

## Supplementary Figure Legends

Fig. S1 Anti-prM responses during primary DENV infection.

Western blots of C6/36 cell lysates infected with DENV1-DENV4 and probed with primary immune DENV serum (A). Plasma diluted 1 in 100 from five cases each of DENV1, DENV2 and DENV3 were analysed by Western blot for anti-prM against the four DENV serotypes and reactivity was then scored (B).

Fig. S2 Reactivity of human anti-prM monoclonal antibodies.

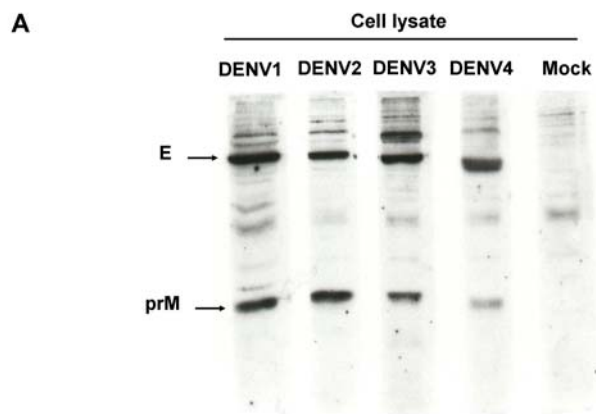
Reactivity of the 6 anti-prM antibodies to reduced (R) and non-reduced (N) DENV infected cell lysates showing loss of reactivity on reduced Western blots (A). To show reactivity to the pr peptide, western blotting of culture supernatant (non-heat/non-reduced) from DENV (B) and mock (C) infected cells was performed. Non reduced gels were run in loading buffer lacking 2-mercaptoethanol which were also non-heat treated.

Fig. S3 Neutralisation and ADE of anti-E and anti-prM antibodies.

Culture supernatants from 20 anti-E and 20 anti-prM cell lines, all of which were specific to DENV2 and cross-reactive with other DENV serotypes, were assayed in neutralization and ADE assays to DENV 2 strain 16681. Neutralisation was performed by focus forming assay on Vero cells using a 1:2 dilution of supernatant while ADE was performed using a 1:100 dilution on U937 cells and infection read by FACS using 4G2 (A and B). Control experiment showing roughly equal levels of infection of monocytes in the presence of the 6 anti-prM monoclonal antibodies when assayed by intracellular staining for either DENV envelope (4G2) or DENV non-structural protein-1 (2G6). Two irrelevant human antibodies are also shown (C). Histograms showing higher amplitude staining with 4G2 (anti-E) compared to 2G6 (anti-NS1), 4G2 was selected for the intracellular staining assays (D).

Fig. S4 Infectivity of virus produced in furin deficient LoVo cells.

LoVo produced virus has a high prM:E ratio measured by ELISA (A). Silver stained gel (non-reduced) of DENV immunoprecipitated with 4G2 showing absence of M in LoVo cells and reduction in M in virus produced in the presence of ammonium chloride (B). Enhancement of infection of LoVo produced virus by anti-prM antibody (C). Infection of U937 cells was detected by FACS with mAb 4G2 at 3 days post infection.



**B Reactivity of primary serum**

Serotype of primary	Western blot			
	DENV1	DENV2	DENV3	DENV4
DENV1 (n=5)	5	5	5	2
DENV2 (n=5)	5	5	5	1
DENV3 (n=5)	3	5	5	5

**Fig. S1**

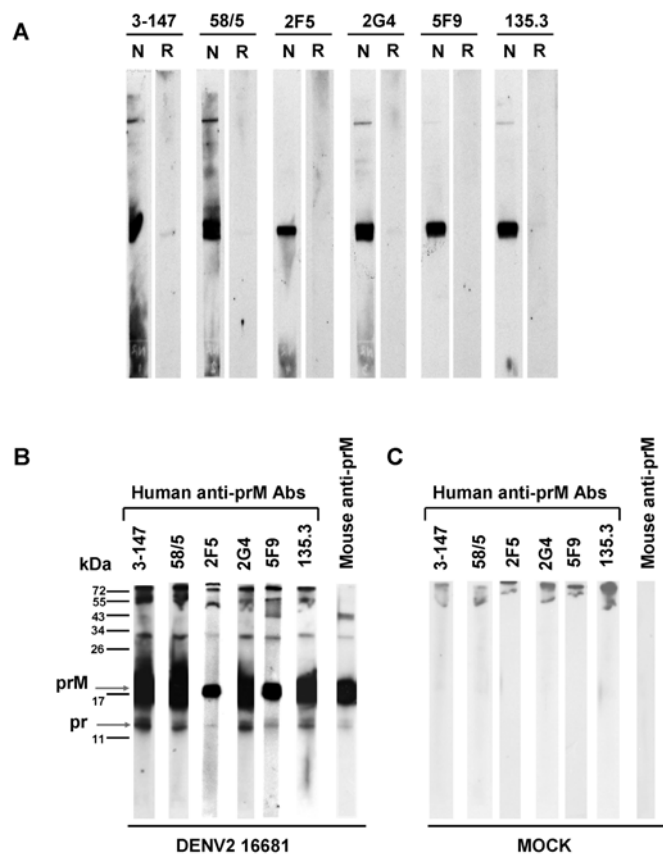


Fig S2

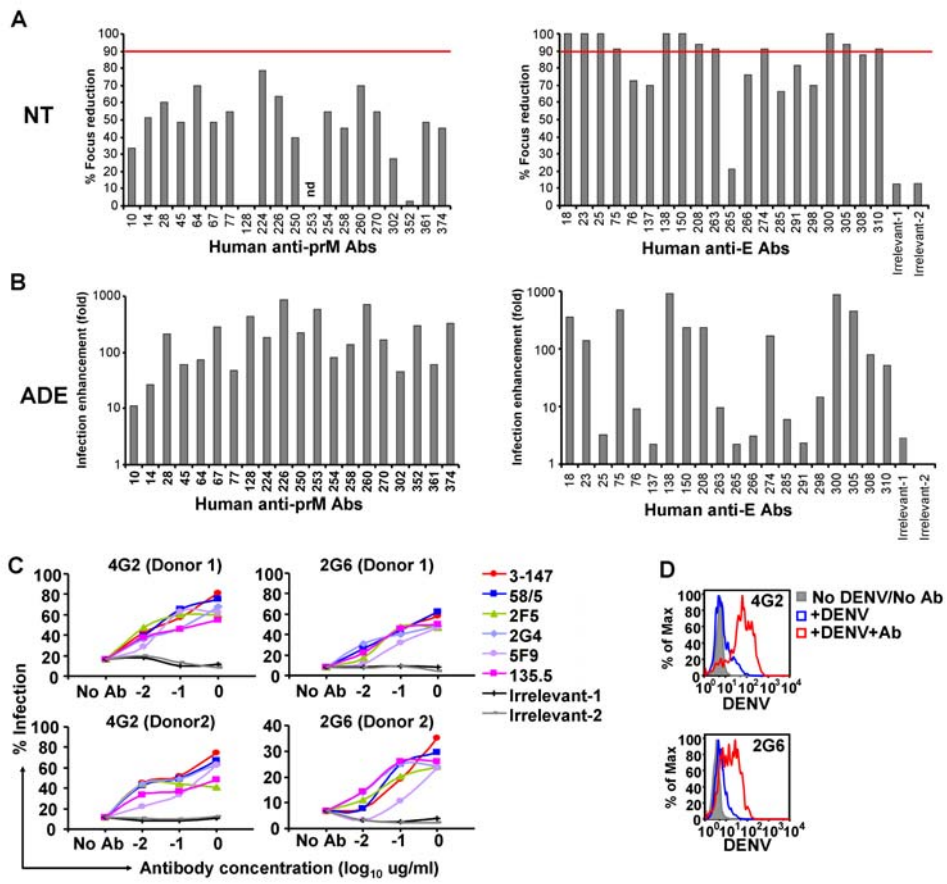


Fig. S3

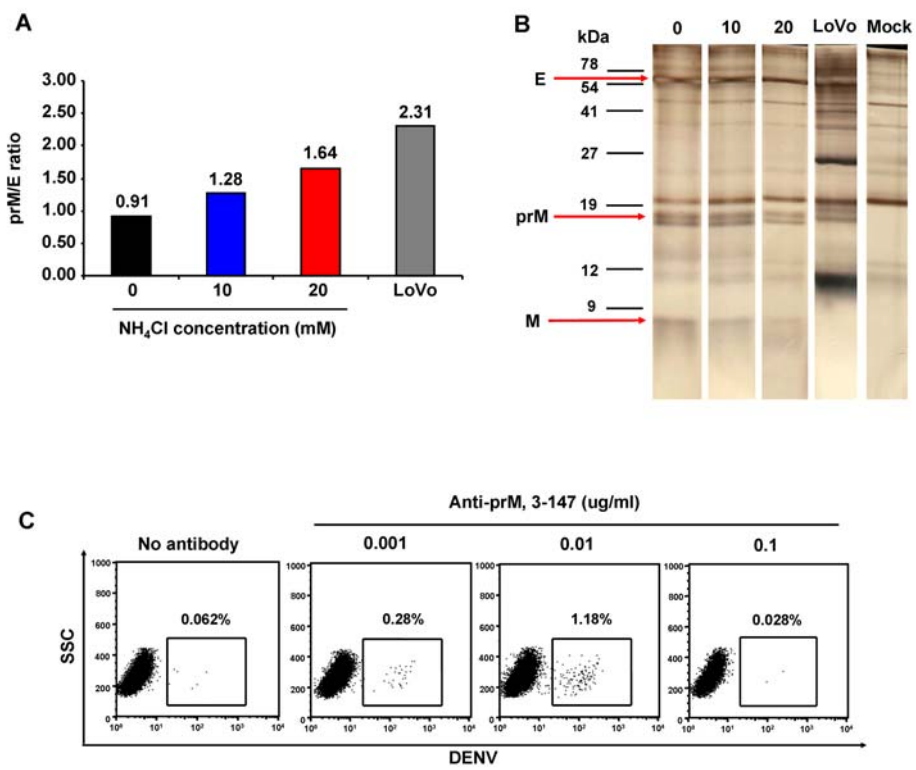


Fig. S4

**Table S1. Summary of DENV-infected patients enrolled in the study**

<b>Patient ID</b>	<b>Severity</b>	<b>Serotype of infection</b>	<b>Day after defervescence</b>	<b>No. of positive BCL (n= 301)</b>
1	DF	DENV2	19	19
2	DHF1	DENV2	23	54
3	DHF1	DENV2	17	53
4	DHF1	Unknown	15	76
5	DHF1	DENV1	17	69
6	DHF2	DENV4	24	20
7	DHF3	DENV2	20	10

**Table S2a . Antibody responses against prM and E**

Patient ID	Serotype	anti-structural (n)	anti-prM(n)	anti-E(n)	%prM
1	2	16	11	5	68.8
2	2	30	12	18	40.0
3	2	33	23	10	69.7
4	unknown	43	26	17	60.5
5	1	44	29	15	65.9
6	4	3	0	3	0.0
7	2	3	2	1	66.7
total		172	103	69	59.9

**Table S2b. Antibody cross reactivity among DENV serotypes**

Patient ID	Serotype	prM			E			NS1		
		full*	partial**	specific***	full	partial	specific	full	partial	specific
1	2	9	2	0	5	0	0	2	1	0
2	2	11	0	1	18	0	0	4	4	8
3	2	23	0	0	10	0	0	12	3	1
4	unknown	24	2	0	12	4	1	6	10	2
5	1	28	0	1	13	2	0	7	4	1
6	4	0	0	0	2	1	0	6	8	1
7	2	2	0	0	1	0	0	1	0	0

\*cross reacts with all 4 serotypes

\*\* cross reacts with 2-3 serotypes

\*\*\* reacts only one serotype

**Table S2c Antibody cross reactivity between DENV and JEV**

Patient ID	Serotype	prM		E		NS1	
		DENV+JEV*	DENV**	DENV+JEV	DENV	DENV+JEV	DENV
1	2	1	10	2	3	0	3
2	2	0	12	17	1	2	14
3	2	1	22	8	2	1	15
4	unknown	0	26	9	8	0	18
5	1	1	28	6	9	0	12
6	4	0	0	2	1	3	12
7	2	0	2	0	1	0	1

\*cross reacts between DENV and JEV

\*\* no cross-reaction to JEV

**Table S3. Amino acid sequence homology among members of *Flaviviridae* family**

	DENV1		
	prM	E	NS1
DENV 1	100	100	100
DENV 2	73	69	73
DENV 3	80	77	78
DENV 4	65	63	69
JEV	35	50	51
KUN	33	50	50
SLE	35	49	53
TBE	22	38	37
WN	34	51	51
YF	33	42	42



**Table S4. Characteristics of the human antibodies**

Monoclonal antibody	Isotype (ELISA)	Immunoblot	Specificity				
			DENV1	DENV2	DENV3	DENV4	JEV
3-147	IgG1 (Kappa)	prM	+	+	+	+	-
58/5	IgG1 (Lamda)	prM	+	+	+	+	-
2F5	IgG1 (Lamda)	prM	+	+	+	+	-
2G4	IgG1 (Kappa)	prM	+	+	+	+	-
5F9	IgG1 (Lamda)	prM	+	+	+	+	-
135.3	IgG1 (Kappa)	prM	+	+	+	+	-