

**Table S1. Viral titers<sup>§</sup> in the blood post-vaccination with ACAM2000 and treatment with vehicle or ST-246.**

Vaccinated Groups	ST-246 Treatment	Assay Day	% of mice with detectable levels of viral DNA <sup>¶</sup>	Genome copies ( $\times 10^3$ /ml) <sup>‡</sup>					P-value <sup>a</sup>
				M1	M2	M3	M4	M5	
<b>Experiment #1<sup>¶¶</sup></b>									
N.D./BALB/c	-	7	80%	3.91	4.05	5.15	7.38	< LLOQ	<b>0.561</b>
	+	7	40%	4.59	5.58	< LLOQ	< LLOQ	< LLOQ	
CD8 <sup>-</sup> /BALB/c	-	7	75%	6.54	32.70	32.90	< LLOQ	N/A	<b>0.066</b>
	+	7	40%	4.09	8.38	< LLOQ	< LLOQ	< LLOQ	
CD4 <sup>-</sup> /BALB/c	-	7	75%	3.74	15.60	17.20	< LLOQ	N/A	<b>0.013</b>
	+	7	40%	3.89	5.52	< LLOQ	< LLOQ	< LLOQ	
N.D./JH-KO	-	7	80%	10.80	30.80	44.20	51.60	< LLOQ	<b>0.118</b>
	+	7	40%	12.30	16.60	< LLOQ	< LLOQ	< LLOQ	
<b>Experiment #2<sup>¶¶</sup></b>									
CD8 <sup>-</sup> CD4 <sup>-</sup> /BALB/c	-	7	60%	4.08	7.37	10.10	< LLOQ	< LLOQ	<b>0.169</b>
	+	7	10%	7.03	< LLOQ	< LLOQ	< LLOQ	< LLOQ	
N.D./JH-KO	-	7	80%	4.06	6.68	7.33	7.70	< LLOQ	<b>0.003</b>
	+	7	0%	< LLOQ	< LLOQ	< LLOQ	< LLOQ	< LLOQ	
CD8 <sup>-</sup> /JH-KO	-	7	60%	3.61	3.63	12.60	< LLOQ	< LLOQ	<b>0.099</b>
	+	7	20%	5.09	< LLOQ	< LLOQ	< LLOQ	< LLOQ	
CD4 <sup>-</sup> /JH-KO	-	7	20%	4.45	< LLOQ	< LLOQ	< LLOQ	< LLOQ	<b>0.594</b>
	+	7	0%	< LLOQ	< LLOQ	< LLOQ	< LLOQ	< LLOQ	
CD8 <sup>-</sup> CD4 <sup>-</sup> /JH-KO*	-	7	100%	5.03	11.60	21.50	29.90	80.90	<b>0.007</b>
	+	7	20%	6.74	< LLOQ	< LLOQ	< LLOQ	< LLOQ	
	-	14	80%	5.88	17.90	28.40	121.00	< LLOQ	
	+	14	40%	4.76	5.94	< LLOQ	< LLOQ	< LLOQ	
	-	21	40%	4.42	5.42	< LLOQ	< LLOQ	< LLOQ	
	+	21	20%	7.13	< LLOQ	< LLOQ	< LLOQ	< LLOQ	

<sup>§</sup> Measured on days 3, 7, 14, 21, and 28 p.v. in whole blood using quantitative real-time polymerase chain reaction (qRT-PCR) as described previously [17].

<sup>¶</sup> Percentage of mice with VV genome copy numbers above the Lower Limit of Quantification (LLOQ) =  $3.5 \times 10^{-3}$  genome copies/ml.

<sup>‡</sup> Numbers shown for each mouse (M) in the group (n = 4 or 5) if above the LLOQ; N/A: Not available since n = 4.

<sup>a</sup> Vaccine/vehicle vs. vaccine/ST-246 comparison using Student's *t*-test on log-transformed data. Extrapolated values were used for those below the LLOQ.

*P*-value <0.050 is considered statistically significant.

<sup>¶¶</sup> The two experiments were performed at different times but were set up in a similar manner.

\* Only day 7 data is shown for all of the above groups since all values were below LLOQ on days 3, 14, 21, and 28 p.v.