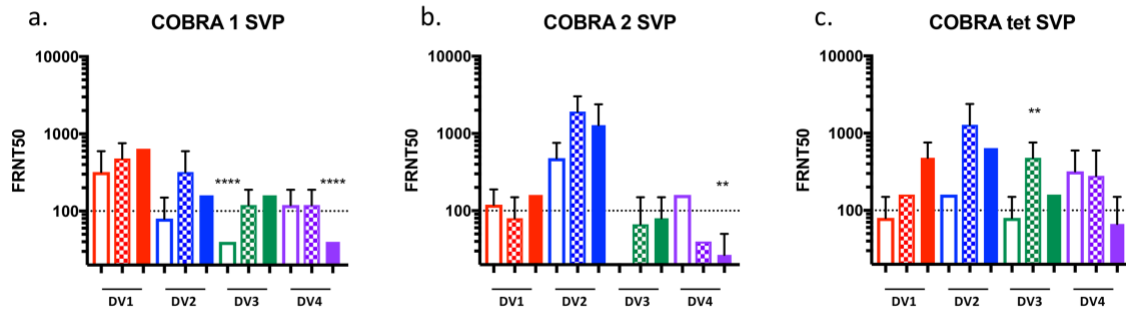
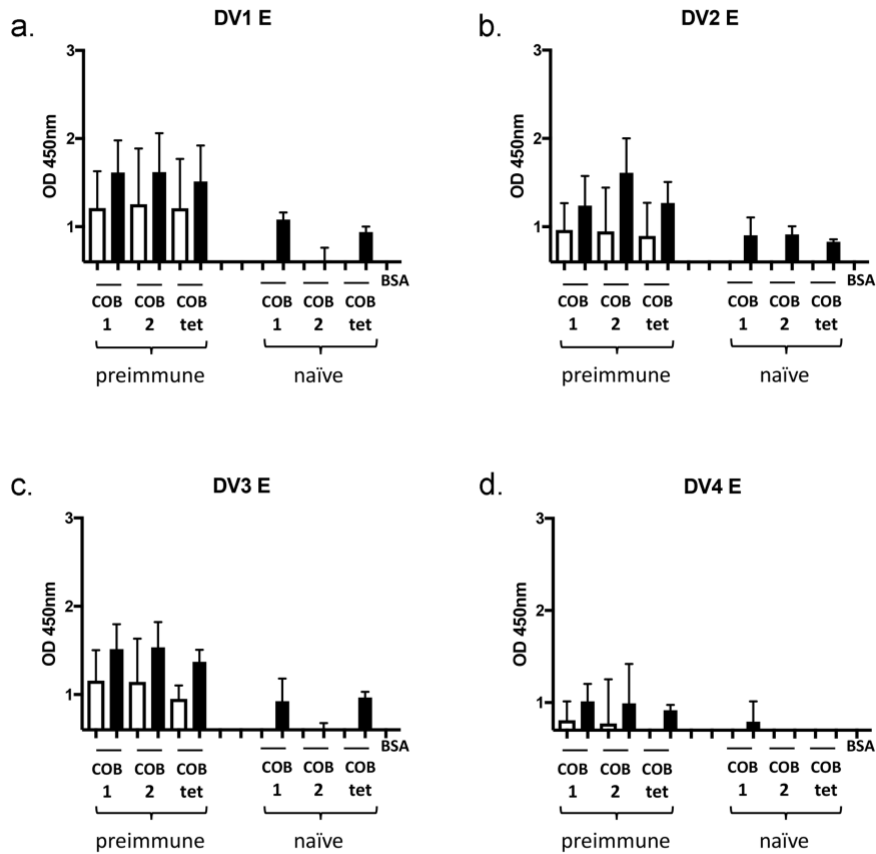


Supplemental figure 1



Supplemental figure 1: Longevity of neutralization ability of WT and COBRA SVP vaccine groups. FRNT₅₀ from pooled sera from C57BL/6 mice 20 weeks after vaccination with a) COBRA 1, b) COBRA 2, or c) COBRA tetravalent SVPs against a panel of prototype (unfilled), American (checkered), and Asian (filled) strains from each serotype. Dashed line indicate 1:100 titer. Statistical differences between 4 weeks and 20 weeks post vaccination calculated by paired t-test. ** for $P \leq 0.01$, **** for $P \leq 0.0001$.

Supplemental figure 2



Supplemental figure 2: Seroconversion of NHP given COBRA SVP vaccination, before second vaccination. a-d) Antibody binding to E of DV 1-4. Vaccine groups listed on x-axis. Total IgG binding of sera (1:100 dilution) from individual NHP were measured by their optical density (OD) values. Absorbance was measured at 405 nm. Unfilled bars are day 0, filled bars are day 42.

Supplemental table 1: One-way analysis of variance (ANOVA) for seroconversion. This analysis was done to determine if there are any statistically significant differences between means in all mouse populations. Vaccine groups were compared in ELISA antibody binding to wild type SVPs (Fig 2a) or soluble E (Fig 2b) from all four serotypes. Additional follow up test was done to compare the mean rank of each vaccine group with the mean rank of control (PBS group) with Dunnett test to correct for multiple comparisons using statistical hypothesis testing. Family-wise significance and confidence level: .05 (95% confidence level).

Comparison of vaccine groups against SVP

Vaccine groups	SVP coating			
	DV1	DV2	DV3	DV4
WT SVPs	****	****	****	****
COBRA SVPs	****	****	****	****
All SVPs	****	****	****	****

Comparison of vaccine groups against soluble E

Vaccine groups	soluble E coating			
	DV1	DV2	DV3	DV4
WT SVPs	****	****	***	**
COBRA SVPs	****	****	**	*
All SVPs	****	****	**	**

Supplemental table 2: Statistically significant differences in antibody binding before and after vaccination with COBRA SVPs. Paired t- tests were done to compare day 0 and day 70 ELISA data from all 4 serotypes. Pre-immune non-human primate (NHP) groups (top rows) were two-tailed paired t-tests and naïve NHP groups (bottom rows) were one-tailed paired t-test. Definition of statistical significance was $p < 0.05$.

		DV1	DV2	DV3	DV4
Preimmune	COBRA 1 SVP	**	**	**	***
	COBRA 2 SVP	*	*	*	*
	COBRA tet SVP	ns	*	***	***
Naïve	COBRA 1 SVP	*	ns	*	ns
	COBRA 2 SVP	**	**	**	**
	COBRA tet SVP	**	*	*	**

Supplemental table 3: Statistically significant differences in neutralization titer in NHP vaccine groups for Figures 5, 6, Table 3. Top table compares day 0 and day 70 FRNT₅₀ data for each vaccine group. Paired t- tests were done. Pre-immune NHP groups (top rows) were two-tailed paired t-tests and naïve NHP groups (bottom row) were one-tailed paired t-test. Bottom table compares day 70 neutralizing antibody titer between COBRA SVP groups. Unpaired two-tailed t-tests were done. For comparisons between NHP vaccine groups with different sample size (pre-immune COBRA 1 vs tetravalent and pre-immune COBRA 2 vs tetravalent), Welch’s t-tests were performed. The virus strains used for FRNT is indicated at the top. P-values less than .05 were considered statistically significant. *ns* for $p > 0.05$, * for $p \leq 0.05$, ** for $p \leq 0.01$, *** for $p \leq 0.001$, **** for $p \leq 0.0001$.

FRNT ₅₀		DENV virus strain panel											
		DV1 Prototype	DV1 American	DV1 Asian	DV2 Prototype	DV2 American	DV2 Asian	DV3 Prototype	DV3 American	DV3 Asian	DV4 Prototype	DV4 American	DV4 Asian
Pre-immune	COBRA 1	*	***	****	ns	**	***	**	***	****	****	**	***
	COBRA 2	**	***	***	**	***	**	**	**	****	**	***	***
	COBRA tet	ns	**	**	**	**	**	**	****	****	***	****	**
Naïve	COBRA 1	**	**	**	**	***	**	**	**	**	**	**	***
	COBRA 2	**	**	**	**	***	**	*	**	**	**	**	**
	COBRA tet	**	**	**	**	****	**	**	***	****	**	**	***

FRNT ₅₀		DENV virus strain panel											
		DV1 Prototype	DV1 American	DV1 Asian	DV2 Prototype	DV2 American	DV2 Asian	DV3 Prototype	DV3 American	DV3 Asian	DV4 Prototype	DV4 American	DV4 Asian
Pre-immune	COBRA 1 vs tetravalent	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	COBRA 2 vs tetravalent	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
	COBRA 1 vs 2	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
Naïve	COBRA 1 vs tetravalent	ns	ns	ns	ns	*	ns	ns	ns	ns	*	ns	*
	COBRA 2 vs tetravalent	**	*	ns	ns	ns	ns	ns	*	*	*	*	**
	COBRA 1 vs 2	**	*	ns	ns	*	ns	ns	ns	ns	ns	ns	*

Supplemental table 4: Statistically significant differences of NHP memory B cell responses for Figure 7. Top table shows paired two-tailed t-tests analysis to compare DENV-specific and non-specific (BSA) memory B cell response. Bottom table shows unpaired two-tailed t-tests to compare differences between vaccine groups. For comparisons between NHP vaccine groups with different sample size (pre-immune COBRA 1 vs tetravalent and pre-immune COBRA 2 vs tetravalent), Welch's t-tests were performed. P-values less than .05 were considered statistically significant. *ns* for $p > 0.05$, * for $p \leq 0.05$, ** for $p \leq 0.01$, *** for $p \leq 0.001$, **** for $p \leq 0.0001$.

		ELISPOT coating			
Vaccine groups		DV1	DV2	DV3	DV4
Preimmune	COBRA 1	**	*	**	*
	COBRA 2	****	****	****	****
	COBRA tet	***	**	***	***
Naïve	COBRA 1	**	*	**	*
	COBRA 2	*	**	*	**
	COBRA tet	*	*	*	ns

		ELISPOT coating			
Vaccine groups		DV1	DV2	DV3	DV4
Preimmune	COBRA 1 vs tetravalent	ns	ns	ns	ns
	COBRA 2 vs tetravalent	ns	*	ns	*
	COBRA 1 vs 2	ns	*	ns	**
Naïve	COBRA 1 vs tetravalent	ns	ns	ns	ns
	COBRA 2 vs tetravalent	*	ns	**	ns
	COBRA 1 vs 2	*	ns	*	ns