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## Supplementary Materials for

### **Allele-specific long-distance regulation dictates IL-32 isoform switching and mediates susceptibility to HIV-1**

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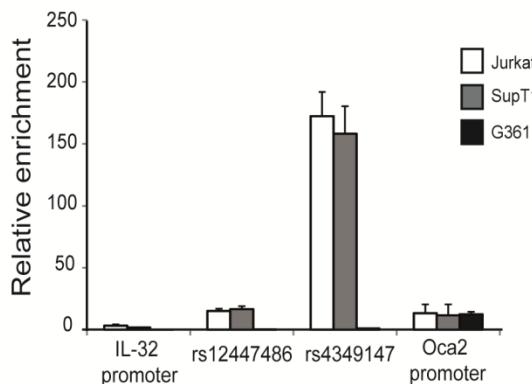
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# Supplementary Figure 1.

A



B

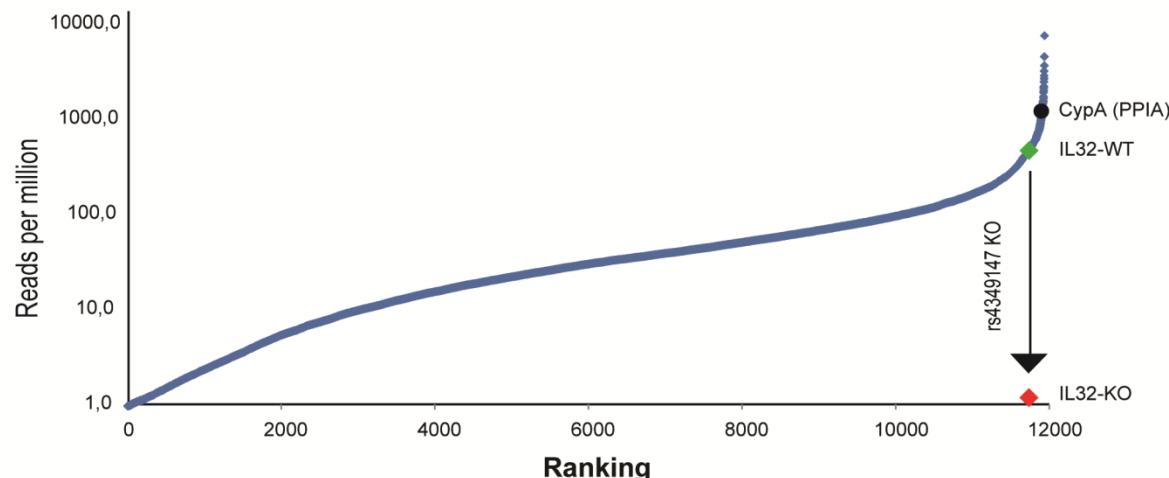
KO -/- WT G/A

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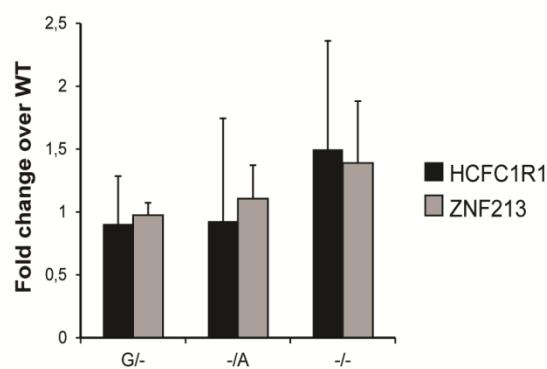
1      AAAAAA.....AGAGACAGAAAAGAAAGTTGGGGCC..... rs12598118 C/T
1      AAAAAA.....AGAGACRAAAAAAGAAAAGTTGGGGCCYGGGCTGGATGRAGCTTGAGGG rs4349147 G/A
38
61  GCTGTGGGCCCTGGCATGGGGCTGAGGGGAGTGCGAGGAGCTGCCTGCCAAAGCCTGGGG
38
121 CAAGGATGATAGGAGGTGCTGGGGCCCCTGTTGACTGCCCTCTGAGAAATCTCGTGAGGCT
38
181 GGGCTGACAGCTGGTIGTGTGIAACTTCCCCAGATGATGGTGTGACAAGGGTGCAG
38
241 GAAGGGGTGCAGGGCCCGAAGCTCAGTGTGGTAAAGASATGCAAGGCAGGGATAGAAGG rs4786376 G/C
38
301 TGAGAGATGAATGATATGCCGTGATCAAAYACCAAACITCAGTTTCAGAAAAAGGA rs12917910 C/T
38
361 CTAGAGCAACAGAGAACCTACAGTCACAAAGGACATTCACTAGCGCACATGTGAATTG
38
421 AGCAAGACCATTGAAGGCCCTGCTGAACGGCAAGCTGGCAGAGCCAGGGTACCTGGCCAT
76  CTACCTTGAAGTCTCTGTGCTCAGTTCCCTCTGTAAAAATGGACATA
481 CTACCTTGAAGTCTCTGTGCTCAGTTCCCTCTGTAAAAATGGACATA

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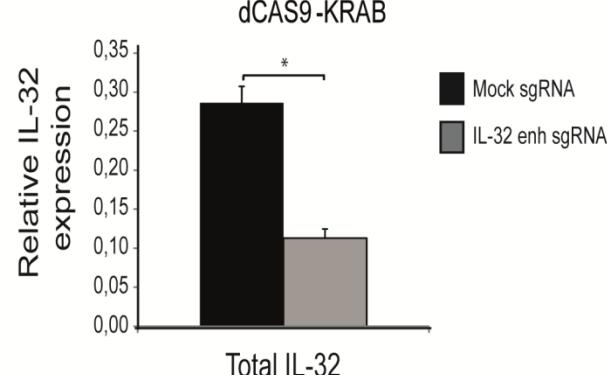
C



D



E

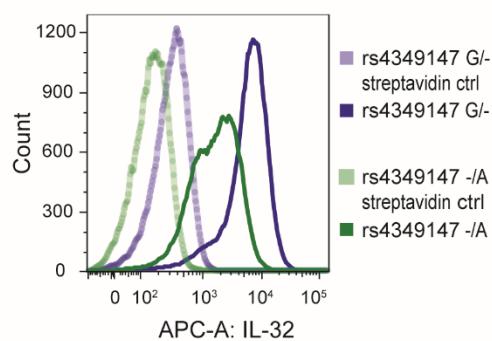


**fig. S1. Characterization of the rs4349147 DHS and the rs4349147 KO clone.** (A) FAIRE analysis of the region surrounding rs4349147 demonstrates significant increase in DNA accessibility indicating this region is depleted of histones and accessible in the T cell derived cell lines Jurkat and SupT1 but not in the melanoma cell line G361. By comparison, control regions rs12447486 and the melanocyte specific Oca2 promoter are less accessible as shown in the FAIRE analysis. (B) Sequencing of PCR

amplicon 1 (see figure 1B) spanning the rs4349147 DHS KO(-/-) line depicts the region deleted using Crispr/CAS9. Top sequence is obtained from the IL-32 rs4349147 DHS KO(-/-) cells; bottom sequence is obtained from the WT(G/A) cells. Sequence of the sgRNA's are indicated by boldface font and underlined. Position of variants is indicated. **(C)** Reads per million of all genes expressed above 1 read per million are ranked in ascending order. In WT(G/A) Jurkat cells IL-32 expression is among the top 5% of highly expressed genes (green diamond). Upon deletion of the rs4349147 regulatory element IL-32 expression drops to the lowest 2% of expressed genes (red diamond). The CypA gene is indicated as reference (black dot). **(D)** Real-time pcr confirmation of invariable expression of surrounding genes. **(E)** Targeting of a dCAS9-KRAB domain fusion to the rs4349147 region in wild type Jurkat cells results in reduced IL-32 expression.

## Supplementary Figure 2.

A



B

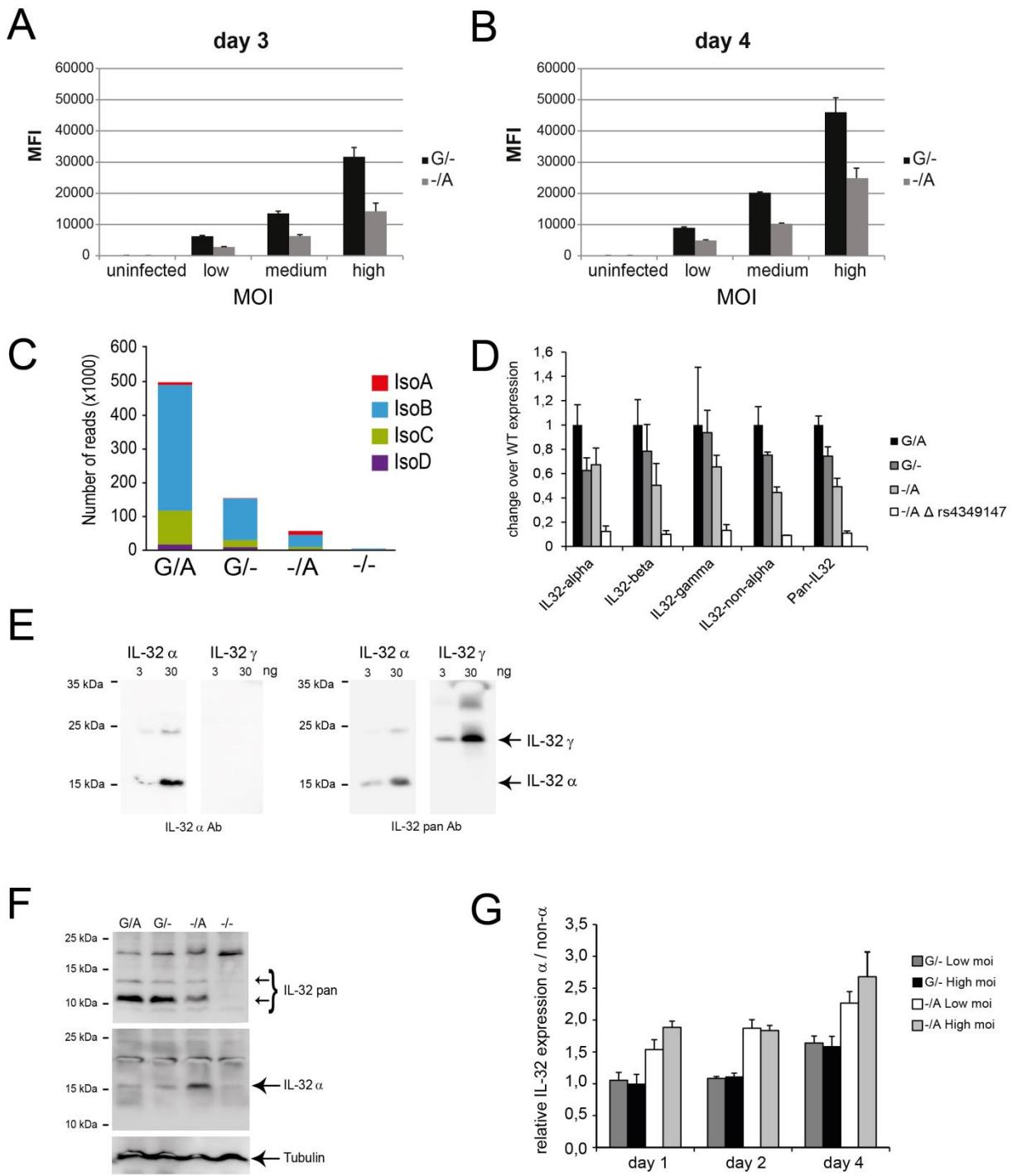
-/A Δ rs4349147	1	AAAAAAAAAAAAAGAGACAGAAAAGAAAGTTGGGG.....	rs12598118-C
-/A	1	AAAAAAAAAAAAAGAGACAGAAAAGAAAGTTGGGGC <span style="color:red">C</span> GGGGCTGGATGA <span style="color:magenta">A</span> AGCTTGAGG	rs4349147-A
	37	.....	
	61	GGCTGTGGCCTGGCATGGGCTGAGGGAGTGTGCAGGAGCTGCCTGCCAAGCCTGG	
	37	.....	
	121	GCAAGGATGATAGGAGGTGCTGGGCCCCTGTGGACTGCCCTTGAGAATCTCGTGAGGC	
	37	.....GTGGTTGTGTAACTTCCCCAGATGCATGGTGTGACAAGGGTGCAG	
	181	TGGGTCTGCACAGCTGTGGTTGTGTAACTTCCCCAGATGCATGGTGTGACAAGGGTGCAG	
	82	GAAGGGGTGCAGGGCCCGGAAGCTCAGTGTGGTAAAGACATGCAAGGCAGGATAGAAGG	rs4786376-C
	241	GAAGGGGTGCAGGGCCCGGAAGCTCAGTGTGGTAAAGACATGCAAGGCAGGATAGAAGG	
	142	TGAGAGATGAATGATATGCCGTGATCAAAACACCAAACCTCAGTTCTCAGAAAAGGA	rs12917910-C
	301	TGAGAGATGAATGATATGCCGTGATCAAAACACCAAACCTCAGTTCTCAGAAAAGGA	

**fig. S2. Characterization of the rs4349147 G/–, rs4349147 –/A, and –/A Δrs4349147 clones. (A)**

Intracellular staining with biotin-conjugated antibody against IL-32 followed by FACS analysis

rs4349147 –/A Jurkat cells and rs4349147 G/– Jurkat cells. Streptavidin-APC only staining is shown to demonstrate specificity. **(B)** Sequencing of PCR amplicon 1 (see figure 1B) spanning the rs4349147 DHS demonstrates the 158bp deletion in the –/A Δrs4349147 clone. Top sequence is obtained from the –/A Δrs4349147 clone; bottom sequence is obtained from the parental rs4349147 –/A cells. Position of variants is indicated.

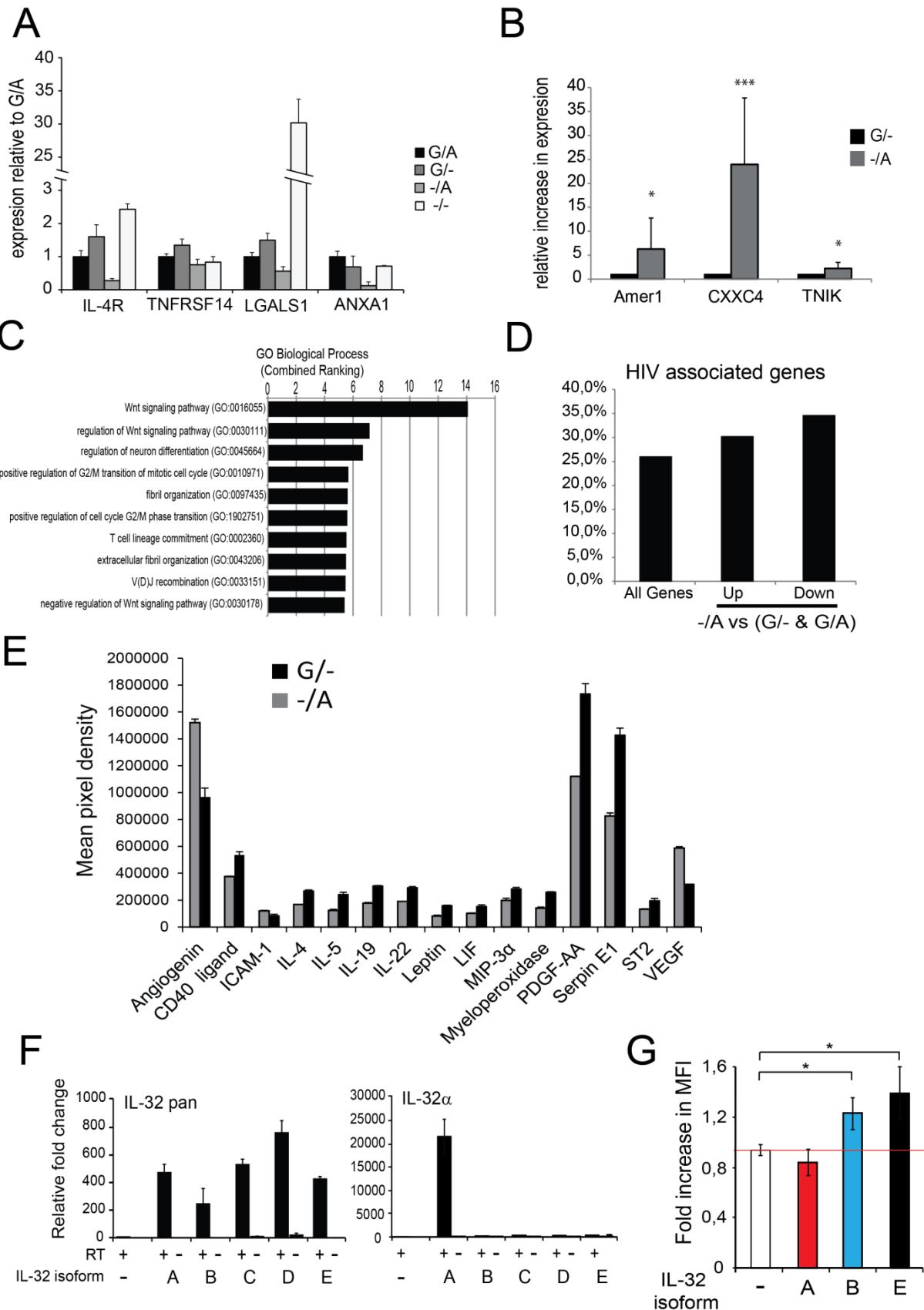
## Supplementary Figure 3.



**fig. S3. HIV infectability and differential expression of IL-32 isoforms between WT, rs4349147 G/-, and rs4349147 -/A clonal Jurkat cell lines.** (A, B) Difference in sensitivity to HIV infection between the rs4349147 -/A and rs4349147 G/- Jurkat cells is independent of MOI and time frame. (A) depicts MFI three days after infection using different MOI and (B) depicts MFI four days after infection using different MOI. Low MOI corresponds to ~20% GFP positive cells, medium MOI to ~50% GFP positive cells and High to ~80% GFP positive cells. (C) IL-32 isoform A expression is relatively elevated in

rs4349147 -/A cells as compared to rs4349147 G/- or WT(G/A) cells. Bar charts show the number of reads for each isoform in the high throughput RNA sequencing analysis (**D**) Relative expression of the IL-32 $\alpha$ , IL-32 $\beta$  and IL-32 $\gamma$  in WT, rs4349147 -/A, rs4349147 G/- and the -/A Δrs4349147 Jurkat cells. The primer pair for IL-32 $\beta$  only recognizes the “short” Var3 isoform originating from the EPD IL32\_1 promoter. (**E**) Determination of specificity of commercial anti-pan IL-32 and anti-IL-32 $\alpha$ -specific antibodies as indicated. Western blot analysis of 3 and 30 ng each of recombinant IL-32 $\alpha$  and IL-32 $\gamma$  protein is shown. (**F**) Western blot analysis using a pan-IL-32 antibody and an antibody specific to IL-32 $\alpha$  in the rs4349147 G/A, G/-, -/A and -/- Jurkat clones. (**G**) The increased ratio of IL-32 $\alpha$  over non- $\alpha$  IL-32 isoforms does not change after infection and is independent of the MOI of infection. Low MOI corresponds to ~20% GFP positive cells and High to ~80% GFP positive cells.

## Supplementary Figure 4.

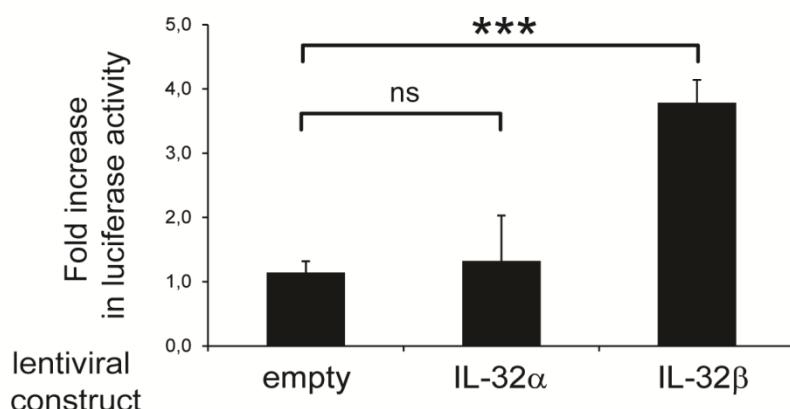


**fig. S4. Analysis of genes that are at least twofold differentially expressed in rs4349147 -/A compared to rs4349147 G/- and WT clonal Jurkat cell lines.** (A) Expression of a selection of genes downregulated between rs4349147 -/A and rs4349147 G/- as well as WT(G/A) clonal Jurkat cell lines

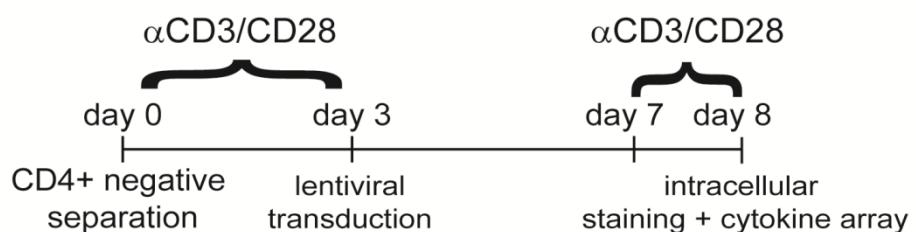
IL-4R, TNFRSF14, LGALS1, and ANXA1 in WT, rs4349147 -/A, rs4349147 G/- and KO Jurkat cells. **(B)** RT-PCR confirmation of a selection of genes upregulated between rs4349147 -/A and rs4349147 G/- as well as WT clonal Jurkat cell lines. **(C)** GO biological process analysis of genes upregulated between rs4349147 -/A and rs4349147 G/- as well as WT clonal Jurkat cell lines. A significant enrichment for factors involved in Wnt signaling and a slight enrichment for factors involved in neuron differentiation is found. **(D)** HIV associated genes, here defined as previously shown to interact with HIV either genetically or via protein-protein interaction (from HIV-1 Human Interaction Database; [www.ncbi.nlm.nih.gov/genome/viruses/retroviruses/hiv-1/interactions/](http://www.ncbi.nlm.nih.gov/genome/viruses/retroviruses/hiv-1/interactions/)) are overrepresented in the downregulated genes when compared to all genes (> 1rpm in Jurkats) and upregulated genes. **(E)** Mean pixel identity as measured by Proteome Profiler Human XL Cytokine Array Kit (R&D systems) in supernatant of rs4349147 -/A Jurkat cells and rs4349147 G/- Jurkat cells. **(F)** RT-PCR confirmation of exogenous expression of distinct IL-32 isoforms in rs4349147 enhancer KO Jurkat cells following nucleofection. Left panel shows IL-32 mRNA expression using PCR primers that detect all isoforms of IL-32. Right panel demonstrates mRNA expression of the IL-32 $\alpha$  isoform using PCR primers that specifically amplify the IL-32 $\alpha$  transcript. **(G)** Levels of infection, measured as fold increase in the MFI, following exogenous expression of IL-32 isoforms A, B, and E in WT Jurkat cells. Color coding is as for Fig. 3h.

## Supplementary Figure 5.

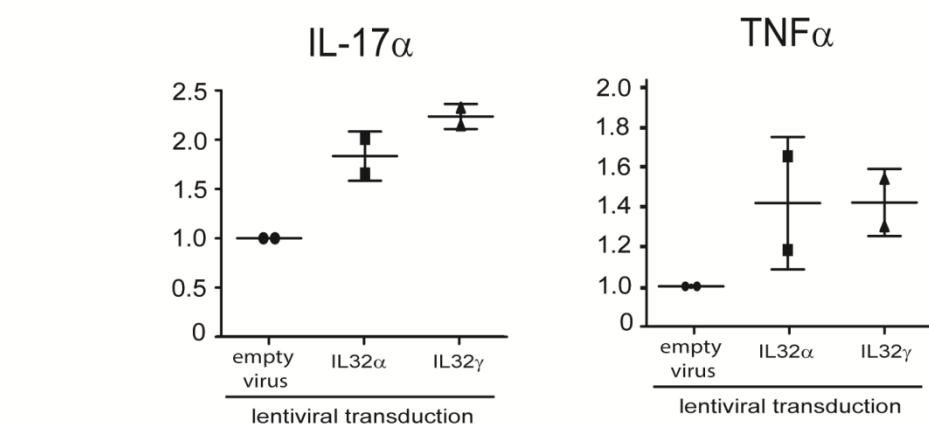
A



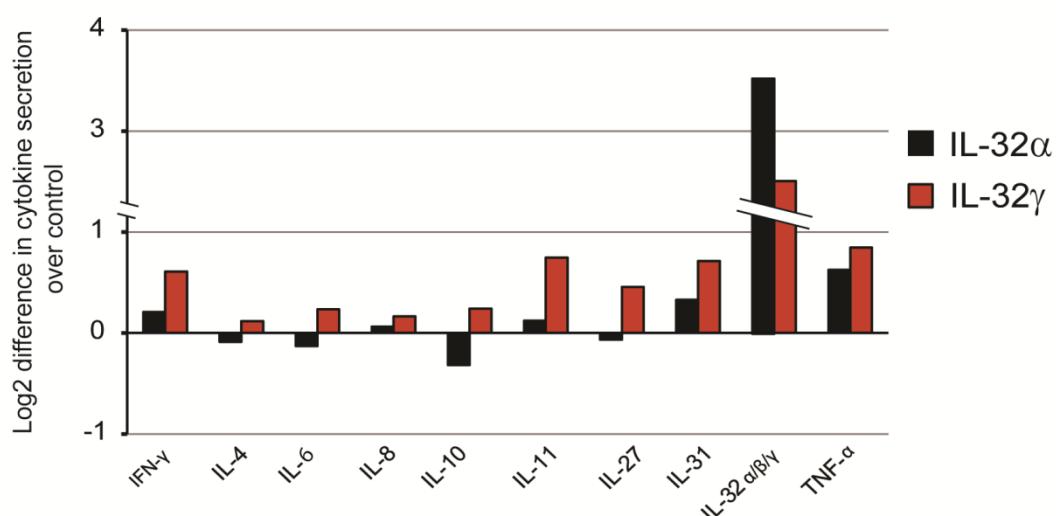
B



C

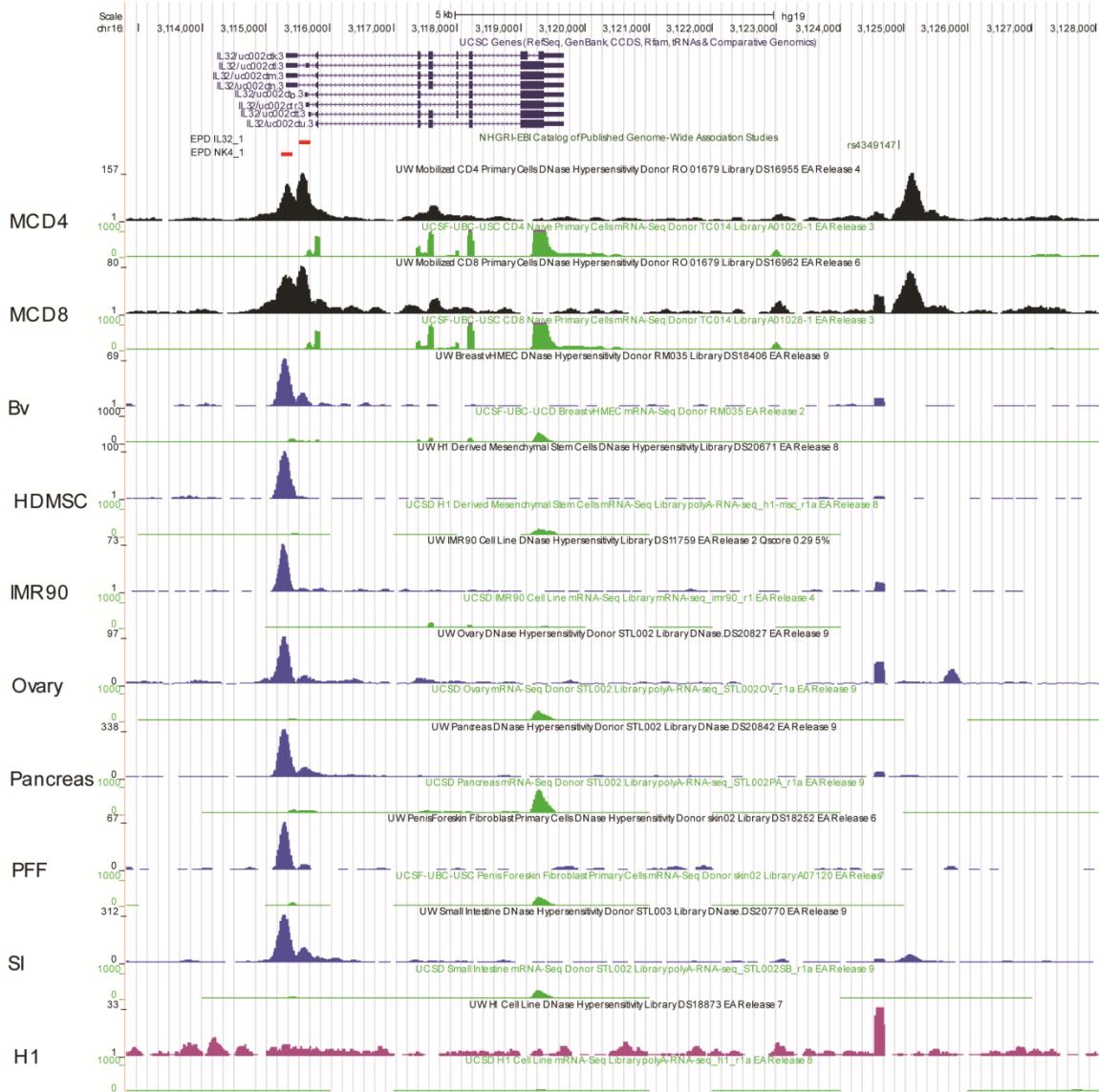


D



**fig. S5. Endogenous lentiviral overexpression of IL-32 isoforms in CD4<sup>+</sup> cells results in altered HIV susceptibility and proinflammatory cytokine expression.** (A) Exogenous lentiviral overexpression of IL-32 $\beta$  results in an increase in HIV infection as compared to CD4 $+$  T cells overexpressing IL-32 $\alpha$  or control cells infected with an empty lentiviral construct. (B) CD4 $+$  T cells isolated from two healthy donors were stimulated with CD3-CD28 coated beads and infected with a control lentiviral vector or a lentiviral vector expressing IL-32 $\alpha$  or IL-32 $\gamma$ . After 4 days the cells were re-stimulated for 24h and cytokine levels were determined by intracellular staining or measured using the Proteome Profiler Human XL Cytokine Array Kit (R&D systems) (C) Frequency of IFN $\gamma$  or TNF $\alpha$ -producing live (Annexin V-negative) purified CD4 $+$  T cells are shown from two different donors. Percentage indicate cytokine positive populations. (D) Cytokine secretion as measured by Proteome Profiler Human XL Cytokine Array Kit (R&D systems) demonstrates increased secretion of pro-inflammatory cytokines in the supernatant of CD4 $+$ T cells exogenously overexpressing IL-32 $\gamma$  as compared to CD4 $+$  T cells that overexpress IL-32 $\alpha$ . Values depicted are log2 fold increase of IL-32 $\alpha$  (black bars) or IL-32 $\gamma$  (red bars) overexpressing cells over control cells. Note that robust overexpression of IL-32 in IL32 $\alpha$  and IL-32 $\gamma$  lentiviral infected CD4 $+$  cells is evident.

## Supplementary Figure 6.



**fig. S6. UCSC genome browser graphic of DNase I hypersensitivity (upper track, black, blue, purple) and mRNA sequencing (lower track, green) data obtained from the Human Epigenome Atlas.** In T-cells, which express high levels of IL-32 (green tracks), a DNasel HS peak (black tracks) is present at the location of rs4349147 and a double DNasel HS peak is present at the IL-32 promoter region indicating the presence of two separate promoters for IL-32. In cell types that lack a DNasel HS peak at the location of rs4349147 (blue tracks) but still express low levels of IL-32 (corresponding green tracks) a single DNasel HS peak is present at the IL-32 promoter for the long IL-32 transcripts. In H1 human ES cells no DNasel HS peaks are detected in the IL-32 locus and the IL-32 gene is not expressed. mRNA-seq tracks are delimited to 1000 to emphasize differences in expression levels, while DNasel HS tracks are not delimited to emphasize IL-32 promoter region peaks. <http://www.genboree.org/epigenomeatlas/index.rhtml>. Promoters as defined by the Eukaryotic Promoter Database (EPD; <http://epd.vital-it.ch>) are indicated as red bars.

**table S1. Overview of SNPs.**

SNP	Celltype	Chromosome	start	end
rs2796163	Th0;Th1	chr1	234978473	234979377
rs2802978	Th1	chr1	234978473	234979377
rs62000984	Th0;Th1	chr6	26017665	26018290
rs41266783	Th0;Th1	chr6	26031942	26032652
rs2230654	Th0;Th1	chr6	26033518	26034104
rs11751732	Th0;Th1	chr6	26043567	26044256
rs9468842	Th0;Th1	chr6	30851403	30854679
rs6901464	Th0;Th1	chr6	30851403	30854679
rs1049622	Th1	chr6	30858647	30859161
rs1049628	Th1	chr6	30866998	30867470
rs2074510	Th0;Th1	chr6	30875522	30876336
rs1052693	Th0;Th1	chr6	30875522	30876336
rs3828917	Th0;Th1	chr6	31465194	31466193
rs3093661	Th1	chr6	31542110	31543783
rs9368699	Th0;Th1	chr6	31802108	31803075
rs8192583	Th0;Th1	chr6	32162969	32164095
rs6990319	Th0;Th1	chr8	66862573	66863027
rs11998618	Th0	chr8	66858410	66858738
rs12447486	Th0;Th1	chr16	3121836	3123558
rs4349147	Th0;Th1	chr16	3124834	3125437
rs2015620	Th0	chr16	3123504	3123607
GRCh37/hg19	assembly			

**table S2. List of differentially regulated genes.**

GENE	WT (RPM)	G/- (RPM)	-/A (RPM)	-/- (RPM)
OR3A2	1,9237	1,4648	0,0000	0,2341
RTP4	0,8630	1,2101	0,0000	0,8993
CARNS1	0,9448	0,5732	0,0000	0,9532
TNS3	0,8009	0,3821	0,0000	0,3086
NIPSNAP3B	0,6478	0,3821	0,0000	0,7406
LGR6	0,5721	0,3821	0,0000	0,2341
GCSAML	0,7887	0,2548	0,0000	0,6926
LRRTM2	0,6880	0,1911	0,0000	0,3938
ZP1	0,8630	0,1274	0,0000	0,2929
CRISPLD1	0,7266	0,0637	0,0000	0,0000
ZCCHC16	0,7206	0,0637	0,0000	0,2929
DPP6	0,6819	0,0637	0,0000	1,2676
ANO9	3,5611	4,0761	0,0622	4,0703
LARGE	3,6491	2,9297	0,0622	3,0995
FAAH2	1,3979	2,6112	0,0622	3,8195
ZNF697	2,5314	3,4392	0,1244	1,9113
C10orf107	6,5094	8,0885	0,3111	14,7982
GPR158	12,6412	7,7064	0,3111	0,3517
TMEM151B	2,0996	2,8023	0,1244	8,8842
ANGPTL6	1,2169	2,0380	0,1244	2,2473
GBGT1	2,2579	1,7833	0,1244	2,5137
TUBA4A	16,4543	31,9081	2,2399	19,5230
TMOD1	1,8556	1,5922	0,1244	1,9808
F2RL2	5,2113	6,7510	0,5600	2,6107
PIANP	4,3288	4,1398	0,3733	3,9537
FXYD2	4,7035	0,6369	0,0622	4,3849
GCA	3,5505	0,6369	0,0622	2,1630
<b>ANXA1</b>	<b>232,6092</b>	<b>158,1394</b>	<b>15,8040</b>	<b>113,4199</b>
PYGL	8,5059	3,6940	0,3733	11,2002
ATP2B2	3,3594	0,5732	0,0622	7,5129
ITGA6	8,0081	26,3035	2,8621	12,5178
GZMA	37,1217	19,3614	2,1155	37,1296
UBXN10	5,5305	8,8528	0,9955	12,4539
LSP1	2,9489	3,1844	0,3733	1,8485
PTCRA	1,6450	1,0190	0,1244	0,8092
<b>TNFRSF14</b>	<b>9,9424</b>	<b>12,4193</b>	<b>1,6177</b>	<b>11,6105</b>
SLC25A21	1,5866	1,4012	0,1867	1,8270
SIGLEC6	5,6690	2,2928	0,3111	1,3156
ITGB2-AS1	5,5804	10,8908	1,4933	5,7023
PCBP3	3,9832	3,6303	0,4978	18,6150
BCAM	1,3267	1,3375	0,1867	1,6673
GPR68	2,7633	2,9934	0,4355	4,4210
GSTM3	37,5542	22,9917	3,3599	18,8696
BST2	44,9524	104,5134	15,3685	66,2490

IER3	8,4907	7,7700	1,1822	5,5692
TRPM2	5,8159	6,4326	0,9955	10,6309
<b>STAT5A</b>	13,3907	17,6418	2,8621	6,8289
LOC90246	1,7427	1,1464	0,1867	0,5114
SMAP1	31,5560	21,7179	3,7955	27,1142
PI16	29,3594	49,1678	8,6487	11,7409
GFRA3	2,1927	2,1017	0,3733	1,3205
CRIM1	1,5820	0,7006	0,1244	1,0972
CD69	12,0947	12,2283	2,2399	12,0202
CTSW	36,0529	52,0338	9,5820	101,1831
EFNB3	3,6847	2,2928	0,4355	2,0768
PLCH1	21,9898	19,9346	3,9821	19,4173
CST7	26,6965	26,3035	5,3510	117,9958
PLEK	54,0085	14,5211	2,9866	106,6130
GNLY	4,6648	0,8916	0,1867	18,0264
PRKCH	198,9677	305,3880	64,2116	196,0620
ADCYAP1	20,7476	20,2531	4,2932	4,2035
CD300A	2,4352	0,5732	0,1244	0,4369
PDE9A	6,0229	8,4069	1,8666	4,0478
IFI35	12,2411	13,6931	3,0488	16,1884
USP40	17,5236	25,5392	5,7243	19,9463
GAS7	94,4084	139,4786	32,3547	101,6567
HECW1	7,2178	2,6749	0,6222	1,8535
LPCAT2	10,7652	10,8908	2,6133	17,6029
<b>LGALS1</b>	63,0176	4,9040	1,1822	107,6043
AKAP7	4,4551	2,8023	0,6844	4,2487
DENND2D	3,8718	3,5666	0,8711	3,7715
SMPD3	3,1254	1,7196	0,4355	0,5701
C16orf74	2,3966	2,4202	0,6222	8,1015
PCCA	11,8957	13,7568	3,5466	14,7032
TNFSF10	14,1815	15,0306	3,9199	21,9496
TDRD9	35,7427	21,4631	5,6621	28,5570
EGR1	10,0812	8,0248	2,1777	11,5017
C19orf59	1,9435	0,8916	0,2489	1,3156
LAIR1	109,1083	81,8402	23,3327	75,0209
LST1	6,2562	5,1588	1,4933	4,6297
SLC2A3	15,1188	13,6294	3,9821	9,4554
KLHL29	20,2388	24,3928	7,1554	40,9360
<b>IL4R</b>	8,4943	11,6551	3,4221	25,3313
BMP10	6,0146	4,0124	1,1822	6,8975
IFI30	22,0016	29,1695	8,8353	29,6365
CHRNA3	24,9003	35,7931	11,0753	52,4075
DPEP2	2,2761	1,4012	0,4355	1,0972
FAM101B	35,2872	54,8361	17,0484	39,8864
NRBP2	9,7002	5,5409	1,7422	11,6457
GPA33	12,0305	14,1389	4,4799	13,1544
SIRPB1	8,5868	5,4136	1,7422	15,4232
MSH5-SAPCD1	5,0689	4,5219	1,4933	5,7269
H6PD	52,2552	60,9502	20,3461	39,6230
HLF	6,9214	2,4202	0,8089	2,6685

SLC16A3	9,5840	9,3623	3,1732	9,0361
AIG1	64,4390	91,5846	31,1103	62,6788
GLDC	34,5223	31,8444	10,8886	23,0093
GALNT6	15,5484	18,6608	6,4709	14,8100
DHX32	22,6168	21,2084	7,4042	26,5959
PTPN3	52,0431	49,8684	17,4840	38,9746
<b>ITGAL</b>	26,2732	30,9528	10,8886	27,9478
KLHL35	5,5144	2,1017	0,7466	1,2725
IL32	621,6479	144,5737	53,5719	1,5067
CD244	7,0395	5,5409	2,0533	11,2276
SQRDL	35,7659	36,5574	13,5641	44,7357
RGS2	3,3898	1,3375	0,4978	1,3950
LIMD2	58,5659	42,7989	16,3640	51,4402
RAET1E	11,4925	9,1712	3,5466	17,3982
EMID1	12,1328	12,1646	4,7288	12,6283
SLA	478,0886	376,9743	146,5916	462,1445
TTC16	27,7892	29,0421	11,3241	15,9542
LACTB2	11,5229	7,0058	2,7377	8,2769
SPINK2	2,4459	0,3184	0,1244	0,4849
SKAP1	18,3071	19,4888	7,6531	20,7486
GVINP1	47,6777	45,6649	18,1062	50,8067
DNTT	37,2784	9,8718	3,9199	66,5260
FLOT1	89,8745	90,6929	36,5235	70,0579
KIAA0125	17,8081	12,9288	5,2265	17,1609
PTPN6	210,8397	164,6357	66,5760	185,7251
<b>HES1</b>	19,0670	16,4317	6,7820	4,6797
TSHZ3	18,5028	20,7626	8,6487	23,3220
CPA4	12,1662	3,5666	1,4933	34,1661
RMRP	19,3306	3,1208	1,3066	1,0600
ZAP70	451,6591	396,3994	166,0044	585,9785
MAL	42,5390	25,5392	10,7642	20,1643
TEX19	26,7968	8,4069	3,5466	9,1418
FAIM3	15,6537	7,6427	3,2355	10,2714
ADC	6,7821	5,8594	2,4888	6,7760
SPSB1	12,3570	10,6360	4,5421	7,0886
CCDC102B	11,6085	5,6683	2,4266	10,3204
RHBDL3	5,6440	3,5666	1,5555	6,2941
ZNF616	12,6664	11,5277	5,0399	12,0964
ABI3	8,4846	7,5153	3,3599	7,8194
<b>JAK3</b>	25,9808	23,6923	10,7642	21,2217
APOBEC3B	26,9777	25,2845	11,5108	25,3480
TSPAN9	9,7492	8,2796	3,7955	10,9797
ERP27	5,5296	3,3755	1,5555	3,8509
LAT	68,6253	69,2935	32,1058	70,2288
LOC100130476	6,2766	4,2035	1,9911	7,7332
CECR1	44,9476	43,6269	20,8439	62,8255
IL16	28,6884	16,8139	8,0887	27,0064
RCBTB2	25,6701	14,3937	6,9687	15,2813
NDFIP2	36,9922	14,6484	7,0931	41,5746
CD82	295,4044	198,7729	96,2552	206,1652

BIN2	78,8526	59,2943	28,8081	89,3595
LPAR5	17,7956	12,4193	6,0354	27,9518
LOC440354	3,2565	1,4012	0,6844	2,6195
MAGEB18	3,5566	0,7643	0,3733	2,2904
C1orf186	3,4482	1,5285	0,7466	3,0368
UGT3A2	5,9909	0,3821	0,1867	5,0902
GYPC	189,0652	170,5587	83,6244	244,8064
HPGD	15,1422	4,7767	2,3644	5,3419
LIMS2	4,3642	9,9355	20,0972	3,9724
ATP2B3	0,0000	2,6749	5,5998	0,1225
DNAJC12	0,0773	0,8916	1,8666	0,0960
SLC9A7	8,6081	12,9288	27,6881	13,0369
TMEM100	0,0000	0,3184	0,6844	0,5055
ZNF211	15,7289	17,2597	37,7057	10,5536
<b>TNIK</b>	<b>28,6610</b>	<b>46,8113</b>	<b>102,6017</b>	<b>26,1868</b>
RAG2	13,0955	17,3234	38,7012	13,9145
TGFB3	3,4467	5,2862	11,8219	4,9706
FAM84B	9,5688	11,4640	25,8837	9,0263
IKZF3	3,7142	5,2225	11,8219	28,8514
MFAP4	0,1129	5,4136	12,3197	2,9055
FKBP9L	0,0000	0,1911	0,4355	0,3194
EPHB6	44,3400	40,1877	92,5842	34,7260
HYDIN	2,5792	3,6303	8,5864	1,9485
PPP2R2B	0,4948	0,9553	2,3022	0,5858
SRGAP1	1,7366	2,8660	6,9065	5,8083
SLC12A6	19,7711	17,8329	43,1811	49,0547
MAT1A	3,5082	5,3499	13,3774	1,0717
TLE1	25,9050	25,4755	64,2738	30,8435
MIR181B1	0,0000	0,1911	0,4978	0,0852
TMEM178B	0,7175	2,1654	5,6621	1,1236
CKM	0,0000	0,4458	1,1822	0,1489
OR2C1	0,0000	0,2548	0,6844	0,0960
IFI44L	0,0386	0,3821	1,0577	0,0372
RGS4	0,0000	0,2548	0,7466	0,1225
ACTC1	0,0000	0,2548	0,7466	0,0000
AP1B1	26,9615	38,0222	113,0547	32,0132
PLEKHG1	0,9835	1,8470	5,8487	0,9640
NYNRIN	0,1531	0,9553	3,0488	0,4154
ADAMTS3	0,1546	0,3821	1,2444	1,8436
SPTLC3	1,8261	2,0380	6,8443	5,4957
ZNF83	15,6750	11,8461	40,0700	0,1969
ZBBX	0,0000	0,1274	0,4355	0,0000
LGALS3BP	0,6509	5,9868	22,7727	3,0995
PSD3	0,3819	0,6369	2,4266	0,6446
CD79A	6,0222	4,4582	17,2351	13,5326
PBX1	0,0758	0,4458	1,7422	0,5006
PRKAA2	0,0742	0,2548	1,0577	0,0000
PHLDB2	7,0419	9,5533	41,8122	19,3164
EOMES	1,3888	2,2291	10,2042	38,4467
GALC	2,0305	1,7833	8,2753	0,3674

PCED1B-AS1	0,1515	0,5732	2,7377	0,7563
CYTH4	0,1485	0,5732	2,7377	2,6549
GPC5	0,3448	0,9553	4,9154	0,0000
TLL1	2,6519	2,2291	11,5108	3,3601
ZNF385B	2,0117	1,1464	5,9732	3,4983
ZNF772	0,6478	3,2481	16,9862	1,6820
RGPD3	2,4769	2,1017	11,1997	0,3409
PRUNE2	1,0236	1,1464	6,5332	0,1440
BEST1	0,0371	0,3821	2,3022	0,6867
SMARCA1	2,1322	6,6873	41,1900	22,0886
EVPLL	0,0742	0,1911	1,1822	0,0480
<b>AMER1</b>	<b>23,2847</b>	<b>10,6360</b>	<b>66,2649</b>	<b>29,5464</b>
CLEC11A	1,7192	4,5219	28,2481	1,3587
SDC2	0,6448	0,3821	2,4266	8,3542
HHEX	0,0773	0,2548	1,6177	0,0000
STX1B	0,1887	0,1911	1,3066	0,3037
LIN28B	0,3864	0,5095	3,5466	0,3252
DBH	0,0000	0,0637	0,4978	0,0000
TC2N	0,1902	0,3821	3,0488	0,0000
PTPRG	0,3046	1,2101	9,8931	1,3685
C11orf74	0,0386	0,5095	4,2310	0,5065
AKR1C6P	5,4213	1,7833	15,3063	1,4538
C2orf16	0,0000	0,0637	0,5600	0,0372
ADAMTS18	2,6595	0,8280	7,2798	15,1500
RAG1	13,1222	10,9545	105,0905	9,2377
PPAP2B	0,0758	0,1911	1,8666	0,0852
RNF43	0,5319	0,3821	3,7332	0,8680
COBL	0,1129	0,3821	3,8577	0,0480
AKR1C3	0,0371	0,1274	1,3066	0,0480
TRPS1	0,0386	0,2548	2,8621	0,4526
<b>CXXC4</b>	<b>0,3804</b>	<b>0,1911</b>	<b>2,3022</b>	<b>0,0745</b>
PTPRD	0,0758	1,9107	23,9549	0,3781
IRF4	0,0386	0,0637	0,8089	0,0852
SORBS2	0,0000	0,5732	7,2798	0,0480
GABRB2	7,0139	3,0571	48,4076	12,4824
HLA-DOA	1,3994	0,5732	9,0842	3,3983
TRIM29	0,0000	0,0637	1,2444	0,2341
STARD13	0,0773	0,0637	1,7422	1,1501
SOX5	0,1485	0,6369	18,1684	0,0745
APP	0,1856	0,1274	3,9821	0,6495
CACNB2	0,0000	0,0637	2,0533	0,2929
TSPEAR	0,3016	0,0637	2,2399	0,0480
RASEF	0,0371	0,3184	14,1241	0,9855
GABRA3	0,0773	0,0637	3,8577	1,8270
INPP4B	0,0000	0,0000	0,4355	0,0000
FLRT3	0,0000	0,0000	0,4355	0,0000
VN1R1	0,0000	0,0000	0,4978	0,0000
PLD1	0,0000	0,0000	0,4978	0,0000
ROR2	0,0000	0,0000	0,5600	0,1225
SCEL	0,0000	0,0000	0,5600	0,0000

HCG23	0,0000	0,0000	0,6222	0,0000
LIX1	0,0758	0,0000	0,8711	0,0000
CAPN6	0,0000	0,0000	0,9333	0,0000
SDSL	0,2258	0,0000	1,5555	1,3156
CREB5	0,1144	0,0000	3,3599	0,0480

**table S3. GO term analysis of -/A versus WT and G/- down-regulated genes.**

Go-term analysis ( <a href="http://amp.pharm.mssm.edu/Enrichr/">http://amp.pharm.mssm.edu/Enrichr/</a> )															
-/A vs T & G/- down regulated genes															
Term	Overlap	P-value	Adjusted P-value	Old P-value	Old Adjusted P-value	Z-score	Combined Score	Genes							
negative regulation of alpha-beta T cell activation (GO:0046636)	4/19	1.14E-05	0.007110384	2.30E-05	0.008985301	-2.81977	13,94712595	IL4R	CD300A	TNFRSF14	JAK3				
regulation of cell activation (GO:0050865)	13/420	2.01E-05	0.007402995	1.94E-05	0.008985301	-5.22587	12,37074968	STAT5A	IL4R	CD300A	LST1				
regulation of lymphocyte activation (GO:0051249)	12/344	1.31E-05	0.007110384	1.329E-05	0.008985301	-5.20051	12,36634498	STAT5A	ZAP70	LGAL51	IL4R				
regulation of nucleotide activation (GO:0050864)	12/390	4.47E-05	0.007110384	4.38E-05	0.008985301	-5.15451	12,32320948	STAT5A	IL4R	CD300A	LST1				
regulation of T cell activation (GO:0050863)	11/311	4.81E-06	0.007110384	4.78E-06	0.008985301	-5.0856	12,32320948	STAT5A	IL4R	CD300A	LST1				
negative regulation of cell motility process (GO:0002683)	10/10	4.97E-05	0.007402995	4.93E-05	0.008985301	-5.05116	12,08626797	STAT5A	IL4R	CD300A	LST1				
negative regulation of muscle hypertrophy (GO:0014741)	8/170	4.8E-05	0.007402995	5.43E-05	0.008985301	-4.99115	11,71474707	STAT5A	ZAP70	CD300A	LST1				
regulation of mononuclear cell proliferation (GO:0032944)	8/171	5.5E-05	0.007402995	5.65E-05	0.008985301	-4.95123	11,70186261	STAT5A	ZAP70	CD300A	LST1				
negative regulation of cardiac muscle hypertrophy (GO:0010614)	3/9	3.5E-05	0.007402995	8.40E-06	0.008985301	-4.94817	11,53665581	BMP10	IL4R	CD300A	LST1				
regulation of leukocyte proliferation (GO:0070663)	8/176	6.13E-05	0.00833752	6.86E-05	0.012458499	-4.88568	11,20202785	STAT5A	ZAP70	CD300A	LST1				
thrombin receptor signaling pathway (GO:0070493)	3/9	3.5E-05	0.007402995	8.40E-06	0.008985301	-4.85187	11,35141795	HPGD	PELX	FBLRL2					
negative regulation of leukocyte mediated immunity (GO:0002704)	4/34	0.000125	0.012345564	0.0001764	0.016945905	-5.03056	11,00176688	STAT5A	CD300A	PTPN6	JAK3				
regulation of B cell receptor signaling pathway (GO:0050855)	3/13	0.000116	0.012345564	0.0002094	0.018991966	-5.02029	10,8953765	PRKCH	CD300A	PTPN6					
regulation of glial cell proliferation (GO:0060251)	3/15	0.000183	0.015739091	0.0003019	0.020530942	-4.87573	10,32725110	ADCVAP1	PRKCH	HES1					
positive regulation of T cell activation (GO:0050870)	8/189	0.000101	0.012345564	0.0001106	0.01389832	-3.2167	10,16290114	STAT5A	ZAP70	LGAL51	IL4R				
negative regulation of lymphocyte activation (GO:0051250)	6/102	0.000129	0.012345564	0.0001531	0.016435011	-2.5827	9,92384018	IL4R	CD300A	LST1	TNFRSF14	PTPN6	JAK3		
negative regulation of immune response (GO:0050777)	6/103	0.000136	0.012345564	0.000161	0.016435011	-2.5043	9,68286287	STAT5A	ADCVAP1	IL4R	CD300A	PTPN6	JAK3		
positive regulation of cell activation (GO:0050867)	9/272	0.000241	0.018715678	0.0002474	0.019649793	-2.39548	9,53006345	STAT5A	ZAP70	LGAL51	IL4R	PELX	TNFRSF14	PTPN6	HES1
regulation of alpha-beta T cell activation (GO:0046634)	5/63	0.000117	0.012345564	0.0001496	0.016435011	-2.1497	9,44674511	STAT5A	IL4R	CD300A	TNFRSF14	JAK3		ITGAL	
-/A vs T & G/- up regulated genes															
Term	Overlap	P-value	Adjusted P-value	Old P-value	Old Adjusted P-value	Z-score	Combined Score	Genes							
Wnt signaling pathway (GO:0016055)	9/234	2.06E-06	0.004206082	5.877E-06	0.006644844	-3.33521	14,08708782	AMER1	RNF43	HHEX	TLE1				
regulation of Wnt signaling pathway (GO:0030111)	7/214	8.28E-05	0.048337881	0.0001808	0.10550927	-3.26173	7,15526760	AMER1	RNF43	HHEX	TLE1				
regulation of neuron differentiation (GO:0045664)	9/405	0.000156	0.060574599	0.0003627	0.141229462	-3.2885	6,68668321	EOMES	PTPRD	APP	SCD2				
positive regulation of G2/M transition of mitotic cell cycle (GO:0010971)	2/14	0.000204	0.113441367	0.0035252	0.180882111	-2.60583	5,671502706	APP	PBX1						
fibfil organization (GO:0097435)	2/14	0.000204	0.113441367	0.0035252	0.180882111	-2.58071	5,616844562	MFP4	ADAMTS3						
positive regulation of cell cycle G2/M phase transition (GO:1902751)	2/14	0.000204	0.113441367	0.0035252	0.180882111	-2.56874	5,590784047	APP	PBX1						
T cell lineage commitment (GO:0002360)	2/12	0.000149	0.110363586	0.0024834	0.180882111	-2.5128	5,58153031	IRF4	RAG2						
extracellular fibril organization (GO:0043206)	2/12	0.000149	0.110363586	0.0024834	0.180882111	-2.49737	5,504152017	MFP4	ADAMTS3						
V(D)J recombination (GO:0033151)	2/16	0.000273	0.130069855	0.0041781	0.206030672	-2.68048	5,467338863	RAG2	RAG1						
negative regulation of Wnt signaling pathway (GO:0030178)	5/126	0.000372	0.093354279	0.0006877	0.172060453	-2.78736	5,402793201	AMER1	RNF43	TLE1	ROR2				
response to light stimuli (GO:0009416)	7/322	0.000079	0.093354279	0.0001808	0.180882111	-2.3809	5,246755311	MFP4	APP	SCD2	AKR1C3	GPC5	DBH	BEST1	
B cell activation (GO:0042113)	5/128	0.0004	0.093354279	0.0007366	0.172060453	-2.16582	5,14232765	C7orf94	HHEX	IRF4	RAG2	IKZF3	RAG1		
lymphocyte activation (GO:0046449)	7/303	0.000699	0.093354279	0.0101843	0.180882111	-2.31394	5,131990594	EOMES	CD79A	HHEX	IRF4	RAG2	IKZF3	RAG1	
leukocyte differentiation (GO:0002521)	6/251	0.0001404	0.110363586	0.0025603	0.180882111	-2.32475	5,123868466	EOMES	CD79A	HHEX	IRF4	RAG2	IKZF3	RAG1	
leukocyte activation (GO:0045321)	7/373	0.0002265	0.120266262	0.0042489	0.206030672	-2.32584	5,927101656	EOMES	CD79A	HHEX	IRF4	RAG2	IKZF3	RAG1	
lymphocyte differentiation (GO:0009898)	2/172	0.000152	0.110363586	0.0026024	0.180882111	-2.31101	5,903686211	C7orf94	HHEX	IRF4	RAG2	IKZF3	RAG1		
regulation of adrenergic development (GO:0050773)	4/68	0.00026	0.110363586	0.0035525	0.180882111	-2.20183	5,803287047	PTPRD	SCD2	AKR1C3	GPC5	DBH	BEST1		
B cell differentiation (GO:0030183)	4/80	0.00062	0.108841518	0.0010709	0.180882111	-2.18121	4,8376100	CD79A	HHEX	IRF4	RAG2	IKZF3	RAG1		
detection of visible light (GO:0009584)	4/104	0.000165	0.113382092	0.0026998	0.180882111	-2.18116	4,74837213	SOC3	AKR1C3	GPC5	BEST1				
transmembrane transport (GO:0098656)	5/172	0.001512	0.110363586	0.0026111	0.180882111	-2.14829	4,734778725	GABRB2	PRKA2	GABRA3	SLC12A6	BEST1			

**table S4. Cytokine secretion in Jurkat cells as measured by Proteome Profiler Human XL Cytokine Array kit.**

Label	96G/A	96(A)	96G/A	96(A)											
Label	Vol + Vol * Weight	Background	Norm'd Vol [percent]	Percent?	Quality	Vol + Vol * Weight	Background	Norm'd Vol [percent]	Percent?	Quality	Vol + Vol * Weight	Background	Norm'd Vol [percent]	Percent?	Quality
A1 Reference	11105988	1412860	2963111.0	n/a	n/a	12722241	12722241	2963111.0	n/a	n/a	13067381	13067381	26072.9	13065517	13065517
A2 Adiponectin	10707895	1174396	2963111.0	n/a	n/a	12139800	12139800	2963111.0	n/a	n/a	103187.7	103187.7	16175.45	2505035	2505035
A3 Adiponectin	10707895	1174396	2963111.0	n/a	n/a	12139800	1213980	2963111.0	n/a	n/a	103187.7	103187.7	16175.45	2505035	2505035
A4 Angrekan	228845	1025459	2963143.0	n/a	n/a	205961.2	2163426	2963143.0	n/a	n/a	438164.9	438164.9	3004.47	220871.7	22171.36
A5 Angrekan	181651.5	1143931	2963151.0	n/a	n/a	205961.2	2163426	2963151.0	n/a	n/a	438164.9	438164.9	3004.47	220871.7	22171.36
A6 Angrekan	181651.5	1143931	2963151.0	n/a	n/a	205961.2	2163426	2963151.0	n/a	n/a	438164.9	438164.9	3004.47	220871.7	22171.36
A7 Angrekan	181651.5	1143931	2963151.0	n/a	n/a	1502309	497380	2963151.0	n/a	n/a	948444	948444	6887.05	252118.6	26048.18
A8 Angrekan	181651.5	1143931	2963151.0	n/a	n/a	122366	303807	2963151.0	n/a	n/a	143883.8	143883.8	2802.21	116074.7	8471.08
A9 Angrekan	181651.5	1143931	2963151.0	n/a	n/a	122366	303807	2963151.0	n/a	n/a	143883.8	143883.8	2802.21	116074.7	8471.08
A10 Angrekan	181651.5	1143931	2963151.0	n/a	n/a	122366	303807	2963151.0	n/a	n/a	143883.8	143883.8	2802.21	116074.7	8471.08
A11 Angrekan	181651.5	1143931	2963151.0	n/a	n/a	122366	303807	2963151.0	n/a	n/a	143883.8	143883.8	2802.21	116074.7	8471.08
A12 Angrekan	181651.5	1143931	2963151.0	n/a	n/a	122366	303807	2963151.0	n/a	n/a	143883.8	143883.8	2802.21	116074.7	8471.08
A13 Angrekan	181651.5	1143931	2963151.0	n/a	n/a	122366	303807	2963151.0	n/a	n/a	143883.8	143883.8	2802.21	116074.7	8471.08
A14 Angrekan	181651.5	1143931	2963151.0	n/a	n/a	122366	303807	2963151.0	n/a	n/a	143883.8	143883.8	2802.21	116074.7	8471.08
A15 EDNF	197126.5	311880	2963186.0	n/a	n/a	205962	317098	2963186.0	n/a	n/a	203684.8	203684.8	8111.87	205452	2187.54
A16 Complement C1q	230070.6	317154	2963186.0	n/a	n/a	203854.4	310598	2963186.0	n/a	n/a	105386	105386	6421.86	130464.4	13824.39
A17 Complement C1q	230070.6	317154	2963186.0	n/a	n/a	203854.4	310598	2963186.0	n/a	n/a	105386	105386	6421.86	130464.4	13824.39
A18 C1QA	182424.2	306241	2963186.0	n/a	n/a	246725.7	310514	2963186.0	n/a	n/a	134651.1	134651.1	2101.73	241337	6123.78
A19 C1QB	182424.2	306241	2963186.0	n/a	n/a	246725.7	310514	2963186.0	n/a	n/a	134651.1	134651.1	2101.73	241337	6123.78
A20 C1QB	182424.2	306241	2963186.0	n/a	n/a	246725.7	310514	2963186.0	n/a	n/a	134651.1	134651.1	2101.73	241337	6123.78
A21 C1R	182424.2	306241	2963186.0	n/a	n/a	246725.7	310514	2963186.0	n/a	n/a	134651.1	134651.1	2101.73	241337	6123.78
A22 CD40 ligand	120341.2	3486317	2963186.0	n/a	n/a	21694.6	314342	2963186.0	n/a	n/a	154642.0	154642.0	2307.56	174004.6	3405.26
A23 Chitinase 3-like 1	219129.5	311767	2963186.0	n/a	n/a	205962	317098	2963186.0	n/a	n/a	205215.1	205215.1	185111.6	141611.6	941986
A24 Chitinase 3-like 1	219129.5	311767	2963186.0	n/a	n/a	205962	317098	2963186.0	n/a	n/a	205215.1	205215.1	185111.6	141611.6	941986
A25 Chitinase 3-like 1	219129.5	311767	2963186.0	n/a	n/a	205962	317098	2963186.0	n/a	n/a	205215.1	205215.1	185111.6	141611.6	941986
A26 Chitinase 3-like 1	219129.5	311767	2963186.0	n/a	n/a	205962	317098	2963186.0	n/a	n/a	205215.1	205215.1	185111.6	141611.6	941986
A27 Complement Factor D	145470.2	310577	2963186.0	n/a	n/a	140841.6	441384	2963186.0	n/a	n/a	140286.8	140286.8	5171.53	130955	10711.30
A28 C-Reactive Protein	137034.4	308780	2963186.0	n/a	n/a	17512.4	151640	2963186.0	n/a	n/a	130781.5	130781.5	2303.76	105615.1	1305.40
A29 C-Reactive Protein	137034.4	308780	2963186.0	n/a	n/a	17512.4	151640	2963186.0	n/a	n/a	130781.5	130781.5	2303.76	105615.1	1305.40
A30 C1QA	182424.2	306241	2963186.0	n/a	n/a	246725.7	310514	2963186.0	n/a	n/a	134651.1	134651.1	2101.73	241337	6123.78
A31 C1QB	182424.2	306241	2963186.0	n/a	n/a	246725.7	310514	2963186.0	n/a	n/a	134651.1	134651.1	2101.73	241337	6123.78
A32 C1R	182424.2	306241	2963186.0	n/a	n/a	246725.7	310514	2963186.0	n/a	n/a	134651.1	134651.1	2101.73	241337	6123.78
A33 C3	15572.6	311879	2963186.0	n/a	n/a	144705.7	311220	2963186.0	n/a	n/a	105084.1	105084.1	1022.22	130757.1	10154.05
A34 C3	144205.6	318134	2963186.0	n/a	n/a	130380.7	309654	2963186.0	n/a	n/a	103616	103616	275.09	144003.1	4668.98
A35 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518.9	110518.9	328.04	144003.1	4668.98
A36 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518.9	110518	328.04	144003.1	4668.98
A37 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A38 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A39 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A40 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A41 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A42 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A43 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A44 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A45 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A46 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A47 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A48 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A49 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A50 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A51 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A52 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A53 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A54 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A55 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A56 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A57 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A58 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A59 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A60 C3nG	136172.9	307195	2963186.0	n/a	n/a	141214.8	130651	2963186.0	n/a	n/a	110518	110518	328.04	144003.1	4668.98
A61 C3nG	136172.9	307195	2963186												

**table S5. Cytokine secretion in CD4<sup>+</sup> T cells after stimulation and infection with HIV as measured by Proteome Profiler Human XL Cytokine Array kit.**

		Control	CD4+alpha	CD4+gamma	control	Average Stddev	CD4+alpha	CD4+gamma	Average Stddev	
A1	Reference	7771469	6053846	4207463	7706370	27537	6307328	613985	4207848	147122
A2	IL-1	778242	393243	452840	7706370	27537	59837	59306	36248	108704
A3	Adiponectin	217090	238055	134837	157971	83006	32438	78533	108704	30249
A4	Angiotensin	98813	103647	81154	98813	2086	64658	13951	78877	571
A5	Aggrcan	92083	93338	73293	92083	2086	64658	13951	78877	571
A6	Angiopoietin	98168	65128	78564	36378	17740	43162	24380	40300	3387
A7	Angiopoietin-1	380324	415811	455457	53938	7351	29202	181	48894	40
A8	Angiopoietin-2	380344	395121	45018	53938	7351	29202	181	48894	40
A9	Angiotensin-1	48731	59121	49018	56037	4418	17951	1720	174045	7877
A10	Angiotensin-2	48732	59121	49018	56037	4418	17951	1720	174045	7877
A11	Angiotensin-3	48733	59121	49018	56037	4418	17951	1720	174045	7877
A12	Angiotensin-4	48734	59121	49018	56037	4418	17951	1720	174045	7877
A13	Angiotensin-5	157213	155881	113120	156403	12996	134028	2639	113378	766
A14	Angiotensin-6	173528	173528	12307	155008	4971	126559	345	13389	6219
A15	Angiotensin-7	114493	120651	109592	155008	4971	126559	345	13389	6219
A16	Angiotensin-8	156511	156511	109592	28731	16219	54462	2325	57159	8886
A17	Complement C1/C2a	17265	57378	50517	28731	16219	54462	2325	57159	8886
A18	Complement C1/C2b	40322	560640	614517	38875	12781	99986	16627	73935	30283
A19	Complement C1/C2c	47611	560640	614517	38875	12781	99986	16627	73935	30283
A20	CD30	256244	108556	83631	131388	27550	120201	11750	104378	32114
A21	CD30L	131187	121047	109056	131388	27550	120201	11750	104378	32114
A22	CD40	715356	660750	562177	777329	16508	689557	71451	547486	21554
A23	CD40L	703262	657498	562177	777329	16508	689557	71451	547486	21554
B1	CD40 Ligand	60494	537388	412755	58137	16204	12629	11482	411882	1206
B2	CD40L Ligand	60495	537388	412755	58137	16204	12629	11482	411882	1206
B3	Chitotriose-1	61217	51962	59315	62899	2395	58049	9873	66679	363
B4	Chitotriose-2	61218	51962	59315	62899	2395	58049	9873	66679	363
B5	Chitotriose-3-like 1	61219	51962	59315	62899	2395	58049	9873	66679	363
B6	Chitotriose-3-like 2	61220	51962	59315	62899	2395	58049	9873	66679	363
B7	Complement Factor D	75527	67425	69522	71836	525	60388	9963	62121	466
B8	Complement Factor H	68134	51336	68049	102101	30501	73138	812	8841	206
B9	Complementary Protein	12084	72598	87896	102101	30501	73138	812	8841	206
B10	C3	95173	72598	87896	102101	30501	73138	812	8841	206
B11	C3 convertase	12084	72598	87896	102101	30501	73138	812	8841	206
B12	C3d	0	2055	30803	30803	2055	29055	2889	40560	4487
B13	C3d	256244	108556	83631	131388	27550	120201	11750	104378	32114
B14	C3d	131187	121047	109056	131388	27550	120201	11750	104378	32114
B15	C3d	74244	85112	108017	73946	3357	83917	851	10388	3125
B16	C3d	74245	85112	108017	73946	3357	83917	851	10388	3125
B17	CFb	203997	164103	164103	203997	164103	164103	164103	164103	164103
B18	CFD basic	115571	217979	561515	104040	14271	79072	3120	95505	5487
B19	CFD	115572	217979	561515	104040	14271	79072	3120	95505	5487
B20	CFD-L	115573	217979	561515	104040	14271	79072	3120	95505	5487
B21	CFD-R	115574	217979	561515	104040	14271	79072	3120	95505	5487
B22	CFD-S	115575	217979	561515	104040	14271	79072	3120	95505	5487
B23	CFD-T	115576	217979	561515	104040	14271	79072	3120	95505	5487
B24	CFD-Y	115577	217979	561515	104040	14271	79072	3120	95505	5487
B25	CFD-Y'	115578	217979	561515	104040	14271	79072	3120	95505	5487
B26	CFD-Y''	115579	217979	561515	104040	14271	79072	3120	95505	5487
B27	CFD-Y'''	115580	217979	561515	104040	14271	79072	3120	95505	5487
B28	CFD-Y''''	115581	217979	561515	104040	14271	79072	3120	95505	5487
B29	CFD-Y'''''	115582	217979	561515	104040	14271	79072	3120	95505	5487
B30	CFD-Y''''''	115583	217979	561515	104040	14271	79072	3120	95505	5487
B31	CFD-Y'''''''	115584	217979	561515	104040	14271	79072	3120	95505	5487
B32	CFD-Y'''''''	115585	217979	561515	104040	14271	79072	3120	95505	5487
B33	CFD-Y''''''''	115586	217979	561515	104040	14271	79072	3120	95505	5487
B34	CFD-Y'''''''''	115587	217979	561515	104040	14271	79072	3120	95505	5487
B35	CFD-Y''''''''''	115588	217979	561515	104040	14271	79072	3120	95505	5487
B36	CFD-Y'''''''''''	115589	217979	561515	104040	14271	79072	3120	95505	5487
B37	CFD-Y''''''''''''	115590	217979	561515	104040	14271	79072	3120	95505	5487
B38	CFD-Y'''''''''''''	115591	217979	561515	104040	14271	79072	3120	95505	5487
B39	CFD-Y''''''''''''''	115592	217979	561515	104040	14271	79072	3120	95505	5487
B40	CFD-Y'''''''''''''''	115593	217979	561515	104040	14271	79072	3120	95505	5487
B41	CFD-Y''''''''''''''''	115594	217979	561515	104040	14271	79072	3120	95505	5487
B42	CFD-Y'''''''''''''''''	115595	217979	561515	104040	14271	79072	3120	95505	5487
B43	CFD-Y''''''''''''''''''	115596	217979	561515	104040	14271	79072	3120	95505	5487
B44	CFD-Y'''''''''''''''''''	115597	217979	561515	104040	14271	79072	3120	95505	5487
B45	CFD-Y''''''''''''''''''''	115598	217979	561515	104040	14271	79072	3120	95505	5487
B46	CFD-Y''''''''''''''''''''	115599	217979	561515	104040	14271	79072	3120	95505	5487
B47	CFD-Y'''''''''''''''''''''	115600	217979	561515	104040	14271	79072	3120	95505	5487
B48	CFD-Y''''''''''''''''''''''	115601	217979	561515	104040	14271	79072	3120	95505	5487
B49	CFD-Y''''''''''''''''''''''	115602	217979	561515	104040	14271	79072	3120	95505	5487
B50	CFD-Y''''''''''''''''''''''	115603	217979	561515	104040	14271	79072	3120	95505	5487
B51	CFD-Y''''''''''''''''''''''	115604	217979	561515	104040	14271	79072	3120	95505	5487
B52	CFD-Y''''''''''''''''''''''	115605	217979	561515	104040	14271	79072	3120	95505	5487
B53	CFD-Y''''''''''''''''''''''	115606	217979	561515	104040	14271	79072	3120	95505	5487
B54	CFD-Y''''''''''''''''''''''	115607	217979	561515	104040	14271	79072	3120	95505	5487
B55	CFD-Y''''''''''''''''''''''	115608	217979	561515	104040	14271	79072	3120	95505	5487
B56	CFD-Y''''''''''''''''''''''	115609	217979	561515	104040	14271	79072	3120	95505	5487
B57	CFD-Y''''''''''''''''''''''	115610	217979	561515	104040	14271	79072	3120	95505	5487
B58	CFD-Y''''''''''''''''''''''	115611	217979	561515	104040	14271	79072	3120	95505	5487
B59	CFD-Y''''''''''''''''''''''	115612	217979	561515	104040	14271	79072	3120	95505	5487
B60	CFD-Y''''''''''''''''''''''	115613	217979	561515	104040	14271	79072	3120	95505	5487
B61	CFD-Y''''''''''''''''''''''	115614	217979	561515	104040	14271	79072	3120	95505	5487
B62	CFD-Y''''''''''''''''''''''	115615	217979	561515	104040	14271	79072	3120	95505	5487
B63	CFD-Y''''''''''''''''''''''	115616	217979	561515	104040	14271	79072	3120	95505	5487
B64	CFD-Y''''''''''''''''''''''	115617	217979	561515	104040	14271	79072	3120	95505	5487
B65	CFD-Y''''''''''''''''''''''	115618	217979	561515	104040	14271	79072	3120	95505	5487
B66	CFD-Y''''''''''''''''''''''	115619	217979	561515	104040	14271	79072	3120	95505	5487
B67	CFD-Y''''''''''''''''''''''	115620	217979	561515	104040	14271	79072	3120	95505	5487
B68	CFD-Y''''''''''''''''''''''	115621	217979	561515	104040	14271	79072	3120	95505	5487
B69	CFD-Y''''''''''''''''''''''	115622	217979	561515	104040	14271	79072	3120	95505	5487
B70	CFD-Y''''''''''''''''''''''	115623	217979	561515	104040	14271	79072	3120	95505	5487
B71	CFD-Y''''''''''''''''''''''	115624	217979	561515	104040	14271	79072	3120	95505	5487
B72	CFD-Y''''''''''''''''									

**table S6. Primer sequences used.**

Primer Name	Sequence
IL-32 enhancer amplicon 1 forward	ACATGGTGAATCCCGTCCC
IL-32 enhancer amplicon 1 reverse	CCCTAAACCACTAGCTGAGCA
IL-32 enhancer amplicon 2 forward	TGAGAATCTGTGAGGCTGG
IL-32 enhancer amplicon 2 reverse	ACTTCACCAAACCTGTCC
Total IL-32 forward	AGGACGTGGACAGGTGATGTC
Total IL-32 reverse	GTCTCCAGGTAGCCCTTTGA
Cyclophilin A (CypA/PPIA) forward	TCATCTGCACTGCCAAGACTG
Cyclophilin A (CypA/PPIA) reverse	CATGCCCTTCTTCACTTGCC
$\beta$ 2-microglobulin (B2M)-fw	ATGAGTATGCCTGCCGTGTG
$\beta$ 2-microglobulin (B2M)-rev	CCAATGCCGATCTTCAAAC
3C primer A	CCTCTATGTGTCTCTGGGTCG
3C primer rs4349147	GCAGGGATAGAAGGTGAGAGATGAAT
3C primer B	GGGAACCTGACCTCAGACAG
3C primer C	GCACCCCTGTGTTCTCTCA
3C primer IL32 promoter	GAGGGAAAGTCCAGACTCGG
3C primer D	TCAGCCAAGCTCAGACAGC
3C primer E	GTGGCTTCCTCTGTCTCCC
IL4R forward	CGTGGTCAGTGCAGATAACTA
IL4R reverse	TGGTGTGAAGTCAGGTTTC
TNFRSF14 forward	GTGCAGTCCAGGTTATCGTGT
TNFRSF14 reverse	CACTGCTTAGGCCATTGAGG
STAT5A forward	CGACGGGACCTTGTGTTG
STAT5A reverse	GTTCGGGGAGTCAAACTTCC
LGALS1 forward	TCGCCAGCAACCTGAATCTC
LGALS1 reverse	GCACGAAGCTCTAGCGTCA
ANXA1 forward	GCAGGCCCTGGTTATTGAAA
ANXA1 reverse	GCTGTGCATTGTTCGCTTA
IL-32 enhancer gRNA 1 forward	ACCGGAAAAGAAAGTTGGGGCCG
IL-32 enhancer gRNA 1 reverse	ACCGGCCAGCCTGCCGTTAGCAG
IL-32 enhancer gRNA 2 forward	AAACCGCCCCAACCTTCTTTC
IL-32 enhancer gRNA 2 reverse	AAACCTGCTGAAACGGCAGGCTGGC
IL-32 promotor forward	GTGGAGCTGGGTATCTCAG
IL-32 promotor reverse	CATGGCGGCCAAAAGTCAA
rs12447486 forward	AGATCTGGCTGGATCCTGGT
rs12447486 reverse	TACTCATGCCTGCCCTCTGC
rs4349147 forward	CCTGGGGCAAGGATGATAGG
rs4349147 reverse	AGACCCAGCCTCACGAGATT
Oca2 promoter forward	TAACCCCTCCCTGCCGTGTT
Oca2 promoter reverse	CCCTCTGAGTTCTTACTTCG
Mock sgRNA 1 forward	ACCGGTCAGGTCACTCAATCGC
Mock sgRNA 1 reverse	AAACGCGATTGAGTCACCTGAC
Mock sgRNA 2 forward	ACCGGTATCATCATCAGGGCCG
Mock sgRNA 2 reverse	AAACCGCCCCCTGATGATGATGC
Amer1 forward	AGTACCCGTGAACAAACAGCA
Amer1 reverse	AGGCAGAGTACAGATACCCCTC
CXXC4 forward	ATGCACCAACCGAACGACTC
CXXC4 reverse	GCAGTGTTCAGGGGATAAGGT
TNIK forward	TAAGGGTCGTATGTCAAAACG
TNIK reverse	CCATGCCCTGGTGGGTTCTT
IL-32 non-alpha forward	TCTTCATGTCCCTTCCAGTCCTA
IL-32 non-alpha reverse	AAGGTGGTGTCACTATCTTCATTTG
IL-32 alpha forward	CTTTGGCCGCCATGTG
IL-32 alpha reverse	GTGCATTGGGCCCTTCAG
IL-32 beta forward	GAAGACTGCGTGCAGAAGGT
IL-32 beta reverse	CTTCTATGGCCTGGTGCAT
IL-32 gamma forward	AGGCCGAATGTTAATGCT
IL-32 gamma reverse	CTGCTCCAGGTAGCCCTCT