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Supplementary Table 1: Clinical Study Participants Characteristics.

	Uninfected study participants	HIV-1 infected study participants
Number of subjects	14	24
Age (yrs)	31 (23-54)	33.5 (22-58)
Male/Female Ratio	9/5	18/6
CD4 count (cells/μl)[*]	724 (468-1071)	445 (221-1248)
Plasma viral load (HIV-1 RNA copies/ml)	-	51,350 (2880-207,000)
Race:		
White/Caucasian	10 (71.4%)	17 (70.8%)
Black/African American	2 (14.3%)	6 (25%)
Asian	2 (14.3%)	1 (4.2%)

Values are shown as median (range) or the number (percentage) of each cohort. Statistical analysis performed using Mann-Whitney test for comparisons between uninfected and HIV-1 infected study participants and the Fisher Exact test or Chi-square test for comparison of categorical data. [*]p=0.001.

Supplementary Table 2: Study Participants Characteristics (RUMC IRB gastrointestinal repository)

	Uninfected study participants	HIV-1 infected study participants
Number of subjects	15	15
Age (yrs)	52 (39-62)	51 (42-59)
Male/Female Ratio	11/4	11/4
CD4 count (cells/μl)	n/d	508 (178-1415)
Plasma viral load (HIV-1 RNA copies/ml)	-	<40
Race:		
White/Caucasian	2 (13.3%)	2 (13.3%)
Black/African American	13 (86.7%)	13 (86.7%)

Values are shown as median (range) or the number (percentage) of each cohort. Statistical analysis performed using Mann-Whitney test for comparisons between uninfected and HIV-1 infected study participants and the Fisher Exact test or Chi-square test for comparison of categorical data. n/d: not determined.

Supplementary Table 3: PBMC and colon biopsies with appropriate RNA or GAPDH levels for accurate Type I IFN and ISG gene measurements.

	UC-AMC Cohorts	
	Uninfected study participants (Total N=14)	**HIV-infected study participants** (Total N=24)
	PBMC	
IFNα	14	24
IFNα subtypes	8	13
IFNβ	14	24
	Colon biopsies	
IFNα	12	18
IFNα subtypes	7	11
IFNβ	12	18
Tetherin	11	16
APOBEC3G	11	16
MX2	13	18
	RUMC Cohorts	
	Uninfected study participants (Total N=11)	**HIV-infected study participants** (Total N=15)
	Colon biopsies	
IFNα	11	15
IFNβ	11	15
Tetherin	11	15
APOBEC3G	11	15
MX2	11	15

Samples were excluded due to insufficient RNA or when GAPDH levels <200 copies/ng.

Supplementary Table 4. Correlations between colonic IFNα and IFNβ gene transcripts and clinical, virological and immunological parameters.[#]

	IFNα	IFNβ
Clinical Parameters		
Blood CD4 T cell count	R=-0.23, P=0.36	R=-0.17, P=0.51
Plasma HIV-1 viral load	R=-0.10, P=0.70	R=-0.02, P=0.95
Systemic inflammation, immune activation, microbial translocation and epithelial barrier disruption parameters		
Plasma IL-6	R=-0.42, P=0.08	R=0.38, P=0.12
Plasma C-reactive protein (CRP)	R=-0.27, P=0.28	R=0.27, P=0.29
Plasma TNFα	R=-0.50, P=0.09	R=0.40, P=0.18
Plasma IFNγ	R=-0.09, P=0.77	**R=0.61, P=0.03**
Plasma IL-10	R=-0.24, P=0.44	**R=0.58, P=0.04**
Activated blood CD4 T cells	R=-0.07, P=0.77	R=-0.18, P=0.48
Activated blood CD8 T cells	R=0.07, P=0.77	R=-0.03, P=0.89
Plasma soluble CD27 (sCD27)	R=0.02, P=0.94	R=0.03, P=0.92
Plasma sCD14	R=-0.45, P=0.09	R=0.31, P=0.26
Plasma lipopolysaccharide (LPS)	R=-0.08, P=0.76	R=-0.18, P=0.51
Plasma lipoteichoic acid (LTA)	R=-0.10, P=0.71	R=-0.30, P=0.27
Plasma intestinal fatty acid binding protein (iFABP)	R=0.05, P=0.83	R=0.09, P=0.74
Colonic immunity parameters		
HIV-1 RNA levels	R=0.12, P=0.63	R=0.03, P=0.88
Number of CD1c^{+} mDC	R=0.12, P=0.64	R=0.38, P=0.14
Number of pDC	R=-0.12, P=0.66	R=0.04, P=0.88
CD40 expression levels on CD1c^{+} mDC	R=0.07, P=0.79	R=0.09, P=0.72
CD40 expression levels on pDC	R=0.04, P=0.87	R=0.00, P=1.0
Percent of CD83-expressing CD1c^{+} mDC	R=0.40, P=0.12	R=0.29, P=0.26
Percent of CD83-expressing pDC	R=0.24, P=0.36	R=0.35, P=0.17
Number of CD4 T cells	R=-0.17, P=0.49	R=0.00, P=1.0
Number of CD8 T cells	R=-0.08, P=0.75	R=0.23, P=0.35
Number of activated CD4 T cells	R=-0.08, P=0.76	R=0.003, P=0.99
Number of activated CD8 T cells	R=0.11, P=0.67	R=0.22, P=0.38
Number of IFNγ-expressing CD4 T cells	R=-0.20, P=0.44	R=0.43, P=0.08
Number of IL-17-expressing CD4 T cells	R=-0.22, P=0.40	R=0.44, P=0.08
Number of IL-22-expressing CD4 T cells	R=0.22, P=0.40	R=0.28, P=0.27
Number of IFNγ-expressing CD8 T cells	R=0.07, P=0.79	R=0.12, P=0.65
Constitutive IL-12p70 production	R=0.13, P=0.67	R=0.30, P=0.30
Constitutive IL-23 production	R=-0.06, P=0.83	R=0.24, P=0.40
Constitutive IL-10 production	R=0.27, P=0.35	R=-0.08, P=0.80
Constitutive IL-1β production	R=-0.19, P=0.51	R=-0.06, P=0.83
Constitutive TNFα production	R=-0.13, P=0.65	R=-0.10, P=0.72
Constitutive IL-6 production	R=-0.19, P=0.51	R=-0.04, P=0.89
Constitutive IFNγ production	R=-0.14, P=0.60	R=0.06, P=0.83
Constitutive IL-17 production	R=-0.18, P=0.50	R=0.02, P=0.95

Statistical analysis performed using the Spearman test. [#]Bold font indicates statistically significant correlation.

Supplementary Table 5. Correlations between colonic Type I IFN gene transcripts.*

	IFNα	IFNβ	Tetherin	APOBEC3G	MX2
IFNα	---				
IFNβ	R=-0.10, P=0.70	---			
Tetherin	R=-0.03, P=0.93	R=0.43, P=0.11	---		
APOBEC3G	R=0.10, P=0.93	R=0.41, P=0.13	**R=0.81, P=0.0002**	---	
MX2	R=-0.12, P=0.66	R=0.26, P=0.30	**R=0.84, P=0.0004**	**R=0.58, P=0.03**	---

Statistical analysis was performed using the Spearman test. *Bold font indicates statistically significant correlation.