SUPPLEMENTARY MATERIALS

Expression of human endogenous retrovirus group K (HERV-K) HML-2 correlates

with immune activation of macrophages and type I interferon response

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List of supplementary tables (Excel files)

Supplementary Table S1. Log_2 (fold-change) and false-discovery rate adjusted p-value following macrophage M1 (LPS + IFN γ), M2 (IL10), and M2 (IL4) polarization for retroelements and HML-2 loci.

Supplementary Table S2. Comparison of FGL1 and HML2_8p22 expression in primary MDMs and TDMs.

Supplementary Table S3. Log₂(fold-change) and false-discovery rate adjusted p-value following TLR agonist (top) or IFN (bottom) treatment for retroelements and HML-2 loci.

Supplementary Table S4. CPM values and relative expression of genes which 1) contain a GAS but not an ISRE site, 2) contain an ISRE but not a GAS site or 3) contain both GAS/ISRE sites.

Supplementary Table S5. Predicted transcription factors binding sites (TFBSs) by the PROMO software algorithm in LTR12F, the 5'LTR of 1q22, and the 5'LTR of 3q12.3.

Supplementary Table S6. Predicted targets of the HML-2-shRNA; Genome analysis data.

Supplementary Table S7. Reagents and resources.

Supplementary figures



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<u>Retroelement</u>	Log2FC	Log2(CPM)
L1PA10:L1:LINE	1.041486	5.343971
L1M1:L1:LINE	1.024448	4.97766
L1MA4:L1:LINE	1.601261	4.721855
MER33:hAT-Charlie:DNA	1.122598	4.635343
HERVK-int:ERVK:LTR	1.358738	4.515872







Figure S1. Retroelement expression in response to macrophage polarization. (**A**) Number of significantly modulated retroelements in response to M1, M2 (IL10) and M2 (IL4) polarization. (**B**) The top five most highly expressed retroelements at the basal state that are significantly modulated in response to M1 polarization. CPM – copies per million. (**C**) Relative expression of CD48, 1q23.3, CR1, and 1q32.2 to compare the expression of the HML-2 loci with the gene they reside within. (**D**) Locus-specific expression of the HML-2 subfamily in response to TDM polarization; ****, P < 0.0001; according to edgeR analysis. (**E**) Relative expression of FGL1 and 8p22 in TDMs.



Figure S2. Correlation between IRF1 and HERV-K102 expression in cutaneous leishmaniasis patients. Pearson's r correlation between HERV-K102 and IRF1 expression in CL patients.



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Antibody target (or ATAC)	Chromosome	Beginning of peak	End of peak	Peak length	Peak summit	Fold-enrichment	Adjusted p value	Cell type
STAT1	chr1	155637480	155637773	294	155637658	7.6404	3.19963E-55	MDM
IRF1	chr1	155637408	155637777	370	155637618	12.0589	5.1523E-142	MDM
H3K27ac	chr1	155635819	155637517	1699	155637434	2.16843	9.49511E-19	MDM
ATAC	chr1	155637202	155637965	764	155637572	3.03479	2.66073E-15	HeLa
H3K4me2	chr1	155635765	155636040	276	155635902	6.88336	2.58941E-13	HeLa
H3K4me2	chr1	155636160	155637384	1225	155636513	6.62564	1.43648E-22	HeLa
H3K79me2	chr1	155636013	155636536	524	155636280	3.8251	0.00014639	HeLa
H3K27ac	chr1	155635965	155637572	1608	155637302	4.08018	2.22382E-14	HeLa

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LTR12F_1q22 Solo LTR (chr1:155637452-155637661):



Conserved IRF-E motif: AANNGAAA (55)

Sequence motifs in LTR12F that are enriched in IRF-1 binding sites (56):

- 1) GA<u>AAGCGAAA</u>GT
- 2) GAAAGTGAAA
- 3) TGA<u>AAGTGAAAA</u>

Figure S3. ChIP-seq and ATAC-seq analysis of HERV-K102. (A) Peaks identified by MACS2 as significantly enriched within 10kb +/- of HERV-K102. **(B)** Location of three potential IRF-E sites within LTR12F.



Figure S4. HML-2 env knockdown efficiency.

Relative HML-2 env expression in controlshRNA and HML-2-shRNA expressing TDMs following IFN γ treatment. The data are presented as mean values ± SEM from three biological replicates. ****, *P* < 0.0001 according to two-way Anova.