Supplemental tables

	Total estimated parameters	a	β	c	δ	γ	k	λ	n	m	θ	p
Model 1	6	-	E	23	E	-	E	0.5	-	-	E	E
Model 2	7	E	E	23	E	-	E	0.5	E	-	E	E
Model 3	7	-	E	23	E	-	E	0.5	-	-	E	E
Model 4	8	E	E	23	E	-	E	0.5	E	-	E	E
Model 5	7	-	E	23	E	E	E	0.5	-	E	E	E

Table S1: Parameter values. Values that were estimated for each model are marked with an E.

	Model 1	Model 2	Model 3 (β)	Model 3 (δ)	Model 3 (k)	Model 4 (β)	Model 4 (δ)	Model 4 (k)	Model 5
Exp. 1	8.51	2.76	12.69	13.77	15.67	7.45	11.02	11.08	17.44
Exp. 2	10.57	3.08	12.81	14.41	13.78	7.39	11.63	11.90	15.72
Exp. 3	7.67	-1.49	11.52	12.52	14.18	1.20	2.50	5.74	14.23
Control 1	7.71	10.37	15.56	15.04	21.47	16.47	24.01	23.95	29.42
Control 2	11.12	14.26	18.31	17.45	22.76	20.11	27.67	27.66	30.02

Table S2: Akaike Information Criteria scores. A lower AIC value corresponds to a better description of the data by the given model, statistically speaking.

	Exp. 1	Exp. 2	Exp. 3	Control 1	Control 2	Mean
Fit to Exp. 1	6.55e-03	1.71e-02	1.84e-02	1.25e-02	1.62e-02	1.42e-02
Fit to Exp 2	7.04e-03	1.97e-02	1.92e-02	1.45e-02	1.85e-02	1.58e-02
Fit to Exp 3	4.60e-03	1.31e-02	1.38e-02	9.63e-03	1.23e-02	1.07e-02
Fit to Control 1	1.26e-02	3.07e-02	3.63e-02	2.53e-02	2.90e-02	2.68e-02
Fit to Control 2	3.55e-03	8.96e-03	7.22e-03	6.58e-03	7.52e-03	6.76e-03

Table S3: Fitted values obtained for the proportion p of SHIV measured in peripheral blood produced by CD4+ T-cells in blood. For each row of the table, Model 2 was individually fit to that particular animal. Then, we carried forward all the parameters obtained through this fit and fit only to parameter p. For example, when fitting to Control 2, we obtained that the value of p for Experiment 1 is $p = 3.55$e-03.

Supplemental figures

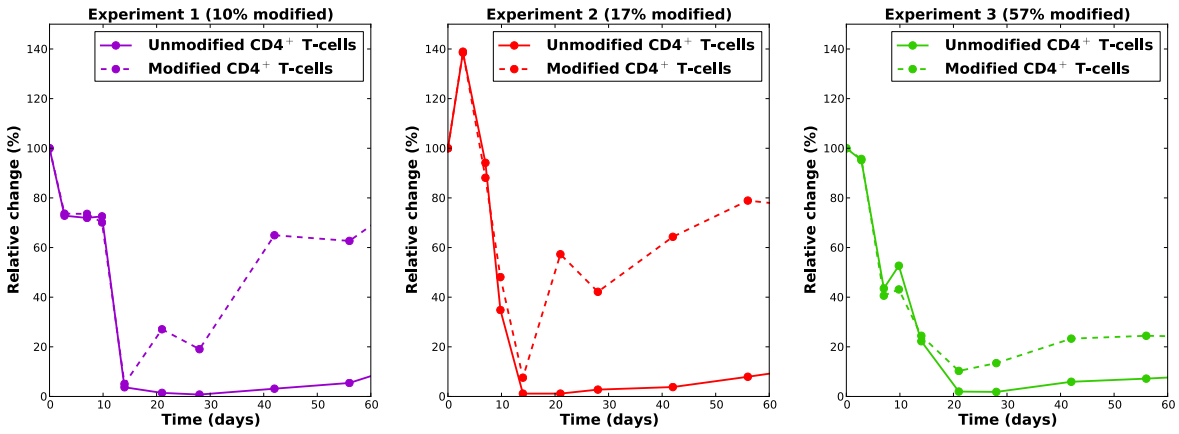

Figure S1: Relative change of $CD4^+$ T-cells in the experimental monkeys. The graphs compare the number of CD4+ T-cells at different time points with respect with the number of CD4+ T-cells on the day of viral inoculation, as a relative percentage. A) Experiment 1, with 10% gene-modified cells. B) Experiment 2, with 17% gene-modified cells. C) Experiment 3, with 57% gene-modified cells

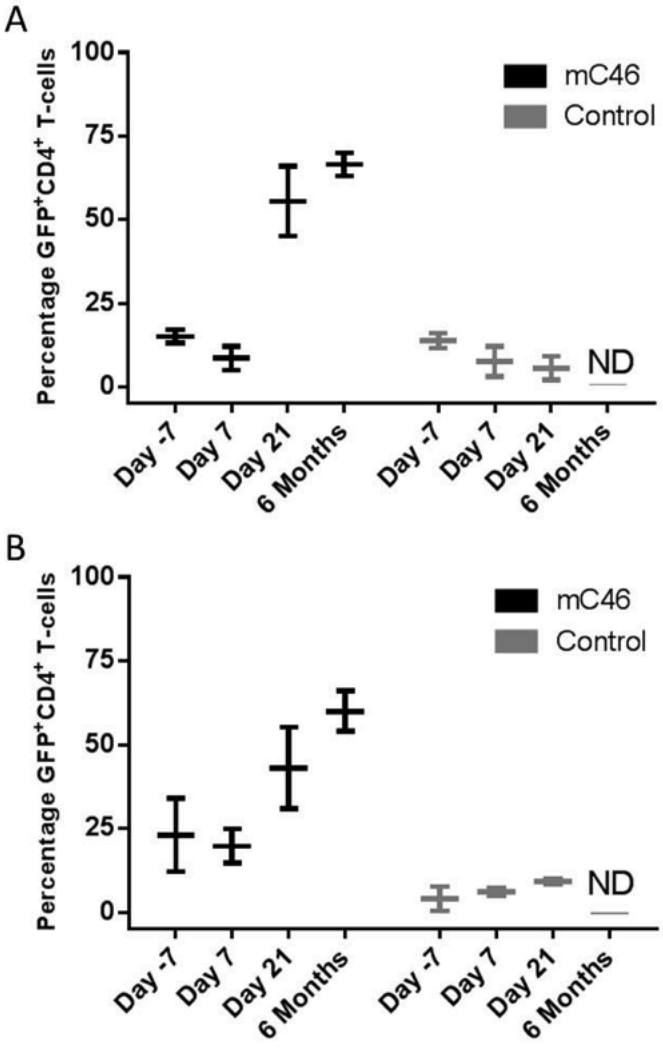

Figure S2: Positive selection of mC46-expressing $CD4^+$ T-cells following SHIV-challenge. (A and B) The percentage of genetically modified cells was determined in (A) GI and (B) LN biopsies harvested at Day(-) 7, Day 7, Day 21 and 6 months following SHIV-challenge. Following gating on CD3+ T-lymphocytes, CD4+ T-cell versus GFP+ cells was determined. ND: Not detected. This research was originally published in Blood. Younan et al. Positive selection of mC46-expressing CD4+ T cells and maintenance of virus specific immunity in a primate AIDS model. Blood. 2013;122 (2):179-87. © the American Society of Hematology.

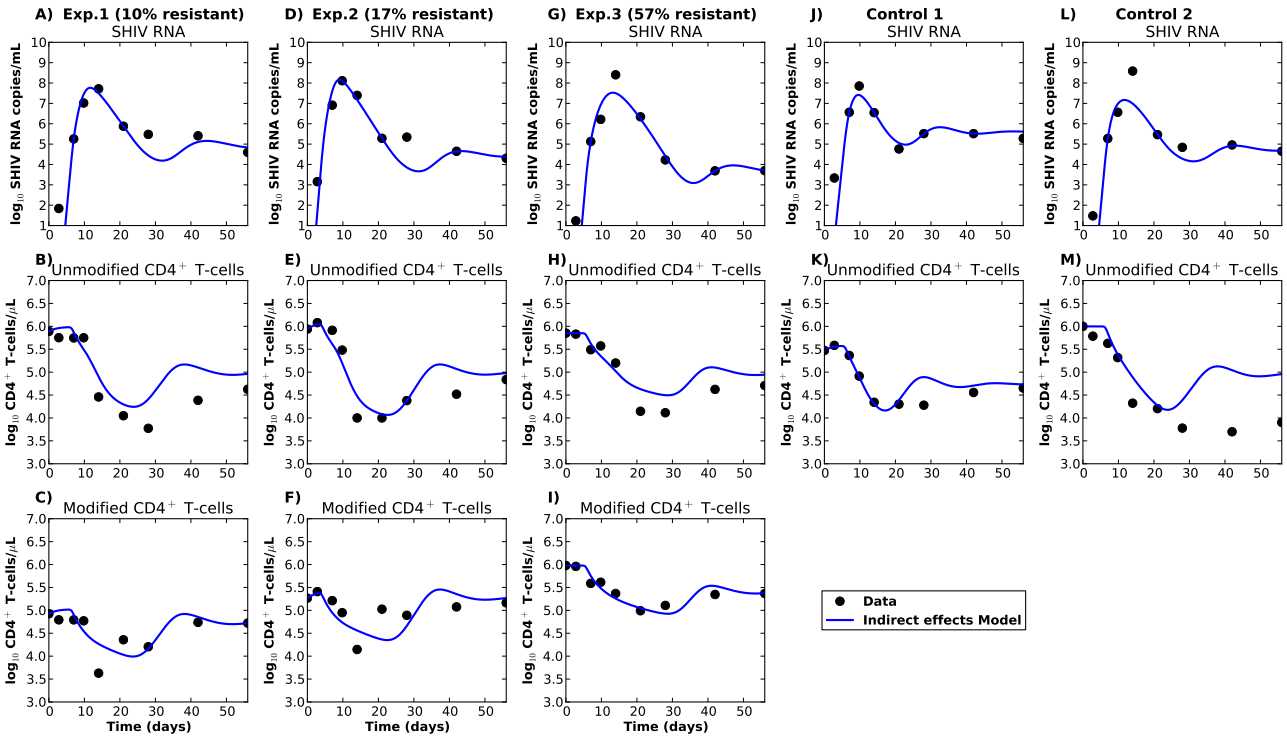

Figure S3: Best-fit trajectories (solid lines) using Model 2 and experimentally observed data (•) for the experimental and control animals. Here, the indirect effects model was fit with 7 unknown parameters for each animal individually. (A-C) Experiment 1, with 10%modified cells prior to infection. (D-F) Experiment 2, with 17% modified cells prior to infection. (G-I) Experiment 3, with 55% modified cells prior to infection. (J-K) Control 1. (L-M) Control 2.

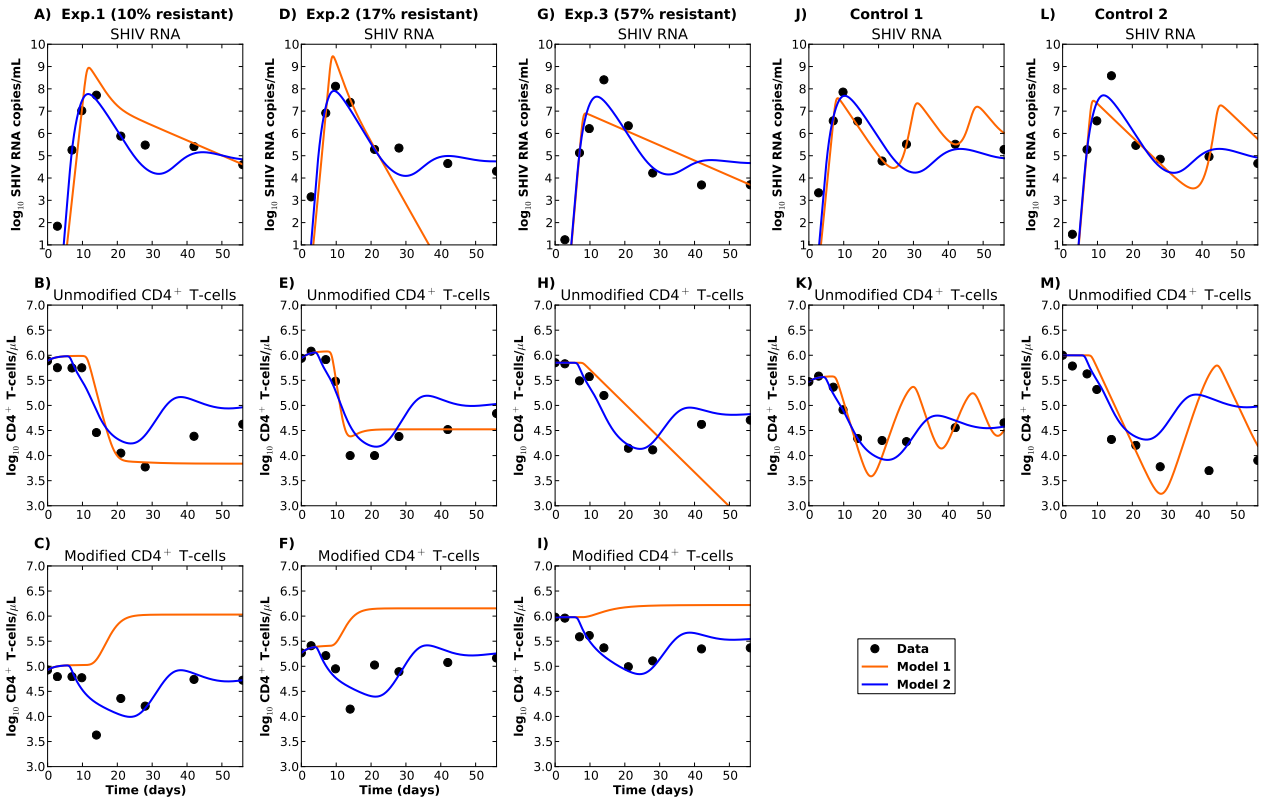

Figure S4: Best-fit trajectories (solid lines) for Model 1 (orange) and Model 2 (blue) and experimentally observed data (•) for the experimental and control animals. (A-C) Experiment 1, with 10% modified cells prior to infection. (D-F) Experiment 2, with 17% modified cells prior to infection. (G-I) Experiment 3, with 55% modified cells prior to infection. (J-K) Control 1. (L-M) Control 2. Here, each monkey was fit individually.

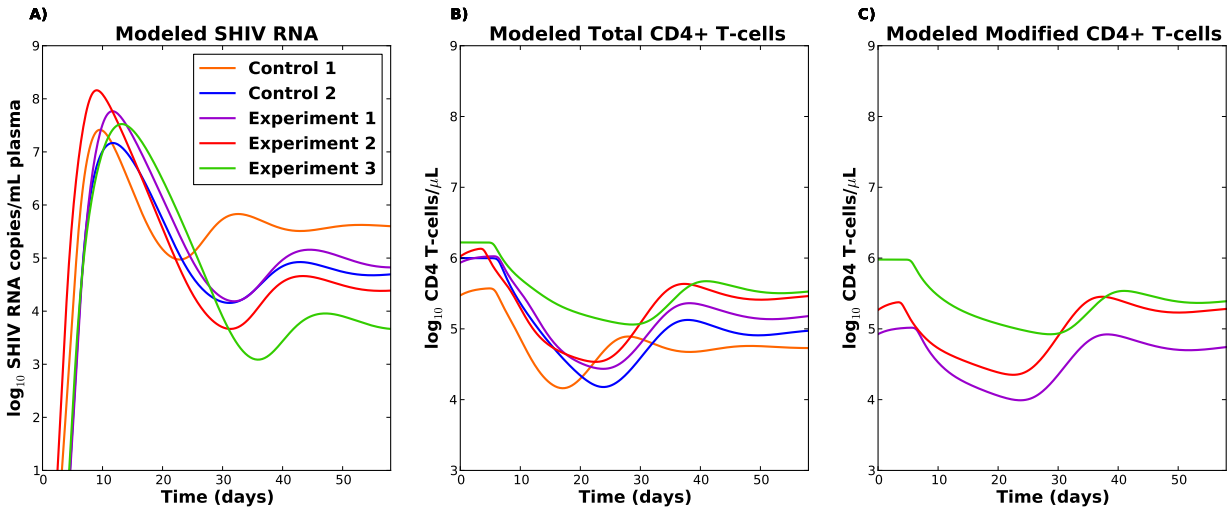

Figure S5: Modeled viral load and CD4+ T-cell trajectories using the individual fits of the "Indirect effects model" (Model 2). Here, Model 2 was fit with 7 unknown parameters for each animal individually. A) Modeled viral loads for the five macaques. B) Modeled total CD4 T-cell counts for the five macaques. C) Modeled modified CD4+ T-cell counts for the experimental macaques.

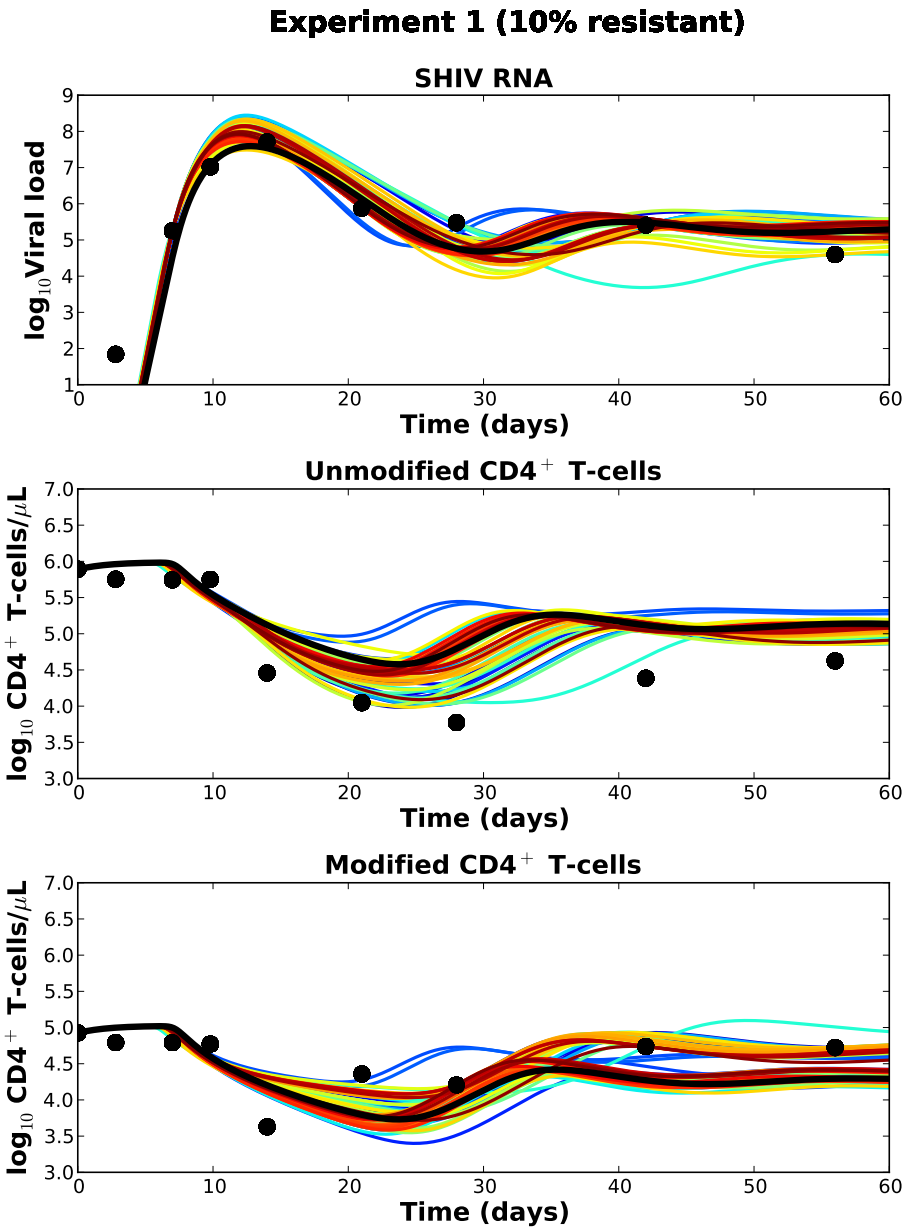

Figure S6: Numerical simulations (solid lines) and experimentally observed data (•) for Experiment 1 (10% of $CD4^+$ T-cells modified). All the solutions obtained for the Indirect effects Model (Model 2) are plotted, and the black solid line represents the median parameter set.

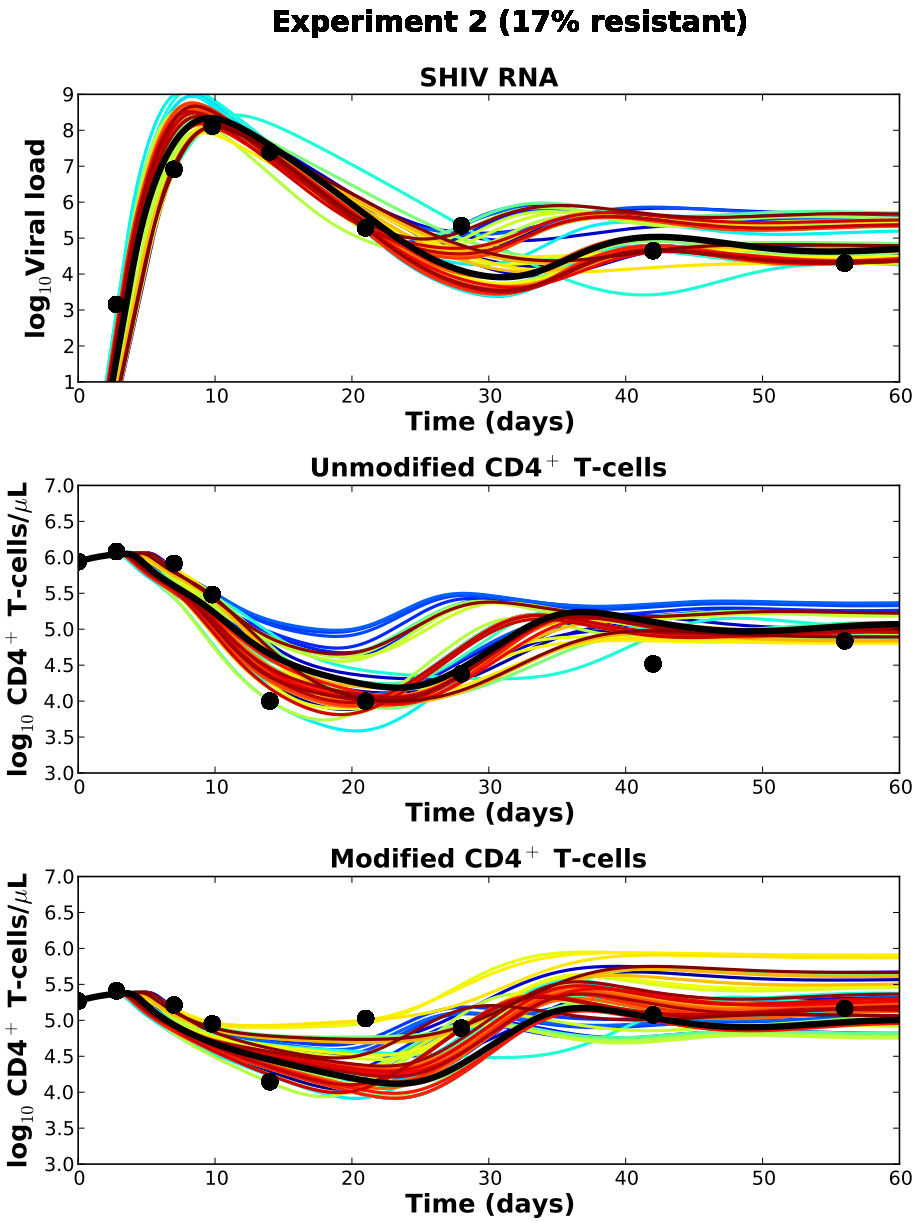

Figure S7: Numerical simulations (solid lines) and experimentally observed data (•) for Experiment 2 (17% of $CD4^+$ T-cells modified). All the solutions obtained for the Indirect effects Model (Model 2) are plotted, and the black solid line represents the median parameter set.

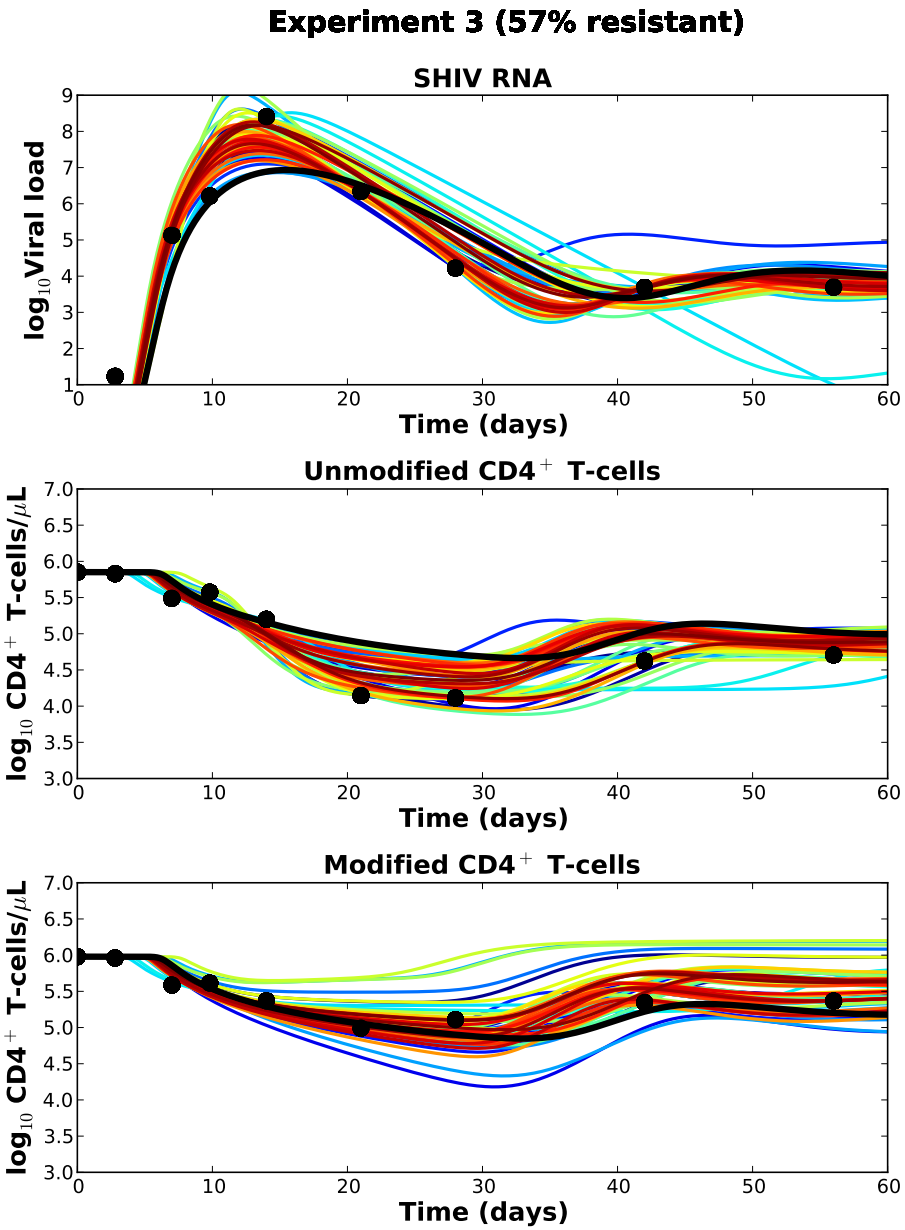

Figure S8: Numerical simulations (solid lines) and experimentally observed data (•) for Experiment 3 (57% of CD4$^+$ T-cells modified). All the solutions obtained for the Indirect effects Model (Model 2) are plotted, and the black solid line represents the median parameter set.

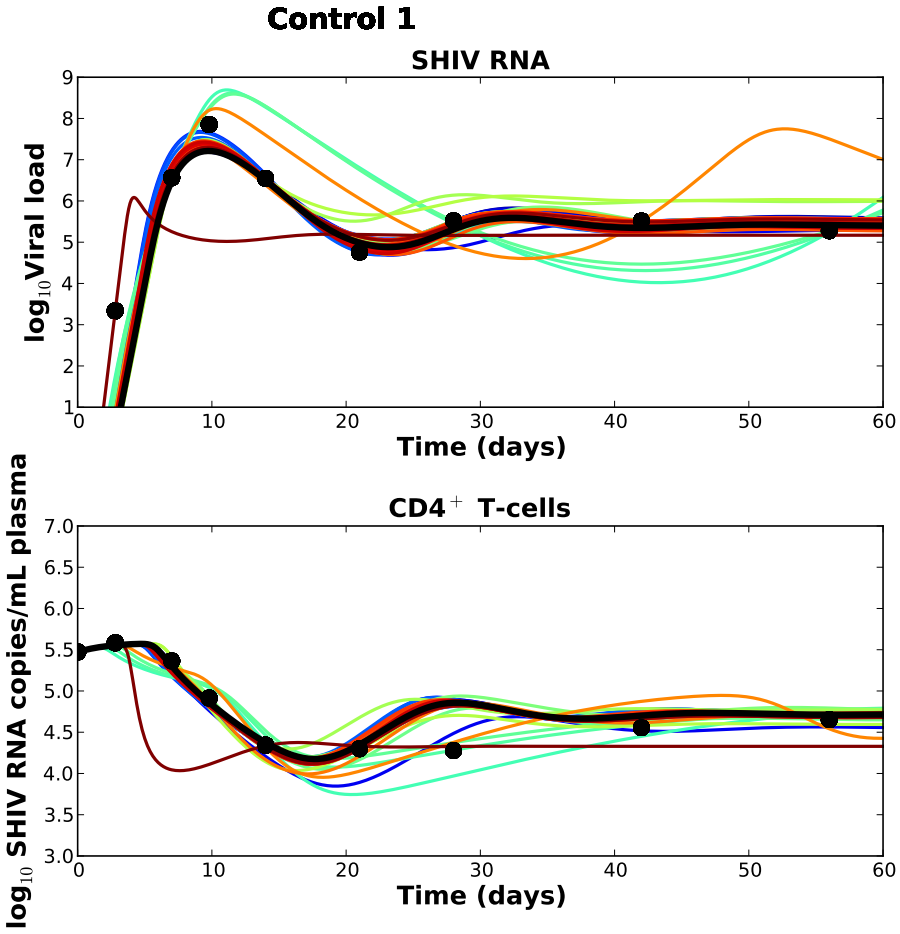

Figure S9: Numerical simulations (solid lines) and experimentally observed data (•) for Control 1. All the solutions obtained for the "Indirect effects Model" (Model 2) are plotted, and the black solid line represents the median parameter set.

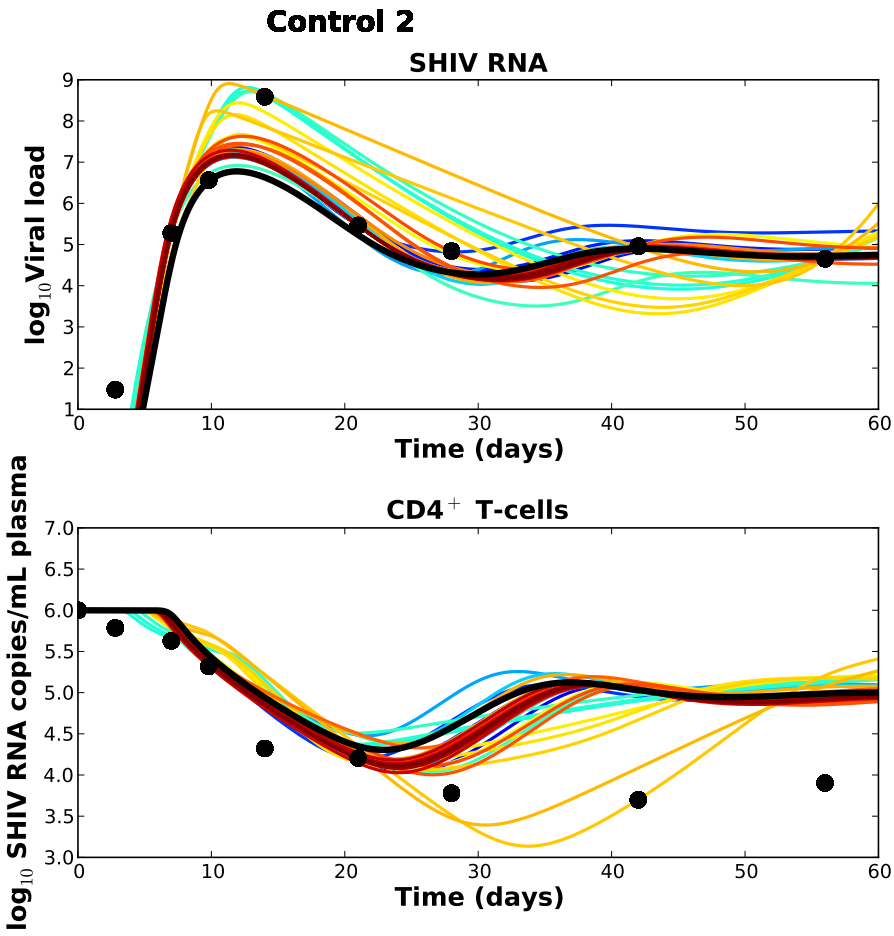

Figure S10: Numerical simulations (solid lines) and experimentally observed data (●) for Control 2. All the solutions obtained for the Indirect effects Model (Model 2) are plotted, and the black solid line represents the median parameter set.

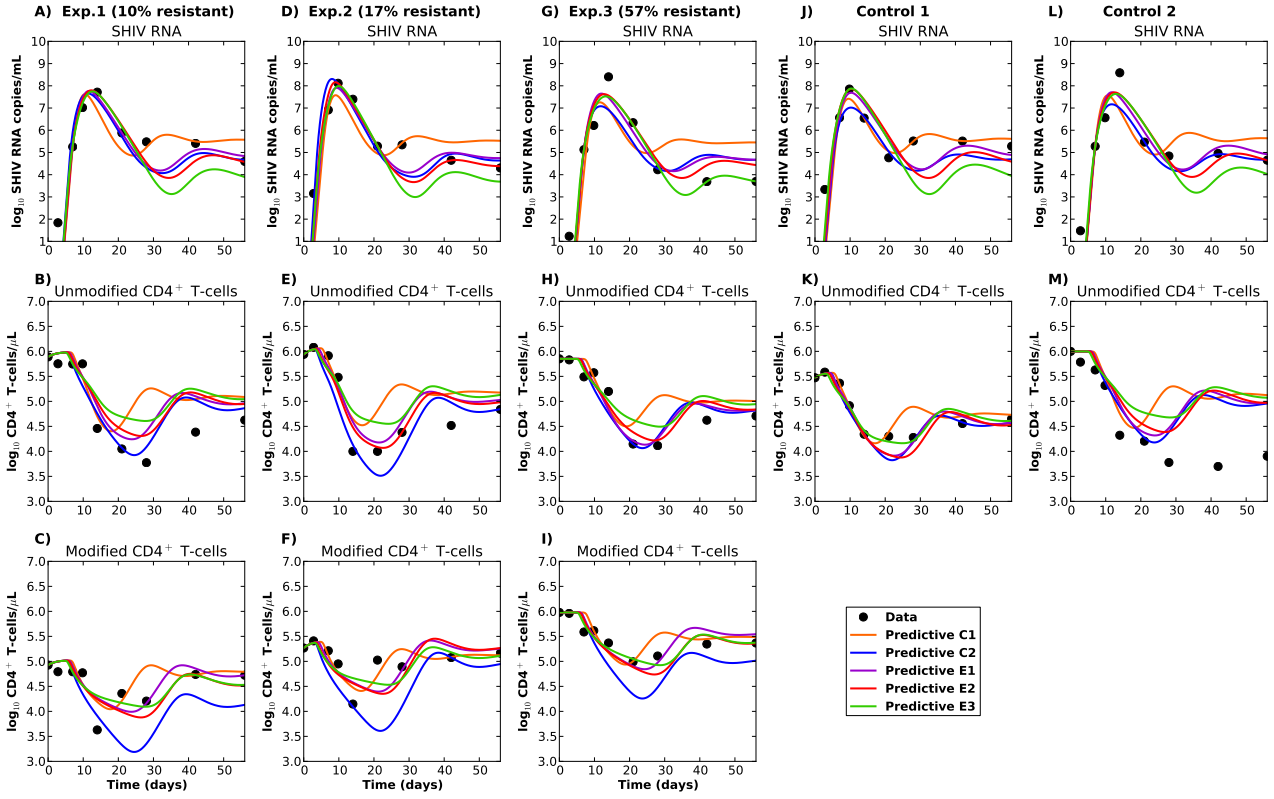

Figure S11: Best-fit trajectories (solid lines) for Model 2 and experimentally observed data (•) for the experimental and control animals. (A-C) Experiment 1, with 10%modified cells prior to infection. (D-F) Experiment 2, with 17% modified cells prior to infection. (G-I) Experiment 3, with 55% modified cells prior to infection. (J-K) Control 1. (L-M) Control 2. Here, each monkey was fit individually. Then, all the parameters obtained for that monkey were carried forward except for parameter p, the proportion of SHIV produced by $CD4^+$ T-cells in blood, which was estimated for the remaining monkeys individually. Orange: best fits for all the monkeys using the parameters from Control 1 and fitting to p only. Blue: best fits for all the monkeys using the parameters from Control 2 and fitting to p only. Purple: best fits for all the monkeys using the parameters from E1 and fitting to p only. Red: best fits for all the monkeys using the parameters from E2 and fitting to p only. Green: best fits for all the monkeys using the parameters from E3 and fitting to p only.

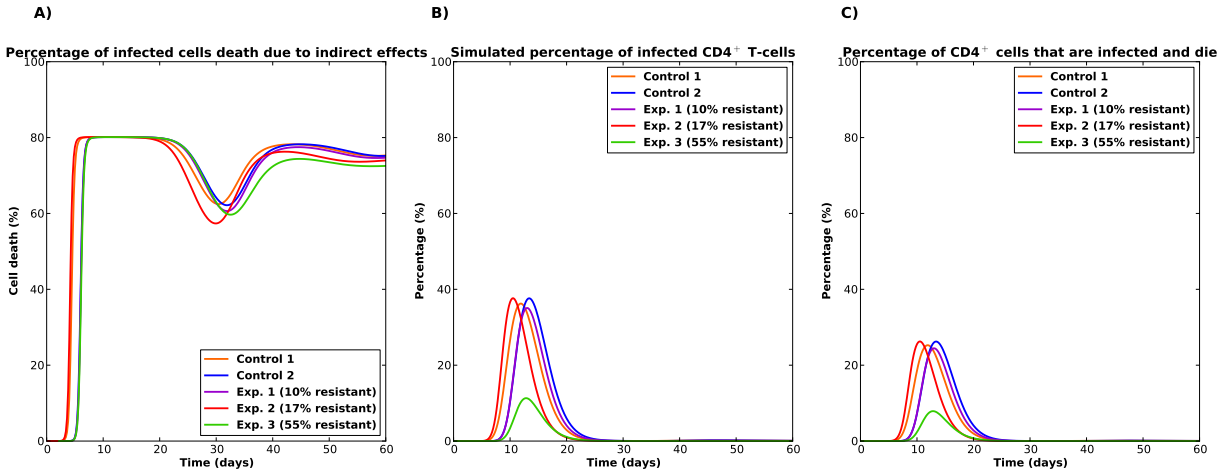

Figure S12: A) Modeled percentage of daily cell-death occurring in the infected compartment due to indirect effects. B) Simulated percentage of infected $CD4^+$ T-Cells during the course of a SHIV infection. C) Simulated percentage of $CD4^+$ T-cells that will become infected and die during the course of a SHIV infection. Here, the parameters obtained by fitting to Experiment 1 were carried over and only the proportion of SHIV produced by $CD4^+$ T-cells in blood (parameter p) was fit to the other animals.

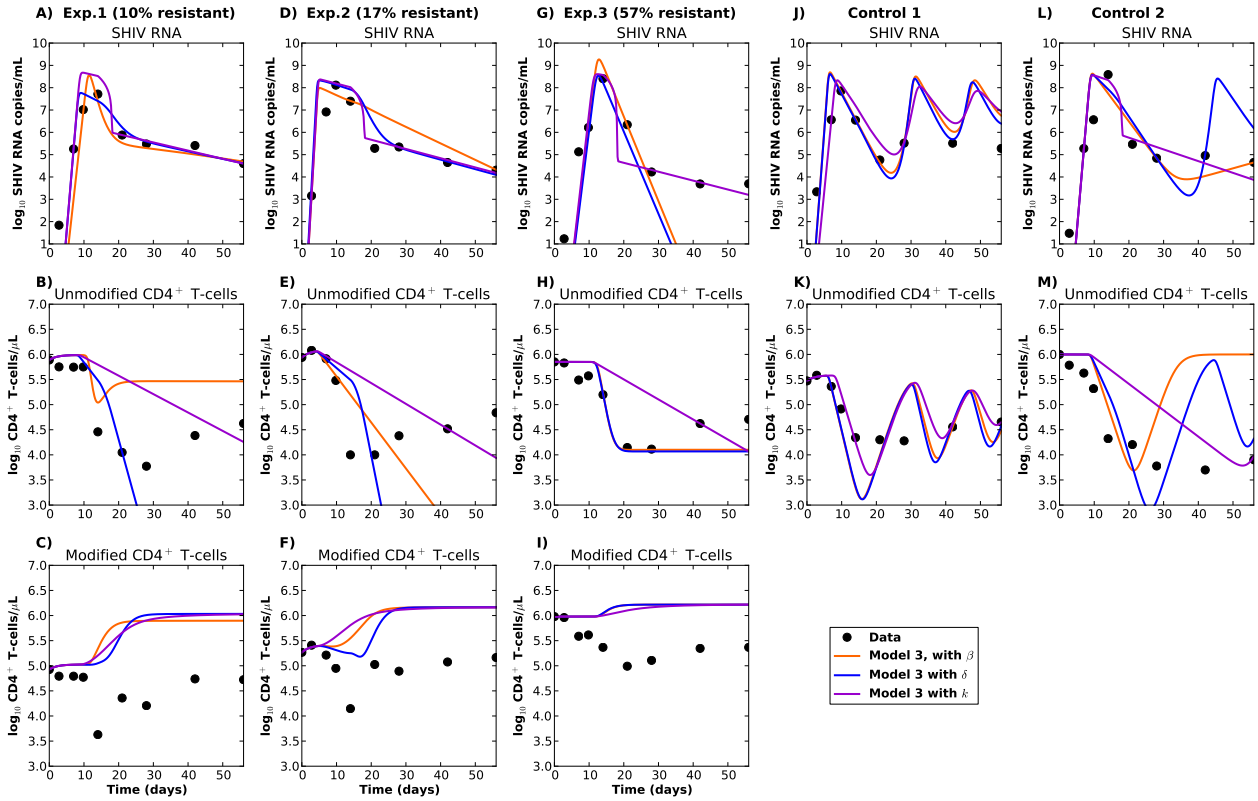

Figure S13: Best-fit trajectories (solid lines) for Model 3 and experimentally observed data (•) for the experimental and control animals. (A-C) Experiment 1, with 10%modified cells prior to infection. (D-F) Experiment 2, with 17% modified cells prior to infection. (G-I) Experiment 3, with 55% modified cells prior to infection. (J-K) Control 1. (L-M) Control 2. Model 3 is similar to Model 1 but it includes a phasing immunity (eq. 3). We assumed immunity could be modeled in three different ways: by decreasing infectivity β (orange), by increasing the infected-cell death rate δ (blue), or by decreasing the burst size k (purple). Here, each monkey was fit individually.

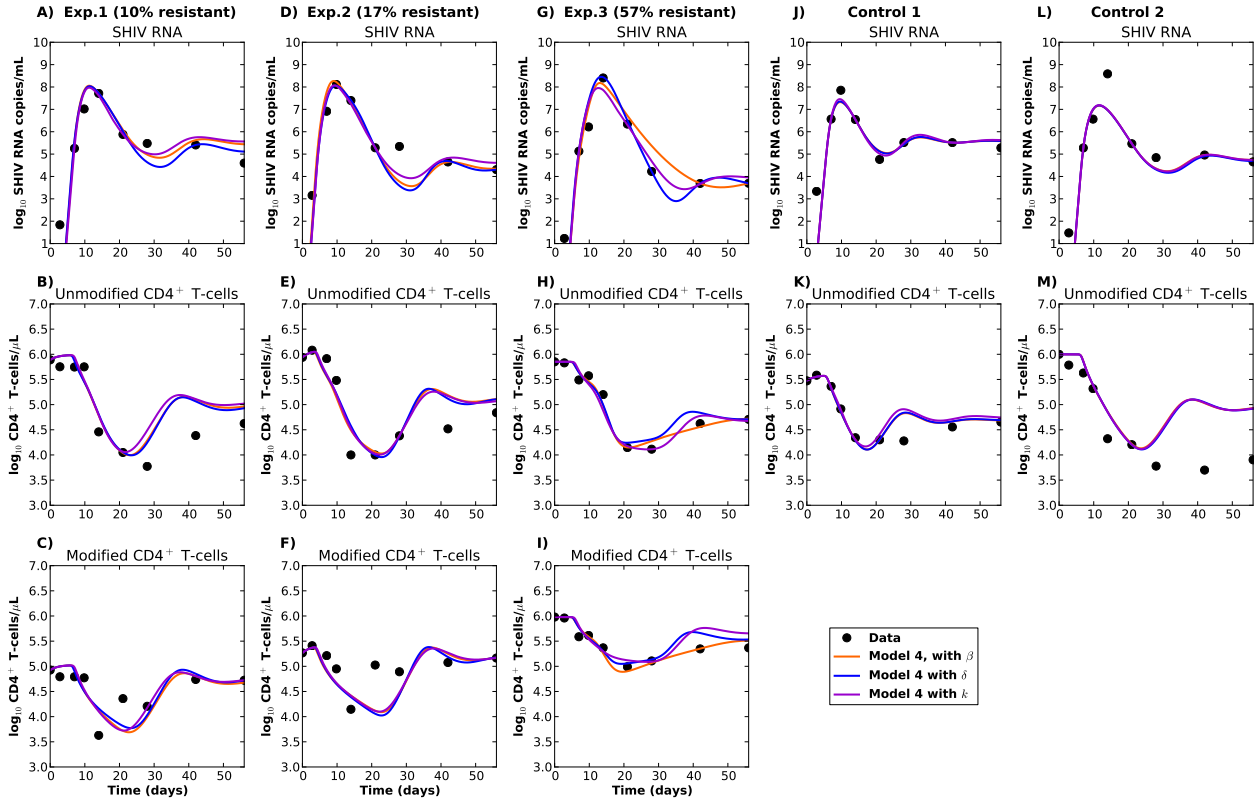

Figure S14: fBest-fit trajectories (solid lines) for Model 4 and experimentally observed data (•) for the experimental and control animals. (A-C) Experiment 1, with 10%modified cells prior to infection. (D-F) Experiment 2, with 17% modified cells prior to infection. (G-I) Experiment 3, with 55% modified cells prior to infection. (J-K) Control 1. (L-M) Control 2. Model 4 is similar to Model 2 but it includes a phasing immunity (eq. 4). We assumed immunity could be modeled in three different ways: by decreasing infectivity β (orange), by increasing the infected-cell death rate δ (blue), or by decreasing the burst size k (purple). Here, each monkey was fit individually.

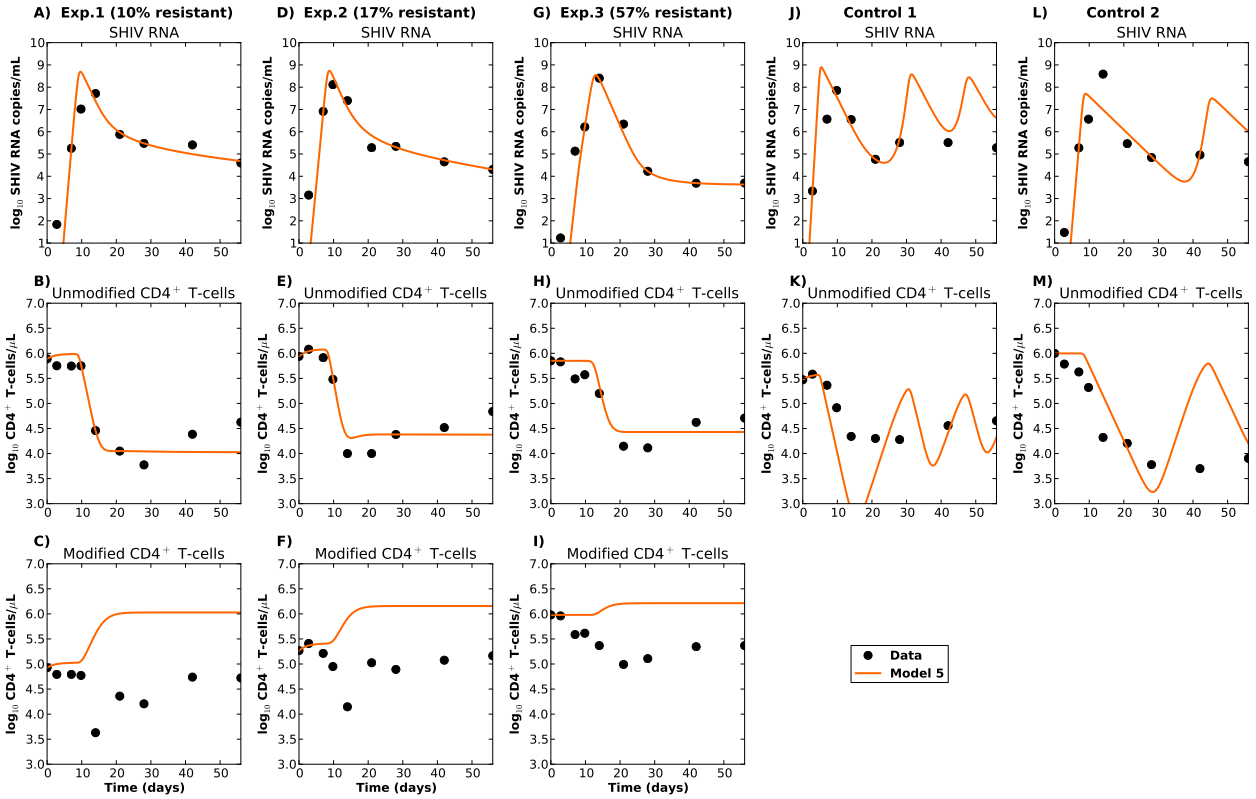

Figure S15: Best-fit trajectories (solid lines) for Model 5 and experimentally observed data (•) for the experimental and control animals. (A-C) Experiment 1, with 10%modified cells prior to infection. (D-F) Experiment 2, with 17% modified cells prior to infection. (G-I) Experiment 3, with 55% modified cells prior to infection. (J-K) Control 1. (L-M) Control 2. Here, each monkey was fit individually.