Table S1. List of antibodies used for characterization of mucosal mononuclear and epithelial cells in rhesus macaques.

Antibody	Isotype	Clone	Working Dilution	Source	Method Used
Anti-human CD3 Pacific Blue	Mouse IgG1	SP34-2	1:2	BD Biosciences	FC
Anti-human CD3	Rabbit polyclonal	-	1:100	Biocare Medical	IF
Anti-human CD4 APCH7	Mouse IgG1	L200	1:1	BD Biosciences	FC
Anti-human CD11c	Mouse IgG1	3.9	1:50	Biolegend	IF
Anti-human CD45	Mouse IgG1	D058-1283	1:50	BD Biosciences	IF
Anti-human CD45 APC	Mouse IgG1	MB4-6D6	1:11	Miltenyi Biotec	FC
Anti-human CD68	Mouse IgG1	KP1	1:50	Dako	IF
Anti-human CD79a	Mouse IgG1	HM47	1:100	BD Biosciences	IF
Anti-human CD210 (IL10R)	Rat IgG2a	3F9	1:100	Biolegend	IF
Anti-human CD210 (IL10R) PE	Rat IgG2a	3F9	1:1	Biolegend	FC
Anti-human IL10	Rat IgG1	JES3-9D7	1:20	Biolegend	IF
Anti-human IL10 PE-Cy7	Rat IgG1	JES3-9D7	1:1	Biolegend	FC
Anti-human IFNγ	Mouse IgG1	4S.B3	1:20	Biolegend	IF
Anti-human IFNγ PerCP-Cy5.5	Mouse IgG1	4S.B3	1: 10	BD Biosciences	FC
Anti-phospho-STAT3	Rabbit IgG	D3A7	1:50	Cell Signaling	IF
Anti-human TNFα	Mouse IgG1	MAb11	1:20	Biolegend	IF
Anti-human TNFα Alexa Flour 700	Mouse IgG1	Mab11	1:2	BD Biosciences	FC
Active Caspase 3	Rabbit polyclonal	-	1:500	Abcam	IF
Anti-human ZO-1	Mouse IgG1	ZO1-1A12	1:30	Invitrogen	IF
Anti-cow Cytokeratin, Wide Spectrum Screening	Rabbit polyclonal IgG	-	1:500	Dako	IF

IOPath®+ Cytokeratin-Large Spectrum	Mouse IgG1	KL1	1:50	Beckman Coulter	IF
Anti-Human Epithelial Antigen FITC	Mouse IgG1	Ber-EP4	1:2	Dako	FC

Note: Before all staining, the dilution of the respective antibodies was determined via serial dilution experiments. IF and FC represent immunofluorescence and flow cytometry respectively.

Table S2: Percentages of active caspase-3 positive enterocytes detected in normal and acute SIV infected rhesus macaques.

Category	Animal Number	Tissue	Days post SIV infection	AC-3+ enterocytes (%) (mean ± standard errors)
Normal	GB61	Colon	-	1.0 ± 0.3
	GJ06	Colon	-	0.5 ± 0.1
	GN70	Colon	-	1.1 ± 0.2
	GN74	Colon	-	0.9 ± 0.1
	FF15	Colon	-	0.6 ± 0.1
	FF23	Colon	-	0.3 ± 0.1
	GB61	Jejunum	-	2.3 ± 0.7
	GJ06	Jejunum	-	0.2 ± 0.1
	GN70	Jejunum	-	3.2 ± 1.1
	GN74	Jejunum	-	1.8 ± 0.8
	FF15	Jejunum	-	0.2 ± 0.1
	FF23	Jejunum	-	0.4 ± 0.1
Acute SIV Infection	AV63	Colon	8	0.8 ± 0.2
	AV85	Colon	21	4.1 ± 0.7
	AV91	Colon	10	0.7 ± 0.3
	BA17	Colon	13	2.3 ± 0.5
	BA57	Colon	8	1.3 ± 0.2
	BN37	Colon	21	0.5 ± 0.1
	HN29	Colon	10	1.7 ± 0.2
	M992	Colon	13	2.0 ± 0.4
	AV63	Jejunum	8	10.9 ± 1.5
	AV85	Jejunum	21	18.0 ± 3.0
	AV91	Jejunum	10	10.5 ± 1.9
	BA17	Jejunum	13	8.6 ± 3.2
	BA57	Jejunum	8	11.5 ± 4.3
	BN37	Jejunum	21	14.3 ± 3.8
	HN29	Jejunum	10	6.8 ± 1.2
	M992	Jejunum	13	11.0 ± 3.5

SUPPLEMENTARY FIGURES:

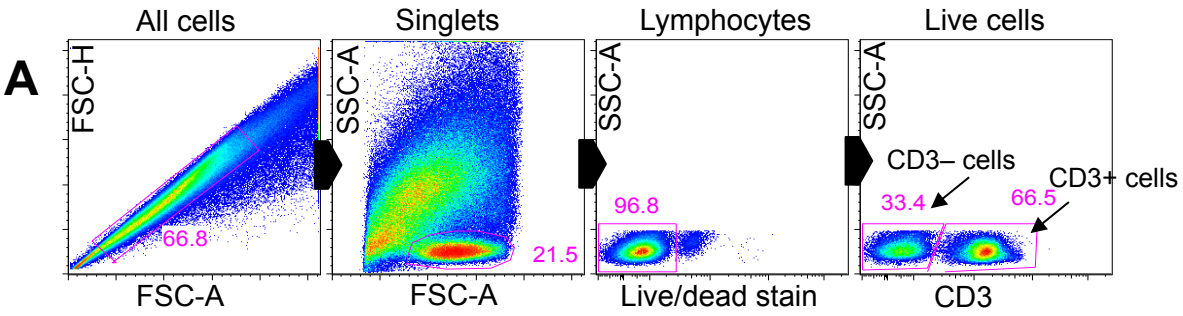
Figure S1: Interferon gamma (IFNγ) expression of CD3+ T-cells and CD3⁻ lymphocytes in jejunum lamina propria mononuclear cells detected by flow cytometry from a representative macaque at day 0 and 21 days post $SIV_{MAC}251$ infection. (A) Cells were gated first on singlets, lymphocytes, followed by live cells and then on CD3+ T-cells and CD3⁻ lymphocytes. (B) The percentages of total IFNγ are shown in each upper box of each plot of CD3+ T-cells and CD3⁻ lymphocytes. (C) The percentages for IFNγ are shown for CD3+ T-cells and CD3⁻ lymphocytes (open histograms) along with fluorescence minus controls (filled histograms).

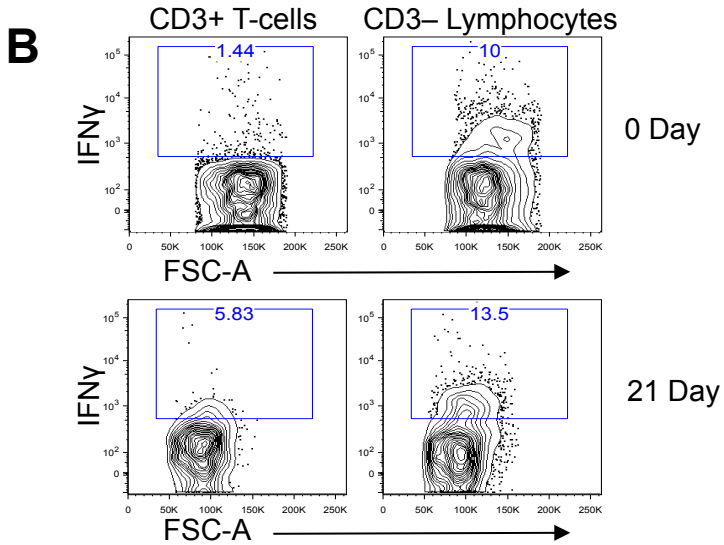
Figure S2. Linear regression analysis was performed comparing mean percentages of active caspase-3+ enterocytes and plasma viral load in acute (A & C) and chronic (B & D) SIV infected macaques. Note there is an inverse correlation between apoptotic enterocytes and plasma viral load during acute phase of infection in both colon (A, n=8) and jejunum (C, n=8). Interestingly, a positive correlation is shown between apoptotic enterocytes and plasma viral load during chronic infection in both colon (B) and jejunum (D) tissues (n=7). However, these data were not statistically significant.

Figure S3. Jejunum villus height, crypt length, and villus to crypt ratio, and colon crypt length and breadth in both normal, and SIV-infected infected macaques. Differences in jejunum villus height (A), jejunum crypt length (B), jejunum villus:crypt ratios (C), colon crypt length (D), and colon crypts breadth (E) with means ± standard errors were plotted from normal, and SIV-infected animals. Increased jejunum and decreased colon crypt length were detected in acute (n=6) and chronic (n=6) SIV infected macaques compared

to uninfected controls (n=7). A minimum of 12 to 20 fields from each animal was considered for morphometric analysis. Astericks indicate statistically significant differences between the respective animal groups (* denotes $p<0.005$ and ** denotes $p<0.0001$).

Figure S4. Detection of p-STAT3 positive cells in normal and SIV infected jejunum tissues. Phosphorylated-STAT3 positive cells were detected in uninfected normal (A), acute (B) and chronic (C) SIV-infected macaques by immunohistochemistry staining using anti-pSTAT3 monoclonal antibodies with nuclear fast red counterstain. (D) Isotype control developed with Mach 3 Rabbit AP-Polymer staining showed no positive brown staining in tissues. Black arrow denotes the presence of pSTAT3 positive cells (dark brown color), majority distributed in lamina propria region.


A
All cells
Singlets
Lymphocytes
Live cells
FSC-H
FSC-A
SSC-A
FSC-A
SSC-A
Live/dead stain
SSC-A
CD3
66.8
21.5
96.8
CD3– cells
CD3+ cells
33.4
66.5


B
CD3+ T-cells
CD3– Lymphocytes
IFNγ
FSC-A
1.44
10
0 Day
5.83
13.5
21 Day

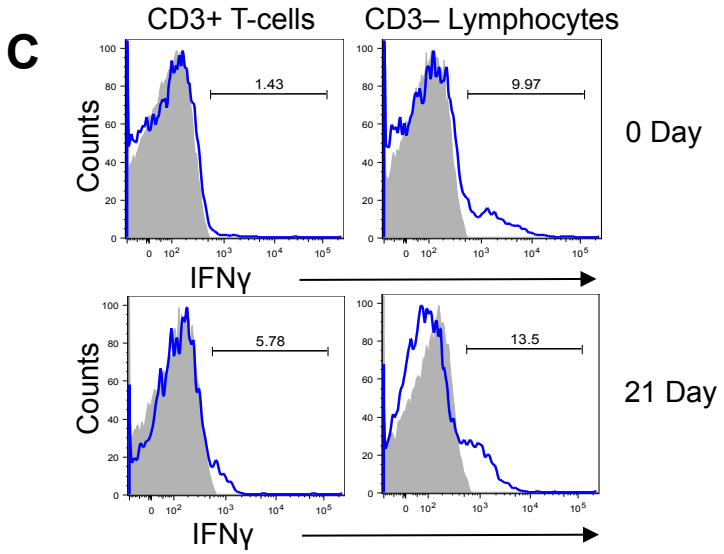

C
CD3+ T-cells
CD3– Lymphocytes
Counts
IFNγ
1.43
9.97
0 Day
5.78
13.5
21 Day

Figure S1

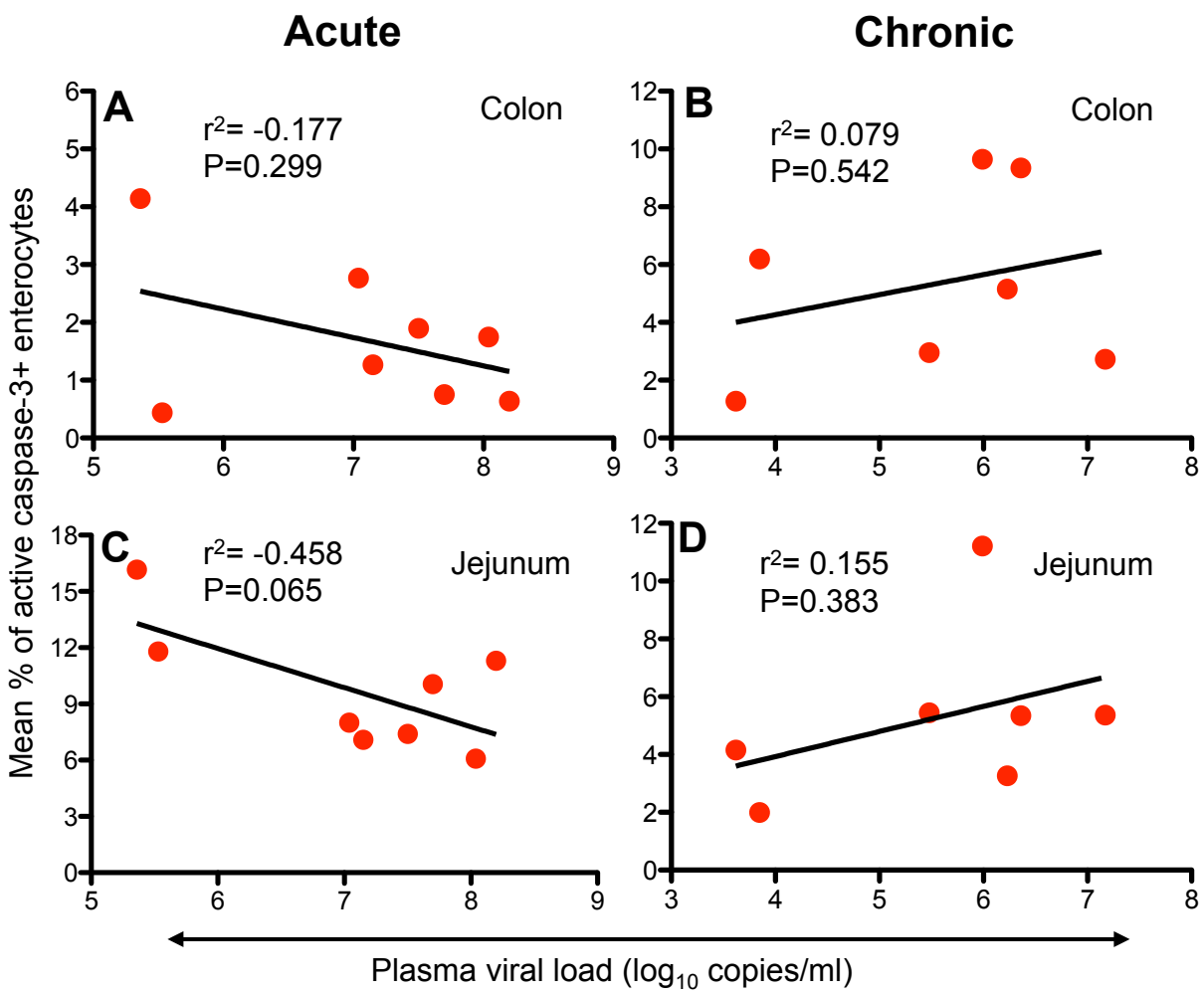

Acute
Chronic
A
r2= -0.177
P=0.299
Colon
B
r2= 0.079
P=0.542
Colon
C
r2= -0.458
P=0.065
Jejunum
D
r2= 0.155
P=0.383
Jejunum
Mean % of active caspase-3+ enterocytes
Plasma viral load (log10 copies/ml)

Figure S2

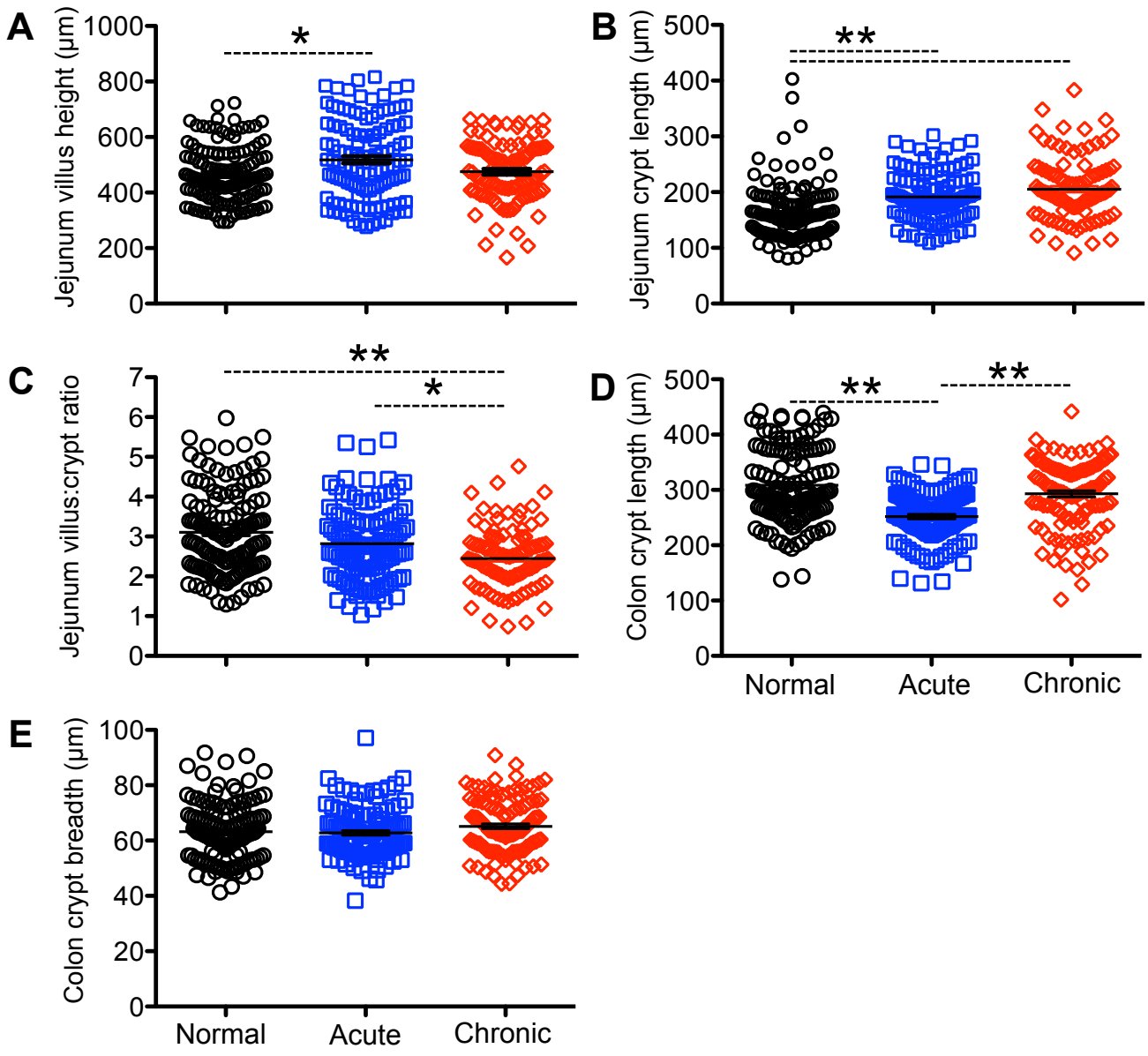

A
Jejunum villus height (µm)
1000
800
600
400
200
0
*
B
Jejunum crypt length (µm)
500
400
300
200
100
0
**
C
Jejunum villus:crypt ratio
7
6
5
4
3
2
1
0
**
*
D
Colon crypt length (µm)
500
400
300
200
100
0
**
**
Normal
Acute
Chronic
E
Colon crypt breadth (µm)
100
80
60
40
20
0
Normal
Acute
Chronic

Figure S3

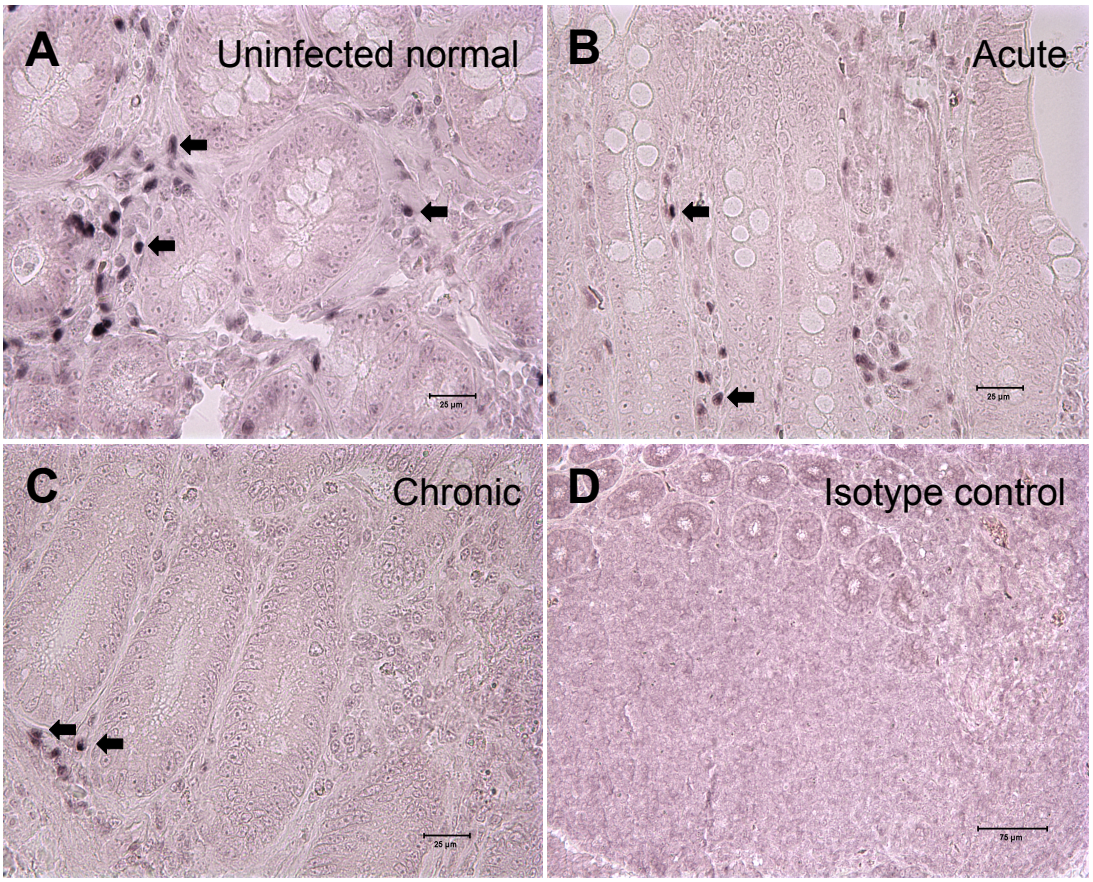


Figure S4