

Supplementary materials

Supplementary Figures

Fig. S1: Characterization of coding, proximal, and distal CAGE peaks

Fig. S2: Activation of LTR retroviral promoters in human HCC tumors

Fig. S3: Activation of LTR retroviral promoters in mouse HCC tumors

Fig. S4: Expression profiles of 43 LTR-derived ncRNAs

Fig. S5: qPCR validation of LTR-derived ncRNAs

Fig. S6: Activity of the ncRNAs in HepG2 cells

Supplementary Tables

Table S1: HCC samples with etiology and map counts

Table S2: Fantom5 data used to measure expression in normal livers

Table S3: A list of up-regulated LTR12C in human HCC

Table S4: mouse liver samples with histology and map counts

Table S5: A list of up-regulated LTR in mouse HCC

Table S6: The most significantly up-regulated distal peaks (43 LTRs and 90 non-LTRs)

Table S7: Targets of 3' RACE validation (15 LTRs and 7 non-LTRs)

Table S8: Full-length ncRNAs determined by 3' RACE

Table S9: Prediction of coding potential using CPAT web system

Table S10: qPCR primers for LTR-derived ncRNAs

Table S11: Clinical features associated with the high LTR class

Table S12: ENCODE data used to measure activities of TSSs in HepG2

Table S13: ENCODE ChIP-Seq data used to measure TF activities in HepG2

Table S14: Targets and sequences of LNAs

Table S15: Significantly dysregulated genes with LTR-001 KD at 48h

Table S16: Significantly dysregulated genes with LTR-002 KD at 48h

Supplementary Data Sets

Human Data

http://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study_id=phs000885.v1.p1

Expression table

File name	: GSE60982_Expression.hg19.HCC.64366peaks.txt.gz
Columns 1-4	: Genomic position of TSS (hg19)
Columns 5	: total read counts of all samples
Columns 6	: strand (+ or -)
Columns 7	: classification (Coding, Proximal, or Distal)
Columns 8-9	: Log2 fold change and FDR (50 tumors vs 50 NTs)
Columns 10-11	: Gene names and IDs
Columns 12-61	: Normalized expression values (tpm) for 50 tumors
Columns 62-111	: Normalized expression values (tpm) for 50 NTs
Columns 112-116	: Normalized expression values (tpm) for 5 normal livers

Mouse Data

<http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE60982>

Expression table

File name	: GSE60982_Expression.mm9.HCC.49096peaks.txt.gz
Columns 1-4	: Genomic position of TSS (mm9)
Columns 5	: total read counts of all samples
Columns 6	: strand (+ or -)
Columns 7	: classification (Coding, Proximal, or Distal)
Columns 8-9	: Log2 fold change and FDR (3 WTs vs 4 high-grade HCC)
Columns 10-11	: Gene names and IDs
Columns 12-17	: Normalized expression values (tpm) for 6 WT
Columns 18-20	: Normalized expression values (tpm) for 3 inflammation
Columns 21-24	: Normalized expression values (tpm) for 4 adenoma
Columns 25-40	: Normalized expression values (tpm) for 16 low-grade HCC
Columns 41-48	: Normalized expression values (tpm) for 8 high-grade HCC

Example of data access and file conversion

```
wget ftp://ftp-trace.ncbi.nlm.nih.gov/sra/sra-instant/reads/ByExp/sra/SRX%2FSRX690%2FSRX690748/SRR1562475/SRR1562475.sra
```

```
sam-dump SRR1562475.sra | samtools view -bhS - > SRR1562475.bam
```

```
samtools index SRR1562475.bam
```

Supplementary Methods

Generation of random dataset to analyze human LTR activities

The significantly up-regulated peaks (genomic positions) were randomized using the shuffleBed function of the Bedtools v2.17.0 with the '-seed' option 1, 2, and 3 for dataset 1, 2, and 3 (Quinlan and Hall 2010). Gapped regions including centromere and telomere filled with 'N' in the human genome were excluded using the '-excl' option. The generated random peaks were classified into coding, proximal, and distal groups in the same way described in the Results section. The coordinates of gapped regions were downloaded from the UCSC table browser. We then counted the number of distal peaks that overlap with LTRs in sense and antisense directions (Fig. S2E) and that overlap with LTR subfamilies in the sense direction (Fig. S2J).

Rapid amplification of 3' cDNA ends (3' RACE)

We manually selected CAGE peaks derived from LTRs for 3' RACE. RNA samples from tumor and non-tumor samples (149T and 149NT respectively) were fractionated into polyA+ and polyA- pools with MicroPurist kit (Ambion). PolyA+ RNA fractions were reverse transcribed with PrimeScript (Takara) and random primers. For each target two subsequent

RACE PCRs were performed using Ex Taq (Takara), gene-specific forward primers and oligo dT reverse primers. Libraries of the RACE products were prepared using Nextera XT DNA Sample Preparation Kit (Illumina) and paired-end sequenced on Miseq platform (Illumina). The sequencing reads were assembled by Trinity with default parameters (Grabherr et al. 2011), and the assembled sequences were mapped to the human genome (hg19/GRCh37) using blat (version 34) (Kent 2002). A missing 5' sequence from the CAGE peak to a primer position was added to the assembled sequence. Coding potential was predicted for the obtained full-length sequences using the CPAT web server with default parameters (Wang et al. 2013).

Quantitative PCR for LTRs

Total RNA was extracted from tumor and non-tumor samples of 71 human HCCs. cDNA was synthesized using SuperScript II reverse transcriptase with random primers. Expressions levels of LTR-001, 002, 004, and 007 were measured by qPCR using target-specific primer sets and normalized to HMBS (Table S10).

Gene Set Enrichment Analysis

Gene set enrichment analysis was performed with GSEA 2.013 from broad institute and MsigDb 4.0 (Subramanian et al. 2005). Molecules known to be target of MYC were used to build a custom gene set compatible with GSEA software from Broad Institute: MYC targets were curated from publications by Cairo and al (Cairo et al. 2008). Genes targets of MYC enriched by GSEA analysis were implemented into Cytoscape version 3.0.1 to build a network (Shannon et al. 2003).

CAGE for LNA Knockdown samples

We prepared CAGE libraries for biological duplicates of Lipofectamine alone, scramble LNAs, two different LNAs targeting LTR-001, and two LNAs targeting LTR-002 at 12h and 48h after the transfection. A total of 24 CAGE libraries were sequenced with single-end reads of 50 bp on the Illumina HiSeq 2000 platform. Extraction of CAGE tags, mapping to the human genome, and TSS peak detections were done as described above. We compared expression levels between 4 knockdown samples using two different LNAs as a case group and 4 Lipofectamine with/without scramble LNAs as a control group with edgeR version 2.6.3. CAGE peaks that had bias to a specific barcode sequence were detected and removed by edgeR (FDR<1.0E-5).

References

- Cairo S, Armengol C, De Reynies A, Wei Y, Thomas E, Renard CA, Goga A, Balakrishnan A, Semeraro M, Gresh L et al. 2008. Hepatic stem-like phenotype and interplay of Wnt/beta-catenin and Myc signaling in aggressive childhood liver cancer. *Cancer cell* **14**: 471-484.
- Grabherr MG, Haas BJ, Yassour M, Levin JZ, Thompson DA, Amit I, Adiconis X, Fan L, Raychowdhury R, Zeng Q et al. 2011. Full-length transcriptome assembly from RNA-Seq data without a reference genome. *Nature biotechnology* **29**: 644-652.
- Kent WJ. 2002. BLAT--the BLAST-like alignment tool. *Genome research* **12**: 656-664.
- Quinlan AR, Hall IM. 2010. BEDTools: a flexible suite of utilities for comparing genomic features. *Bioinformatics* **26**: 841-842.
- Shannon P, Markiel A, Ozier O, Baliga NS, Wang JT, Ramage D, Amin N, Schwikowski B, Ideker T. 2003. Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome research* **13**: 2498-2504.
- Subramanian A, Tamayo P, Mootha VK, Mukherjee S, Ebert BL, Gillette MA, Paulovich A, Pomeroy SL, Golub TR, Lander ES et al. 2005. Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. *Proceedings of the National Academy of Sciences of the United States of America* **102**: 15545-15550.
- Wang L, Park HJ, Dasari S, Wang S, Kocher JP, Li W. 2013. CPAT: Coding-Potential Assessment Tool using an alignment-free logistic regression model. *Nucleic acids research* **41**: e74.

Supplementary Figure legends

Figure S1. Characterization of coding, proximal, and distal CAGE peaks. **A.** Distribution of distances between proximal peaks to their closest coding peaks. Sense indicates that coding and proximal peaks are the same strands and antisense indicates that they are the opposite strands. **B.**

Spearman's correlations for proximal vs. coding peaks and distal vs. coding peaks. **C.** Robustness of coding, proximal, and distal CAGE peaks. Graphs show how many tumor samples support CAGE peaks. A great majority of peaks in all groups are supported by more than half samples. **D.** Expression pattern of proximal peaks across human body. (see also Fig. 1E for coding and distal peaks)

Figure S2. Activation of LTR retroviral promoters in human HCC tumors. **A.** Expression levels of *GPC3*, the most significantly up-regulated coding gene in tumors. As reported by previous papers, *GPC3* is largely up-regulated in HCC. **B.** Fraction of peaks in repeats in the sense direction. **C.** Fraction of peaks in repeats in the anti-sense direction. **D.** Fraction of non-up-regulated peaks in repeats repetitive elements in the anti-sense direction. **E.** Fraction of randomized peaks in repeats in the sense direction. R1, 2, and 3 represent three sets of randomized peaks. **F.** Fraction of peaks in repeats excluding ERV internal domains (“-int” elements). **G.** Fraction of peaks in repeats using tags with mapping quality 30 or above. **H.** Fraction of peaks in repeats using the Gencode ver.19 (the latest for the hg19 genome) for the promoter classification instead of Gencode ver.12. **I.** Expression levels of non-LTR distal peaks in tumor, non-tumor (NT), and normal liver tissues. 'Liver' (normal adult and fetus liver tissues)

and 'Hepato' (three biological replicates of primary hepatocytes) data from the Fantom 5 Project are shown for comparison. To avoid log of zero, 0.005 is added to the tpm values. The median values of 'Normal', 'Liver', and 'Hepato' are 0.005, indicating no expression. **J.** Random overlap counts versus copy numbers for LTR subfamilies in the human genome. One dot represents one LTR subfamily. **K.** Sequence patterns of promoters in LTR12C elements. The upper panel shows a sequence logo generated by WebLogo based on the multiple alignment of significantly up-regulated LTR12C sequences. The lower panel shows a sequence logo for non-expressed LTR12C elements that retain the promoter region. **L.** Size distribution of all and up-regulated LTR12C and MER52A elements. **M.** Relative position of CAGE peaks on the LTRs excluding LTR12C subfamily members **N.** Distribution of CAGE tags on long (>5kb) LINE elements for different etiology groups. Blue (purple) bars: sense (antisense) direction with respect to the LINE elements. **O.** Significantly up-regulated repeat families (FDR<0.05) in tumor compared to non-tumor. The analysis was done using single-map as well as multi-map tags (mapping quality below 10). The vast majority of up-regulated families are LTR, whereas no SINE families are significantly changed.

Figure S3. Activation of LTR retroviral promoters in mouse HCC tumors. **A.** Numbers of peaks for coding, proximal, and distal peaks **B.** Fractions of significantly upregulated coding, proximal, and distal peaks in high-grade HCC tumors compared to WT. The threshold is set to $p < 0.05$ (FDR, calculated with edgeR). **C.** Fractions of up-regulated or non-upregulated peaks in repeats in the sense or anti-sense (AS) directions **D.** Fractions of up-regulated peaks excluding “-int” elements or using tags with mapping quality 30 or above. **E.** Significantly up-regulated repeat families (FDR<0.05) in HCC (high) compared to WT. The analysis was done using single-map as well as multi-map tags (mapping quality below 10). The vast majority of up-regulated families are LTR, whereas no SINE families are significantly changed.

Figure S4. Expression profiles of 43 LTR-derived ncRNAs. **A.** Expression values of 43 LTRs for tumors (red), non-tumors (yellow), and normal (green) samples. **B.** Expression values of LTRs (LTR-007 to LTR-043) in Fantom 5 samples: 133 human normal tissues (red), 421 primary cells (yellow), and 252 cell lines (green). **C.** Determination of all transcripts in LTR-001 and 002 loci by PCRs using 10 primer pairs designed on different exons. F1 and F1.1 were used as forward primers with reverse primers, R1-4 and R5-6 respectively. F2 and F2.1 were used as forward primers with reverse primers, R8-9 and R9-10 respectively. The obtained

bands marked by arrows were subjected to sequence by MiSeq 250bp paired-end and determined full-length transcripts.

Figure S5. qPCR validation of LTR-derived ncRNAs. Fold changes of LTR-001, 002, 004, and 007 in tumor compared to non-tumor samples were measured by qPCR in the first 50 samples and the second 21 samples.

Figure S6. Activity of the distal ncRNAs in HepG2 cells. **A.** Transcription factors significantly associated with up-regulated ncRNAs. TBP (TATA box-binding protein) had the lowest p-value, and ARID3A (AT-rich interactive domain-containing protein 3) had the highest binding counts around TSSs of the ncRNAs. **B.** Enrichment of ChIP-Seq peaks of RNA-Polymerase II, H3K4me3, H3K27ac, and DNase Footprints within 2 kb from CAGE peaks in LTR elements. The red and blue lines represent active and inactive peaks in the HepG2 cell line, respectively. **C.** Enrichment of ChIP-seq peaks of 6 transcription factors within 2kb from CAGE peaks in LTR elements. **D.** Knockdown efficiency of LTR-001 and 002 measured by qPCR at 12h, 24h, 48h, and 72h after transfection of LNAs into HepG2 cells. CT1: Lipofectamine alone, CT2: Lipofectamine with scramble LNAs, KD1: Lipofectamine with

LNA designed on the LTR. KD2: Lipofectamine with another LNA designed on the LTR. **E.**

Knockdown efficiency of LTR-001 and 002 at 12h and 48h measured by CAGE. **F.**

Representative correlation plots between two different LNAs targeting LTR-001 and LTR-002.

The average spearman's correlation coefficient between two different LNAs is 0.935 whereas

the correlation between biological replicates of the same LNAs is 0.928.

Figure S1

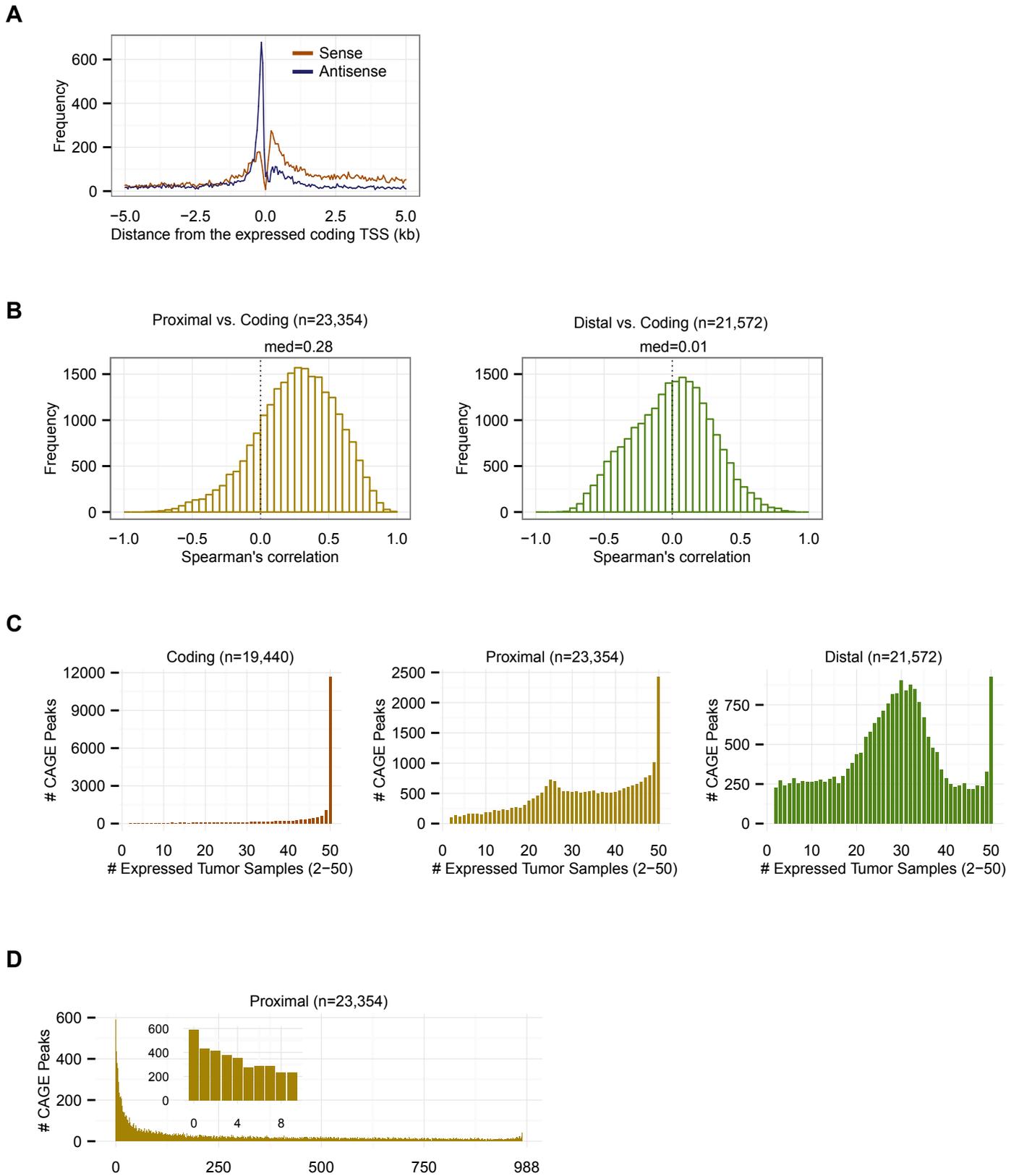
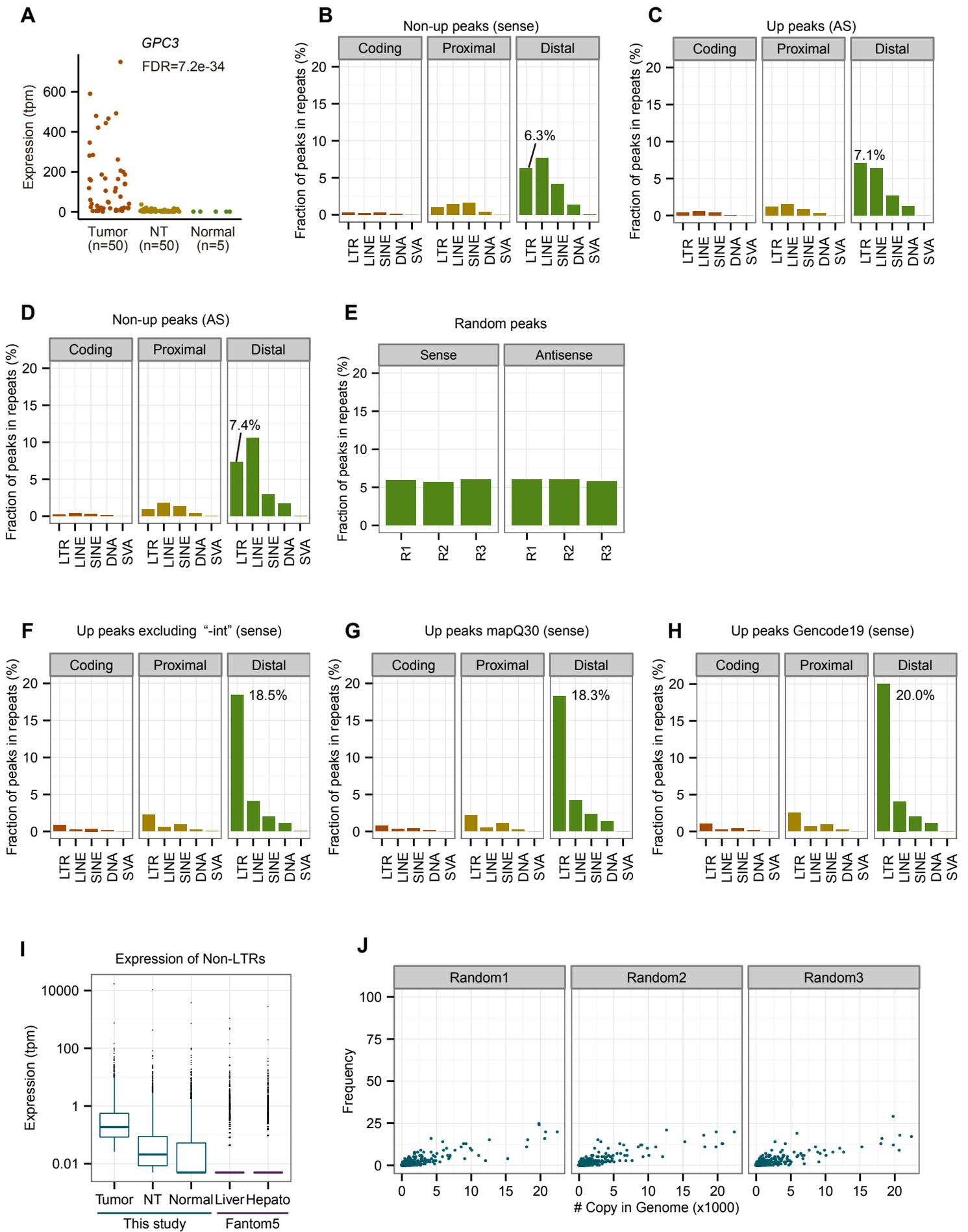


Figure S2



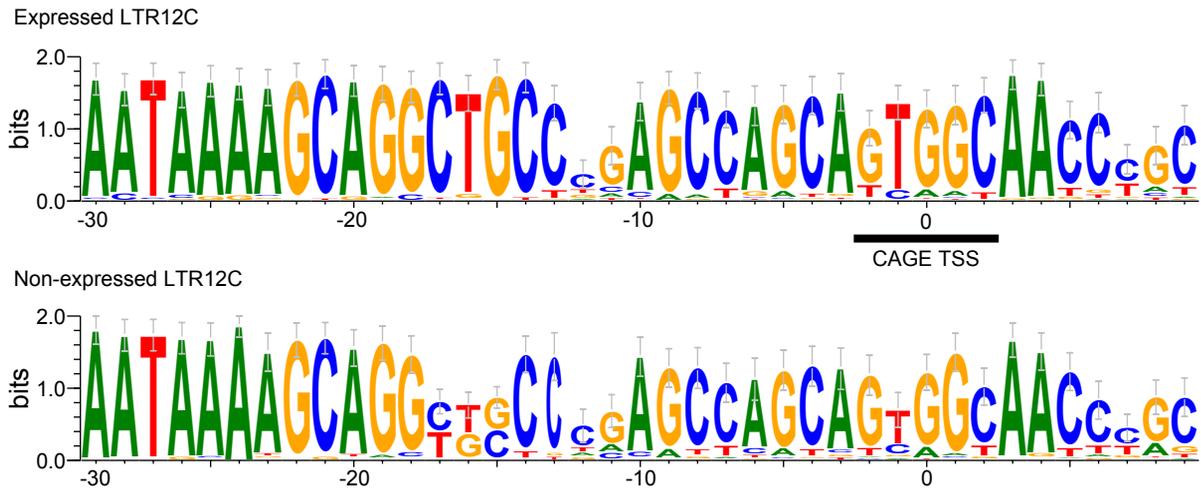
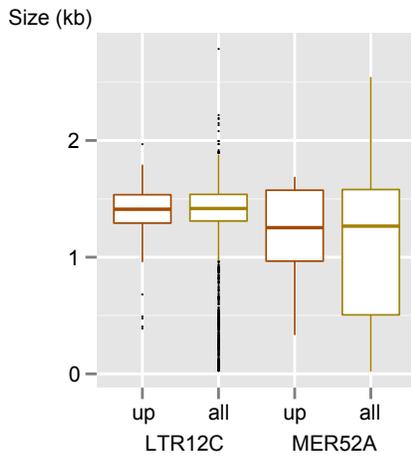
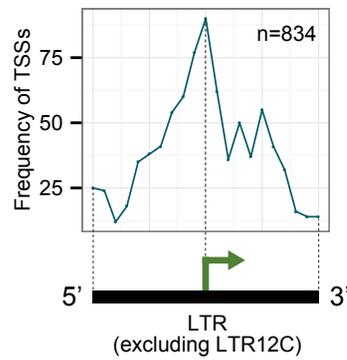
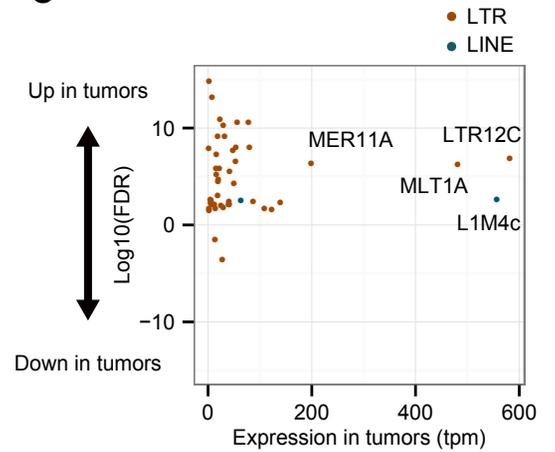
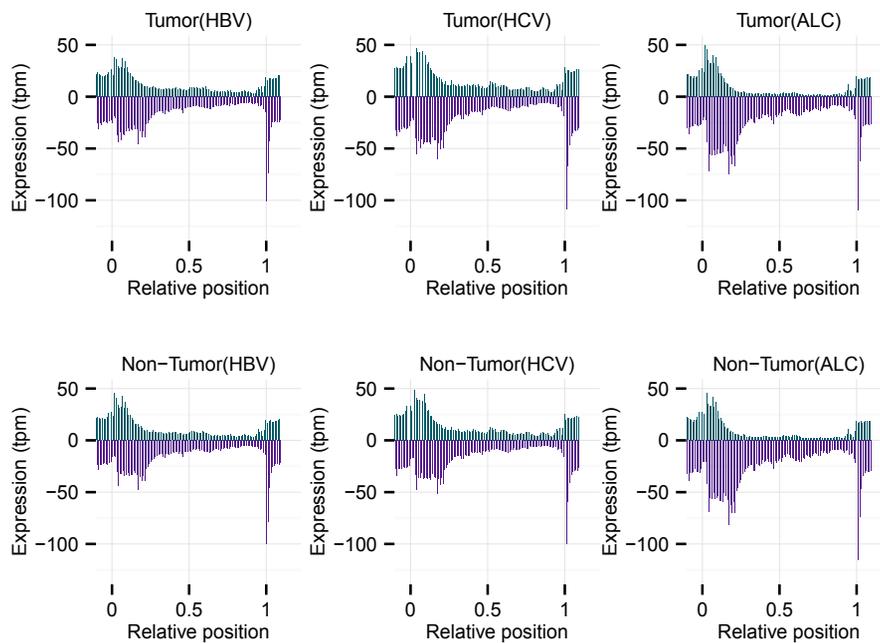
K**L****M****O****N**

Figure S3

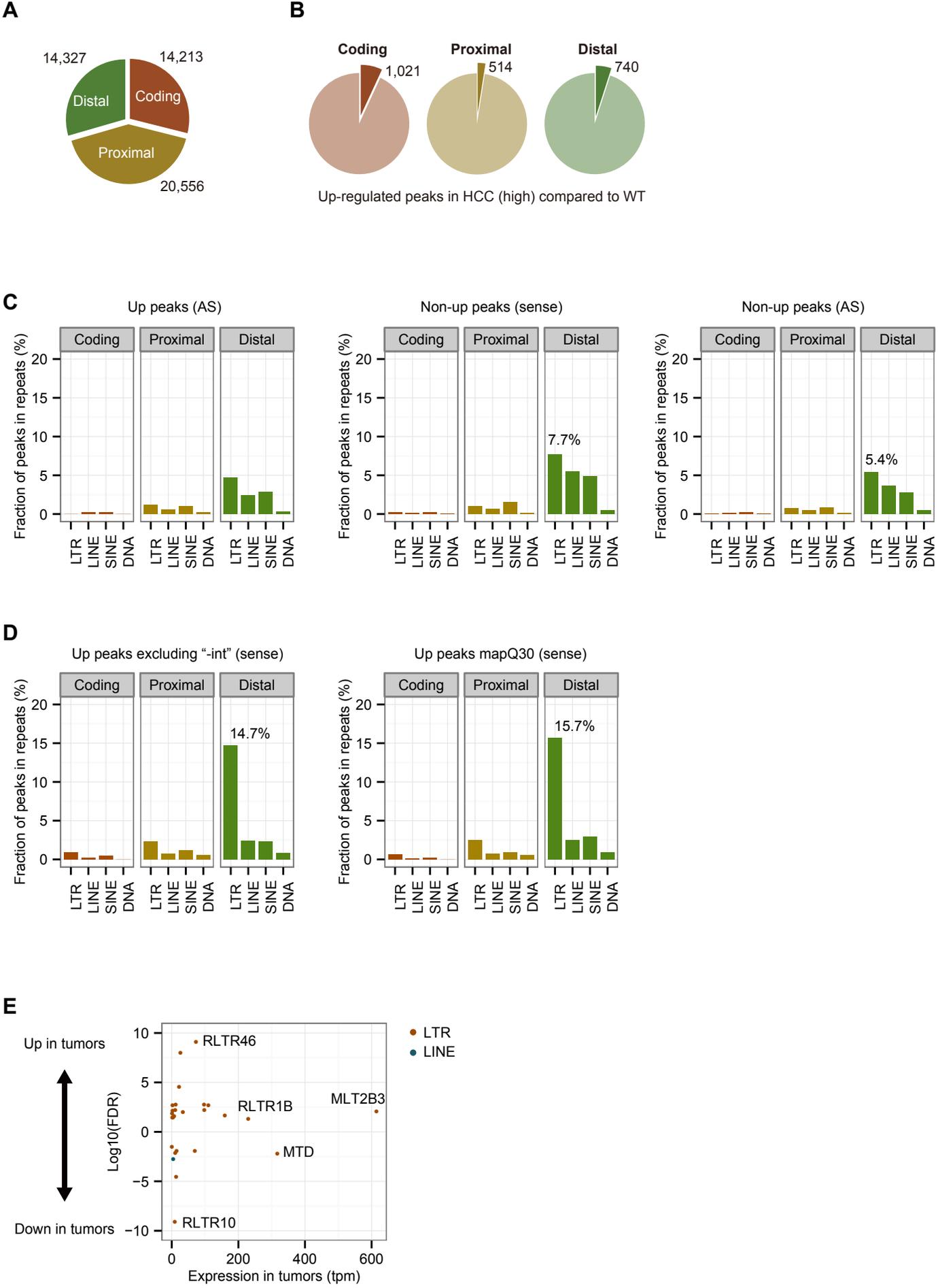


Figure S4A

Expression profiles of
43 LTRs in liver tissues

- Tumor (n=50)
- Non-tumor (n=50)
- Normal (n=5)

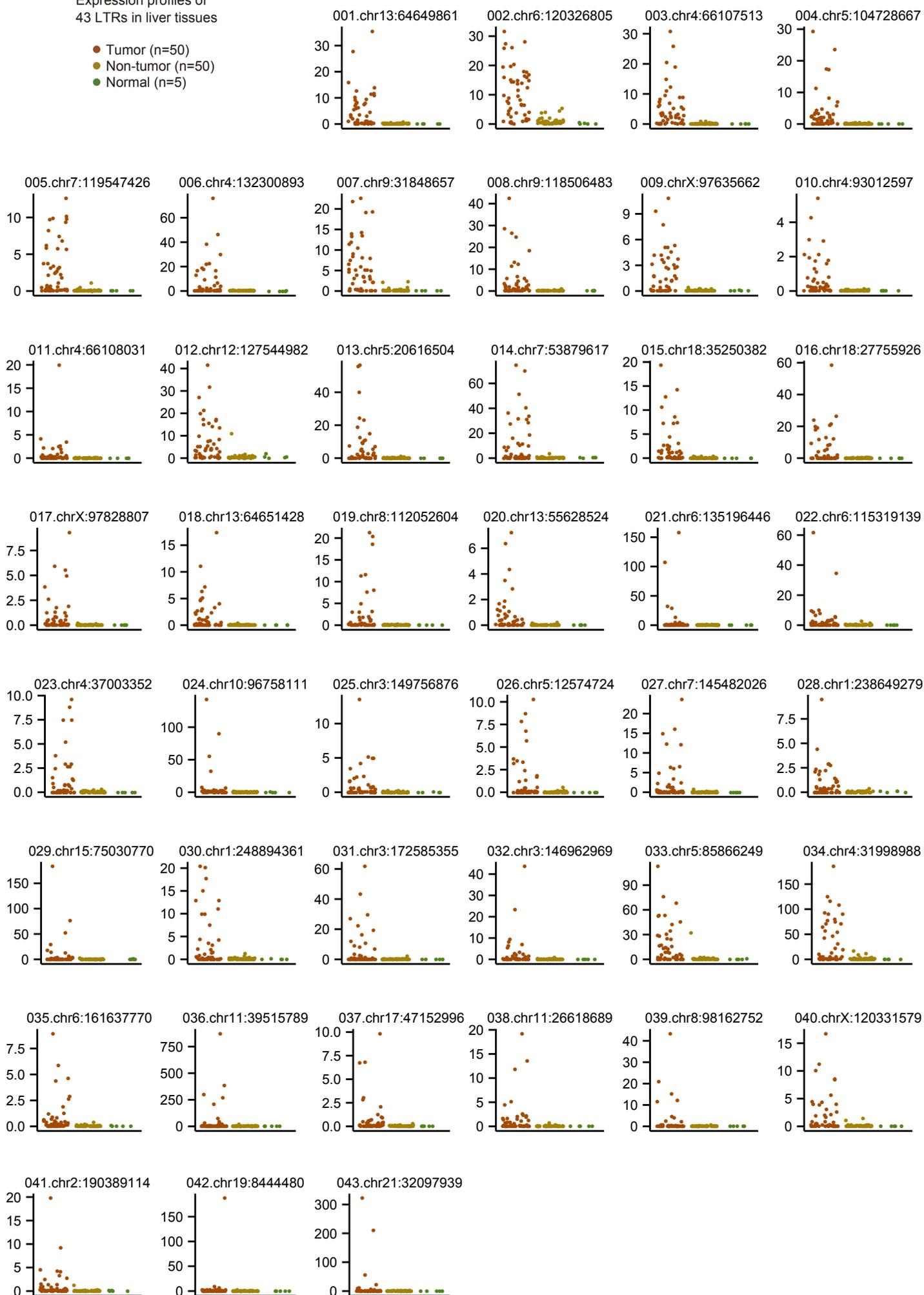


Figure S4B

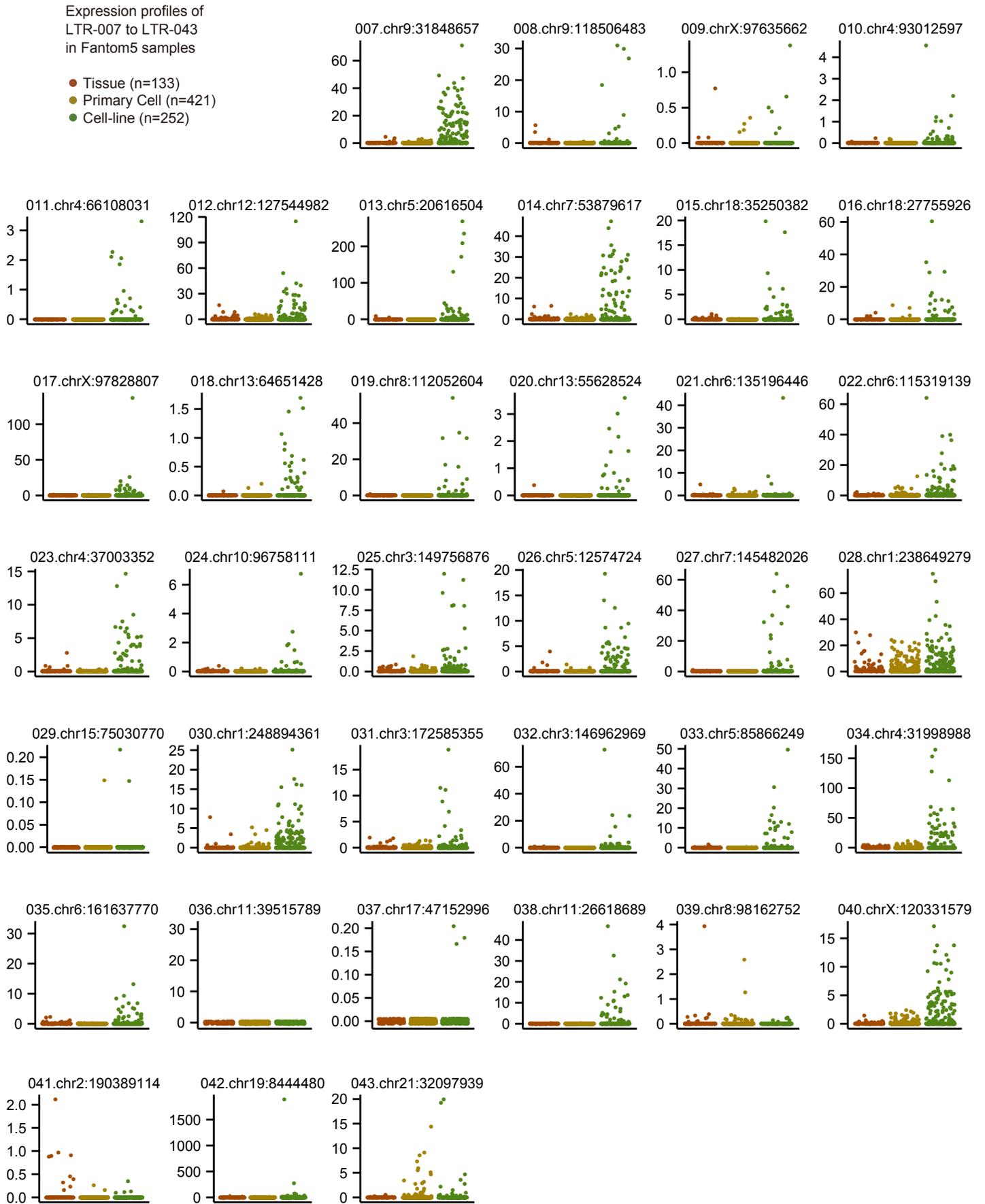
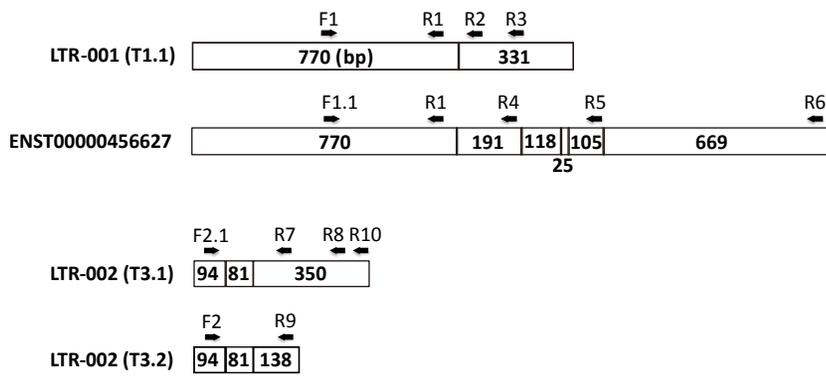


Figure S4C

Primer design



Forward Primers

F1 GACGCCCTGCCTATGGAAC
 F1.1 ACCAGCTGTCACTCTGGGTCTC
 F2 TCGCTTTCTGCCATGATTGC
 F2.1 TGTTTCCTACCGCGTTGTGAAG

Reverse Primers

R1 CCCAGAAAGGGTGTACAGT
 R2 CTGTGTCCATCCCTCCTCTG
 R3 AAATCCGACTTGCCCTTGAA
 R4 GCACATTGGCGTGATACAAC
 R5 GGCAGCGTTTCTTATCTGATGG
 R6 GAGGGAAGGATGGCAACTCATGG
 R7 AGTGTTATTTAATGTTACTATGGT
 R8 GGGTCTTTGTCCACATTTT
 R9 ATGAACCTGCAGATCCAGTG
 R10 AATTTACTTCACTTTATTGTGC

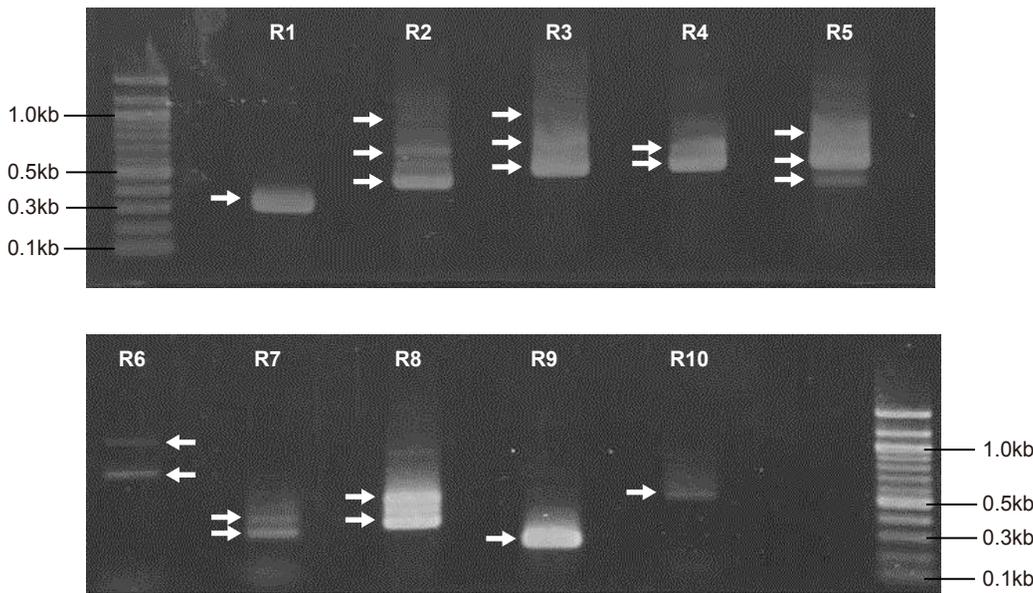
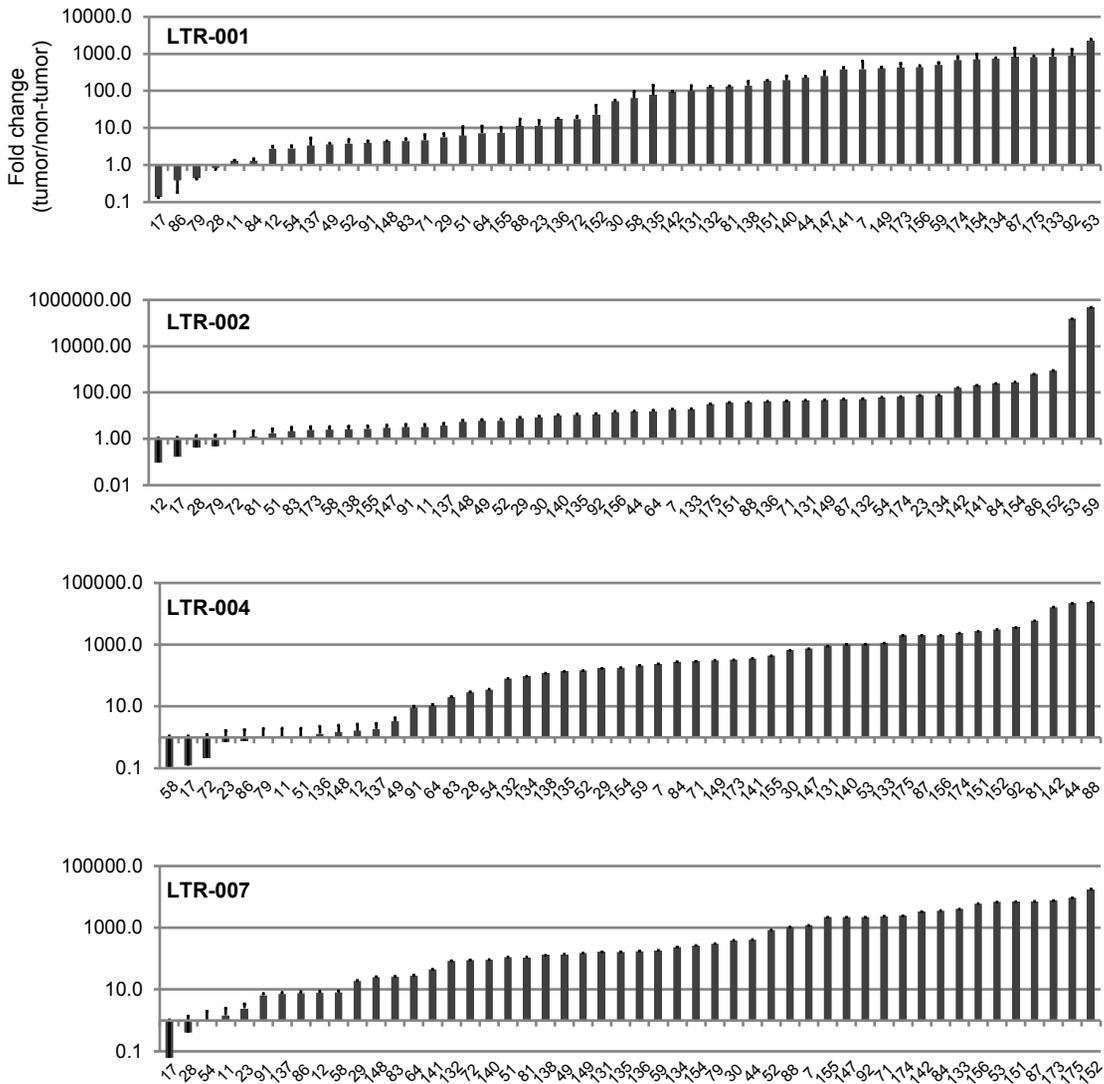
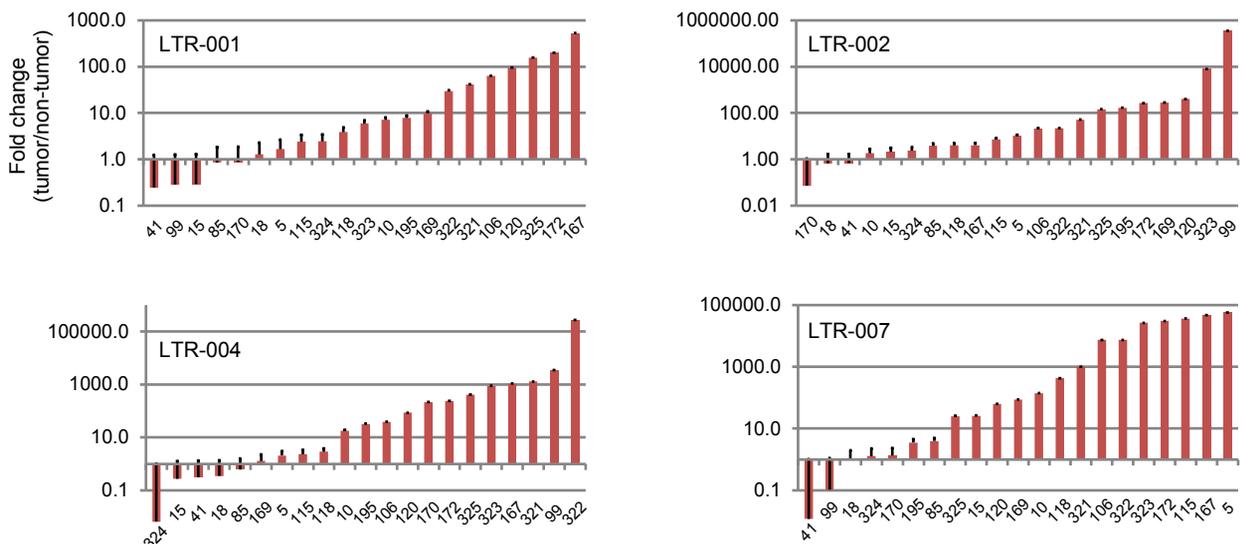


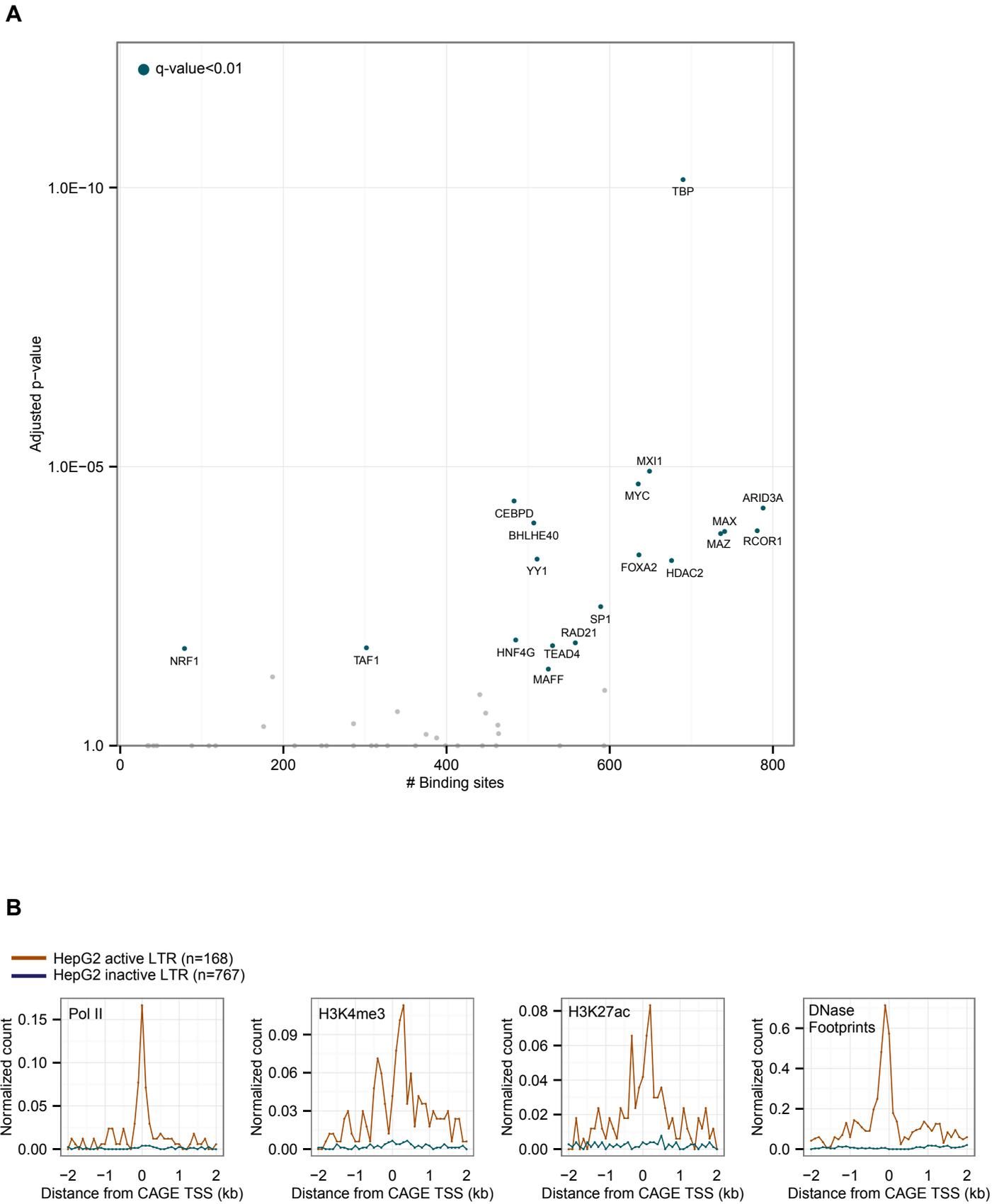
Figure S5

The first set: 50 samples



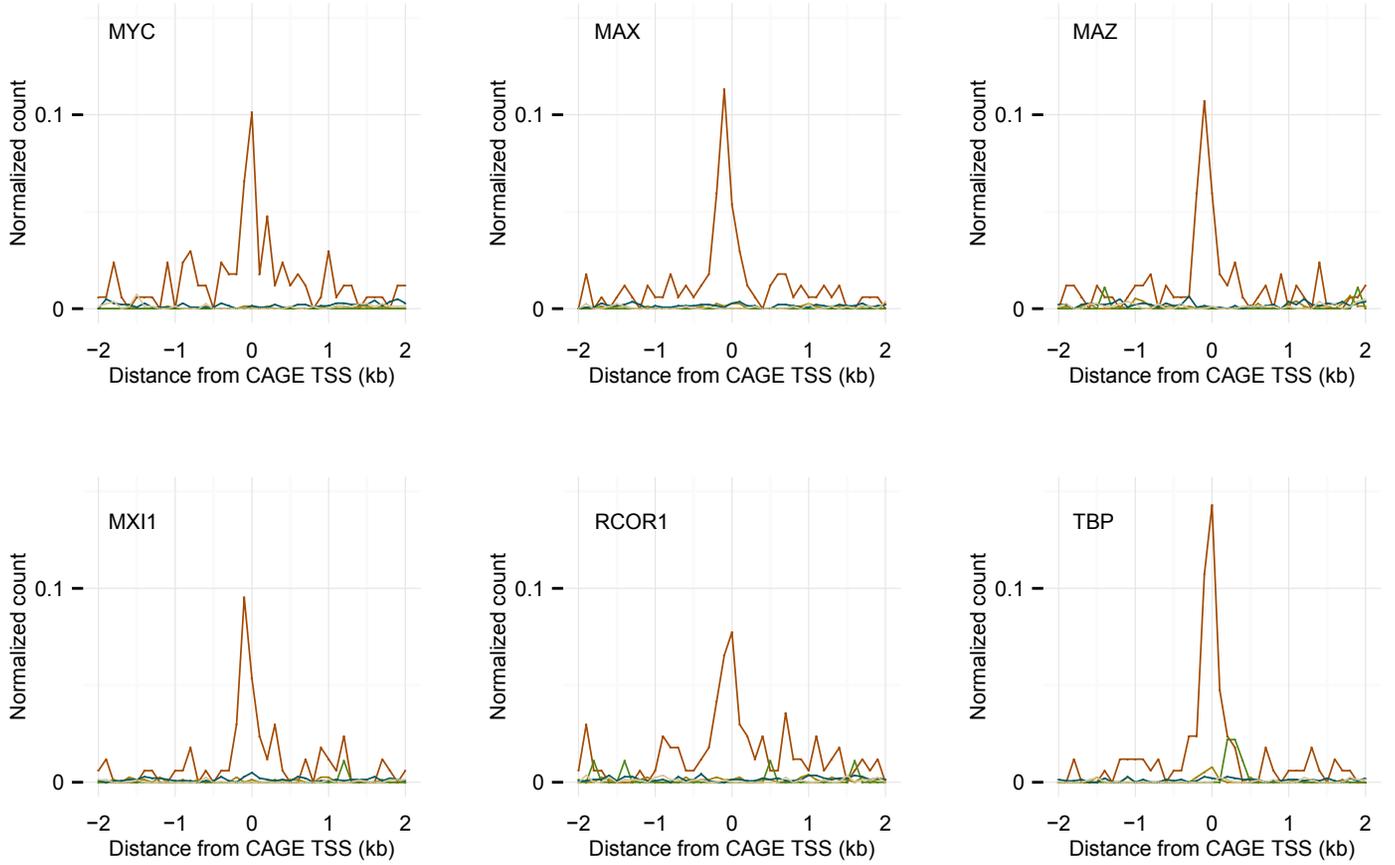
The second set: 21 samples





C

- HepG2 active LTR (n=168)
- HepG2 inactive LTR (n=767)
- HepG2 inactive LTR12C (n=91)
- LTR12B,C,D,E, or F (n=1418)
- LTR17 (n=831)



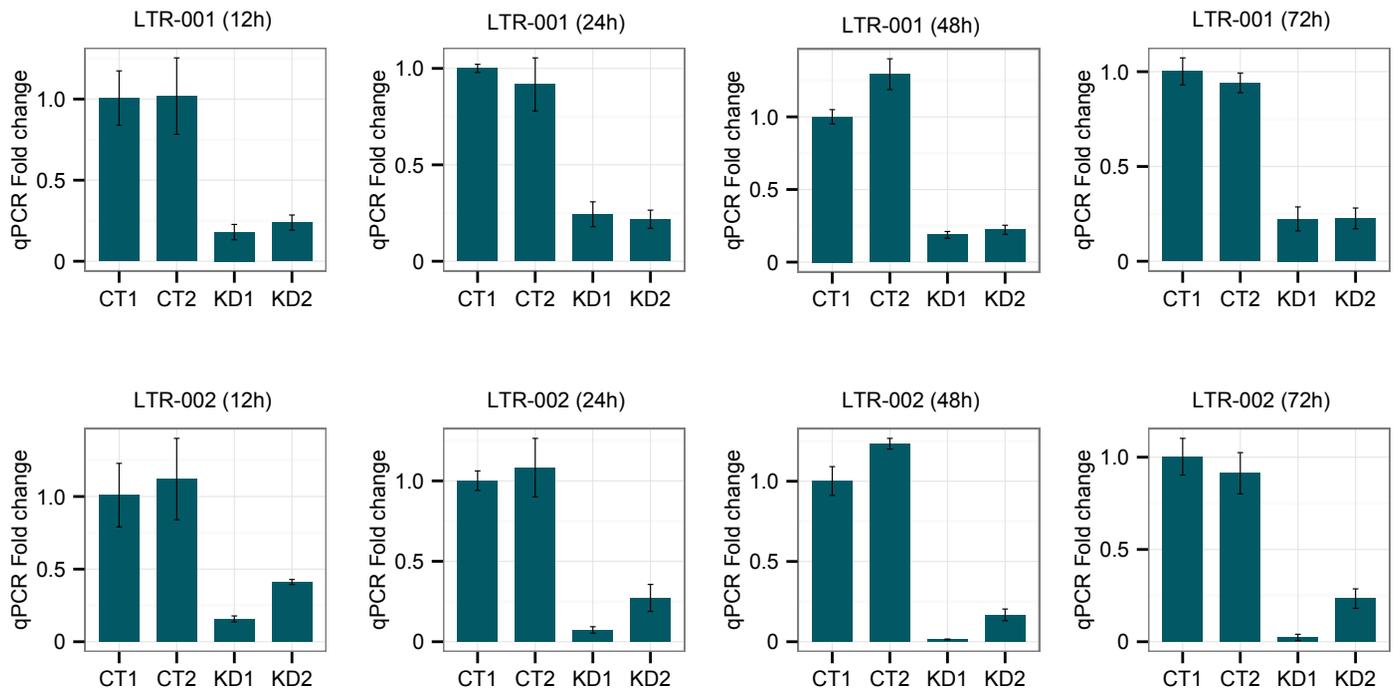
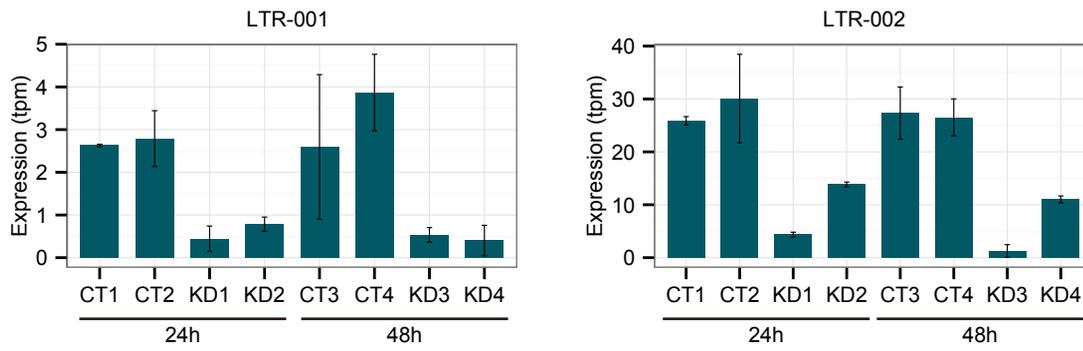
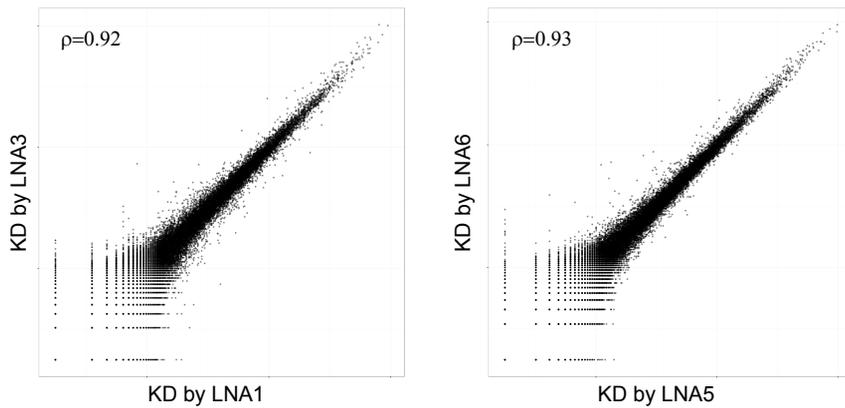
D**E****F**

Table S1. HCC samples with etiology and map counts

Number	Sample ID	Type	Etiology	Gender	RIN	Read count	Mapped	Single map	Map rate
1	17T	Tumor	HBV	male	8.6	13,704,114	11,131,494	10,057,951	81%
2	23T	Tumor	HBV	male	10	34,526,410	32,495,689	28,344,846	94%
3	52T	Tumor	HBV	male	8.7	9,393,758	8,529,410	7,986,553	91%
4	71T	Tumor	HBV	male	9.5	9,448,052	8,794,498	7,902,752	93%
5	81T	Tumor	HBV	male	7.9	29,757,451	27,673,138	24,261,335	93%
6	86T	Tumor	HBV	female	9	13,982,080	12,941,944	11,148,718	93%
7	133T	Tumor	HBV	male	7.9	13,554,448	12,241,611	10,706,465	90%
8	137T	Tumor	HBV	male	8.2	18,361,250	16,760,712	13,689,986	91%
9	140T	Tumor	HBV	male	7.1	25,775,615	23,950,279	19,768,074	93%
10	141T	Tumor	HBV	male	8	19,346,705	17,575,608	15,395,218	91%
11	154T	Tumor	HBV	male	7.7	18,581,260	16,944,580	15,187,136	91%
12	155T	Tumor	HBV	male	7.5	19,044,662	17,100,978	15,549,557	90%
13	156T	Tumor	HBV	male	7.6	11,163,135	10,290,388	9,269,347	92%
14	173T	Tumor	HBV	male	9.2	33,628,289	31,429,432	27,814,369	93%
15	174T	Tumor	HBV	male	8.4	13,286,218	12,318,911	10,806,132	93%
16	175T	Tumor	HBV	male	8.6	32,000,160	29,904,230	25,970,240	93%
17	11T	Tumor	HCV	male	8.8	31,347,758	29,386,132	25,245,047	94%
18	12T	Tumor	HCV	male	8.9	12,274,044	11,399,462	9,891,139	93%
19	29T	Tumor	HCV	male	8.8	17,434,011	16,246,397	14,100,265	93%
20	49T	Tumor	HCV	male	8.4	26,189,069	24,588,064	21,310,469	94%
21	72T	Tumor	HCV	male	8.5	26,938,828	25,199,079	22,030,051	94%
22	91T	Tumor	HCV	male	8.8	8,618,017	7,586,177	6,504,774	88%
23	131T	Tumor	HCV	female	8.2	24,397,405	22,003,796	18,310,187	90%
24	132T	Tumor	HCV	male	7.9	33,973,535	30,725,852	26,996,995	90%
25	134T	Tumor	HCV	male	8.1	30,285,017	26,693,466	22,398,364	88%
26	135T	Tumor	HCV	male	7.2	23,799,961	21,659,035	18,219,428	91%
27	136T	Tumor	HCV	male	8	19,114,206	17,332,811	14,978,015	91%
28	138T	Tumor	HCV	female	8.3	22,710,452	20,889,761	17,315,752	92%
29	142T	Tumor	HCV	male	6.9	21,295,859	19,295,625	16,544,160	91%
30	147T	Tumor	HCV	female	7.7	24,177,262	22,069,033	19,554,254	91%
31	148T	Tumor	HCV	female	8.2	12,114,410	10,897,676	9,860,845	90%
32	149T	Tumor	HCV	male	9	39,997,354	36,590,187	32,581,254	91%
33	151T	Tumor	HCV	female	8.4	15,890,142	14,356,824	12,764,379	90%
34	152T	Tumor	HCV	female	9	13,669,240	12,590,006	11,505,888	92%
35	28T	Tumor	Alcohol abuse	male	8.4	29,346,572	26,563,450	22,997,478	91%
36	30T	Tumor	Alcohol abuse	male	8.2	18,963,155	17,913,140	15,327,709	94%
37	44T	Tumor	Alcohol abuse	male	7.8	14,571,524	13,685,675	11,835,762	94%
38	7T	Tumor	Alcohol abuse	male	8.4	27,360,816	25,390,730	22,321,213	93%
39	83T	Tumor	Alcohol abuse	male	7.6	10,892,088	9,896,427	8,679,861	91%
40	88T	Tumor	Alcohol abuse	male	8.9	37,410,176	34,755,389	31,355,638	93%
41	92T	Tumor	Alcohol abuse	male	7.6	13,889,818	12,667,987	11,214,084	91%
42	59T	Tumor	Alcohol abuse	male	5.6	10,969,469	9,630,605	8,741,640	88%
43	58T	Tumor	Alcohol abuse	male	8	20,262,303	19,185,690	16,985,353	95%
44	64T	Tumor	Alcohol abuse	male	7	8,239,372	7,499,221	6,606,183	91%
45	51T	Tumor	HBV+HCV	male	9.5	22,472,479	20,667,558	19,046,624	92%
46	53T	Tumor	Autoimmune	female	8.6	13,127,042	12,008,177	10,593,579	91%
47	87T	Tumor	NASH	male	7.9	14,370,235	12,816,899	11,632,369	89%
48	54T	Tumor	WIL	male	7.7	9,866,988	8,832,359	8,123,513	90%
49	84T	Tumor	Unknown	male	8.1	16,839,679	15,081,376	13,596,219	90%
50	79T	Tumor	Unknown	male	8.8	11,366,739	10,671,947	9,450,468	94%
51	17NT	Non-tumor	HBV	male	8.2	4,952,149	4,089,802	3,657,964	83%
52	23NT	Non-tumor	HBV	male	9.3	31,859,986	29,345,240	25,672,297	92%
53	52NT	Non-tumor	HBV	male	9.2	15,459,585	14,346,903	12,737,372	93%
54	71NT	Non-tumor	HBV	male	7.8	24,525,111	22,857,897	19,659,022	93%
55	81NT	Non-tumor	HBV	male	8.6	36,083,947	33,644,047	29,861,955	93%
56	86NT	Non-tumor	HBV	female	6.3	13,267,499	11,990,398	10,084,745	90%

57	133NT	Non-tumor	HBV	male	8.3	15,809,573	13,918,837	12,073,071	88%
58	137NT	Non-tumor	HBV	male	8.2	14,928,380	13,576,095	11,586,526	91%
59	140NT	Non-tumor	HBV	male	7.9	18,848,537	16,907,315	14,932,883	90%
60	141NT	Non-tumor	HBV	male	7.4	20,099,768	18,015,093	15,331,814	90%
61	154NT	Non-tumor	HBV	male	7.3	22,278,862	20,214,152	18,398,102	91%
62	155NT	Non-tumor	HBV	male	6.2	10,352,268	9,422,626	8,656,389	91%
63	156NT	Non-tumor	HBV	male	6.9	8,100,277	7,449,314	6,746,743	92%
64	173NT	Non-tumor	HBV	male	9	31,890,433	30,102,764	26,417,530	94%
65	174NT	Non-tumor	HBV	male	8.6	19,465,347	18,041,909	15,775,145	93%
66	175NT	Non-tumor	HBV	male	6.5	26,287,447	25,091,661	21,805,115	95%
67	11NT	Non-tumor	HCV	male	8	16,738,091	15,788,083	13,572,802	94%
68	12NT	Non-tumor	HCV	male	8.4	22,067,957	20,430,729	17,695,368	93%
69	29NT	Non-tumor	HCV	male	8.7	8,921,719	8,238,391	7,187,997	92%
70	49NT	Non-tumor	HCV	male	8.5	25,164,907	23,470,166	20,504,277	93%
71	72NT	Non-tumor	HCV	male	7.9	28,129,758	25,898,262	22,881,340	92%
72	91NT	Non-tumor	HCV	male	9	16,859,719	15,062,680	13,230,514	89%
73	131NT	Non-tumor	HCV	female	7.8	11,434,712	10,215,653	8,671,702	89%
74	132NT	Non-tumor	HCV	male	7.8	24,134,839	21,738,928	18,785,473	90%
75	134NT	Non-tumor	HCV	male	7.8	18,354,742	16,665,006	14,186,414	91%
76	135NT	Non-tumor	HCV	male	7.4	21,285,078	19,269,560	16,079,945	91%
77	136NT	Non-tumor	HCV	male	7.8	10,372,005	9,213,917	8,114,142	89%
78	138NT	Non-tumor	HCV	female	7.8	25,810,748	23,327,876	19,663,074	90%
79	142NT	Non-tumor	HCV	male	8.8	30,947,952	28,213,004	24,865,650	91%
80	147NT	Non-tumor	HCV	female	7	20,920,849	18,814,767	16,594,177	90%
81	148NT	Non-tumor	HCV	female	8.1	16,256,292	14,614,583	13,176,739	90%
82	149NT	Non-tumor	HCV	male	8	25,049,915	22,501,418	20,198,693	90%
83	151NT	Non-tumor	HCV	female	9	18,103,115	16,333,599	14,602,482	90%
84	152NT	Non-tumor	HCV	female	8.2	15,227,304	13,819,750	12,623,047	91%
85	28NT	Non-tumor	Alcohol abuse	male	9.4	18,415,109	17,427,849	15,212,504	95%
86	30NT	Non-tumor	Alcohol abuse	male	8	36,677,681	34,582,453	29,705,982	94%
87	44NT	Non-tumor	Alcohol abuse	male	7.1	27,601,475	25,721,122	22,322,225	93%
88	7NT	Non-tumor	Alcohol abuse	male	7.6	15,400,894	14,500,578	12,649,686	94%
89	83NT	Non-tumor	Alcohol abuse	male	7.9	12,302,344	11,156,455	9,982,624	91%
90	88NT	Non-tumor	Alcohol abuse	male	7.1	23,386,207	21,203,361	19,163,055	91%
91	92NT	Non-tumor	Alcohol abuse	male	10	19,870,942	18,158,308	16,594,194	91%
92	59NT	Non-tumor	Alcohol abuse	male	6.8	14,761,194	13,053,058	11,926,456	88%
93	58NT	Non-tumor	Alcohol abuse	male	6.5	7,582,225	7,014,493	6,356,770	93%
94	64NT	Non-tumor	Alcohol abuse	male	7.3	9,943,414	9,286,654	8,327,211	93%
95	51NT	Non-tumor	HBV+HCV	male	7.6	11,586,463	10,097,726	8,866,281	87%
96	53NT	Non-tumor	Autoimmune	female	8.9	16,597,955	15,458,580	13,510,315	93%
97	87NT	Non-tumor	NASH	male	9.2	32,470,921	29,524,474	26,649,603	91%
98	54NT	Non-tumor	WIL	male	8.3	26,703,622	24,828,555	21,077,564	93%
99	84NT	Non-tumor	Unknown	male	7.9	25,205,759	22,195,075	19,733,852	88%
100	79NT	Non-tumor	Unknown	male	8.6	18,129,437	17,250,865	14,572,380	95%
101	NL2	Normal	Normal	undefined	7.8	16,883,878	15,142,360	13,574,375	90%
102	NL3	Normal	Normal	undefined	7.2	33,157,781	26,822,976	23,340,295	81%
103	NL4	Normal	Normal	undefined	7.4	24,782,874	22,339,733	19,748,343	90%
104	NL5	Normal	Normal	undefined	7.8	24,054,644	21,695,420	19,453,471	90%
105	NL6	Normal	Normal	undefined	7.3	14,627,021	13,160,229	11,571,324	90%

Table S2. Fantom5 data used to measure expression in normal livers

Number	Technology	Definition	Sample ID
1	CAGE	adult liver tissue	CNhs10624
2	CAGE	fetul liver tissue	CNhs11798
3	CAGE	primary hepatocyte donor1	CNhs12340
4	CAGE	primary hepatocyte donor2	CNhs12349
5	CAGE	primary hepatocyte donor3	CNhs12626

Table S3. A list of up-regulated LTR12C in human HCC

	Peak	Log2FC	FDR
1	chr13_64651428_64651436_-	6.1	2.8E-16
2	chr8_112052604_112052671_-	6.2	7.3E-16
3	chr2_108363389_108363407_-	6.9	1.0E-13
4	chr2_140168479_140168533_+	5.7	2.9E-13
5	chr5_12574724_12574910_-	5.5	3.3E-13
6	chr3_172585355_172585370_+	5.5	5.7E-13
7	chr3_146962969_146962989_-	6.3	6.8E-13
8	chr4_31998988_31999006_+	4.7	1.2E-12
9	chr2_88803503_88803509_+	7.5	1.3E-12
10	chr3_145051902_145051917_+	6.4	7.2E-12
11	chr11_21774394_21774408_-	5.6	2.3E-11
12	chr7_148141630_148141638_-	6.6	8.8E-11
13	chr8_83354646_83354651_+	5.9	1.2E-10
14	chr1_79735629_79735638_+	6.0	2.4E-10
15	chr3_83267071_83267112_-	5.1	8.7E-10
16	chr4_187812082_187812090_+	5.8	1.8E-09
17	chr4_163661593_163661651_+	5.5	2.0E-09
18	chr1_194327154_194327213_-	5.3	2.0E-09
19	chr11_29735181_29735221_+	5.7	9.8E-09
20	chr14_44854772_44854777_+	7.2	1.1E-08
21	chr1_154644064_154644071_+	4.0	1.3E-08
22	chr8_80289026_80289041_-	6.4	2.0E-08
23	chr22_26149438_26149489_+	5.6	5.4E-08
24	chr1_81643879_81643889_-	5.6	9.5E-08
25	chr11_42896529_42896534_+	6.3	1.1E-07
26	chr18_63273306_63273317_+	6.8	1.7E-07
27	chr4_138864174_138864179_+	6.1	2.0E-07
28	chr5_13579412_13579422_+	7.7	2.0E-07
29	chr1_187042495_187042523_-	4.7	6.3E-07
30	chr2_181556732_181556740_+	5.7	6.5E-07
31	chr3_163217645_163217657_+	5.8	1.6E-06
32	chr2_52007008_52007022_-	3.4	2.4E-06
33	chr6_28606947_28606954_-	7.4	2.6E-06
34	chr14_88200640_88200666_-	4.9	4.1E-06
35	chr8_84315924_84315972_+	4.7	4.2E-06
36	chr4_90412098_90412103_+	3.8	5.1E-06
37	chr8_117544072_117544076_+	8.7	5.7E-06
38	chr3_165635822_165635825_-	6.1	6.2E-06
39	chr14_41099157_41099160_-	4.3	7.8E-06
40	chr2_175412747_175412762_-	5.7	8.5E-06
41	chr3_145052033_145052038_+	5.8	9.3E-06
42	chr4_70441336_70441356_-	4.4	1.2E-05
43	chr9_87024408_87024421_+	6.3	1.8E-05
44	chr16_64377812_64377899_+	3.2	1.9E-05
45	chr1_210061899_210061905_-	8.3	2.0E-05
46	chr5_150689584_150689588_+	5.5	2.2E-05
47	chr6_30989607_30989611_+	7.7	3.4E-05
48	chr1_171350384_171350391_-	4.4	3.8E-05
49	chr3_79552183_79552188_+	4.1	4.0E-05
50	chr12_20936266_20936299_-	3.8	5.9E-05
51	chr7_83303632_83303637_+	8.2	7.3E-05
52	chr3_85554118_85554157_-	2.5	8.0E-05
53	chrX_118343588_118343600_-	3.5	8.3E-05
54	chr11_21774185_21774220_-	5.0	1.0E-04
55	chr5_19288676_19288683_+	7.7	1.1E-04
56	chr6_28926720_28926729_+	4.7	1.4E-04

57	chr14_70722346_70722352_+	3.5	1.5E-04
58	chr12_92028652_92028706_+	2.2	1.7E-04
59	chr10_62801186_62801190_+	8.3	1.8E-04
60	chr1_154644441_154644443_+	3.8	1.9E-04
61	chr4_14361000_14361038_+	3.9	1.9E-04
62	chr4_34336965_34336974_-	4.2	2.4E-04
63	chr6_122601794_122601878_+	2.6	3.0E-04
64	chr10_15467620_15467650_-	6.2	3.8E-04
65	chr3_137432930_137432963_-	5.3	5.0E-04
66	chr9_105248812_105248816_-	4.7	5.0E-04
67	chr13_91147974_91147983_+	4.7	5.7E-04
68	chr9_91300401_91300406_-	5.7	6.7E-04
69	chr15_62478283_62478287_-	4.3	9.0E-04
70	chr6_113010124_113010129_-	5.4	9.2E-04
71	chr4_142253763_142253785_-	1.2	9.3E-04
72	chr6_52652225_52652242_+	1.6	1.1E-03
73	chr13_55311031_55311041_-	4.0	1.1E-03
74	chr2_52234734_52234741_+	3.6	1.6E-03
75	chr8_127726265_127726269_-	3.9	2.6E-03
76	chr5_105582640_105582705_+	3.8	2.6E-03
77	chr10_67188563_67188589_-	4.2	3.1E-03
78	chr2_192787301_192787319_+	4.0	3.1E-03
79	chr12_6826148_6826150_+	4.5	3.5E-03
80	chr7_79369447_79369452_+	5.1	3.6E-03
81	chr12_72579863_72579867_+	6.3	4.0E-03
82	chr18_56127649_56127652_+	5.6	4.3E-03
83	chr13_81913922_81913954_-	6.7	4.6E-03
84	chr22_39754393_39754398_+	3.7	5.4E-03
85	chr9_21959870_21959874_+	4.2	5.8E-03
86	chr1_115904381_115904395_-	2.5	6.1E-03
87	chr11_84019132_84019170_-	2.8	8.8E-03
88	chrX_118341749_118341754_-	3.3	9.4E-03
89	chr6_36331397_36331401_-	2.0	9.7E-03
90	chr6_28833662_28833666_-	3.2	1.1E-02
91	chr6_24765752_24765756_-	2.9	1.6E-02
92	chr6_30774806_30774810_-	2.9	1.8E-02
93	chr6_64152249_64152258_-	2.7	1.8E-02
94	chr4_6310364_6310369_-	3.1	2.1E-02
95	chr4_88784227_88784231_-	3.2	2.5E-02
96	chrX_118055535_118055549_-	2.6	2.9E-02
97	chr1_191701634_191701668_+	2.4	2.9E-02
98	chr12_6818234_6818238_+	2.6	3.5E-02
99	chr11_124960335_124960376_+	2.7	4.1E-02
100	chr6_28436674_28436680_-	3.7	4.3E-02
101	chr7_152235561_152235568_-	1.5	4.4E-02
102	chr2_178701305_178701309_+	2.4	4.6E-02
103	chr12_71771003_71771009_+	3.0	4.6E-02
104	chr19_39313478_39313484_+	2.2	4.7E-02

Table S4. mouse liver samples with histology and map counts

Number	ID	Category	Histology	Gender	RIN	Read count	Mapped	Single map	Map rate	Used for statistics
1	71	WT	WT tissues	male	7.9	24,948,298	23,275,609	17,015,995	93%	Y
2	72	WT	WT tissues	male	7.5	12,925,948	11,701,886	8,936,593	91%	Y
3	73	WT	WT tissues	male	9.2	51,083,095	47,115,296	34,089,432	92%	Y
4	66	WT	WT cells	male	8.5	24,667,464	21,967,015	17,166,449	89%	N
5	67	WT	WT cells	male	7.3	7,594,431	6,955,074	5,124,318	92%	N
6	68	WT	WT cells	male	9.1	46,641,665	43,485,158	29,644,387	93%	N
7	58	INFL	Inflammation	male	7.5	40,776,157	37,669,539	32,020,059	92%	N
8	60	INFL	Inflammation	male	7.4	12,189,140	10,323,740	8,750,051	85%	N
9	59	INFL	Inflammation	male	5.9	4,396,831	3,423,206	3,074,718	78%	N
10	50	AD	40% AD, 0% HCC	female	8.2	5,747,335	5,110,778	4,625,606	89%	N
11	25	AD	30% AD, 0% HCC	male	6.4	7,122,524	5,031,920	4,542,201	71%	N
12	27	AD	20% AD, 0% HCC	male	6.9	4,613,660	3,909,734	3,520,529	85%	N
13	43	AD	60% AD, 0% HCC	male	6.1	11,085,453	9,407,793	8,580,968	85%	N
14	39	HCC (low)	70% AD, 20% HCC	male	7.5	12,784,580	11,687,696	10,565,343	91%	N
15	35	HCC (low)	70% AD, 10% HCC	male	7.6	22,446,560	20,513,738	18,559,098	91%	N
16	51	HCC (low)	10% AD, 20% HCC	female	7.1	15,155,881	12,725,069	11,857,857	84%	N
17	32	HCC (low)	60% AD, 10% HCC	male	7.3	21,738,865	19,081,480	17,519,961	88%	N
18	48	HCC (low)	50% AD, 20% HCC	male	7.6	3,163,218	2,354,036	2,192,109	74%	N
19	45	HCC (low)	30% AD, 40% HCC	female	7.2	11,416,625	10,515,674	9,597,571	92%	N
20	36	HCC (low)	80% AD, 10% HCC	male	7.6	6,674,328	5,274,349	4,833,128	79%	N
21	40	HCC (low)	80% AD, 20% HCC	male	7	3,634,863	3,115,385	2,770,311	86%	N
22	41	HCC (low)	70% AD, 30% HCC	male	8	9,433,303	8,432,116	7,712,509	89%	N
23	31	HCC (low)	70% AD, 10% HCC	male	6.5	6,082,739	4,954,134	4,493,532	81%	N
24	46	HCC (low)	80% AD, 10% HCC	female	6	2,007,420	1,780,884	1,630,205	89%	N
25	47	HCC (low)	80% AD, 10% HCC	female	6.2	4,055,905	3,670,159	3,354,484	90%	N
26	42	HCC (low)	70% AD, 20% HCC	male	5.2	5,703,096	4,828,486	4,319,918	85%	N
27	34	HCC (low)	70% AD, 20% HCC	male	5.9	6,373,320	5,603,402	5,062,103	88%	N
28	49	HCC (low)	0% AD, 50% HCC	female	7.5	2,798,209	2,271,901	2,110,452	81%	N
29	28	HCC (low)	20% AD, 50% HCC	male	6.1	2,856,689	2,266,860	2,042,043	79%	N
30	29	HCC (high)	0% AD, 90% HCC	male	7.4	12,809,505	11,879,489	10,653,463	93%	Y
31	37	HCC (high)	20% AD, 70% HCC	male	7.9	26,022,427	22,719,787	19,571,009	87%	Y
32	38	HCC (high)	20% AD, 70% HCC	male	9	25,638,306	21,871,072	19,641,767	85%	Y
33	30	HCC (high)	10% AD, 70% HCC	male	7.2	29,985,584	25,454,293	23,145,872	85%	Y
34	24	HCC (high)	20% AD, 80% HCC	male	4	3,332,081	2,318,807	2,169,238	70%	N
35	44	HCC (high)	10% AD, 60% HCC	female	5.4	3,364,254	2,679,636	2,415,675	80%	N
36	26	HCC (high)	10% AD, 60% HCC	male	5.3	2,859,731	2,122,221	1,936,007	74%	N
37	33	HCC (high)	0% AD, 60% HCC	male	4.8	5,682,756	4,096,510	3,692,358	72%	N

Table S5. A list of up-regulated LTR in mouse HCC

Num	Chr	Peak Start	Peak End	STR	FDR	LTR	Num	Chr	Start	End	STR	FDR	LTR
1	chr10	35166197	35166483	-	2.32E-09	RLTR4_MM-int	71	chr3	6375406	6375657	+	5.55E-03	RLTR27
2	chr2	80144374	80144811	-	2.35E-09	RLTR47_MM	72	chr8	25522802	25522807	+	5.65E-03	RLTR12B
3	chr6	141824559	141824573	+	3.81E-08	RLTR41	73	chr10	30354461	30354541	+	5.71E-03	MuRRS4-int
4	chr17	53181751	53181960	-	4.83E-08	RLTR47_MM	74	chr17	21611849	21612028	+	5.75E-03	MMVL30-int
5	chr7	5685012	5685128	+	8.19E-08	RLTR10A	75	chr13	33233239	33233486	-	5.75E-03	MMVL30-int
6	chr16	56116366	56116452	-	3.49E-07	RLTR17	76	chr9	1.22E+08	1.22E+08	-	6.21E-03	MLT1F1
7	chr4	107806906	107806917	+	5.71E-07	RLTR41	77	chr4	75046957	75047195	+	6.30E-03	RLTR44A
8	chr8	129409521	129409604	-	6.34E-07	ORR1E	78	chr12	49549721	49549825	-	6.34E-03	RLTR44E
9	chr3	84445398	84445413	-	7.00E-07	RMER19B	79	chr4	88626393	88626504	+	6.55E-03	RLTR20A2
10	chr11	31445733	31445973	+	1.45E-06	RLTR10D	80	chr10	1.05E+08	1.05E+08	+	8.16E-03	IAPLTR4_I
11	chr3	45018416	45018449	+	1.45E-06	RLTR10D	81	chr13	43444677	43445033	+	8.41E-03	RMER19B
12	chr1	123242725	123242859	-	6.02E-06	ORR1B1	82	chr12	41770170	41770262	+	8.41E-03	MTD
13	chr10	84525235	84525412	-	1.10E-05	RLTR47_MM	83	chr4	55355611	55355680	-	8.64E-03	ORR1A4
14	chr18	74508653	74508811	+	1.15E-05	RLTR47_MM	84	chr14	14766737	14766763	+	9.42E-03	RLTR1B-int
15	chr3	21857346	21857736	-	1.17E-05	MT2C_Mm	85	chr18	38388181	38388256	+	9.78E-03	RMER19B
16	chr4	118616054	118616058	-	2.57E-05	MTA_Mm	86	chr15	57416215	57416222	+	1.01E-02	RLTR10D
17	chr6	43466689	43466920	+	3.27E-05	RMER6A	87	chr4	1.08E+08	1.08E+08	+	1.05E-02	MMVL30-int
18	chr18	64793437	64793497	-	4.16E-05	MTC	88	chrX	12999375	12999753	+	1.07E-02	RMER19B
19	chr15	10762808	10762885	+	4.50E-05	RLTR15	89	chr3	63045386	63045393	+	1.11E-02	RLTR41
20	chr6	141825999	141826123	+	5.57E-05	MMVL30-int	90	chr6	1.4E+08	1.4E+08	+	1.19E-02	RLTR20D
21	chr9	76274130	76274268	-	5.64E-05	MMVL30-int	91	chr12	86392448	86392577	+	1.23E-02	MYSERV6-int
22	chr17	11097002	11097167	+	6.27E-05	MTD	92	chr18	74452655	74452872	-	1.24E-02	MMVL30-int
23	chr5	58968860	58969002	+	7.26E-05	RLTR10A	93	chr12	19125205	19125336	+	1.36E-02	MMVL30-int
24	chr8	25522830	25522945	+	8.36E-05	RLTR12B	94	chr4	85706515	85706551	-	1.37E-02	MLT1A1
25	chr6	54359293	54359449	-	9.01E-05	LTR81C	95	chr10	17724993	17725182	-	1.49E-02	RLTR15
26	chr2	107805033	107805355	+	9.15E-05	MTEa	96	chr10	40537776	40537847	+	1.58E-02	RMER16-int
27	chr13	104285139	104285262	+	1.10E-04	MTD	97	chr17	63653523	63653555	-	1.63E-02	RMER19B
28	chr6	11138865	11138951	+	1.79E-04	RLTR1B-int	98	chrX	1.47E+08	1.47E+08	+	1.64E-02	MMVL30-int
29	chr7	93987704	93987785	+	2.40E-04	RLTR10A	99	chr2	16813973	16814215	-	1.74E-02	MuRRS4-int
30	chr2	7531849	7531853	+	2.93E-04	RLTR6_Mm	100	chr3	40732912	40733009	-	1.78E-02	RLTR44B
31	chr17	17641623	17641633	+	3.07E-04	RLTR1B	101	chrX	1.13E+08	1.13E+08	+	1.86E-02	MMVL30-int
32	chr2	34689323	34689327	-	3.19E-04	RLTR27	102	chr2	1.72E+08	1.72E+08	+	1.91E-02	RLTR47_MM
33	chr14	14767874	14767925	+	3.28E-04	RLTR1B-int	103	chrX	93450865	93451028	+	2.01E-02	MTEa
34	chr15	36656474	36656694	+	3.31E-04	RMER17C-int	104	chr13	52118311	52118373	+	2.18E-02	RLTR31B_Mm
35	chr5	87007787	87008202	+	3.88E-04	MMVL30-int	105	chr1	54379933	54379982	-	2.20E-02	MMVL30-int
36	chr17	49103178	49103236	-	4.22E-04	ORR1E	106	chr1	84846537	84846631	-	2.30E-02	ORR1D1
37	chr17	50560909	50561112	+	4.65E-04	MuRRS4-int	107	chrX	11901036	11901150	+	2.32E-02	RLTR40
38	chr14	14765074	14765109	+	4.81E-04	RLTR1B	108	chr14	36501981	36501987	+	2.33E-02	RLTR44B
39	chr6	81971172	81971284	-	5.23E-04	MTD	109	chr3	28753069	28753183	-	2.53E-02	MuRRS4-int
40	chr15	41747509	41747753	+	6.10E-04	RMER6C	110	chr17	18695410	18695693	+	2.53E-02	IAPLTR4
41	chr16	9176527	9176567	-	6.39E-04	RLTR47_MM	111	chr4	7622683	7622686	-	2.64E-02	RLTR27
42	chr1	15062947	15062972	+	6.64E-04	RLTR10A	112	chr12	49546462	49546535	-	2.72E-02	RLTR44E
43	chr6	130348617	130348728	+	9.81E-04	RLTR27	113	chr6	37489670	37489792	+	2.78E-02	RLTR18B
44	chr15	47199928	47200124	+	9.99E-04	RLTR1B-int	114	chr9	1.23E+08	1.23E+08	+	2.78E-02	ORR1A2
45	chr12	105615772	105615840	+	1.23E-03	RLTR9E	115	chr1	23170919	23171084	+	2.81E-02	ORR1A4
46	chr19	23360512	23360831	+	1.24E-03	RMER19B	116	chr15	32743923	32743925	-	2.82E-02	RLTR10D
47	chr13	35689821	35690130	-	1.27E-03	RMER19B	117	chr2	23893179	23893221	+	2.84E-02	MuRRS-int
48	chr10	102969968	102969996	+	1.40E-03	RLTR10D	118	chr5	23762526	23762531	+	2.86E-02	RLTR13D3
49	chr19	58975066	58975072	-	1.55E-03	RLTR10D	119	chr2	1.04E+08	1.04E+08	+	2.95E-02	RLTR17
50	chr16	31927072	31927135	+	1.57E-03	RLTR47_MM	120	chr1	1.67E+08	1.67E+08	-	2.96E-02	MTD
51	chr1	31217413	31217422	+	1.59E-03	RMER19B	121	chr17	17644928	17644945	+	2.97E-02	RLTR1B-int
52	chr2	122771825	122771892	+	1.77E-03	LTR88c	122	chr3	1.37E+08	1.37E+08	-	3.05E-02	ORR1E
53	chr5	45686513	45686641	-	1.86E-03	MLT2B2	123	chr5	1.09E+08	1.09E+08	+	3.24E-02	RLTR31A_Mm
54	chrX	83781606	83781690	-	1.93E-03	RLTR10A	124	chr18	11215228	11215313	+	3.27E-02	RLTR20B3
55	chr16	78460645	78460697	+	2.07E-03	MuRRS4-int	125	chr15	74762666	74762737	+	3.42E-02	RLTR6-int
56	chr3	11036473	11036567	+	2.18E-03	RLTR41	126	chr11	66795121	66795128	+	3.45E-02	RLTR31A_Mm
57	chr7	10774537	10774707	+	2.42E-03	RLTR10A	127	chr1	58672684	58672752	-	3.45E-02	ORR1E-int
58	chr11	12566633	12566804	+	2.68E-03	RLTR16	128	chr17	18692758	18692892	+	3.52E-02	RLTR9E
59	chr8	3309684	3309830	-	2.86E-03	RLTR44B	129	chr3	17450800	17450803	+	3.53E-02	RLTR10A
60	chr2	84371467	84371639	-	2.90E-03	MTEa	130	chr15	41057268	41057300	+	3.81E-02	LTRIS_Mus
61	chr3	39689498	39689558	-	3.24E-03	RLTR10A	131	chr5	1.48E+08	1.48E+08	-	3.90E-02	MTEa
62	chr10	31023041	31023233	-	3.36E-03	RLTR47_MM	132	chrX	23411012	23411093	+	3.90E-02	RLTR10A
63	chr9	70082940	70083016	+	3.44E-03	MTD	133	chr1	1.8E+08	1.8E+08	-	4.02E-02	RLTR16
64	chr2	59503383	59503529	+	3.83E-03	LTR33A_	134	chr8	42237597	42237645	-	4.16E-02	RLTR20D
65	chr3	85150410	85150547	+	3.90E-03	RMER19B	135	chr19	10042810	10042861	+	4.16E-02	RLTR25B
66	chr14	14765421	14765438	+	4.03E-03	RLTR1B-int	136	chr18	19012082	19012118	+	4.21E-02	MMERGLN-int
67	chr17	10888438	10888508	-	4.46E-03	MTE2b	137	chrX	1.1E+08	1.1E+08	-	4.30E-02	ORR1A4
68	chr4	118669814	118669906	-	4.56E-03	RLTR44B	138	chr3	1.11E+08	1.11E+08	-	4.85E-02	RLTR10D
69	chr17	75219028	75219367	-	5.46E-03	RMER19C	139	chr12	19846033	19846036	+	4.92E-02	MMERGLN-int
70	chr16	31557436	31557768	-	5.50E-03	RLTR47_MM	140	chr7	10724062	10724232	+	4.98E-02	IAPLTR4

Table S6. The most significantly up-regulated distal peaks (43 LTRs and 90 non-LTRs, Y: tested, N: not tested)

	TYPE	Name	Peak	LTR	Log2FC	FDR	RACE	qPCR	KD
1	LTR	LTR-001	chr13_64649861_64650181_-	MER52A	5.2	2.4E-27	Y	Y	Y
2	LTR	LTR-002	chr6_120326805_120326870_+	THE1D	3.5	1.5E-24	Y	Y	Y
3	LTR	LTR-003	chr4_66107513_66107548_-	MER52A	6.1	2.4E-24	Y	N	N
4	LTR	LTR-004	chr5_104728667_104728706_-	MER52A	6.1	2.9E-21	Y	Y	N
5	LTR	LTR-005	chr7_119547426_119547433_-	THE1A	5.8	1.9E-20	N	N	N
6	LTR	LTR-006	chr4_132300893_132300970_+	LTR12D	6.0	3.5E-20	N	N	N
7	LTR	LTR-007	chr9_31848657_31848713_+	MER61A	5.0	2.6E-19	Y	Y	N
8	LTR	LTR-008	chr9_118506483_118506625_-	MER50B	5.5	1.4E-18	Y	N	N
9	LTR	LTR-009	chrX_97635662_97635698_-	MER61B	5.6	4.2E-18	Y	N	N
10	LTR	LTR-010	chr4_93012597_93012646_-	MER41A	4.9	4.2E-18	N	N	N
11	LTR	LTR-011	chr4_66108031_66108092_-	MER52A	6.1	1.6E-17	N	N	N
12	LTR	LTR-012	chr12_127544982_127545366_+	LTR1	3.6	1.6E-17	Y	N	N
13	LTR	LTR-013	chr5_20616504_20616510_+	THE1B	6.7	3.4E-17	Y	N	N
14	LTR	LTR-014	chr7_53879617_53879660_-	MLT2B3	4.9	7.7E-17	Y	N	N
15	LTR	LTR-015	chr18_35250382_35250447_+	MLT1K	6.0	1.6E-16	N	N	N
16	LTR	LTR-016	chr18_27755926_27756006_-	LTR1	6.3	1.8E-16	Y	N	N
17	LTR	LTR-017	chrX_97828807_97828900_+	LTR49	6.6	2.6E-16	N	N	N
18	LTR	LTR-018	chr13_64651428_64651436_-	LTR12C	6.1	2.8E-16	N	N	N
19	LTR	LTR-019	chr8_112052604_112052671_-	LTR12C	6.2	7.3E-16	Y	N	N
20	LTR	LTR-020	chr13_55628524_55628539_+	LTR17	6.0	4.8E-15	N	N	N
21	LTR	LTR-021	chr6_135196446_135196589_-	LTR18A	5.9	1.4E-14	N	N	N
22	LTR	LTR-022	chr6_115319139_115319436_+	LTR12F	4.1	3.5E-14	N	N	N
23	LTR	LTR-023	chr4_37003352_37003605_+	MER48	4.7	1.2E-13	N	N	N
24	LTR	LTR-024	chr10_96758111_96758263_-	LTR10A	6.1	2.6E-13	N	N	N
25	LTR	LTR-025	chr3_149756876_149757003_+	MER51A	5.5	2.9E-13	N	N	N
26	LTR	LTR-026	chr5_12574724_12574910_-	LTR12C	5.5	3.3E-13	N	N	N
27	LTR	LTR-027	chr7_145482026_145482125_+	MER50B	6.0	3.8E-13	Y	N	N
28	LTR	LTR-028	chr1_238649279_238649353_-	MER61A	4.3	3.9E-13	N	N	N
29	LTR	LTR-029	chr15_75030770_75030854_-	THE1B	6.4	5.1E-13	N	N	N
30	LTR	LTR-030	chr1_248894361_248894428_-	MER50B	4.9	5.3E-13	N	N	N
31	LTR	LTR-031	chr3_172585355_172585370_+	LTR12C	5.5	5.7E-13	N	N	N
32	LTR	LTR-032	chr3_146962969_146962989_-	LTR12C	6.3	6.8E-13	N	N	N
33	LTR	LTR-033	chr5_85866249_85866735_-	LTR2C	4.0	9.5E-13	N	N	N
34	LTR	LTR-034	chr4_31998988_31999006_+	LTR12C	4.7	1.2E-12	Y	N	N
35	LTR	LTR-035	chr6_161637770_161637904_-	THE1A	4.7	1.5E-12	N	N	N
36	LTR	LTR-036	chr11_39515789_39515794_+	MER11A	4.4	6.3E-12	N	N	N
37	LTR	LTR-037	chr17_47152996_47153073_-	MER41-int	4.9	8.3E-12	N	N	N
38	LTR	LTR-038	chr11_26618689_26618774_-	LTR17	5.5	8.7E-12	N	N	N
39	LTR	LTR-039	chr8_98162752_98162840_+	THE1B	5.6	1.0E-11	N	N	N
40	LTR	LTR-040	chrX_120331579_120331716_+	LTR25	3.9	1.5E-11	Y	N	N
41	LTR	LTR-041	chr2_190389114_190389189_-	THE1D	4.1	1.9E-11	N	N	N
42	LTR	LTR-042	chr19_8444480_8444487_+	LTR12D	4.9	1.9E-11	N	N	N
43	LTR	LTR-043	chr21_32097939_32098065_-	MLT2D	4.9	5.0E-11	N	N	N
44	non-LTR	nLTR-044	chr4_19456991_19457094_+		6.6	2.3E-29	N	N	N
45	non-LTR	nLTR-045	chr2_145425502_145425854_+		5.7	8.3E-24	Y	N	N
46	non-LTR	nLTR-046	chr22_48027406_48027559_+		5.7	5.2E-23	N	N	N
47	non-LTR	nLTR-047	chr14_25501764_25501806_-		4.8	3.1E-22	N	N	N
48	non-LTR	nLTR-048	chr10_54515147_54515384_-		4.4	1.4E-21	N	N	N
49	non-LTR	nLTR-049	chr9_11065016_11065169_-		6.1	3.5E-21	N	N	N
50	non-LTR	nLTR-050	chr1_143467553_143467742_-		4.8	9.1E-21	N	N	N
51	non-LTR	nLTR-051	chr4_66864638_66864906_+		4.3	2.0E-20	N	N	N
52	non-LTR	nLTR-052	chr6_23177196_23177334_-		5.5	8.0E-20	Y	N	N
53	non-LTR	nLTR-053	chr13_89815398_89815500_-		6.3	1.2E-19	N	N	N
54	non-LTR	nLTR-054	chr17_70396473_70396561_-		4.8	2.3E-19	Y	N	N
55	non-LTR	nLTR-055	chr4_135248598_135248657_-		5.2	2.3E-19	N	N	N
56	non-LTR	nLTR-056	chr1_192708603_192708714_-		4.6	7.3E-19	Y	N	N
57	non-LTR	nLTR-057	chr10_102880778_102880935_+		3.1	7.7E-19	Y	N	N
58	non-LTR	nLTR-058	chr8_47529222_47529328_-		7.2	8.3E-18	N	N	N
59	non-LTR	nLTR-059	chr8_107072668_107072827_-		3.3	1.4E-17	Y	N	N
60	non-LTR	nLTR-060	chr4_66107613_66107620_+		6.7	1.9E-17	N	N	N
61	non-LTR	nLTR-061	chrX_92951158_92951236_+		6.5	3.4E-17	N	N	N
62	non-LTR	nLTR-062	chr21_11098925_11098996_-		5.8	5.9E-17	N	N	N
63	non-LTR	nLTR-063	chr8_124697229_124697426_-		6.8	1.0E-16	N	N	N
64	non-LTR	nLTR-064	chr19_55845276_55845520_-		3.4	2.0E-16	N	N	N
65	non-LTR	nLTR-065	chr1_156426321_156426375_-		3.7	2.1E-16	N	N	N

66	non-LTR	nLTR-066	chr2_133094884_133094955_+	5.6	3.9E-16	N	N	N
67	non-LTR	nLTR-067	chr12_111497811_111497862_-	6.5	7.8E-16	N	N	N
68	non-LTR	nLTR-068	chr14_54080422_54080745_-	3.5	9.6E-16	Y	N	N
69	non-LTR	nLTR-069	chr2_78768982_78769323_-	5.4	1.3E-15	N	N	N
70	non-LTR	nLTR-070	chr8_49088774_49088921_+	3.7	1.6E-15	N	N	N
71	non-LTR	nLTR-071	chr16_76268983_76269339_+	5.4	1.8E-15	N	N	N
72	non-LTR	nLTR-072	chr5_35237985_35238069_-	4.2	2.3E-15	N	N	N
73	non-LTR	nLTR-073	chr1_202830852_202830914_+	3.5	4.3E-15	N	N	N
74	non-LTR	nLTR-074	chr12_127544890_127544992_-	3.5	6.4E-15	N	N	N
75	non-LTR	nLTR-075	chr7_34797830_34797945_-	4.7	9.6E-15	N	N	N
76	non-LTR	nLTR-076	chr4_188593870_188594125_-	4.8	2.5E-14	N	N	N
77	non-LTR	nLTR-077	chr1_147727218_147727318_-	5.7	3.5E-14	N	N	N
78	non-LTR	nLTR-078	chr3_147088170_147088274_-	6.3	6.6E-14	N	N	N
79	non-LTR	nLTR-079	chr22_44242951_44243047_-	5.2	1.8E-13	N	N	N
80	non-LTR	nLTR-080	chr12_70944080_70944102_+	6.4	2.0E-13	N	N	N
81	non-LTR	nLTR-081	chrX_149115424_149115504_+	5.5	2.6E-13	N	N	N
82	non-LTR	nLTR-082	chr6_124669729_124669754_+	6.1	2.9E-13	N	N	N
83	non-LTR	nLTR-083	chr15_66694188_66694236_+	3.7	3.1E-13	N	N	N
84	non-LTR	nLTR-084	chr5_3536011_3536189_-	6.0	3.3E-13	N	N	N
85	non-LTR	nLTR-085	chr1_170143736_170143807_+	5.5	3.8E-13	N	N	N
86	non-LTR	nLTR-086	chr1_246339776_246339914_-	5.1	4.6E-13	N	N	N
87	non-LTR	nLTR-087	chr6_105384844_105384950_+	5.2	5.0E-13	N	N	N
88	non-LTR	nLTR-088	chr7_64734221_64734308_+	4.3	5.6E-13	N	N	N
89	non-LTR	nLTR-089	chr13_110242600_110242753_+	4.0	5.7E-13	N	N	N
90	non-LTR	nLTR-090	chr3_4941365_4941578_-	6.1	5.9E-13	N	N	N
91	non-LTR	nLTR-091	chr4_115068285_115068322_+	4.6	5.9E-13	N	N	N
92	non-LTR	nLTR-092	chr5_173155159_173155203_-	4.4	6.5E-13	N	N	N
93	non-LTR	nLTR-093	chr4_44018712_44018944_+	4.9	7.4E-13	N	N	N
94	non-LTR	nLTR-094	chr10_10836846_10836976_-	3.2	9.6E-13	N	N	N
95	non-LTR	nLTR-095	chr13_68831761_68831830_-	5.9	9.8E-13	N	N	N
96	non-LTR	nLTR-096	chr16_14580591_14580873_+	3.1	1.1E-12	N	N	N
97	non-LTR	nLTR-097	chrX_7511587_7511814_+	5.8	1.3E-12	N	N	N
98	non-LTR	nLTR-098	chr1_145390399_145390478_-	4.3	1.3E-12	N	N	N
99	non-LTR	nLTR-099	chr2_210359776_210360229_+	3.4	1.4E-12	N	N	N
100	non-LTR	nLTR-100	chr5_59837919_59838042_-	4.4	1.9E-12	N	N	N
101	non-LTR	nLTR-101	chr14_28142441_28142491_-	5.3	3.1E-12	N	N	N
102	non-LTR	nLTR-102	chr12_74686399_74686456_-	5.3	4.7E-12	N	N	N
103	non-LTR	nLTR-103	chr3_145829119_145829280_-	4.0	5.6E-12	N	N	N
104	non-LTR	nLTR-104	chr8_36636633_36636738_-	5.3	5.6E-12	N	N	N
105	non-LTR	nLTR-105	chr16_79018417_79018492_+	3.2	7.8E-12	N	N	N
106	non-LTR	nLTR-106	chr1_155618329_155618374_-	4.0	8.6E-12	N	N	N
107	non-LTR	nLTR-107	chr1_201874446_201874513_-	4.9	1.1E-11	N	N	N
108	non-LTR	nLTR-108	chr11_35425907_35426227_-	3.6	1.1E-11	N	N	N
109	non-LTR	nLTR-109	chr12_103292981_103293117_+	3.6	1.1E-11	N	N	N
110	non-LTR	nLTR-110	chr5_557071_557102_-	3.5	1.6E-11	N	N	N
111	non-LTR	nLTR-111	chr16_12713528_12713697_-	4.2	1.8E-11	N	N	N
112	non-LTR	nLTR-112	chr12_34200857_34200951_-	5.1	1.9E-11	N	N	N
113	non-LTR	nLTR-113	chr1_244256324_244256377_-	4.6	2.0E-11	N	N	N
114	non-LTR	nLTR-114	chr12_113644190_113644252_-	4.4	2.1E-11	N	N	N
115	non-LTR	nLTR-115	chr1_237634114_237634543_+	4.3	2.3E-11	N	N	N
116	non-LTR	nLTR-116	chr12_97856596_97856613_+	3.5	2.3E-11	N	N	N
117	non-LTR	nLTR-117	chr19_22966865_22966986_-	3.1	2.5E-11	N	N	N
118	non-LTR	nLTR-118	chr3_150454151_150454451_-	3.6	2.9E-11	N	N	N
119	non-LTR	nLTR-119	chr13_94958159_94958162_+	3.8	3.1E-11	N	N	N
120	non-LTR	nLTR-120	chrX_21788738_21788791_-	3.4	3.2E-11	N	N	N
121	non-LTR	nLTR-121	chr12_128108501_128108573_+	4.7	3.5E-11	N	N	N
122	non-LTR	nLTR-122	chrX_49558230_49558478_+	4.3	3.6E-11	N	N	N
123	non-LTR	nLTR-123	chrX_27417076_27417151_-	4.2	3.9E-11	N	N	N
124	non-LTR	nLTR-124	chr19_29492135_29492199_+	5.3	4.3E-11	N	N	N
125	non-LTR	nLTR-125	chr7_25471788_25471824_-	4.9	5.0E-11	N	N	N
126	non-LTR	nLTR-126	chr1_117008795_117008884_+	3.3	5.1E-11	N	N	N
127	non-LTR	nLTR-127	chr8_144490327_144490432_+	5.1	5.2E-11	N	N	N
128	non-LTR	nLTR-128	chr6_25920064_25920202_+	4.5	5.9E-11	N	N	N
129	non-LTR	nLTR-129	chr10_71850872_71851017_+	3.9	6.1E-11	N	N	N
130	non-LTR	nLTR-130	chr1_187929553_187929791_+	4.2	6.8E-11	N	N	N
131	non-LTR	nLTR-131	chr5_55354832_55354890_+	4.9	6.8E-11	N	N	N
132	non-LTR	nLTR-132	chr3_39839148_39839168_-	4.6	6.9E-11	N	N	N
133	non-LTR	nLTR-133	chr4_69922667_69922730_-	4.3	7.6E-11	N	N	N

Table S7. Targets of 3' RACE validation (15 LTRs and 7 non-LTRs)

Number	Name	TSS	Gencode 19	Primer1	Primer2	# Transcripts
1	LTR-001	chr13_64649861_64650181_-	ENST00000456627.1	CACTGTGGGCTTCGTCTCTG	GACGCCCTGCCTATGGA AAC	7
2	LTR-002	chr6_120326805_120326870_+	Not annotated	CTTGCTGCTTCTTCGCTTTC	TCGCTTTCTGCCATGATTGC	4
3	LTR-003	chr4_66107513_66107548_-	Not annotated	CCGTGTACCTCATTCTTGTC	ACCCTGGGACCCAGTGAATG	2
4	LTR-004	chr5_104728667_104728706_-	ENST00000503650.1	CGTTAGGAGCTACCGTCTTC	TCTTCTCCACCGTGCTCACC	1
5	LTR-007	chr9_31848657_31848713_+	Not annotated	CCGGGTCTTACTCATCATT	TTTGTGGCCGTGGGACAAAG	2
6	LTR-008	chr9_118506483_118506625_-	ENST00000433546.2	CTTGCTTCCCAAAGCTAAGG	AAGCTAAGGAGGGCTCTGTG	1
7	LTR-009	chrX_97635662_97635698_-	Not annotated	GAAACCTGCCAGCAGGACTC	TTCTGTGGGTTCTGTTTCC	3
8	LTR-012	chr12_127544982_127545366_+	Not annotated	CCCAGCCTGGGCCTATAAAC	ACGACCCTAGCAAGGCAGAG	0
9	LTR-013	chr5_20616504_20616510_+	ENST00000512688.1	TTTGCTCCTGCTTCGTCTTC	CGTCTTCTGCCGTGATTGTG	3
10	LTR-014	chr7_53879617_53879660_-	ENST00000380970.2	TCTTACTGTGCTGGGCGGTT	GAGTCAGACTCCAGGTTCTTC	4
11	LTR-016	chr18_27755926_27756006_-	Not annotated	ATCCGAGACCCTAGCAAGAC	AGAAACGGAAGCTGCTGGAC	1
12	LTR-019	chr8_112052604_112052671_-	Not annotated	TCATTCCCGAAGTCAGTGAG	CCAATTCCGGGCACGGTATG	1
13	LTR-027	chr7_145482026_145482125_+	Not annotated	TGTGCCTAGGTCTCTTGTT	AGATTTAAAGTTGCGGCCGAC	1
14	LTR-034	chr4_31998988_31999006_+	ENST00000513211.1	GGAGGAAGGAACA ACTACAG	TTCACTCTTGAGCCAGAGAC	2
15	LTR-040	chrX_120331579_120331716_+	Not annotated	CCCACAGTGAGTATTCCTGTT	CTCTACTGACAGAGAGCTTTC	1
16	nLTR-045	chr2_145425502_145425854_+	ENST00000597655.1	GGTCGAAGGGGAAGAAAAGC	TGTTGAGATCTGGCGACTTG	2
17	nLTR-052	chr6_23177196_23177334_-	Not annotated	GACTTTCGAGGCTCCATTG	CATGCGGCAAATAGGAAACC	2
18	nLTR-054	chr17_70396473_70396561_-	ENST00000453722.2	ATGCCAGGCTGGTGGAGAAC	GCCTGAAGACAGCCCTAAAC	2
19	nLTR-056	chr1_192708603_192708714_-	Not annotated	TTTCTGCCTCCAGACTCTAC	CTACTCTCCTGCCTCAATTC	1
20	nLTR-057	chr10_102880778_102880935_+	Not annotated	CCTCCAGCAGTGTGGATT	GAGGTAAGGGTGCCGATGAG	1
21	nLTR-059	chr8_107072668_107072827_-	ENST00000520433.1	CGCATTCTACTTTTCTAC	CCAGCAGAAATTCCTGTACAC	4
22	nLTR-068	chr14_54080422_54080745_-	ENST00000436530.1	TGATGAAAGTCAGCCTAGGG	CAGAGACCAAAGGGCCATAC	1

Table S8. Full-length ncRNAs determined by 3' RACE

Number	Name	chr	start	end	Exon size	strand	# Exon	Exon length	Exon start position	id
1	LTR-001	chr13	64425460	64650144	1101	-	2	331,770	0,223914	T1.1
2	LTR-001	chr13	64425460	64650144	1176	-	3	331,75,770	0,2357,223914	T1.2
3	LTR-001	chr13	64560503	64650144	1878	-	6	669,105,25,118,191,770	0,3725,16014,16977,47976,88871	T1.3
4	LTR-001	chr13	64560503	64650144	1687	-	5	669,105,25,118,770	0,3725,16014,16977,88871	T1.4
5	LTR-001	chr13	64560503	64650144	1735	-	4	669,105,191,770	0,3725,47976,88871	T1.5
6	LTR-001	chr13	64560503	64650144	1569	-	4	669,105,25,770	0,3725,16014,88871	T1.6
7	LTR-001	chr13	64560503	64650144	1544	-	3	669,105,770	0,3725,88871	T1.7
8	LTR-002	chr6	120326868	121027885	525	+	3	94,81,350	0,456788,700667	T3.1
9	LTR-002	chr6	120326868	120892061	313	+	3	94,80,139	0,456788,565054	T3.2
10	LTR-002	chr6	120326868	121027885	600	+	4	94,75,81,350	0,122844,456788,700667	T3.3
11	LTR-002	chr6	120326868	121027885	650	+	5	94,75,50,81,350	0,122844,345860,456788,700667	T3.4
12	LTR-003	chr4	66072125	66107533	1242	-	4	376,151,81,634	0,19452,31976,34774	T2.1
13	LTR-003	chr4	66103988	66107533	828	-	2	194,634	0,2911	T2.2
14	LTR-004	chr5	104253029	104728668	971	-	4	570,143,51,207	0,38246,91532,475432	T5.1
15	LTR-007	chr9	31848669	32112835	1002	+	3	236,98,668	0,124343,263498	T10.1
16	LTR-007	chr9	31848669	31977997	839	+	3	236,98,505	0,124343,128823	T10.2
17	LTR-008	chr9	118403718	118506541	749	-	3	542,101,106	0,100022,102717	T15.1
18	LTR-009	chrX	97009741	97635670	581	-	3	273,98,210	0,597260,625719	T18.1
19	LTR-009	chrX	97288808	97635670	616	-	4	149,159,98,210	0,154631,318193,346652	T18.2
20	LTR-009	chrX	97418996	97635670	771	-	5	201,103,159,98,210	0,834,24443,188005,216464	T18.3
21	LTR-013	chr5	20616506	20936877	1257	+	8	83,57,147,61,85,98,108,618	0,44314,120557,191455,279085,316485,318534,319753	T13.1
22	LTR-013	chr5	20616506	20899593	585	+	6	83,57,147,61,85,152	0,44314,120557,191455,279085,282935	T13.2
23	LTR-013	chr5	20616506	20737349	426	+	3	83,57,286	0,44314,120557	T13.3
24	LTR-014	chr7	53724161	53879642	1991	-	6	980,163,174,141,91,442	0,35458,114965,120019,123477,155039	T16.1
25	LTR-014	chr7	53724161	53879642	1676	-	4	980,163,91,442	0,35458,123477,155039	T16.2
26	LTR-014	chr7	53758873	53879642	1757	-	5	909,174,141,91,442	0,80253,85307,88765,120327	T16.3
27	LTR-014	chr7	53838091	53879642	1883	-	4	1209,141,91,442	0,6089,9547,41109	T16.4
28	LTR-016	chr18	27737296	27755981	546	-	2	270,276	0,18409	T17.1
29	LTR-019	chr8	111995211	112052619	992	-	7	158,37,109,120,128,154,286	0,20431,21678,22547,44323,56106,57122	T21.1
30	LTR-027	chr7	145482073	145545509	668	+	3	453,94,121	0,57510,63315	T19.1
31	LTR-034	chr4	31998999	32157445	1170	+	3	445,215,510	0,148675,157936	T22.1
32	LTR-034	chr4	31998999	32157445	955	+	2	445,510	0,157936	T22.2
33	LTR-040	chrX	120331632	120332713	1081	+	1	1081	0	T12.1
34	nLTR-045	chr2	145425550	145940216	888	+	4	125,183,134,446	0,100114,504014,514220	T4.1
35	nLTR-045	chr2	145425550	145612387	532	+	4	125,183,105,119	0,100114,185299,186718	T4.2
36	nLTR-052	chr6	23056524	23177316	1052	-	3	771,86,195	0,118957,120597	T14.1
37	nLTR-052	chr6	23175151	23177316	611	-	2	416,195	0,1970	T14.2
38	nLTR-054	chr17	70319276	70396542	1012	-	3	185,590,237	0,59907,77029	T7.1
39	nLTR-054	chr17	70319276	70396542	576	-	3	185,154,237	0,2657,77029	T7.2
40	nLTR-056	chr1	192460585	192708626	830	-	5	514,70,59,81,106	0,75691,102143,135885,247935	T9.1
41	nLTR-057	chr10	102880846	102897510	1035	+	2	329,706	0,15958	T6.1
42	nLTR-059	chr8	106797034	107072753	1044	-	6	411,155,148,118,67,145	0,2260,2642,13518,142844,275574	T8.1
43	nLTR-059	chr8	106797034	107072753	889	-	5	411,148,118,67,145	0,2642,13518,142844,275574	T8.2
44	nLTR-059	chr8	106673911	107072753	853	-	6	285,169,69,118,67,145	0,1089,69410,136641,265967,398697	T8.3
45	nLTR-059	chr8	106697116	107072753	418	-	5	38,50,118,67,145	0,856,113436,242762,375492	T8.4
46	nLTR-068	chr14	54074027	54080669	614	-	2	315,299	0,6343	T11.1

Table S9. Prediction of coding potential using CPAT web system

Number	Name	Size (bp)	Exon	Genomic Size	Coding Probability	Coding Label
1	T1.1	1101	2	224684	0.07	no
2	T1.2	1176	3	224684	0.02	no
3	T1.3	1878	6	89641	0.04	no
4	T1.4	1687	5	89641	0.05	no
5	T1.5	1735	4	89641	0.03	no
6	T1.6	1569	4	89641	0.03	no
7	T1.7	1544	3	89641	0.03	no
8	T2.1	1242	4	35408	0.02	no
9	T2.2	828	2	3545	0.02	no
10	T3.1	525	3	701017	0.02	no
11	T3.2	313	3	565193	0.02	no
12	T3.3	600	3	701017	0.01	no
13	T3.4	650	3	701017	0.12	no
14	T4.1	888	4	514666	0.08	no
15	T4.2	532	4	186837	0.05	no
16	T5.1	971	4	475639	0.02	no
17	T6.1	1035	2	16664	0.03	no
18	T7.1	1012	3	77266	0.00	no
19	T7.2	576	3	77266	0.00	no
20	T8.1	1044	6	275719	0.02	no
21	T8.2	889	5	275719	0.02	no
22	T8.3	853	6	398842	0.02	no
23	T8.4	418	5	375637	0.02	no
24	T9.1	830	5	248041	0.01	no
25	T10.1	1002	3	264166	0.02	no
26	T10.2	839	3	129328	0.01	no
27	T11.1	614	2	6642	0.03	no
28	T12.1	1081	1	1081	0.00	no
29	T13.1	1257	8	320371	0.00	no
30	T13.2	585	6	283087	0.00	no
31	T13.3	426	3	120843	0.00	no
32	T14.1	1052	3	120792	0.00	no
33	T14.2	611	2	2165	0.00	no
34	T15.1	749	3	102823	0.02	no
35	T16.1	1991	6	155481	0.17	no
36	T16.2	1676	4	155481	0.17	no
37	T16.3	1757	5	120769	0.17	no
38	T16.4	1883	4	41551	0.17	no
39	T17.1	546	2	18685	0.06	no
40	T18.1	581	3	625929	0.02	no
41	T18.2	616	4	346862	0.00	no
42	T18.3	771	5	216674	0.00	no
43	T19.1	668	3	63436	0.05	no
44	T21.1	992	7	57408	0.00	no
45	T22.1	1170	3	158446	0.01	no
46	T22.2	955	2	158446	0.00	no

Table S10. qPCR primers for LTR-derived ncRNAs

Number	Target	Experiments	Forward	Reverse
1	LTR-001	qPCR / LNA KD	TTGAAACATGCCCTTGCTC	AGAAAGGGTGTACAGTCTTGG
2	LTR-002	LNA KD	TCGCTTTCTGCCATGATTGC	TTCCTGGCCCAGACTTCAATC
3	LTR-002	qPCR	GCAGTCCATGGAGCAGTTACA	CCCTGCATCGAGCAAGTCTA
4	LTR-004	qPCR	AGCTTTTTCTCGCTGCTGAG	AGCGTTACAGCCCTTTTTGC
5	LTR-007	qPCR	AGCCCTGCAACAATTTTGGC	TTTCAAAGGTCCCCAACTCG
6	HMBS	qPCR	GGCAATGCGGCTGCAA	GGGTACCCACGCGAATCAC
7	GAPDH	LNA KD	GAAATCCCATCACCATCTTCCAGG	GAGCCCCAGCCTTCTCCATG

Table S11. Clinical features associated with the high LTR class

Study	high-LTR	low-LTR	Odds	95% CI
Gender (Male)	14/16	10/14	2.8	0.427 to 18.376
Age (≥55 years)	12/16	5/14	5.4	1.120 to 26.045
Viral etiology	14/16	7/14	7	1.140 to 42.971
Cirrhosis	8/16	10/14	0.4	0.0876 to 1.826
AFP (≥50 ng/ml)	8/15	4/12	2.286	0.475 to 11.003
Pre-operative treatment	4/16	9/14	0.185	0.0384 to 0.893
Liver transplantation	4/16	11/14	0.0909	0.0165 to 0.501
Multinodular HCC	6/16	12/14	0.1	0.0164 to 0.609
Tumor size (≥50 mm)	5/16	4/14	1.136	0.237 to 5.457
Satellite nodules	6/16	2/14	3.6	0.591 to 21.932
Microvascular invasion	7/16	3/14	2.852	0.568 to 14.326
Recurrence	10/16	2/14	10	1.641 to 60.923
Metastasis	4/16	1/14	4.333	0.423 to 44.430
Differentiation - Well	5/16	11/14	0.124	0.0236 to 0.650
Differentiation - Moderate	10/16	2/14	10	1.641 to 60.923
Differentiation - Poor	1/16	1/14	0.867	0.0492 to 15.280
Total (fixed effects)	118/255	93/222	1.199	0.830 to 1.732
Total (random effects)	118/255	93/222	1.355	0.586 to 3.134

Table S12. ENCODE data used to measure activities of TSSs in HepG2

Number	Technology	Definition	UCSC Accession	FileName
1	CAGE	cell PolyA+ rep1	wgEncodeEH001149	wgEncodeRikenCageHepg2CellPapAlnRep1.bam
2	CAGE	cell PolyA+ rep2	wgEncodeEH001149	wgEncodeRikenCageHepg2CellPapAlnRep2.bam
3	CAGE	nucleus PolyA+ rep1	wgEncodeEH001148	wgEncodeRikenCageHepg2NucleusPapAlnRep1.bam
4	CAGE	nucleus PolyA+ rep2	wgEncodeEH001148	wgEncodeRikenCageHepg2NucleusPapAlnRep2.bam
5	CAGE	nucleus PolyA-	wgEncodeEH000345	wgEncodeRikenCageHepg2NucleusPamAln.bam
6	CAGE	cytosol PolyA+ rep1	wgEncodeEH001147	wgEncodeRikenCageHepg2CytosolPapAlnRep1.bam
7	CAGE	cytosol PolyA+ rep2	wgEncodeEH001147	wgEncodeRikenCageHepg2CytosolPapAlnRep2.bam
8	CAGE	cytosol PolyA-	wgEncodeEH000343	wgEncodeRikenCageHepg2CytosolPamAln.bam
9	CAGE	nucleolus	wgEncodeEH000344	wgEncodeRikenCageHepg2NucleolusTotalAln.bam
10	DNase-Seq	narrowPeak rep1	wgEncodeEH000482	wgEncodeUwDnaseHepg2PkRep1.narrowPeak.gz
11	DNase-Seq	narrowPeak rep2	wgEncodeEH000482	wgEncodeUwTfbsHepg2CtcfStdPkRep2.narrowPeak.gz
12	FAIR-Seq	narrowPeak	wgEncodeEH000546	wgEncodeOpenChromFaireHepg2Pk.narrowPeak.gz
13	ChIP-Seq	RNA pol II	wgEncodeEH002278	wgEncodeHaibTfbsHepg2Pol24h8V0416102PkRep1.broadPeak.gz
14	ChIP-Seq	H3K4me3	wgEncodeEH000413	wgEncodeUwHistoneHepg2H3k4me3StdPkRep1.narrowPeak.gz
15	ChIP-Seq	H3K27ac	wgEncodeEH000094	wgEncodeBroadHistoneHepg2H3k27acStdPk.broadPeak.gz
16	ChIP-Seq	chromatin state	wgEncodeEH000789	wgEncodeBroadHmmHepg2HMM.bed.gz

Table S13. ENCODE ChIP-Seq data used to measure TF activities in HepG2

Number	Name	GEO accession	UCSC Accession	FileName
1	ARID3A	GSM935275	wgEncodeEH002858	wgEncodeSydhTfbsHepg2Arid3anb100279lggrabPk.narrowPeak.gz
2	ATF3	GSM803503	wgEncodeEH001568	wgEncodeHaibTfbsHepg2Atf3V0416101PkRep1.broadPeak.gz
3	BHLHE40	GSM935566	wgEncodeEH002032	wgEncodeSydhTfbsHepg2Bhlhe40clggrabPk.narrowPeak.gz
4	BRCA1	GSM935609	wgEncodeEH001859	wgEncodeSydhTfbsHepg2Brca1a300lggrabPk.narrowPeak.gz
5	CEBPB	GSM1010778	wgEncodeEH002304	wgEncodeHaibTfbsHepg2Cebpbsc150V0416101PkRep2.broadPeak.gz
6	CEBPD	GSM1010777	wgEncodeEH002305	wgEncodeHaibTfbsHepg2Cebpdsc636V0416101PkRep1.broadPeak.gz
7	CHD2	GSM935307	wgEncodeEH001840	wgEncodeSydhTfbsHepg2Chd2ab68301lggrabPk.narrowPeak.gz
8	cJUN	GSM935364	wgEncodeEH001794	wgEncodeSydhTfbsHepg2CjunlggrabPk.narrowPeak.gz
9	cMYC	GSM822291	wgEncodeEH000545	wgEncodeOpenChromChipHepg2CmycPk.narrowPeak.gz
10	CREB1	GSM1010808	wgEncodeEH003312	wgEncodeHaibTfbsHepg2Creb1sc240V0422111PkRep1.broadPeak.gz
11	CTCF	GSM733645	wgEncodeEH000080	wgEncodeBroadHistoneHepg2CtcfStdPk.broadPeak.gz
12	ELF1	GSM803415	wgEncodeEH001641	wgEncodeHaibTfbsHepg2Elf1sc631V0416101PkRep2.broadPeak.gz
13	EZH2	GSM1003487	wgEncodeEH002416	wgEncodeBroadHistoneHepg2Ezh239875Pk.broadPeak.gz
14	FOSL2	GSM803451	wgEncodeEH001501	wgEncodeHaibTfbsHepg2Fosl2V0416101PkRep1.broadPeak.gz
15	FOXA1	GSM803432	wgEncodeEH001630	wgEncodeHaibTfbsHepg2Foxa1sc101058V0416101PkRep1.broadPeak.gz
16	FOXA2	GSM803403	wgEncodeEH001650	wgEncodeHaibTfbsHepg2Foxa2sc6554V0416101PkRep2.broadPeak.gz
17	GABPA	GSM803343	wgEncodeEH001548	wgEncodeHaibTfbsHepg2GabpPcr2xPkRep1.broadPeak.gz
18	HDAC2	GSM803493	wgEncodeEH001618	wgEncodeHaibTfbsHepg2Hdac2sc6296V0416101PkRep1.broadPeak.gz
19	HNF4A	GSM803460	wgEncodeEH001595	wgEncodeHaibTfbsHepg2Hnf4asc8987V0416101PkRep1.broadPeak.gz
20	HNF4G	GSM803404	wgEncodeEH001651	wgEncodeHaibTfbsHepg2Hnf4gsc6558V0416101PkRep1.broadPeak.gz
21	JUND	GSM803500	wgEncodeEH001470	wgEncodeHaibTfbsHepg2JundPcr1xPkRep2.broadPeak.gz
22	MAFF	GSM935306	wgEncodeEH001841	wgEncodeSydhTfbsHepg2Maffm8194lggrabPk.narrowPeak.gz
23	MAFK	GSM935305	wgEncodeEH001842	wgEncodeSydhTfbsHepg2Mafkab50322lggrabPk.narrowPeak.gz
24	MAX	GSM935406	wgEncodeEH002796	wgEncodeSydhTfbsHepg2MaxlggrabPk.narrowPeak.gz
25	MAZ	GSM935335	wgEncodeEH002860	wgEncodeSydhTfbsHepg2Mazab85725lggrabPk.narrowPeak.gz
26	MBD4	GSM1010740	wgEncodeEH002318	wgEncodeHaibTfbsHepg2Mbd4sc271530V0422111PkRep1.broadPeak.gz
27	MXI1	GSM935437	wgEncodeEH002029	wgEncodeSydhTfbsHepg2Mxi1StdPk.narrowPeak.gz
28	NR2F2	GSM1010810	wgEncodeEH003314	wgEncodeHaibTfbsHepg2Nr2f2sc271940V0422111PkRep2.broadPeak.gz
29	NRF1	GSM935648	wgEncodeEH001802	wgEncodeSydhTfbsHepg2Nrf1lggrabPk.narrowPeak.gz
30	NRSF	GSM1010784	wgEncodeEH002263	wgEncodeHaibTfbsHepg2NrsfV0416101PkRep2.broadPeak.gz
31	P300	GSM803499	wgEncodeEH001612	wgEncodeHaibTfbsHepg2P300V0416101PkRep1.broadPeak.gz
32	RAD21	GSM935647	wgEncodeEH001803	wgEncodeSydhTfbsHepg2Rad21lggrabPk.narrowPeak.gz
33	RCOR1	GSM935579	wgEncodeEH002845	wgEncodeSydhTfbsHepg2Corestsc30189lggrabPk.narrowPeak.gz
34	RXRA	GSM803452	wgEncodeEH001506	wgEncodeHaibTfbsHepg2RxraPcr1xPkRep2.broadPeak.gz
35	SIN3AK20	GSM803530	wgEncodeEH001471	wgEncodeHaibTfbsHepg2Sin3ak20Pcr1xPkRep2.broadPeak.gz
36	SMC3	GSM935542	wgEncodeEH001861	wgEncodeSydhTfbsHepg2Smc3ab9263lggrabPk.narrowPeak.gz

37	SP1	GSM803507	wgEncodeEH001561	wgEncodeHaibTfbsHepg2Sp1Pcr1xPkRep1.broadPeak.gz
38	SP2	GSM1010787	wgEncodeEH002264	wgEncodeHaibTfbsHepg2Sp2V0422111PkRep1.broadPeak.gz
39	SRF	GSM803502	wgEncodeEH001611	wgEncodeHaibTfbsHepg2SrfV0416101PkRep2.broadPeak.gz
40	TAF1	GSM803367	wgEncodeEH001551	wgEncodeHaibTfbsHepg2Taf1Pcr2xPkRep1.broadPeak.gz
41	TBP	GSM935280	wgEncodeEH001793	wgEncodeSydhTfbsHepg2TbplggrabPk.narrowPeak.gz
42	TCF12	GSM803336	wgEncodeEH001544	wgEncodeHaibTfbsHepg2Tcf12Pcr1xPkRep1.broadPeak.gz
43	TCF7L2	GSM782122	wgEncodeEH001780	wgEncodeSydhTfbsHepg2Tcf7l2UcdPk.narrowPeak.gz
44	TEAD4	GSM1010875	wgEncodeEH002345	wgEncodeHaibTfbsHepg2Tead4sc101184V0422111PkRep1.broadPeak.gz
45	TR4	GSM935596	wgEncodeEH000675	wgEncodeSydhTfbsHepg2Tr4UcdPk.narrowPeak.gz
46	USF1	GSM803527	wgEncodeEH001472	wgEncodeHaibTfbsHepg2Usf1Pcr1xPkRep2.broadPeak.gz
47	USF2	GSM935646	wgEncodeEH001804	wgEncodeSydhTfbsHepg2Usf2lggrabPk.narrowPeak.gz
48	YY1	GSM803381	wgEncodeEH001661	wgEncodeHaibTfbsHepg2Yy1sc281V0416101PkRep1.broadPeak.gz
49	ZBTB33	GSM803449	wgEncodeEH001503	wgEncodeHaibTfbsHepg2Zbtb33Pcr1xPkRep1.broadPeak.gz
50	ZBTB7A	GSM1010831	wgEncodeEH002296	wgEncodeHaibTfbsHepg2Zbtb7aV0416101PkRep2.broadPeak.gz
51	ZEB1	GSM1010809	wgEncodeEH003315	wgEncodeHaibTfbsHepg2Zeb1V0422111PkRep1.broadPeak.gz

Table S14. Targets and sequences of LNAs

Number	Name	Target	LNA sequence 5'-3'
1	L1	LTR-001	GCGAGTAAGCAGAAGA
2	L3	LTR-001	AAATGGAGGGCGAGTA
3	L4	LTR-001	TGTCCAGGATGAATGA
4	L5	LTR-002	CTTCACAACGCGGTA
5	L6	LTR-002	CCCACAATTACCGTTG

Table S15. Significantly dysregulated genes with LTR-001 KD at 48h

Number	TYPE	TSS	Log2(FC)	FDR	Name
1	DOWN	chr10_77191031_77191479_+	-1.2	1.8E-09	C10ORF11
2	DOWN	chr13_64650089_64650181_-	-2.9	2.2E-08	LTR-001
3	DOWN	chr4_19456965_19457245_+	-1.5	7.1E-07	RP11-608O21.1
4	DOWN	chr6_56819437_56819862_-	-1.3	2.5E-05	DST
5	DOWN	chr3_61547207_61547322_+	-1.4	5.2E-05	PTPRG
6	DOWN	chr5_60240918_60241225_+	-0.7	4.3E-04	MIMITIN
7	DOWN	chr16_15528316_15528473_+	-1.4	2.7E-03	C16ORF45
8	DOWN	chr17_43971780_43972028_+	-0.8	3.2E-03	MAPT
9	DOWN	chr1_246670461_246670642_-	-0.8	4.2E-03	SMYD3
10	DOWN	chr8_9911725_9911878_+	-1.2	4.4E-03	MSRA
11	DOWN	chr6_52668605_52668722_-	-0.8	6.6E-03	GSTA1
12	DOWN	chr13_93879056_93879322_+	-0.8	7.5E-03	GPC6
13	DOWN	chr6_5261619_5261844_+	-0.8	8.9E-03	FARS2
14	DOWN	chr8_58906933_58907302_+	-1.1	1.4E-02	FAM110B
15	DOWN	chrX_33760071_33760534_+	-1.3	1.6E-02	RP11-305F18.1
16	DOWN	chr17_64298632_64298764_+	-0.6	1.7E-02	PRKCA
17	DOWN	chr6_144329324_144329589_-	-1.1	1.7E-02	HYMAI
18	DOWN	chr12_4713988_4714206_+	-0.6	1.9E-02	DYRK4
19	DOWN	chr6_120326805_120326902_+	-0.6	2.3E-02	-
20	DOWN	chr7_101458933_101459327_+	-0.8	2.7E-02	CUX1
21	DOWN	chr11_8615481_8615854_-	-0.8	3.1E-02	STK33
22	DOWN	chr13_112025173_112025276_+	-1.1	3.1E-02	-
23	DOWN	chr4_74281767_74281993_+	-0.6	3.1E-02	ALB
24	DOWN	chr13_43597508_43597846_+	-0.5	3.3E-02	DNAJC15
25	DOWN	chr20_18568521_18568735_+	-1.0	3.9E-02	DTD1
26	DOWN	chr5_78281472_78281476_-	-2.5	4.1E-02	ARSB
27	DOWN	chr13_93879552_93879586_+	-1.1	4.2E-02	GPC6
28	DOWN	chr8_81786428_81786911_-	-0.7	4.3E-02	ZNF704
29	DOWN	chr5_43313227_43313616_-	-0.6	4.3E-02	HMGCS1
30	DOWN	chr3_126423023_126423364_+	-0.5	4.6E-02	CHCHD6
31	DOWN	chr19_13106214_13106424_+	-0.8	4.6E-02	NFIX
32	DOWN	chr18_32073222_32073328_+	-1.1	4.6E-02	DTNA
33	DOWN	chr3_99536634_99536855_+	-0.6	4.6E-02	C3ORF26
34	DOWN	chr3_13324361_13324814_-	-0.7	4.6E-02	-
35	DOWN	chr20_36322307_36322533_+	-0.5	4.7E-02	CTNBL1
36	UP	chr7_45927983_45928256_+	2.1	1.1E-04	IGFBP1
37	UP	chr16_24548998_24549082_+	1.2	2.2E-03	RBBP6
38	UP	chr11_67120745_67121095_-	0.8	5.8E-03	POLD4
39	UP	chr10_114154436_114154612_+	1.2	5.8E-03	ACSL5
40	UP	chr8_117658735_117658838_-	4.1	6.6E-03	EIF3H
41	UP	chr12_7052070_7052116_+	1.6	7.5E-03	AK310266
42	UP	chr2_192542809_192542896_+	0.9	8.9E-03	DKFZP313C2412
43	UP	chr10_102046091_102046118_-	1.3	1.5E-02	BLOC1S2
44	UP	chr22_35817451_35817454_+	1.7	2.1E-02	MCM5
45	UP	chr1_151804257_151804322_-	2.5	2.1E-02	RORC
46	UP	chr1_110879128_110879228_-	3.0	2.1E-02	-
47	UP	chr12_53343796_53343854_+	1.0	2.4E-02	KRT18
48	UP	chr11_18258262_18258666_-	0.9	2.4E-02	SAA4
49	UP	chr9_140119596_140119649_+	1.5	2.4E-02	C9ORF169
50	UP	chr1_53556536_53556699_-	1.2	2.7E-02	SLC1A7
51	UP	chrX_70331389_70331494_-	1.6	2.7E-02	IL2RG
52	UP	chr17_74547140_74547349_-	0.7	2.7E-02	CYGB
53	UP	chr19_39826638_39826764_-	0.8	2.8E-02	GMFG
54	UP	chr7_45933004_45933231_+	1.5	2.8E-02	-
55	UP	chr17_48351783_48351864_+	1.7	2.8E-02	TMEM92

56	UP	chr5_38468352_38468731_-	1.8	2.9E-02	CTD-2263F21.1
57	UP	chr17_40715271_40715276_+	1.4	3.1E-02	COASY
58	UP	chr12_96390065_96390144_-	1.9	3.1E-02	HAL
59	UP	chr17_74261257_74261463_+	0.7	3.2E-02	FAM100B
60	UP	chr12_50132698_50132740_+	1.3	3.3E-02	TMBIM6
61	UP	chr1_198126084_198126296_+	0.7	3.4E-02	NEK7
62	UP	chrX_102884608_102884683_+	1.4	3.7E-02	TCEAL1
63	UP	chr6_43595017_43595132_-	1.6	4.1E-02	GTPBP2
64	UP	chr2_208734583_208734798_-	0.9	4.3E-02	AC083900.1
65	UP	chr13_76209878_76209953_-	1.5	4.4E-02	LMO7
66	UP	chr9_33447490_33447641_-	1.7	4.6E-02	AQP3
67	UP	chr7_32933645_32933792_-	1.1	4.6E-02	KBTBD2

Table S16. Significantly dysregulated genes with LTR-002 KD at 48h

Number	TYPE	TSS	Log2(FC)	FDR	Name
1	DOWN	chr10_77191031_77191479_+	-1.2	2.3E-12	C10ORF11
2	DOWN	chr2_145425267_145425610_+	-1.0	2.0E-03	AC074093
3	DOWN	chr6_120326805_120326902_+	-2.1	6.7E-03	LTR-002
4	DOWN	chr3_171758299_171758374_+	-0.7	4.6E-02	FNDC3B
5	UP	chr8_117658735_117658838_-	5.7	2.1E-06	EIF3H
6	UP	chr2_204055410_204055413_+	1.6	6.7E-03	AC011737.2
7	UP	chr1_22234544_22234549_+	1.0	6.7E-03	RP11-26H16.1