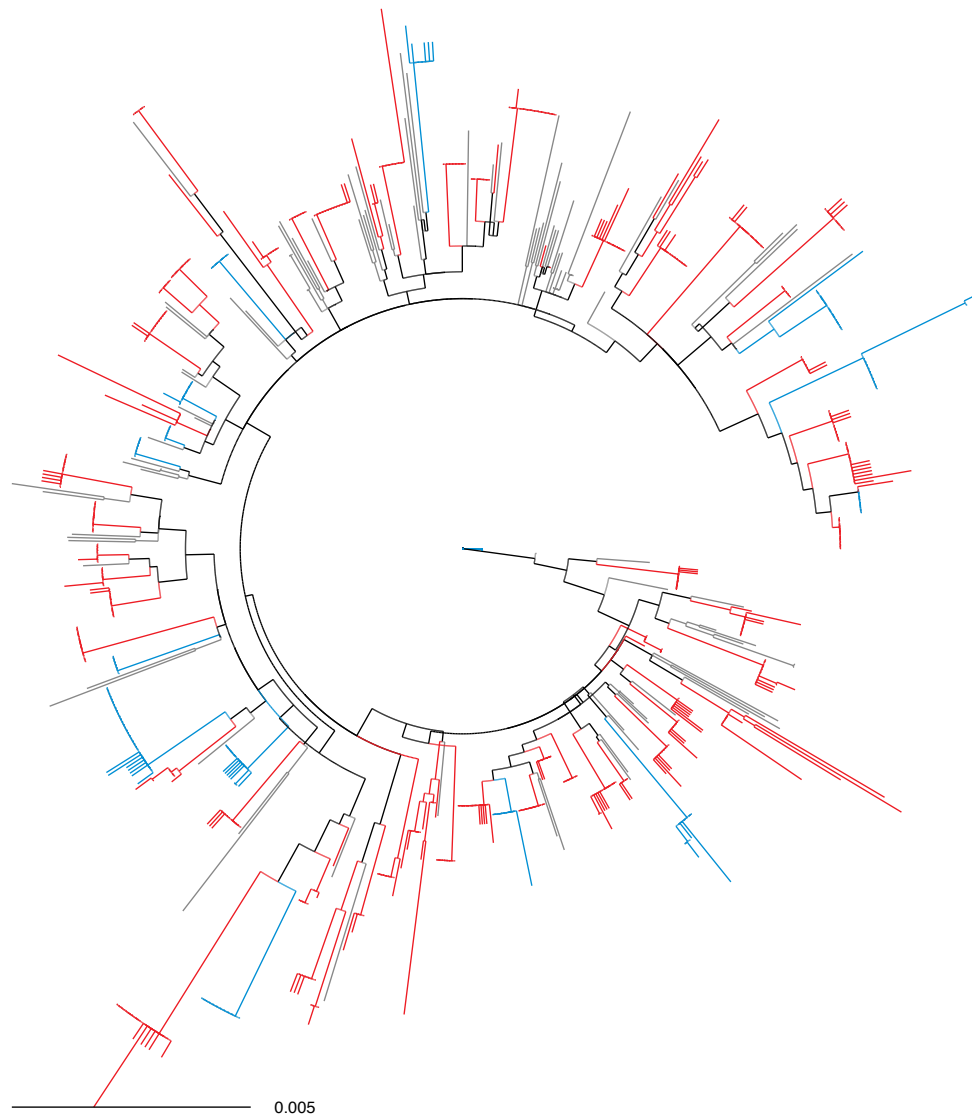


Supplementary Figure Legends

Supplemental Figure 1. Phylogenetic tree of SGA-derived *env* nucleotide sequences from the challenge stocks, and T/F Envs from vaccinated breakthrough and unvaccinated control infections. A FASTA file of a Geneious v6 nucleotide alignment containing all T/F Env and challenge stock sequences was uploaded to the LANL Treemaker tool to generate a Neighbor-joining phylogenetic tree, which was annotated using the LANL Rainbow Tree tool. The distance model was Felsenstein F84, with gaps stripped, and equal site rates. T/F Env sequences from vaccinated animals appear in red, T/F Env sequences from control animals appear in blue, and sequences from the two challenge stocks appear in grey. The horizontal bar shows the scale of genetic distance.

Supplemental Table 1. P values for all Fisher's exact tests. P values are shown for all comparisons at positions 23 (I-V), 45 (A-T), 47 (K-R), and 70 (N-S), as calculated by Prism v6.0 for Mac. Due to multiple comparisons, a P value equal to or less than 0.01 was considered significant.



— Vaccinated

— Control

— Stock

Variable	Group 1	Group 2	Position	Amino acids	P value
Transmission	Challenge Stock	All T/F Envs	23	I-V	0.017
			45	A-T	0.002
			47	K-R	0.0007
			70	N-S	0.003
Vaccination	Control T/F Envs	Vaccinated T/F Envs	23	I-V	0.743
			45	A-T	0.336
			47	K-R	0.506
			70	N-S	1.000
Challenge Route	Intra-rectal T/F Envs	Intra-vaginal T/F Envs	23	I-V	0.776
			45	A-T	0.580
			47	K-R	0.561
			70	N-S	0.592
Challenge Number	Infected at dose 1-6	Infected at dose 7-12	23	I-V	0.552
			45	A-T	0.553
			47	K-R	0.762
			70	N-S	0.785
TRIM5 α susceptibility	^a Permissive	^b Restrictive	23	I-V	0.783
			45	A-T	0.577
			47	K-R	0.777
			70	N-S	1.000

^aTFP/Q, Q/CYPA, Q/Q

^bTFP/TFP, TFP/CYPA, CYPA/CYPA