

Supplementary Table 1. SHCS Subjects characteristics at baseline (pre IFN- α /riba treatment).

Subject	Gender	Age (y)	Risk group ¹	Duration of HIV-1 infection (y)	CDC disease stage ²	HIV-1 viral load (copies/ml)	CD4+ count (cells/ μ l)	INF- α dose (μ g/wk) ⁴	Riba dose (mg/d) ⁴	Treatment duration (wk)	HIV-1 subtype
A	M	38	IDU	11	A	43200	404	120	1000	51	B
B	M	45	OTHER	13	B	55215	270	180	1200	14	B
C	M	42	MSM	5	A	78886	587	100	800	26	B
D	F	26	HET	2	A	13100	374	80	800	48	B
E	M	28	HET	3	A	167500	501	180	800	26	B
I	M	32	MSM	6	A	4070	755	180	800	47	B
J	M	39	IDU	19	A	8620	590	120	1000	47	B
K	M	37	HET	4	B	34050	570	50	600	48	B
L	M	52	MSM	5	A	28600	444	180	800	25	B
M	F	27	IDU	6	C	3360	510	180	800	23	B
N	M	42	IDU	18	C	183	332	180	1000	48	B
O	F	24	HET	4	A	6490	839	135	800	24	J/B/F ³
P	M	39	HET	19	A	4110	336	180	800	21	B
Q	F	37	IDU	10	B	2425	599	72	800	47	B
S	M	30	IDU	7	A	9550	696	180	1200	48	B

¹Risk groups are defined as follows: BLOOD = transfusion recipient, HET = heterosexual, IDU = intravenous drug use, MSM = men who have sex with men.

² CDC disease stage is defined as follows: A = asymptomatic, acute infection or persistent generalized lymphadenopathy, B = symptomatic conditions, C = AIDS-indicator conditions.

³*pol* sequence did not correspond to any particular HIV-1 subtype or circulating recombinant form; subregions exhibited homology to subtypes J, B and F.

⁴ Doses shown are doses at the time of the on-treatment sampling, and in some cases, they reflect dose modifications in response to treatment side effects.

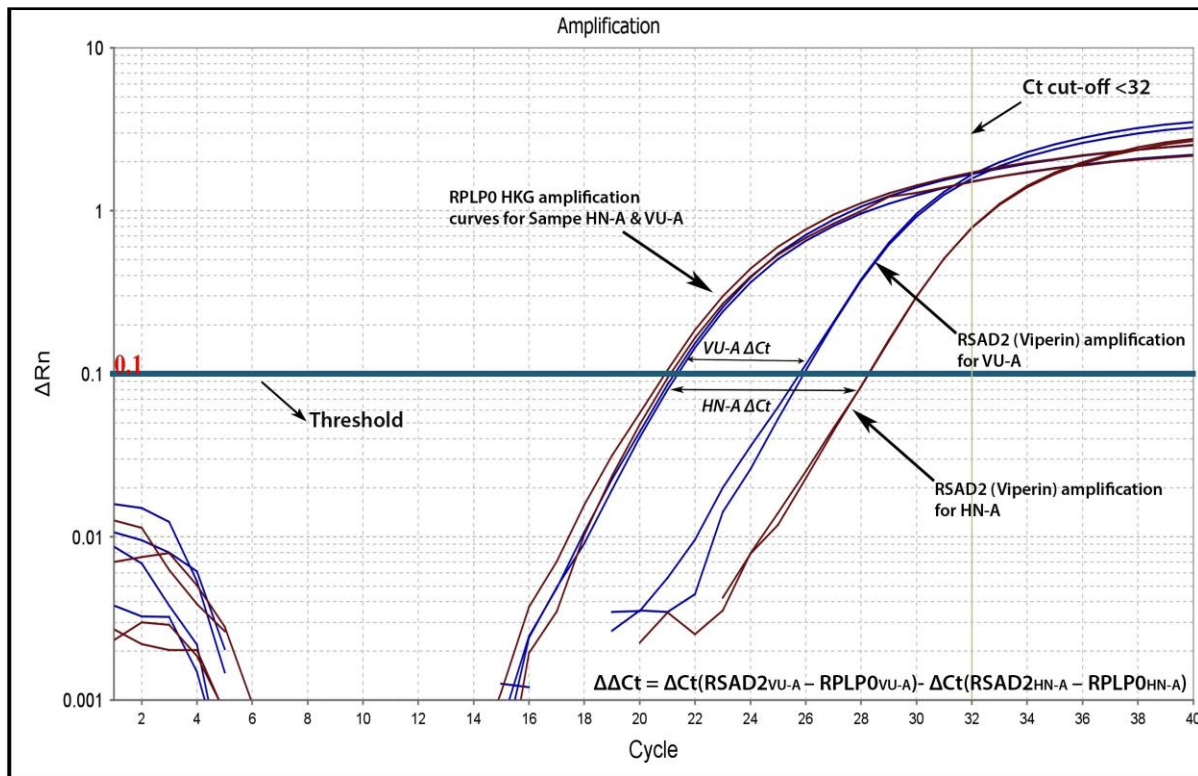
Supplementary Table 2. SCOPE cohort subject characteristics.

	Subject ID	Gender	Age (y)	CD4+ count (cells/μl)	CD4%	HIV-1 viral load (copies/ml)
HIV-negative controls	HN-A	M	54	684	46	Not Detected
	HN-B	M	49	1263	49	Not Detected
	HN-C	M	45	460	40	Not Detected
	HN-D	M	52	1077	52	Not Detected
	HN-E	M	45	741	49	Not Detected
	HN-F	M	49	493	51	Not Detected
	HN-G	M	36	708	45	Not Detected
	HN-H	M	58	1438	64	Not Detected
	HN-I	M	47	465	25	Not Detected
	HN-J	M	51	780	27	Not Detected
	HN-K	M	38	885	39	Not Detected
	HN-L	M	29	750	35	Not Detected
	HIV-infected, ART-untreated	VU-A	F	52	551	24
VU-B		M	52	497	22	11023
VU-C		M	20	501	23	89965
VU-D		M	46	473	16	39719
VU-E		M	27	414	16	43463
VU-F		F	42	492	34	7015
VU-G		M	55	402	34	79418
VU-H		M	42	503	32	7408
VU-I		M	32	269	20	21604
VU-J		M	41	434	21	48131
VU-K		M	52	252	33	18559
VU-L		M	33	938	32	10515

Supplementary Table 3. List of the 34 anti-HIV-1 host restriction factors measured by our CuRe Array.

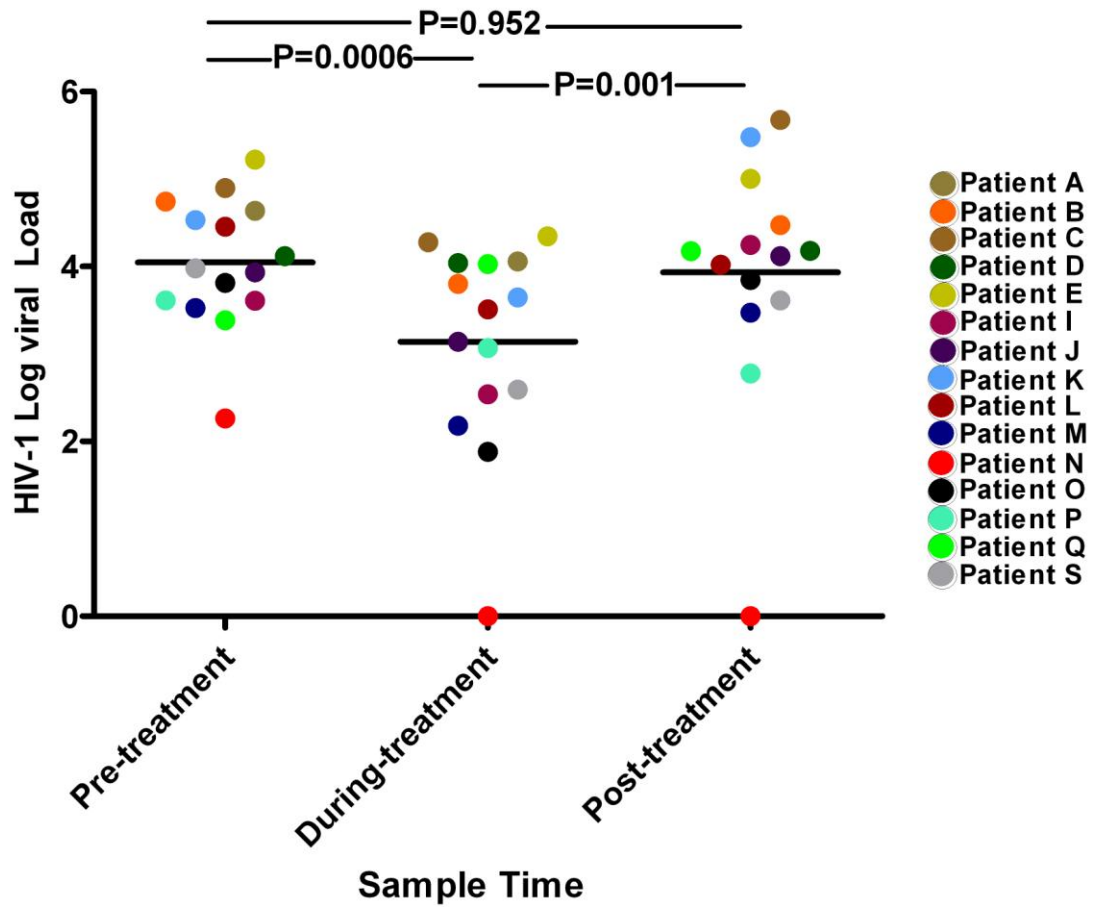
NAME	NCBI ENTREZ GENE DESCRIPTION	KEY ANTI-HIV-1 ROLE(S)	REFS
APOBEC3 (A-H)	Apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like3	Hypermutation; lethal mutations in viral DNA; Inhibition of reverse transcription; Inhibition of integration	(1-9)
TRIM5 α	Tripartite motif-containing protein 5	Targeting of viral capsid; Inhibition of viral transcription	(10-12)
TRIM11, TRIM14, TRIM15, TRIM19, TRIM21, TRIM26, TRIM28, TRIM31, TRIM32	Tripartite motif family	Targeting of viral capsid; Inhibition of viral transcription	(11, 12)
TRIM22	Tripartite motif-containing protein 22	Targeting of viral capsid; Inhibition of viral transcription	(11-13)
BST2/tetherin	Bone marrow stromal cell antigen 2	Blocks release of enveloped viruses	(14, 15)
CDKN1A (P21)	Cyclin-dependent kinase inhibitor 1A (p21, Cip1)	Blocks reverse transcription; Blocks RNA transcription by reducing activity of CDK9	(16-18)
PAF1	Paf1, RNA polymerase II associated factor	Inhibits early events of viral life cycle from reverse transcription to integration	(19)
CTR9	Ctr9, Paf1/RNA polymerase II complex component	Inhibits early events of viral life cycle from reverse transcription to integration	(19)
RTF1	Rtf1, Paf1/RNA polymerase II complex component	Inhibits early events of viral life cycle from reverse transcription to integration	(19)
EIF2AK2 (PKR)	Eukaryotic translation initiation factor 2-alpha kinase 2	Inhibits viral protein translation by protein phosphorylation; promotes innate immune signaling	(20)
HERC5	HECT domain and RLD 5	Blocks early stage of retroviral particle assembly	(21)
IFITM Family (3 members)	Interferon induced transmembrane protein	Inhibits cytosolic entry	(22)
ISG15	ISG15 ubiquitin-like modifier	Blocks interaction between HIV-1 Gag and Tsg101 (ESCRT-I) required for efficient budding of HIV-1	(23)
MOV10	Mov10, Moloney leukemia virus 10, homolog	Inhibits proteolytic processing of Gag and reverse transcription	(24)
RNASEL	Ribonuclease L (2',5'-oligoadenylate synthetase-dependent)	Cleaves single-stranded RNA in U-rich sequences; activates antiviral innate immunity	(25)
RSAD2 (viperin)	Radical S-adenosyl methionine domain containing 2	Inhibits viral production	(26)
SAMHD1	SAM domain and HD domain 1	Inhibits HIV replication in myeloid cells, probably by regulating cellular dNTP supply	(27)
SLFN11	Schlafen family member 11	Inhibits viral protein synthesis	(28)

Supplementary Figure 1.



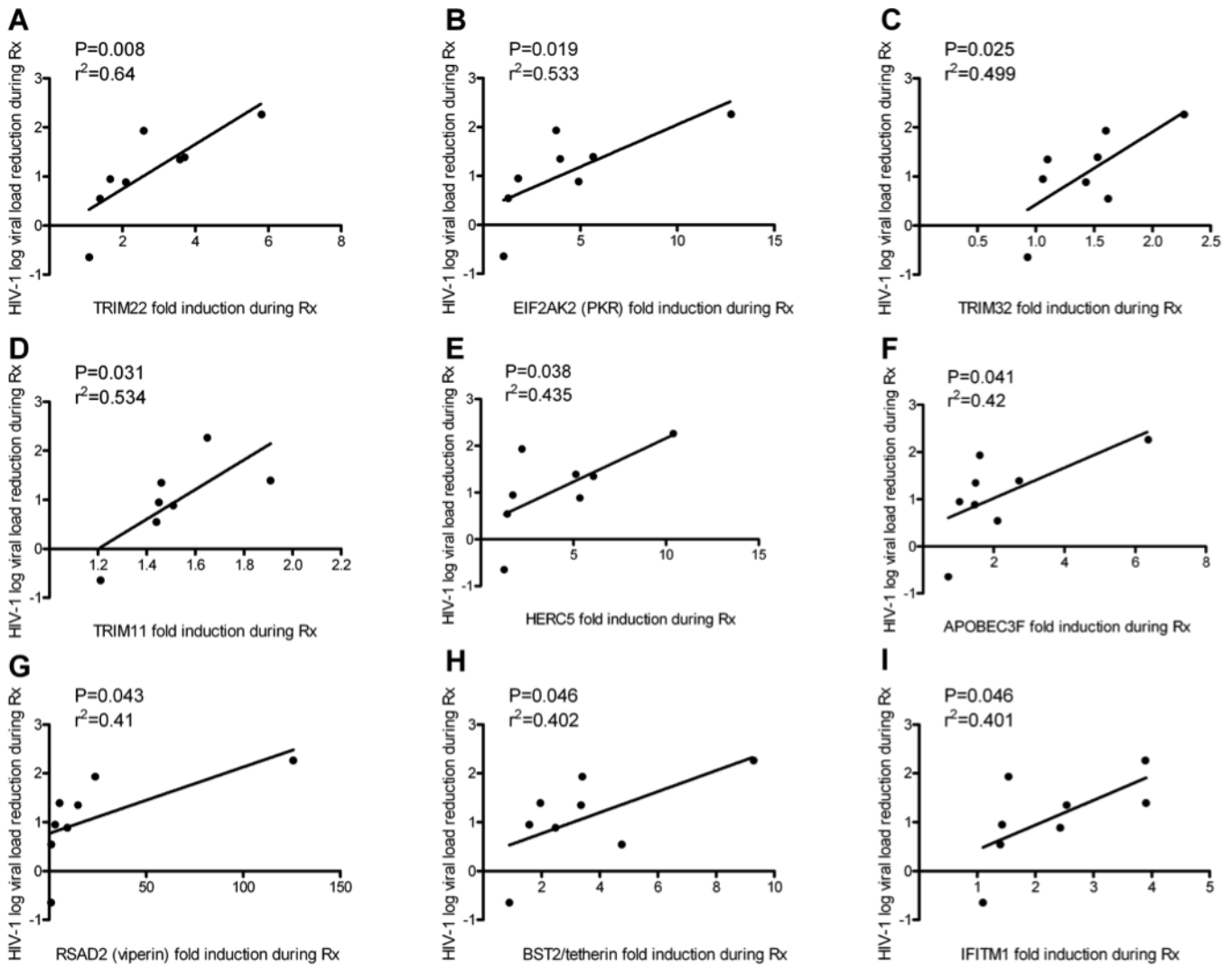
Supplementary Figure 1. Example of quantitative PCR analysis strategy. The DNase-treated RNA was measured using the NanoDrop 1000 to assess RNA quantity and quality. Based on the NanoDrop reading, an equal input of the DNase-treated RNA from each sample was added to the cDNA synthesis reaction. GeNorm was used to choose the most stable housekeeping gene to normalize the data. We excluded (re-purified) any RNA with a low 260:280 ratio (<1.8) or 260:230 ratio (<1.6), or RNA Integrity Number (RIN) <6 based on Bioanalyzer quantification. The threshold cycle (Ct) was calculated by the Life technologies ViiA 7 software (manual threshold at 0.1 and automatic baseline). A cutoff of 32 was applied to discard the late Ct values as recommended by the manufacturer. For each TLDA, quality controls were performed on the raw data by checking negative controls, and samples with coefficient of variation (CV) of the replicates (CV%<3). The comparative Ct($\Delta \Delta Ct$) method was used to calculate gene expression relative quantification.

Supplementary Figure 2.



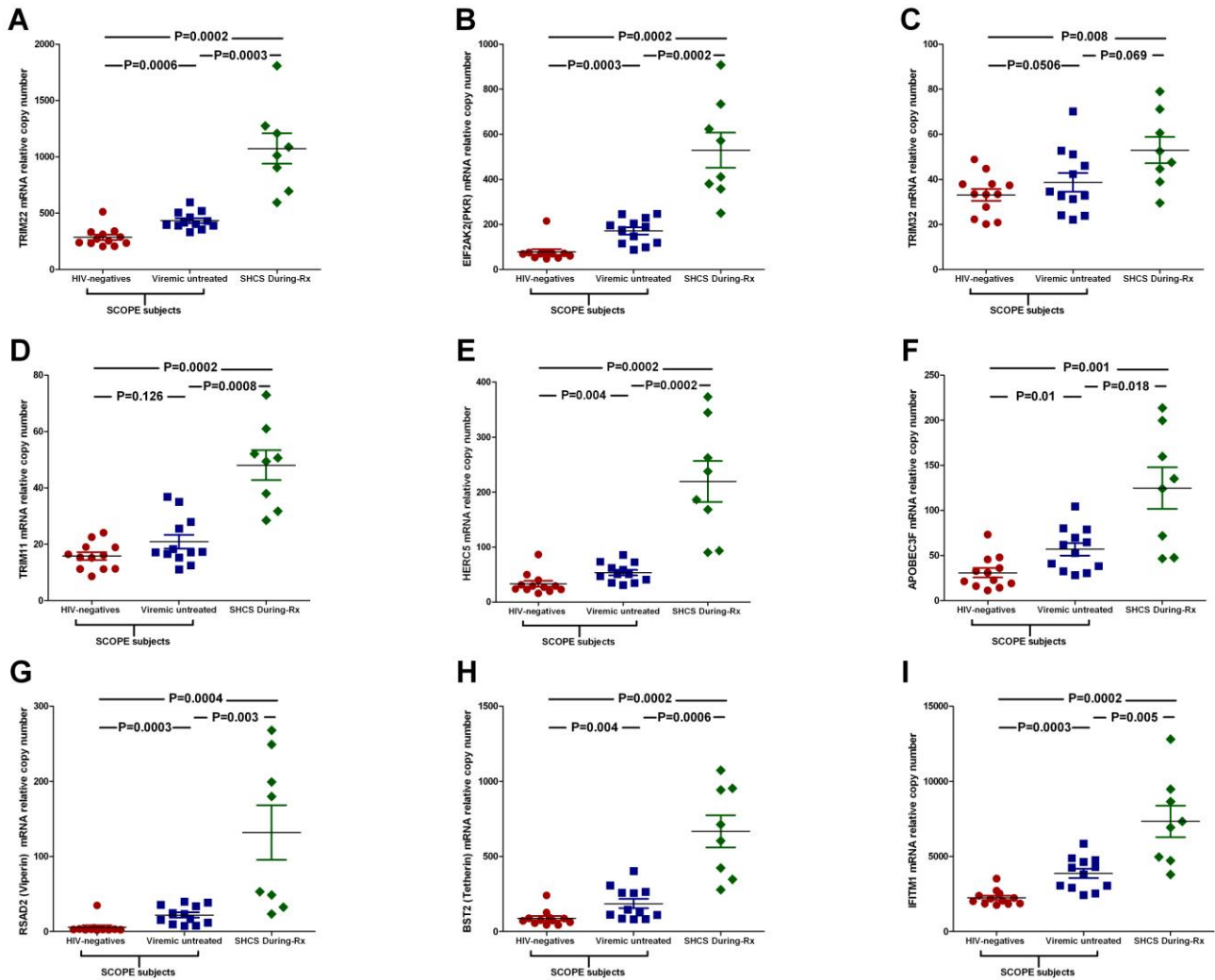
Supplementary Figure 2. Effect of IFN- α /riba therapy on HIV-1 plasma viral load. Pre-treatment, during treatment, and post-treatment viral loads are displayed. Paired Wilcoxon tests were employed to determine significance.

Supplementary Figure 3.



Supplementary Figure 3. Nine IFN- α /riba-induced genes that exhibited significant correlations between fold-induction and HIV-1 viral load reduction during IFN- α /riba therapy. Correlations between viral load reduction and fold-induction of each gene were assessed using the Pearson's r correlation coefficient.

Supplementary Figure 4.



Supplementary Figure 4. Comparison of the nine IFN- α /riba-induced genes that exhibited significant correlations between fold-induction and HIV-1 viral load reduction during IFN- α /riba therapy, between SHCS subjects during IFN- α /riba therapy and HIV-1-negative and HIV-1-infected (ART-untreated) viremic individuals enrolled in the SCOPE cohort. Mann-Whitney tests were employed to determine significance.

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