

Supplementary Table 1. Subset demographics.

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Supplementary Figure 1 | DENV2 viremia after rDEN2Δ30 infection.

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**Supplementary Table 1. Subset demographics.**

	<i>Parent study (n = 20)</i>	<i>Gene expression subset (n = 11)</i>
<i>Female</i>	6 (30%)	2 (18%)
<i>Male</i>	14 (70%)	9 (82%)
<i>Black</i>	9 (45%)	5 (45%)
<i>White</i>	11 (55%)	6 (55%)
<i>Baltimore</i>	11 (55%)	6 (55%)
<i>Vermont</i>	9 (45%)	5 (45%)

**Supplementary Table 2. List of reagents used.**

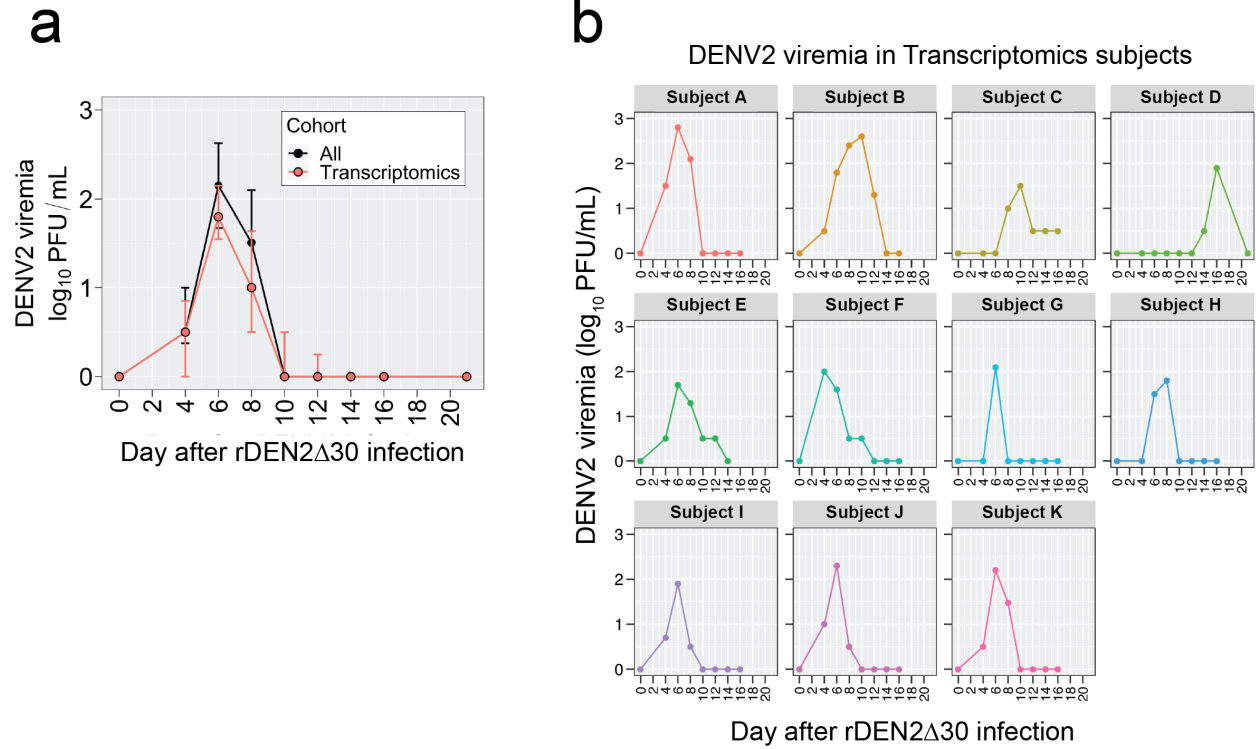
REAGENT or RESOURCE		SOURCE	IDENTIFIER
Antibodies			
Anti-human CD3 (UCHT1) FITC-conjugated	0.25 µL/test	Biolegend	Cat. #300406 Lot #B279208
Anti-human CD4 (OKT4) BV510-conjugated	1 µL/test	Biolegend	Cat. #317444 Lot #B248141
Anti-human CD8 (RPA-T8) BV650-conjugated	0.5 µL/test	Biolegend	Cat. #301041 Lot #B275821
Anti-human CD14 (M5E2) BV711-conjugated	1 µL/test	Biolegend	Cat. #301837 Lot #B275829

Anti-human CD16 (3G8) APC-Cy7-conjugated	0.25 µL/test	Biolegend	Cat. #302017 Lot #B295391
Anti-human CD19 (HIB19) PE-Dazzle594-conjugated	0.5 µL/test	Biolegend	Cat. #302252 Lot #B277039
Anti-human CD25 (M-A251) BV421-conjugated	0.5 µL/test	Biolegend	Cat. #356113 Lot #B301467
Anti-human CD27 (M-T271) PE-Cy7-conjugated	0.125 µL/test	Biolegend	Cat. #356412 Lot #B279971
Anti-human CD38 (HIT2) Alexa Fluor 647-conjugated	0.125 µL/test	Biolegend	Cat. #303514 Lot #B233813
Anti-human CD45RA (HI100) BUV395-conjugated	0.25 µL/test	BD OptiBuild	Cat. #740298 Lot #0293615
Anti-human CD56 (NCAM16.2) BUV563-conjugated	0.125 µL/test	BD Horizon	Cat. #612929 Lot #0044064
Anti-human CD57 (QA17A04) BV605-conjugated	0.5 µL/test	Biolegend	Cat. #393303 Lot #270939
Anti-human CD127 (HIL-7R-M21) BUV805-conjugated	0.25 µL/test	BD OptiBuild	Cat. #748486 Lot #0294340
Anti-human CD134 (ACT35) BUV737-conjugated	0.125 µL/test	BD OptiBuild	Cat. #749286 Lot #0294339
Anti-human CD154 (24-31) BV785-conjugated	0.5 µL/test	Biolegend	Cat. #310841 Lot #B264809
Anti-human HLA-DR (L243) BV570-conjugated	2.5 µL/test	Biolegend	Cat. #307637 Lot #B314475
Anti-human IgM (MHM-88) PerCP-Cy5.5-conjugated	0.5 µL/test	Biolegend	Cat. #314512 Lot #B231968
Anti-human CCR7 (2-L1-A) APC-R700-conjugated	0.5 µL/test	BD Horizon	Cat. #566767 Lot #0283646
Anti-human CD279 (EH12.2H7) PE-conjugated	0.5 µL/test	Biolegend	Cat. #329905 Lot #B252642
Human TruStain FcX blocker	5 µL/test	Biolegend	Cat. #422302 Lot #B313422
True-Stain Monocyte blocker	5 µL/test	Biolegend	Cat. #426102 Lot #B311012
Live/Dead Blue Viability Dye	0.5 µL/test	Invitrogen	Cat. #L23105 A Lot #2214471
Brilliant stain buffer	50 µL/test	BD Horizon	Cat. #566349 Lot #9192749

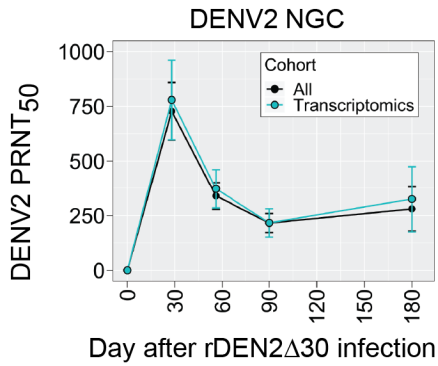
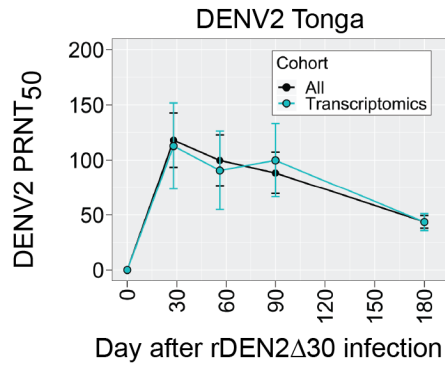
<b>Bacterial and Virus Strains</b>			
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Dengue virus serotype 1 (West Pacific 74) WHO reference strain	Stephen Whitehead, National Institute of Allergy and Infectious Disease (NIAID)	Genbank AY145121
Dengue virus serotype 2 (New Guinea C)	Stephen Whitehead, NIAID	Genbank AF038403.1
Dengue virus serotype 2 (strain S-16803) WHO reference strain	Aravinda De Silva, University of North Carolina-Chapel Hill (UNC)	Genbank GU289914
Dengue virus serotype 3 (Sleman/78)	Stephen Whitehead, NIAID	Genbank AY656169

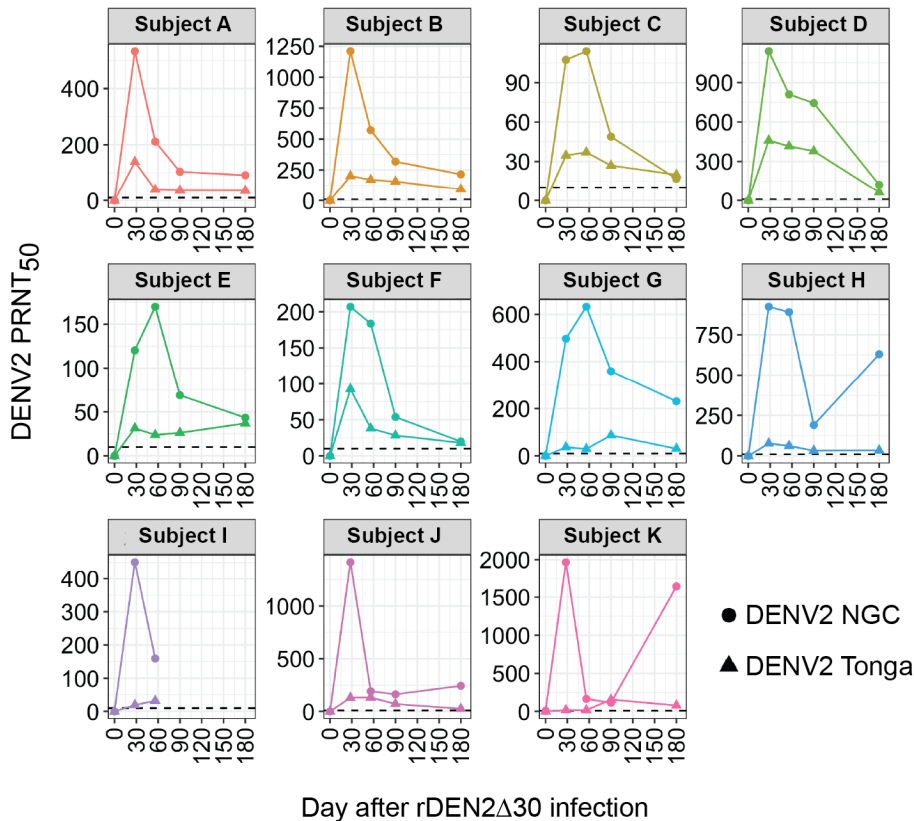
Dengue virus serotype 3 (CH53489) WHO reference strain	Aravinda De Silva, UNC	Genbank DQ863638
Dengue virus serotype 4 Dominica/81	Stephen Whitehead, NIAID	Genbank AY648301
Dengue virus serotype 4 (TVP-376) WHO reference strain	Aravinda De Silva, UNC	Genbank KC963424
<b>Biological Samples</b>		
Human Serum	University of Vermont Vaccine Testing Center and Johns Hopkins Center for Immunization Research	Clinicaltrials.gov identifiers: NCT01072786, NCT02021968
Peripheral blood mononuclear cells (PBMC)	University of Vermont Vaccine Testing Center and Johns Hopkins Center for Immunization Research	Clinicaltrials.gov identifiers: NCT01072786, NCT02021968
<b>Experimental Models: Cell Lines</b>		
African green monkey kidney cells (Vero-81)	Stephen Whitehead, NIAID	RRID:CVC_0059



**Supplementary Figure 1 | DENV2 viremia after rDEN2Δ30 infection. (a)** Comparison of DENV2 serum viremia as assessed by plaque assay (expressed as  $\log_{10}$  plaque-forming units/mL of serum) in the parent cohort (All,  $n = 20$ ) from which a subset was selected for transcriptomics analysis ( $n = 11$ ). Median  $\pm$  standard deviation is plotted. **(b)** Individual viremia profiles for each of the subjects in the transcriptomics analysis.

**a****b****c**

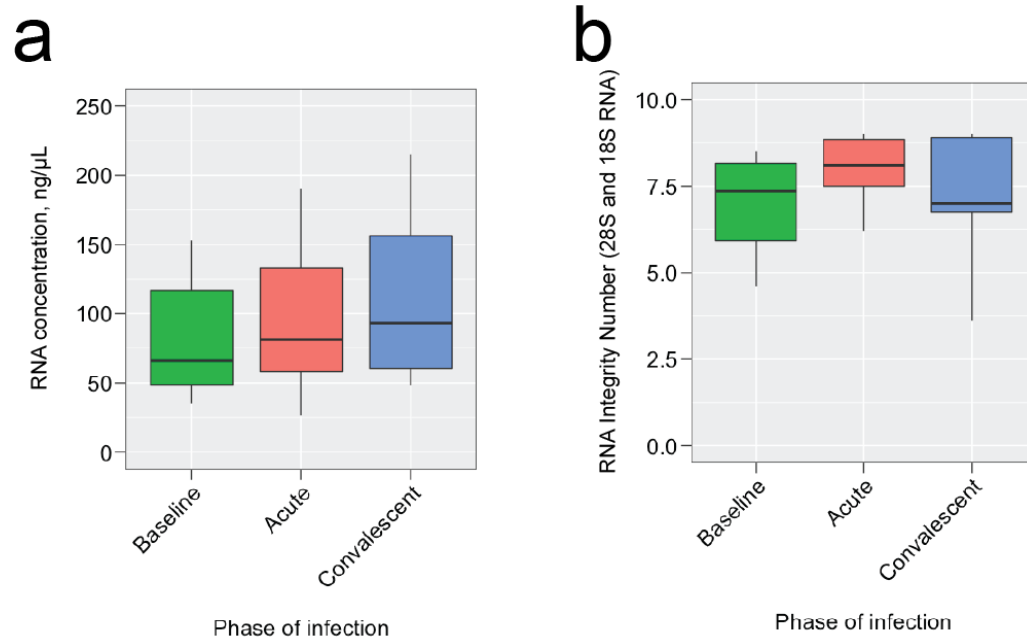
DENV2 serum neutralizing antibodies in transcriptomics subjects



**Supplementary Figure 2 | DENV2 serum neutralizing antibodies after rDEN2Δ30 infection.**

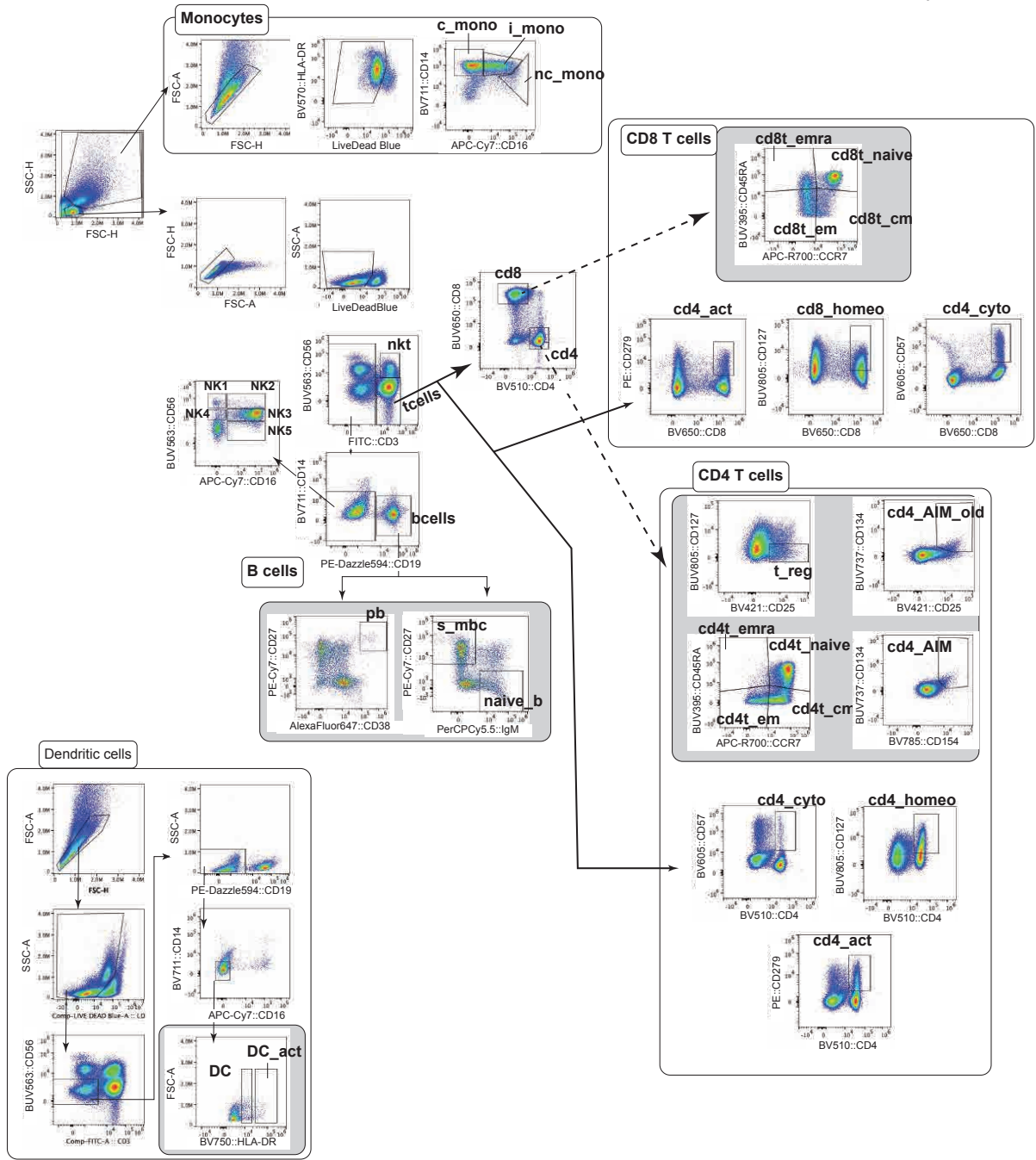
(a) Comparison of DENV2 serum neutralizing antibodies as assessed by plaque reduction neutralization titer 50% (PRNT<sub>50</sub>) to (a) DENV2 NGC (b) DENV2 Tonga in the parent cohort (All,

n = 20) and the subset selected for transcriptomics analysis (n = 11). Mean  $\pm$  standard deviation values are shown. (c) Individual PRNT<sub>50</sub> profiles for DEN2-NGC (circles) and -Tonga (triangles) for each of the subjects in the transcriptomics analysis.



**Supplementary Figure 3 | Quantity and quality of whole blood mRNA during rDEN2 $\Delta$ 30 infection.** (a) RNA quantity (a) and quality (b) in samples isolated at Day 0 (baseline), day 8 (acute) and day 28 (convalescent) after primary rDEN2 $\Delta$ 30 infection (see methods). Boxplots show the median (horizontal line), 95% confidence level (box bounds), and minimum and maximum values (whiskers).

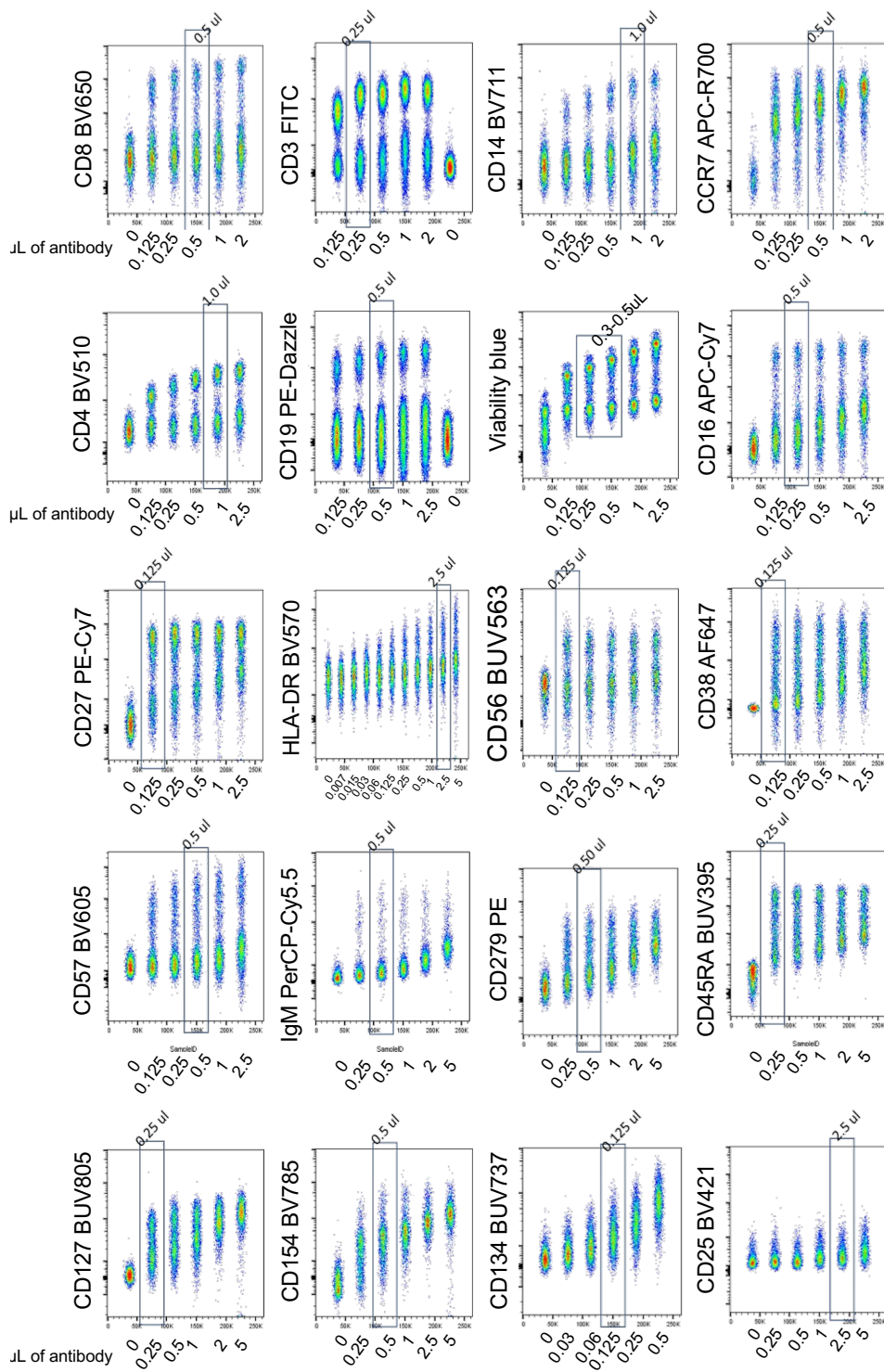
Flow cytometric gating strategy and cell population identifiers for Hanley et al.



**Supplementary Figure 4 | Flow cytometric gating strategy.** Labels in bold on plots correspond to graph headings in Figure 4. Lineage-negative (CD3<sup>-</sup>CD19<sup>-</sup>CD56<sup>-</sup>CD14<sup>-</sup>CD16<sup>-</sup>) HLA-DR<sup>+</sup> Dendritic cells (**DC**), HLA-DR<sup>hi</sup> activated DC (**DC\_act**); monocytes: classical (**c\_mono**), intermediate (**i\_mono**), and non-classical (**nc\_mono**); natural killer T cells (**nkt**), natural killer cell (**NK**)1-5 populations (defined by CD56 and CD16 staining; CD3<sup>+</sup> T cells (**tcells**), CD4<sup>+</sup> T

cells (**cd4**), and CD8<sup>+</sup> T cells (**cd8**); CD8<sup>+</sup> T cell populations: Activated CD279<sup>+</sup> (**cd8\_act**), cytotoxic CD57<sup>+</sup> (**cd8\_cyto**), CCR7<sup>-</sup>CD45RA<sup>+</sup> T effector re-expressing CD45RA (**cd8t\_emra**), CCR7<sup>+</sup>CD45RA<sup>+</sup> naïve (**cd8t\_naive**), CCR7<sup>-</sup>CD45RA<sup>-</sup> effector memory (**cd8t\_em**), CCR7<sup>+</sup>CD45RA<sup>-</sup> central memory (**cd8t\_cm**), and homeostatic CD127<sup>+</sup> (**cd8\_homeo**); CD4<sup>+</sup> T cell populations: activated CD279<sup>+</sup> (**cd4\_act**), cytotoxic CD57<sup>+</sup> (**cd4\_cyto**), activation-induced marker (AIM)-positive CD154<sup>+</sup>CD134<sup>+</sup> (**cd4\_AIM**), CD25<sup>+</sup>CD134<sup>+</sup> (**cd4\_AIM\_old**), regulatory T cells CD127<sup>-</sup>CD25<sup>+</sup> (**t\_regs**), homeostatic CD127<sup>+</sup> (**cd4\_homeo**), CCR7<sup>-</sup>CD45RA<sup>+</sup> T effector re-expressing CD45RA (**cd4t\_emra**), CCR7<sup>+</sup>CD45RA<sup>+</sup> naïve (**cd4t\_naive**), CCR7<sup>-</sup>CD45RA<sup>-</sup> effector memory (**cd4t\_em**), CCR7<sup>+</sup>CD45RA<sup>-</sup> central memory (**cd4t\_cm**); CD19<sup>+</sup> B cells (**bcells**), plasmablasts CD19<sup>+</sup>CD38<sup>hi</sup>CD27<sup>hi</sup> (**pb**), IgM<sup>+</sup>CD27<sup>-</sup> naïve B cells (**naïve\_b**), and IgM<sup>-</sup>CD27<sup>+</sup> switched memory B cells (**s\_mbc**).





**Supplementary Figure 5 | Titration of flow cytometry staining antibodies for multi-color staining panel.** A range of dilutions of each single antibody was used to stain  $10^6$  PBMCs in 50

$\mu\text{L}$  of staining buffer. The fluorescence profiles of each individual antibody dilution ( $\mu\text{L}$  of antibody used on x-axis) was plotted on a single plot with fluorescent intensity on y-axis). Based on the brightness and separation of signal (positive or negative or range of staining), the final staining amount for each antibody required in the multi-color panel are indicated by the box and label.