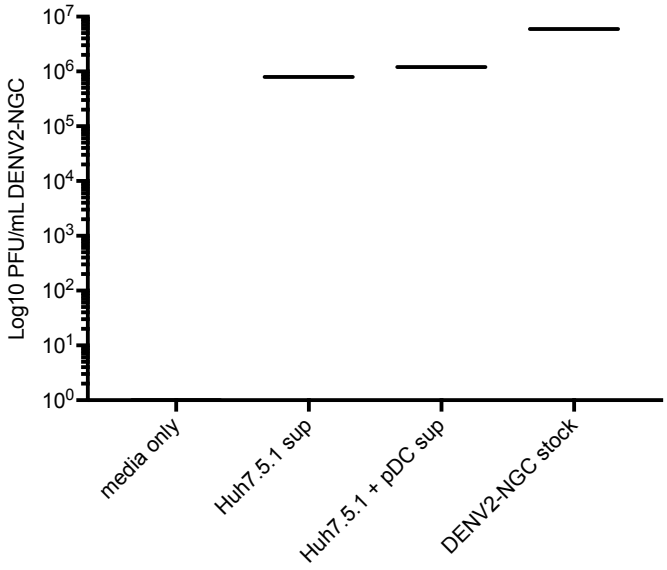
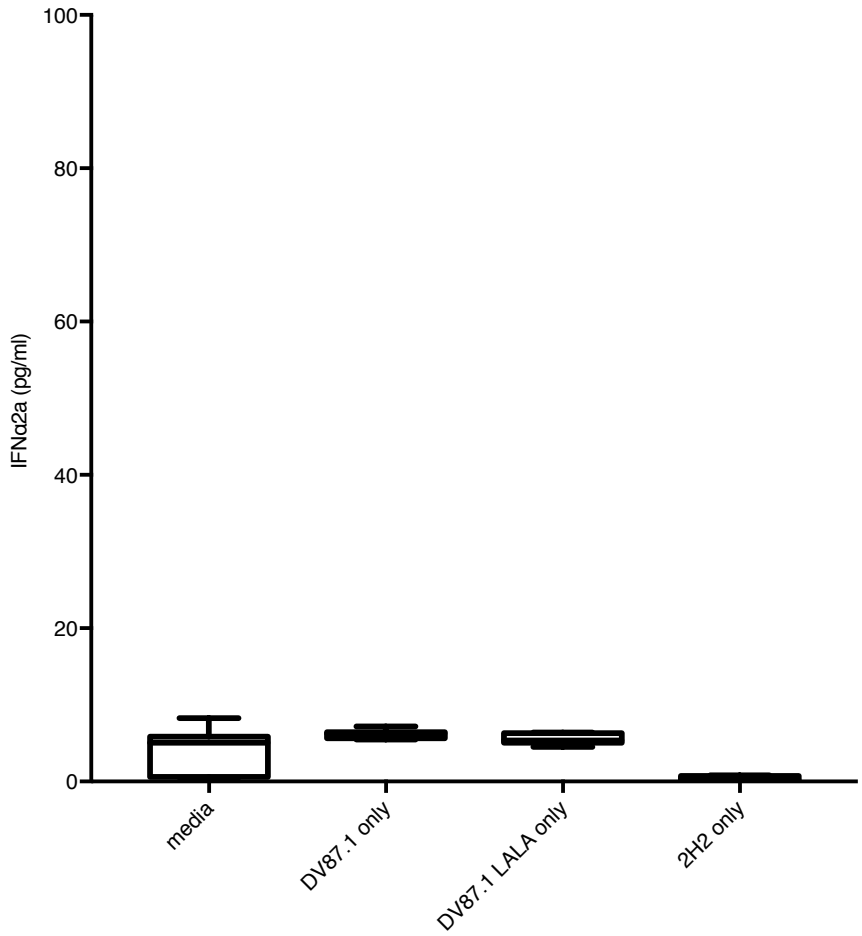
Supplemental figures and figure legends:



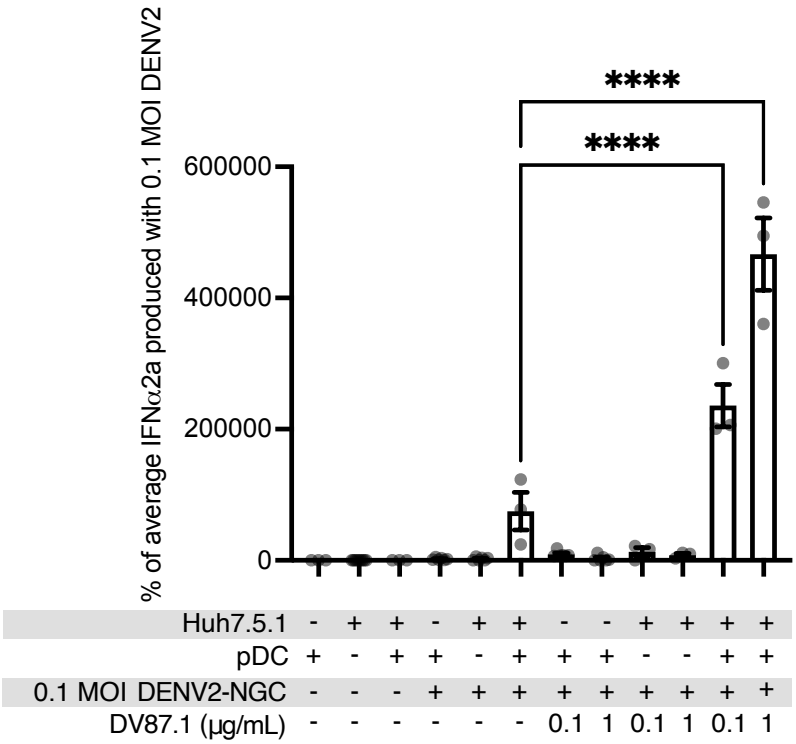
Supplemental Figure 1: Infectious virus is present in supernatant of infected Huh 7.5.1 cells after 48 hours

Supernatant were collected from Huh7.5.1 after 48 hours of infection with 0.1 MOI DENV2-NGC and 24 hours of co-culture with primary human pDCs (Huh7.5.1 + pDC sup) or without co-culture (Huh7.5.1 sup). Supernatant were assayed for PFU/ml of infectious DENV2-NGC using a vero cell based plaque assay and were compared to media alone and DENV2-NGC stock. The figure represents a single experiment with n greater than or equal to 3 per condition.



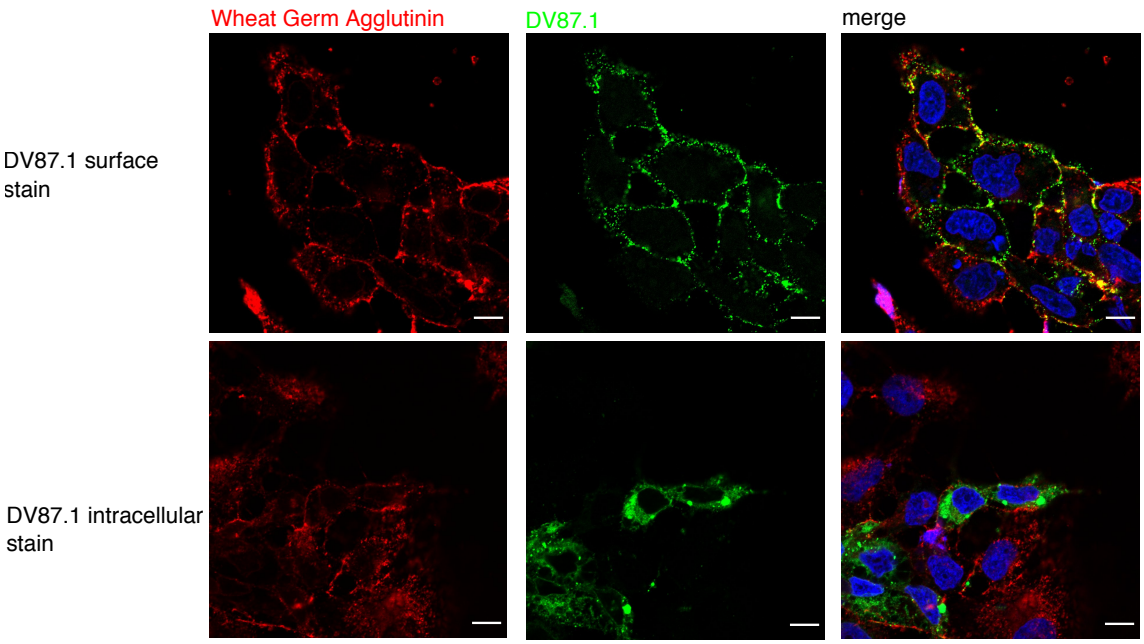
Supplemental Figure 2: Anti-DENV antibodies do not generate pDC IFN response in the absence of virus

Huh7.5.1 cells were left uninfected for 48h. After 48h, anti-DENV envelope antibody DV87.1 or anti-DENV prM antibody 2H2 were added to Huh7.5.1 cells and incubated for 1 hour. After an hour of antibody treatment, primary human pDCs were co-cultured with antibody-treated Huh7.5.1 cells for 24 hours. Supernatants were collected and IFN-α2a levels measured (pg/ml). The figure represents 3 independent experiments with 3 unique pDC donors and n greater than or equal to 3 per condition per experiment.



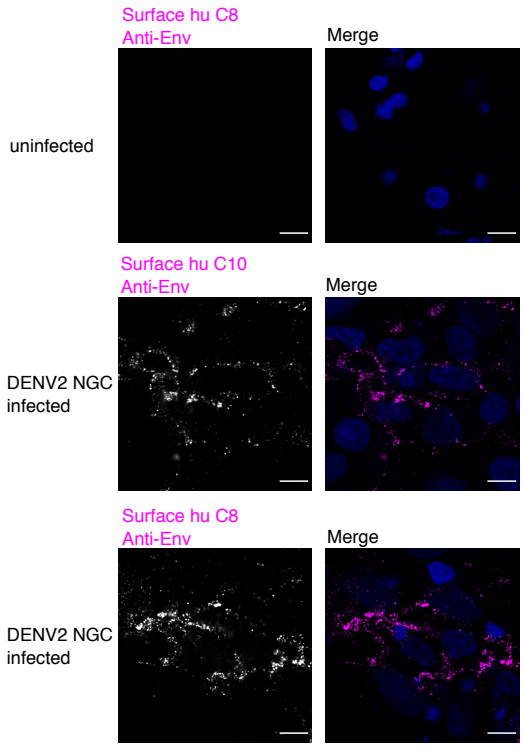
Supplemental Figure 3: Anti-DENV antibodies are unable to increase the sensing of virus in the absence of Huh7.5.1

Huh7.5.1 cells were plated and infected with 0.1 MOI of DENV2-NGC for 48 hours, or left uninfected. Cells were replated and pre-incubated for 1 hour with 0.1-1 ug/mL anti-DENV DV87.1, or left without antibody. After pre-incubation, primary human pDCs were isolated and co-cultured with infected and antibody-treated Huh7.5.1 cells for 24 hours, or both cell types were incubated alone. Additionally, 0.1 MOI of DENV2-NGC was pre-incubated with DV87.1 and subsequently added to pDC. All conditions were incubated for 24 hours, after which supernatants were assessed for IFNα2a by MSD analysis. Figure represents 1-2 independent experiments with unique pDC donors with n greater than or equal to 3 per condition per experiment. * = $p<0.05$, ** = $p<0.01$, *** = $p<0.001$, **** = $p<0.0001$, ns = not significant



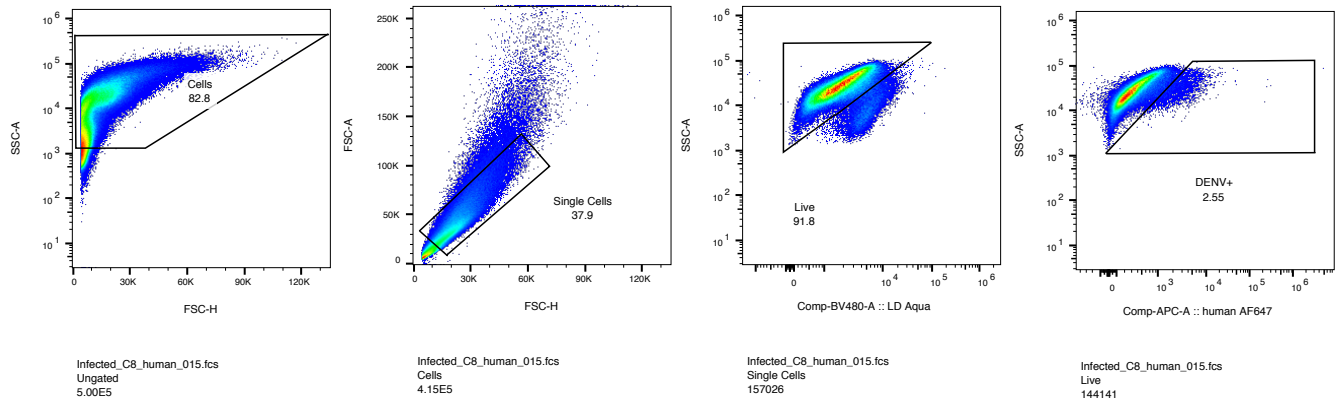
Supplemental Figure 4: DV87.1 anti-DENV antibody binds unpermeabilized DENV infected Huh7.5.1 cells in a manner consistent with surface staining

Huh7.5.1 cells were infected with DENV at 0.1 MOI for 48h. Top panel: Huh7.5.1 cells were treated with human anti-DENV E antibody DV87.1 or wheat germ agglutinin to permit surface binding. Bottom panel: Huh7.5.1 cells were treated with wheat germ agglutinin to permit surface binding, then were permeabilized and stained with DV87.1 for intracellular DENV. Secondary AF488 was added and images were acquired on a Zeiss Airyscan LSM 800. Blue in merged images represents DAPI nuclear stain. Representative images are displayed for 2 conducted experiments. Scale bars represent 10uM.

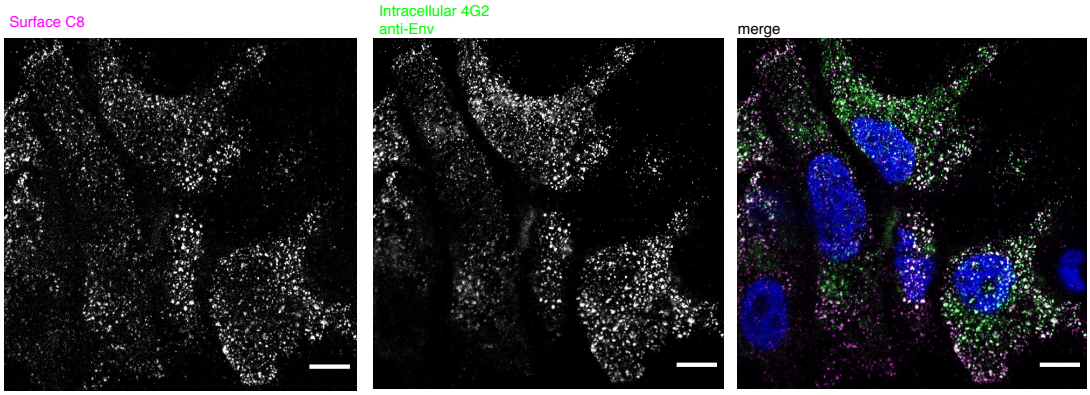


Supplemental Figure 5: Anti-DENV antibodies C8 and C10 bind the surface of infected Huh7.5.1 cells

Huh7.5.1 cells were infected with DENV at 0.1 MOI for 48h or left uninfected for 48h. Huh7.5.1 cells were treated with human anti-dengue env antibodies C8 or C10 to permit surface binding. Secondary goat-anti-human DyLight 650 was added and images were acquired on a Zeiss Airyscan LSM 800. Blue in merged images represents DAPI nuclear stain. Representative images are displayed for 5 conducted experiments. Scale bars represent 10uM.

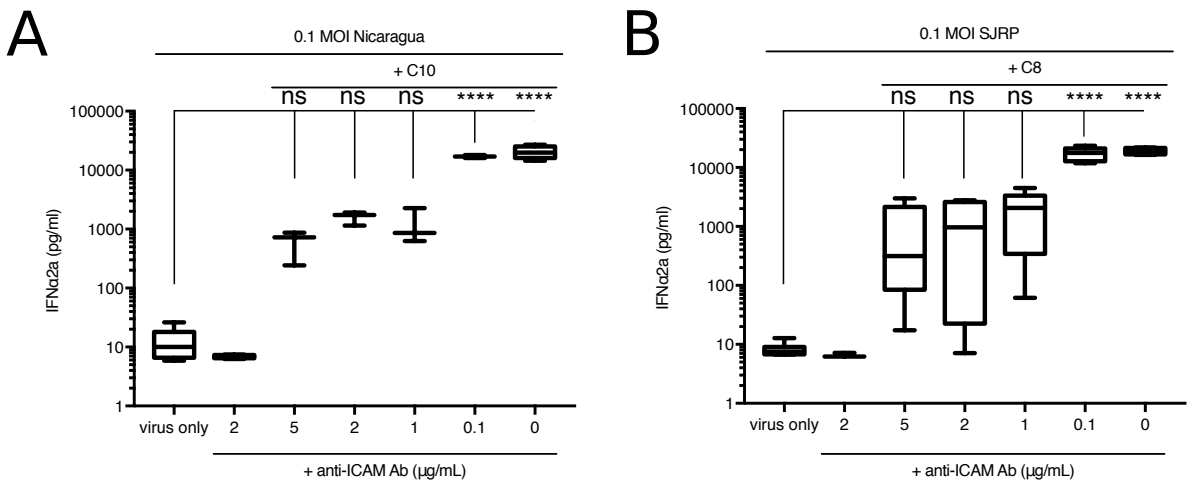


Supplemental Figure 6: Gating strategy for DENV-infected Huh7.5.1 cells
Uninfected or DENV infected Huh7.5.1 cells were surface stained with primary human antibodies against DENV Env protein DV87.1, C8, and C10. Primary antibody stained cells were then stained with secondary anti-human AF647. An example gating scheme is shown here, demonstrating gating for cells, singlets, live cells, and then for DENV infected cells by AF647. Analysis was performed using Flowjo v10 software.



Supplemental Figure 7: Anti-DENV antibody C8 binds the surface of ZIKV infected Huh7.5.1 cells

Huh 7.5.1 cells were infected with ZIKV SJRP and then re-plated for 24 h, at which point they were stained with C8 mAbs for 1 h at 4ºC. Following surface Ab staining, the cells were fixed and permeabilized and stained for intracellular DENV E with mouse mAb 4G2. Representative images are displayed for 4 conducted experiments(ZIKV SJRP used in displayed images). Scale bars represent 10 μM.



Supplemental Figure 8: Anti-ICAM blockade can suppress the C8/C10 augmented IFN response in the presence of ZIKV

Huh7.5.1 cells were plated and infected with 0.1 MOI of (a) Zika Nicaragua or (b) Zika SJRP for 48 hours. Infected cells were replated and pre-incubated for 1 hour with anti-ICAM antibody at 0.1-5ug/ml and (a) C10 or (b) C8 monoclonal antibodies. After pre-incubation, primary human pDCs were isolated and co-cultured with infected and antibody-treated Huh7.5.1 cells for 24 hours, after which supernatants were assessed for IFN-α2a by MSD analysis. Each figure panel represents at least two independent experiments with unique pDC donors with n greater than or equal to 3 per condition per experiment. * = $p<0.05$, ** = $p<0.01$, *** = $p<0.001$, **** = $p<0.0001$, ns = not significant

	Binding to whole virus in ELISA, for the indicated serotype, at 1ug/mL				Binding to Protein				50% neutralization conc. (ug/mL) against indicated serotype				Fold enhancement of infection, for indicated serotype, at 1ug/mL				Critical residues identified by shotgun mutagenesis epitope mapping						
					ELISA		Western Blot																
mAb	D1	D2	D3	D4	rE	rPr	rE	rPr	D1	D2	D3	D4	D1	D2	D3	D4	F1	L3	S5	E9	E18	L24	K26
4G21	+	+	+	+	-	+	-	+	-	-	-	-	18	22	32	0.5	-	-	+	-	+	-	-
1H10	+	+	+	+	-	+	-	+	-	-	-	-	16	23	31	30	-	+	+	-	-	-	-
2H21	+	+	+	+	-	+	-	+	-	-	-	-	3	1	1	4	+	-	-	-	+	+	+
1E23	+	+	+	+	-	+	-	+	-	-	-	-	4	1	5	4	-	+	+	+	-	-	+
1B22	+	+	+	+	-	+	-	+	-	-	-	-	2	1	1	3	-	+	-	-	-	-	-

Supplemental Table 1:
Characterization of anti-prM antibodies supplied by Desilva lab adapted from Smith et al. (68)

Supplemental Methods:

Titration of viral stocks and supernatants

PFU/ml was determined by modified plaque assay and immunostaining. Briefly, Vero cells were plated in 24-well plates and cultured to 90% confluency. Virus was plated in duplicate in serum free OPTIMEM at 6 serial 10-fold dilutions and incubated for 1 hour. An overlay of 1% methylcellulose in OPTIMEM was applied to cultures. Plates were incubated for 4-5 days. Titration plates were fixed with methanol and stained with anti-DENV antibodies (2H2 & 4G2, supplied by the Durbin laboratory), followed by a secondary goat-anti-mouse HRP-conjugated antibody (VWR 074-1806). TrueBlue KPL substrate (VWR 50-78-02) was used to develop plaques.