

Figure S1. Rapamycin treatment does not alter blood chemistry or hematology profiles.

Blood chemistry, liver enzymes, kidney enzymes, and hematology following the second MVA.

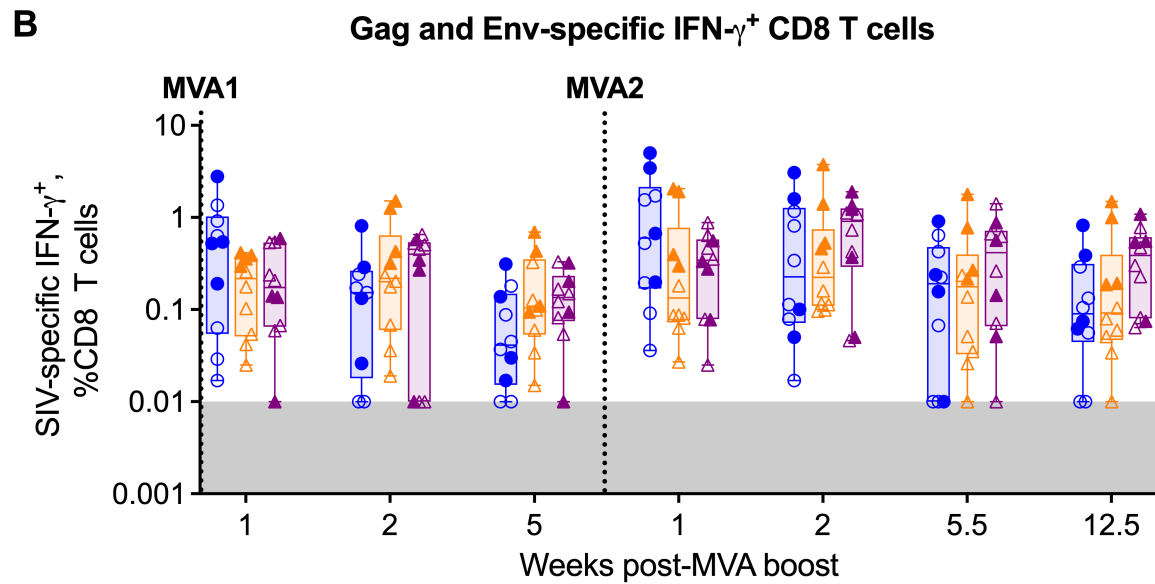
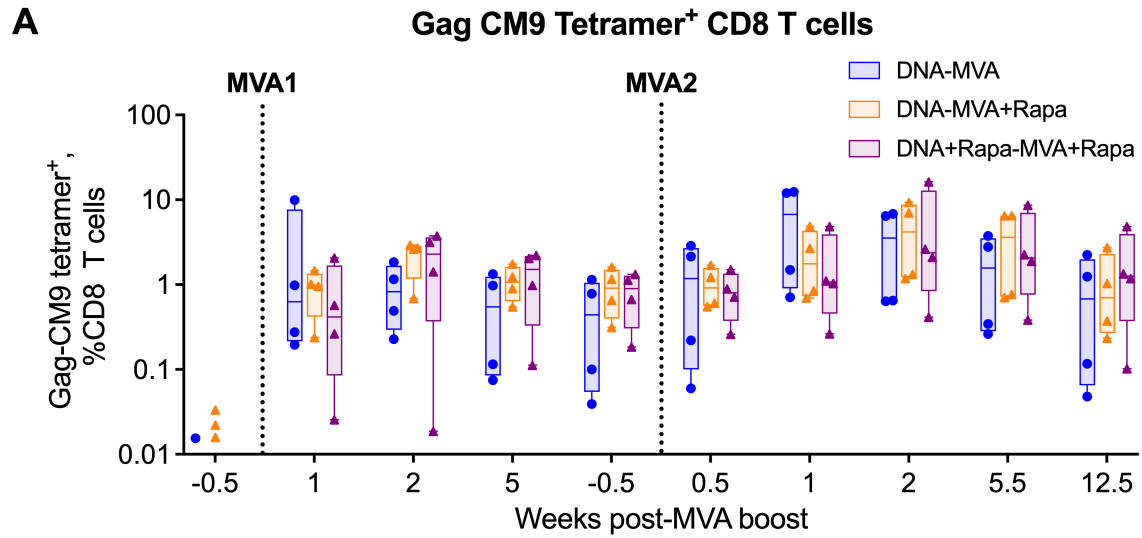


Figure S2. Rapamycin treatment delays peak and reduces Gag- and Env- specific tetramer cells. **A.** Frequency of Gag-CM9 tetramer⁺ CD8 T cells shown individually after MVA vaccinations (n = 4/group). **B.** Frequency of SIV-specific IFN- γ ⁺ CD8 T cells shown individually after MVA vaccinations (n = 10/group).

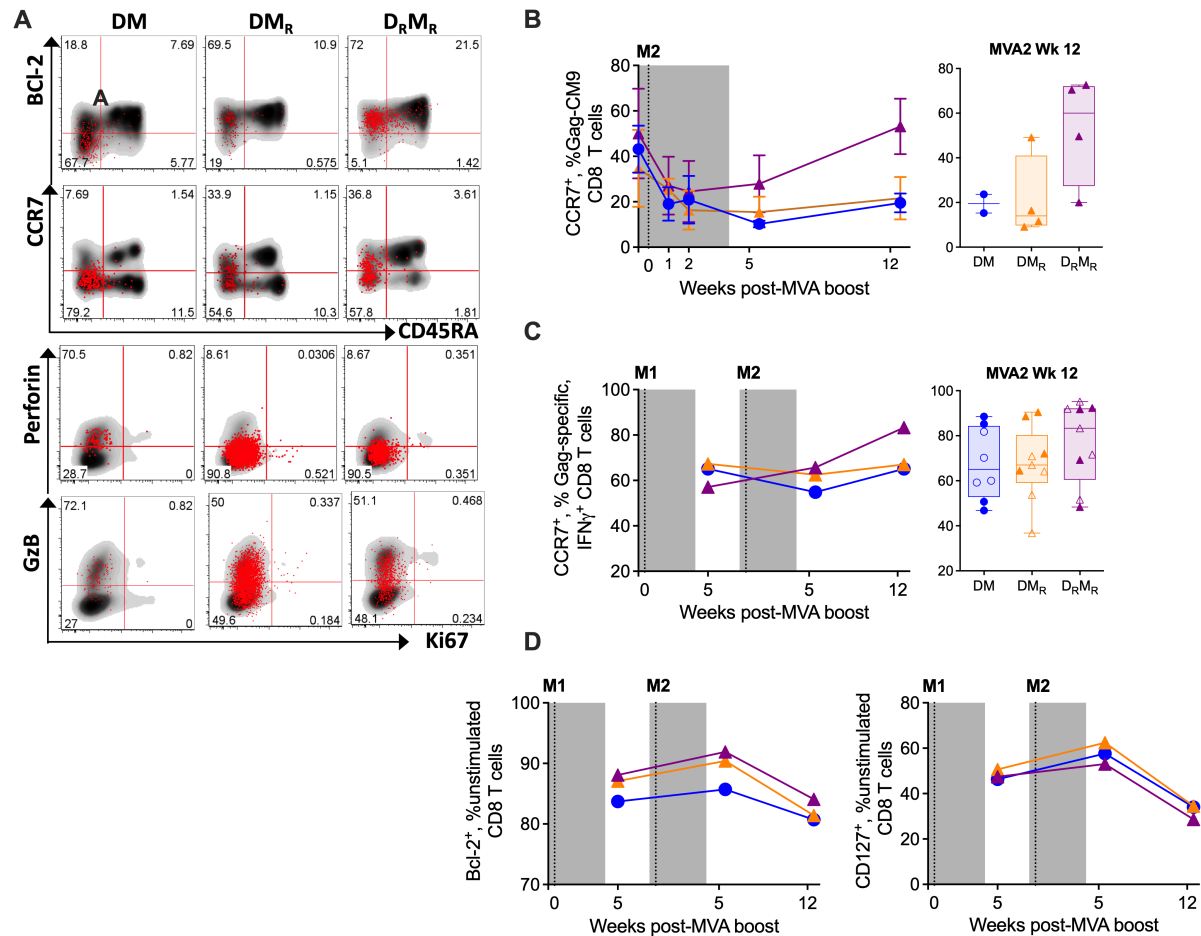


Figure S3. Rapamycin specifically enhances Bcl-2 and CD127 expression in vaccine-induced CD8 T cells. **A.** Representative flow plots of Bcl-2 and CCR7 against CD45RA, and Perforin and GzB against Ki67 on total CD8 T cells (black and gray density plot) and tetramer⁺ CD8 T cells (red dots). **B.** Geometric means of CCR7⁺ frequencies on Gag-CM9 specific tetramer⁺ CD8 T cells measured temporally post-MVA2. Individual data at MVA2 week 12 (n = 4/group). **C.** Geometric means of CCR7⁺ frequencies on Gag-specific IFN- γ ⁺ CD8 T cells measured temporally post-MVA vaccinations. Individual data at MVA2 week 12 (n = 10/group). **D.** Geometric means of Bcl-2⁺ and CD127⁺ frequencies on total CD8 T cells measured temporally post-MVA vaccinations. Statistics: Unpaired, non-parametric Mann-Whitney tests were used to compare marker⁺ frequencies between groups.

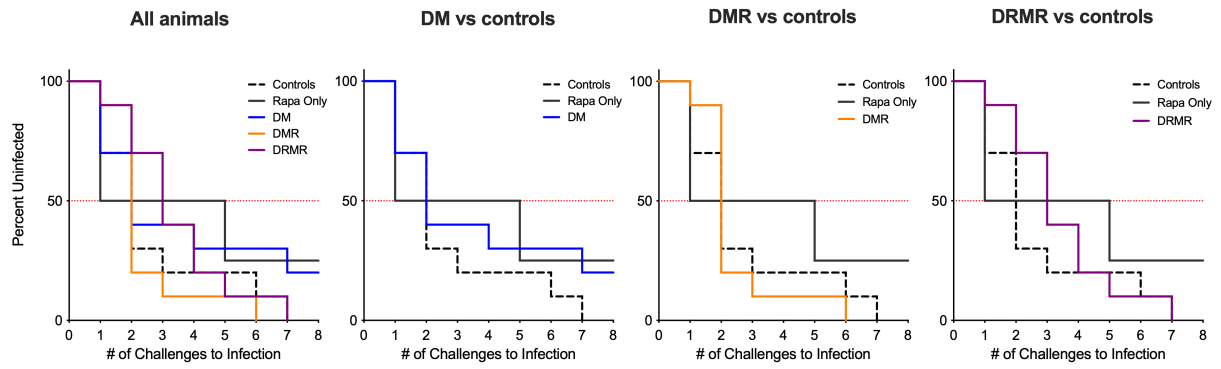


Figure S4. Kaplan-Meier Acquisition Curve. Infection curve for all groups. Statistics: Log-rank (Mantel-Cox) test.

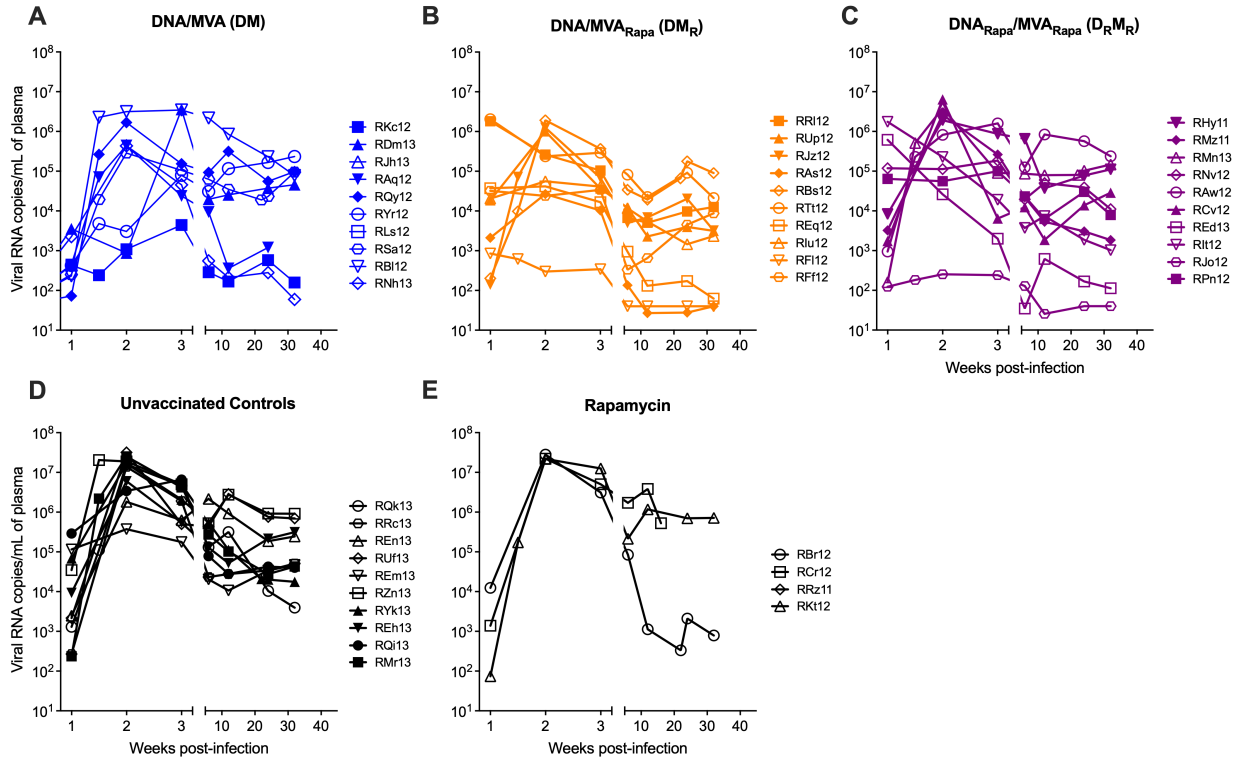


Figure S5. Viral load data of individual animals across all experimental groups. A–E. Plasma viral load data for individual macaques belonging to groups in the following order: DM, DM_R, D_RM_R, UC, and Rapa.

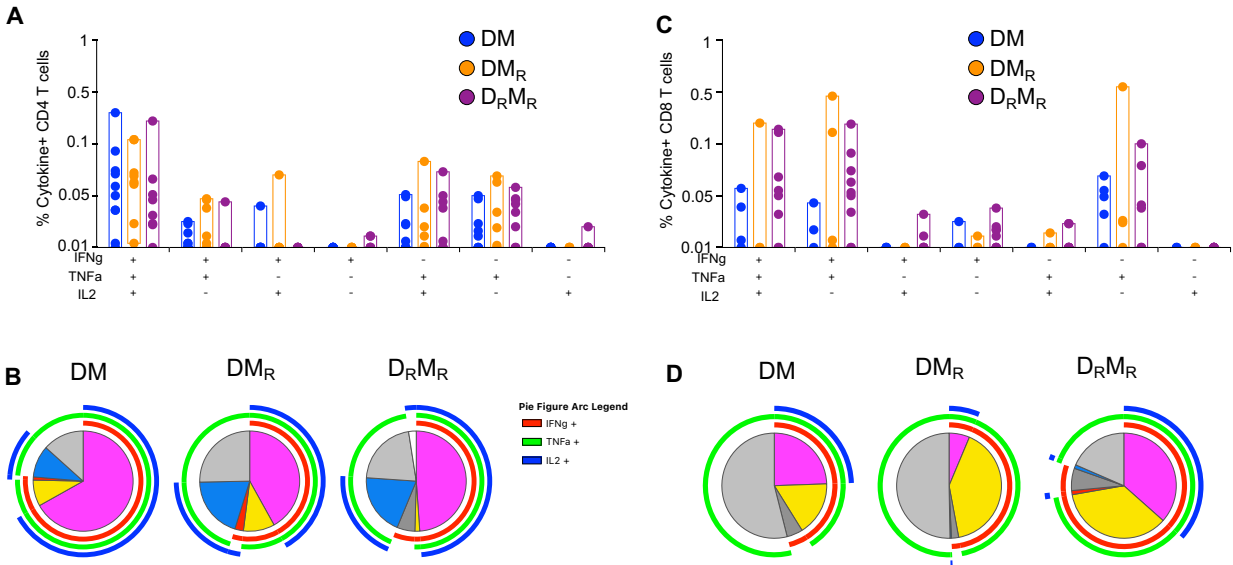


Figure S6. Polyfunctionality of Gag-specific CD4 and CD8 T cells at week 12 post 2nd MVA boost in blood of vaccinated animals. (A, C) The magnitude of triple, double and single cytokine+ cells as a percent of total (A) CD4 or (C) CD8 T cells. Each dot represents an individual monkey. **(B, D)** The relative distribution of triple, double and single cytokine+ cells as a percent of total cytokine+ (B) CD4 or (D) CD8 T cells. For the pie graphs, the mean value for each subset for all animals in a group is plotted.

Group	red A01+ Monkey	Challenge # infected	Macaque Genotypes			Group	Monkey	Challenge # infected	Macaque Genotypes		
			A*01	B*08	B*17				A*01	B*08	B*17
DM	RKc12	2	+	-	-	DRMR	RHy11	7	+	-	-
DM	RDm13	2	+	-	-	DRMR	RMz11	5	+	-	-
DM	RJh13	UI	-	+	-	DRMR	RMn13	1	-	-	-
DM	RAq12	4	+	-	-	DRMR	RNv12	4	-	-	-
DM	RQy12	1	+	-	-	DRMR	RAw12	4	-	-	-
DM	RYr12	7	-	-	-	DRMR	RPh12	3	+	-	-
DM	RLs12	UI	-	-	+	DRMR	RCv12	2	+	-	-
DM	RSa12	1	-	-	-	DRMR	REd13	2	-	+	-
DM	RBI12	1	-	-	-	DRMR	RIt12	3	-	-	-
DM	RNh13	2	-	-	-	DRMR	RJo12	3	-	-	+
DMR	RRI12	2	+	-	-	UC	RQk13	1	-	-	-
DMR	RUp12	2	+	-	-	UC	RRc13	2	-	-	-
DMR	RJz12	2	+	-	-	UC	REn13	2	-	-	-
DMR	RAr12	3	+	-	-	UC	RUf13	2	-	-	-
DMR	RBs12	1	-	-	-	UC	REm13	7	-	-	-
DMR	RTt12	2	-	-	-	UC	RZn13	6	-	-	-
DMR	REq12	2	-	-	-	UC	RYk13	1	+	-	-
DMR	Rlu12	6	-	+	-	UC	REh13	2	+	-	-
DMR	RFI12	2	-	-	+	UC	RQi13	3	+	-	-
DMR	RFf12	2	-	-	-	UC	RMr13	1	+	-	-
						R	RBr12	1	-	+	-
						R	RCr12	1	-	-	-
						R	RRz11	UI	-	-	-
						R	RKt12	5	-	-	-

Table S1. The Mamu typing information for study animals along with the challenge number at which an animal was productively infected. UI, uninfected.