

Supplemental Materials

Supplemental Table S1. SIVkrc infection prevalence from HIV-2 Western blot and RT-qPCR.

	N	Prevalence (95% CI)
Males	21	52.6% (31.7%-72.7%)
Females	8	25% (7.1%-59.1%)
Total	29	41.4% (25.5%-59.3%)

Supplemental Table S2. Enriched GO Pathways for PC loadings of first four PCs.
FDR: False Discovery Rate.

PC	FDR	GO Pathway
PC1	1E-292	RNA Processing
	1E-284	Cellular protein localization
	4E-287	Cellular macromolecule localization
	1E-293	Single-organism organelle organization
PC2	1E-56	Ribonucleoprotein complex biogenesis
	1E-64	NcRNA processing
	5E-61	NcRNA metabolic process
	7E-49	Ribosome biogenesis
PC3	9E-19	Cotranslational protein targeting to membrane
	2E-21	SRP-dependent co-translational protein targeting
	2E-21	Protein targeting to ER
	5E-17	Protein localization to endoplasmic reticulum
	8E-20	Establishment of protein localization to endoplasm
PC4	9E-15	Viral Process
	4E-14	Multi-organism metabolic process
	2E-14	Symbiosis, encompassing mutualism
	2E-14	Interspecies interaction between organisms
	2E-14	Multi-organism cellular process

Supplemental Table S3A. Enriched GO pathways for clusters of genes identified by k-means clustering in uninfected individuals.

Uninfected			
Cluster	FDR	Genes	Pathways
A	1.30E-06	68	Immune response
	2.30E-06	56	Defense response
	7.30E-06	80	Immune system process
	7.30E-06	75	Cell surface receptor signaling pathway
	1.50E-05	35	Response to biotic stimulus
	1.80E-05	59	Response to external stimulus
	1.80E-05	19	Response to virus
	1.80E-05	33	Response to external biotic stimulus
	1.80E-05	71	Regulation of multicellular organismal process
	1.80E-05	16	Defense response to virus
	B	5.10E-10	40
5.40E-10		36	Angiogenesis
7.10E-10		42	Blood vessel development
7.10E-10		43	Vasculature development
7.10E-10		86	Movement of cell or subcellular component
9.80E-10		43	Cardiovascular system development
9.90E-10		157	System development
1.80E-09		26	Regulation of vasculature development
3.30E-09		53	Circulatory system development
6.30E-09		24	Regulation of angiogenesis
C	3.20E-42	187	Immune response
	1.20E-41	221	Immune system process
	2.70E-35	123	Immune effector process
	7.70E-35	91	Myeloid leukocyte activation
	7.70E-35	142	Secretion
	1.90E-33	93	Cell activation involved in immune response
	2.50E-33	133	Secretion by cell
	5.60E-33	92	Leukocyte activation involved in immune response
	6.20E-33	83	Myeloid leukocyte mediated immunity
1.00E-32	82	Leukocyte degranulation	
D	2.50E-06	33	Inflammatory response
	3.60E-05	78	Immune system process
	4.90E-05	72	Cell surface receptor signaling pathway
	6.50E-05	49	Locomotion
	8.10E-05	45	Cell activation
	1.50E-04	87	Regulation of response to stimulus

	1.50E-04	21	Leukocyte migration
	1.70E-04	54	Cell proliferation
	1.70E-04	51	Movement of cell or subcellular component
	1.70E-04	42	Cell motility
E	1.60E-10	38	Neutrophil activation involved in immune response
	1.60E-10	50	Exocytosis
	1.60E-10	38	Neutrophil activation
	1.60E-10	38	Neutrophil degranulation
	1.60E-10	47	Regulated exocytosis
	1.60E-10	38	Neutrophil mediated immunity
	1.60E-10	38	Granulocyte activation
	1.90E-10	39	Leukocyte degranulation
	2.40E-10	39	Myeloid cell activation involved in immune response
	2.60E-10	39	Myeloid leukocyte mediated immunity

Supplemental Table S3B. Enriched GO pathways for clusters of genes identified by k-means clustering in infected individuals.

Infected			
Cluster	FDR	# of Genes	Pathways
A	1.00E-22	65	Cell division
	3.30E-17	44	Chromosome segregation
	3.10E-16	74	Mitotic cell cycle
	5.50E-15	84	Cell cycle process
	6.10E-15	102	Cell cycle
	1.20E-14	64	Mitotic cell cycle process
	6.80E-14	32	Sister chromatid segregation
	1.70E-13	33	Mitotic nuclear division
	2.20E-13	36	Nuclear chromosome segregation
	2.90E-13	41	Nuclear division
B	2.10E-10	65	Homeostatic process
	2.10E-10	16	Iron ion homeostasis
	4.40E-09	11	Porphyrin-containing compound metabolic process
	2.00E-08	46	Chemical homeostasis
	2.00E-08	100	Regulation of biological quality
	2.60E-08	12	Tetrapyrrole metabolic process
	3.00E-08	16	Transition metal ion homeostasis
	3.70E-08	35	Inorganic ion homeostasis
	6.30E-08	40	Cellular homeostasis
	6.30E-08	36	Ion homeostasis
C	1.20E-40	120	Regulated exocytosis
	3.50E-40	174	Secretion
	9.00E-40	165	Secretion by cell
	4.20E-38	124	Exocytosis
	2.80E-37	106	Myeloid leukocyte activation
	1.70E-35	157	Cell activation
	1.20E-34	245	Immune system process
	1.30E-34	95	Leukocyte degranulation
	3.10E-34	95	Myeloid cell activation involved in immune response
	4.80E-34	95	Myeloid leukocyte mediated immunity
D	1.60E-16	134	Immune system process
	3.70E-14	118	Regulation of multicellular organismal process
	6.70E-12	50	Inflammatory response

6.70E-12	94	Response to external stimulus
6.90E-12	99	Immune response
2.30E-11	104	Regulation of localization
2.80E-11	112	Cell surface receptor signaling pathway
6.80E-11	26	B cell activation
7.10E-11	72	Cell activation
1.20E-10	59	Positive regulation of immune system process

Supplemental Table S4A. Enriched transcription factor binding motifs (and associated transcription factors and transcription factors families) in promoters of genes in gene clusters identified by k-means clustering in uninfected individuals.

Uninfected				
Cluster	TF Binding Motif	TF	TF family	FDR
B	TGTCAGGGGGC	INSM1	C2H2 ZF	3.30E-03
	GGGGCCCAAGGGGG	PLAG1	C2H2 ZF	3.30E-03
	CAGCTG	ASCL2	bHLH	7.00E-02
	GGGGGGGGGGCC	PATZ1	C2H2 ZF	7.00E-02
	GGGGATTCCCC	NFKB2	Rel	7.00E-02
	GGGGGGT	ZIC5	C2H2 ZF	7.00E-02
	CACAGCGGGGGGTC	ZIC4	C2H2 ZF	7.00E-02
	GTGGGCGTGG	SP8	C2H2 ZF	1.80E-01
	TTGGCACCGTGCCA	NFIX	SMAD	1.80E-01
	GCAGCTG	NHLH2	bHLH	1.80E-01
C	GGGGGGGGGGCC	PATZ1	C2H2 ZF	1.10E-02
	TTTCGCCTGGCACGTCA	ZBTB49	C2H2 ZF	1.10E-02
	TGTCAGGGGGC	INSM1	C2H2 ZF	1.20E-01
	TGCAGTG	ZBTB3	C2H2 ZF	1.80E-01
	GGGGATTCCCC	NFKB2	Rel	1.80E-01
D	GGGGATTCCCC	NFKB2	Rel	1.40E-01
	GGGGGGGGGGCC	PATZ1	C2H2 ZF	1.50E-01

Supplemental Table S4B. Enriched transcription factor binding motifs (and associated transcription factors and transcription factors families) in promoters of genes in gene clusters identified by k-means clustering in uninfected individuals.

Infected				
Cluster	TF Binding Motif	TF	TF family	FDR
A	GGGCGTG	KLF7	C2H2 ZF	1.30E-02
	GTGGGCGTGG	SP8	C2H2 ZF	1.30E-02
	TGCGGG	ZBTB1	C2H2 ZF	1.30E-02
	GGGGGGGGGCC	PATZ1	C2H2 ZF	1.70E-02
	GTGGGCGTGCC	SP6	C2H2 ZF	1.70E-02
	GGGGGCGGGGC	SP2	C2H2 ZF	2.50E-02
	GGCGGGAA	E2F4	E2F	4.10E-02
	GGGCGGGAA	E2F6	E2F	4.10E-02
	GCCAATCA	PBX3	Homeodomain	5.80E-02
	TAACGG	KLF9	C2H2 ZF	6.10E-02
	CACAGCGGGGGGTC	ZIC4	C2H2 ZF	6.50E-02
	GGCCGGAG	MBD2	MBD	9.80E-02
	TTTGCGCC	MYPOP	Myb/SANT	1.20E-01
	GGGGGGT	ZIC5	C2H2 ZF	1.50E-01
	CAATAGCGGTGGTG	ZBTB4	C2H2 ZF	1.80E-01
	TGTCAGGGGGC	INSM1	C2H2 ZF	1.80E-01
B	GGGGGGGGGCC	PATZ1	C2H2 ZF	2.50E-02
	TTTCGCCTGGCACGTCA	ZBTB49	C2H2 ZF	2.50E-02
	TGTCAGGGGGC	INSM1	C2H2 ZF	3.50E-02
	GGGCGTG	KLF7	C2H2 ZF	6.20E-02
	GGGGGCGGGGC	SP2	C2H2 ZF	1.40E-01
	GGCCGGAG	MBD2	MBD	1.80E-01
	GGGGCCCAAGGGGG	PLAG1	C2H2 ZF	2.40E-01
	TGCAGTG	ZBTB3	C2H2 ZF	2.40E-01
	TTTGCGCC	MYPOP	Myb/SANT	2.40E-01
C	GGGGGGGGGCC	PATZ1	C2H2 ZF	5.80E-03
	TGTCAGGGGGC	INSM1	C2H2 ZF	2.30E-02
	GGGGCCCAAGGGGG	PLAG1	C2H2 ZF	2.30E-02
	GCAGCTG	NHLH2	bHLH	1.00E-01
	GGGGGCGGGGC	SP2	C2H2 ZF	1.10E-01

CAGCTG	ASCL2	bHLH	1.10E-01
CGCAGCTGCG	NHLH1	bHLH	1.10E-01
CACAGCGGGGGGTC	ZIC4	C2H2 ZF	1.10E-01
GGGCGTG	KLF7	C2H2 ZF	1.30E-01
GTGGGCGTGG	SP8	C2H2 ZF	1.30E-01
GGGGATTCCCC	NFKB2	Rel	1.30E-01
GGGGGGT	ZIC5	C2H2 ZF	1.30E-01
GTAACAGCTG	FERD3L	bHLH	1.30E-01

Supplemental Table S5. Enriched GO pathways for weighted gene co-expression networks in uninfected and infected individuals.

Uninfected		
GO Pathway	Genes	FDR
Immune system process	810	3.50E-77
Cell activation	460	1.50E-66
Response to external stimulus	577	4.80E-61
Leukocyte activation	403	3.00E-56
Immune response	592	3.10E-53
Immune effector process	374	1.50E-51
Secretion	453	7.00E-51
Secretion by cell	424	9.70E-50
Inflammatory response	255	5.30E-45
Regulated exocytosis	265	4.00E-43
Exocytosis	289	5.80E-43
Regulation of multicellular organismal process	646	5.80E-43
Cellular response to chemical stimulus	690	5.80E-43
Cell surface receptor signaling pathway	658	2.60E-42
Regulation of response to stimulus	832	1.50E-41
Infected		
Immune system process	806	2.90E-75
Cell activation	460	2.40E-66
Leukocyte activation	406	2.10E-57
Immune effector process	378	3.90E-53
Immune response	585	2.10E-50
Response to external stimulus	548	1.20E-49
Secretion	449	4.90E-49
Secretion by cell	419	1.90E-47
Regulation of response to stimulus	845	8.30E-45
Cell activation involved in immune response	256	2.60E-44
Leukocyte activation involved in immune response	254	9.60E-44
Regulated exocytosis	265	4.30E-43
Cellular response to chemical stimulus	689	2.00E-42
Regulation of multicellular organismal process	643	8.00E-42
Myeloid leukocyte activation	236	2.90E-41

Supplemental Table S6. Differentially expressed gene lists for infected vs. uninfected individuals, controlling for sex and RIN score.

Model: ~sex+RIN+Infection (Fold changes relative to uninfected baseline)			
Symbol	Q value	log2 Fold Change	Ensembl ID
CD4	3.24E-05	-1.58	ENSG00000010610
DGKG	2.04E-04	0.81	ENSG00000058866
CTSA	1.39E-03	0.48	ENSG00000064601
GPIHBP1	1.39E-03	0.95	ENSG00000277494
AATK	3.04E-03	1.00	ENSG00000181409
ACSS2	8.19E-03	0.57	ENSG00000131069
SLC6A6	8.19E-03	0.43	ENSG00000131389
TPCN2	8.19E-03	0.60	ENSG00000162341
MGAM	8.19E-03	0.55	ENSG00000257335
CCDC93	5.27E-02	0.24	ENSG00000125633
ARHGAP25	5.91E-02	0.42	ENSG00000163219
ABHD2	6.66E-02	0.55	ENSG00000140526
YTHDC2	7.52E-02	-0.47	ENSG00000047188
BCL2L13	7.79E-02	0.31	ENSG00000099968
TGIF2	7.79E-02	-0.40	ENSG00000118707
TNNI2	7.79E-02	0.91	ENSG00000130598
ANAPC5	7.98E-02	0.21	ENSG00000089053
ECE1	7.98E-02	0.33	ENSG00000117298
CCDC189	7.98E-02	0.90	ENSG00000196118
SRXN1	7.98E-02	0.40	ENSG00000271303
VPS25	9.08E-02	0.34	ENSG00000131475
TBC1D14	9.74E-02	0.43	ENSG00000132405
SLC11A1	1.10E-01	0.72	ENSG00000018280
CD93	1.13E-01	0.67	ENSG00000125810
IGF1R	1.20E-01	0.45	ENSG00000140443
LRRC27	1.22E-01	0.72	ENSG00000148814
SLAMF6	1.25E-01	-0.39	ENSG00000162739
TM6SF1	1.26E-01	0.31	ENSG00000136404
SDC2	1.26E-01	1.98	ENSG00000169439
DENND3	1.29E-01	0.35	ENSG00000105339
GAB2	1.33E-01	0.47	ENSG00000033327

NINJ1	1.40E-01	0.42	ENSG00000131669
CD101	1.40E-01	0.96	ENSG00000134256
PTX4	1.49E-01	0.70	ENSG00000251692
DDX3Y	1.61E-01	4.96	ENSG00000067048
SLC25A16	1.69E-01	1.02	ENSG00000122912
KBTBD11	1.74E-01	0.96	ENSG00000176595
FES	1.74E-01	0.45	ENSG00000182511
TBXA2R	1.75E-01	-1.74	ENSG00000006638
CADM3	1.76E-01	1.32	ENSG00000162706
ADPGK	1.77E-01	0.40	ENSG00000159322
ARHGEF40	1.79E-01	0.91	ENSG00000165801
STAG3	1.81E-01	-0.26	ENSG00000066923
SGK1	1.81E-01	0.62	ENSG00000118515
ADAM33	1.81E-01	0.90	ENSG00000149451
CALM1	1.81E-01	-0.23	ENSG00000198668
MAPKAPK5	1.86E-01	0.32	ENSG00000089022
GIT2	1.86E-01	0.23	ENSG00000139436
KIF13A	1.88E-01	0.66	ENSG00000137177
SMCR8	1.95E-01	0.32	ENSG00000176994
TCN2	1.95E-01	0.96	ENSG00000185339
TFB2M	2.00E-01	-0.29	ENSG00000162851
CLEC7A	2.00E-01	0.43	ENSG00000172243

Supplemental Table S7. Full results of GO analysis.

Up		Down	
<i>Top Enriched GO Term</i>	<i>Corrected GO P Value</i>	<i>Top Enriched GO Term</i>	<i>Corrected GO P Value</i>
cellular metabolic process	8.09E-09	positive regulation of biological process	4.65E-04
vesicle-mediated transport	3.70E-07	positive regulation of cytosolic calcium ion-concentration	4.99E-03
regulation of catalytic activity	7.49E-07		
biological regulation	8.45E-07		
response to stimulus	1.19E-06		
regulation of biological process	1.53E-06		
positive regulation of molecular function	1.56E-06		
regulation of molecular function	4.98E-06		
transport	6.19E-06		
positive regulation of catalytic activity	7.76E-06		
establishment of localization	8.57E-06		
organonitrogen compound metabolic process	3.12E-05		
organic substance metabolic process	4.03E-05		
catabolic process	7.83E-05		
regulation of cellular process	8.50E-05		
primary metabolic process	1.04E-04		
signaling	2.52E-04		
phosphorylation	3.71E-04		
signal transduction	4.10E-04		
protein metabolic process	4.52E-04		
cellular catabolic process	1.07E-03		
cellular response to stimulus	1.44E-03		
cell communication	1.47E-03		
positive regulation of hydrolase activity	1.66E-03		
establishment of localization in cell	1.67E-03		
phosphorus metabolic process	2.42E-03		
cellular protein metabolic	2.60E-03		

process	
regulated exocytosis	3.43E-03
cellular component organization	3.59E-03
intracellular transport	3.72E-03
nitrogen compound metabolic process	4.69E-03

Supplemental Table S8. CIBERSORT output for relative immune cell proportions.

Sample	Sex	Mem B	CD8	naive CD4+	Mem rest CD4+	Mem act CD4+	rest NK	Monocytes	Macrophages	Neutrophils
RC108	F	0.10	0.31	0.00	0.04	0.10	0.17	0.08	0.06	0.15
RC109	F	0.16	0.25	0.00	0.00	0.13	0.21	0.09	0.05	0.10
RC111	F	0.08	0.34	0.00	0.09	0.12	0.18	0.06	0.04	0.09
RC124	F	0.11	0.31	0.04	0.00	0.07	0.25	0.11	0.02	0.08
RC125	F	0.08	0.27	0.00	0.05	0.10	0.25	0.08	0.02	0.15
RC127	F	0.09	0.27	0.04	0.04	0.08	0.14	0.08	0.04	0.22
RC128	F	0.13	0.26	0.00	0.05	0.08	0.18	0.06	0.04	0.19
RC130	F	0.17	0.30	0.00	0.07	0.09	0.28	0.05	0.02	0.01
RC100	M	0.08	0.36	0.00	0.00	0.08	0.26	0.10	0.04	0.07
RC101	M	0.10	0.25	0.01	0.00	0.14	0.21	0.07	0.03	0.19
RC102	M	0.13	0.40	0.02	0.00	0.08	0.22	0.04	0.01	0.09
RC103	M	0.04	0.37	0.00	0.04	0.12	0.21	0.08	0.03	0.12
RC104	M	0.08	0.39	0.03	0.00	0.10	0.17	0.08	0.03	0.09
RC105	M	0.12	0.34	0.13	0.00	0.10	0.18	0.06	0.02	0.05
RC106	M	0.10	0.43	0.01	0.00	0.10	0.21	0.06	0.03	0.06
RC107	M	0.08	0.46	0.00	0.01	0.09	0.22	0.04	0.02	0.08
RC110	M	0.08	0.32	0.00	0.01	0.12	0.17	0.05	0.08	0.15
RC112	M	0.06	0.20	0.06	0.05	0.10	0.22	0.05	0.04	0.21
RC115	M	0.09	0.19	0.00	0.06	0.17	0.25	0.05	0.03	0.15
RC116	M	0.05	0.30	0.00	0.00	0.11	0.22	0.07	0.07	0.17
RC117	M	0.06	0.22	0.07	0.01	0.14	0.19	0.10	0.06	0.15
RC118	M	0.12	0.21	0.03	0.15	0.05	0.12	0.08	0.06	0.17
RC119	M	0.06	0.37	0.00	0.00	0.13	0.19	0.08	0.03	0.14
RC120	M	0.11	0.32	0.07	0.00	0.08	0.22	0.07	0.02	0.10
RC121	M	0.09	0.23	0.10	0.00	0.14	0.23	0.04	0.07	0.08
RC122	M	0.10	0.36	0.00	0.07	0.10	0.19	0.04	0.04	0.09
RC123	M	0.14	0.13	0.00	0.07	0.08	0.18	0.09	0.09	0.21
RC126	M	0.07	0.23	0.02	0.00	0.10	0.21	0.06	0.03	0.29
RC129	M	0.23	0.18	0.03	0.00	0.07	0.15	0.08	0.03	0.22
Average		0.10	0.30	0.02	0.03	0.10	0.20	0.07	0.04	0.13

Supplemental Figure S1. (Above) Cluster (k) selection for k-means clustering based on the elbow method. (Below) t-SNE maps for infected and uninfected individuals based on the number of clusters.

