

Figure S1: Cell line specificity analysis of the network nodes. a) Distribution of expression of protein coding genes for tissue-specific and ubiquitously expressed gene determined from 24 ENCODE cell lines. b) Distribution of expression of lnc-RNAs for tissue-specific and ubiquitously expressed lncRNAs determined from 24 ENCODE cell lines. 'No expression' refers to lncRNA with no detectable expression in any of the ENCODE cell lines (whole cell RNA-seq) but with detectable expression in the RNA-seq libraries of the chromatin RNA fraction in K562, reflecting expression of nascent transcripts. c) Distribution of gene-lncRNAs Mutual Information values (MI) for tissue-specific and ubiquitously expressed lncRNAs computed from 24 ENCODE cell lines. d) Degree distribution for tissue-specific and ubiquitously expressed lncRNAs.





Table S1: Network properties of different genomic regions

| | | | | | | | - | | | | | | |
|-----|----------|-------|------|----------|--------|------|-------|-------|------|----------|--------|--------|----------|
| ann | notation | min_d | q1_d | median_d | mean_d | q3_d | max₋d | min_b | q1_b | median_b | mean_b | q3_b | max_b |
| | CTCF | 1 | 1 | 1 | 1.09 | 1 | 8 | 0 | 0 | 0 | 3.34 | 0 | 1410 |
| eı | nhancer | 1 | 1 | 1 | 1.18 | 1 | 30 | 0 | 0 | 0 | 31.5 | 0 | 61845 |
| | gene | 1 | 1 | 2 | 2.78 | 4 | 49 | 0 | 0 | 3 | 211.67 | 51 | 62024.27 |
| g | gene_Inc | 1 | 2 | 3 | 3.51 | 4 | 26 | 0 | 0 | 12 | 236.41 | 85.375 | 27307.88 |
| li | incRNA | 1 | 1 | 1 | 1.87 | 2 | 26 | 0 | 0 | 0 | 134.99 | 4.895 | 45314.76 |
| Т,Т | rss,pfi | 1 | 1 | 1 | 1.14 | 1 | 14 | 0 | 0 | 0 | 30.52 | 0 | 84898.53 |
| u | nknown | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

For each genomic annotation we report minimum degree, 25% lower quantile of the degree distribution, median degree, mean degree, 75% upper quantile of the degree distribution and maximum degree. The same quantities are reported for different annotations regarding the betweenness distribution.



Figure S3: Cumulative distributions of lncRNA node degree for different biological properties. Upper left: positional conservation for lncRNAs; upper right: disease annotation for lncRNAs; lower left: chromHMM enhancer annotation for lncRNAs; lower right: chromHMM enhancer annotation for lncRNAs. Numbers in brackets indicate the sample size, i.e. the number of lncRNAs corresponding to each cumulative distribution.



Figure S4: Analysis of small connected components a) Small connected component on chromosome 6 highlighting the functionally validated interactions between the lncRNA overlapping the AHI1 gene and BCLAF1 (circled in red). b) Small connected component on chromosome 8 highlighting the validated regulatory interaction between PVT1 lncRNA and MYC (circled in red). c) Connected component on chromosome 20 highlighting the validated regulatory interaction between TRERNAI lncRNAs and SNAI1 gene (circled in red). d) Small connected component on chromosome 1 highlighting two validated regulatory interactions of the two enhancer-like lncRNAs ncRNA-a3 (CYP4A22-AS1) and ncRNA-a4 (linc00853) on TAL1 gene (circled in red). e) Small connected component on chromosome X involving the lncRNA Xist, major effector of the X inactivation process. Validated regulators of Xist (FTX and JPX) are circled in red.

| IncRNA | degree | to_gene degree | betweenness | expression |
|----------------------|--------|-------------------|-------------|------------|
| RP11-442N24B.1,RNU11 | 26 | 12 | 28958.62 | 5.465 |
| RP4-798A10.7 | 21 | 6 | 32092.38 | 16.0232 |
| RP11-495P10.3 | 12 | 0 | 5456 | 1.0816 |
| SNHG12 | 9 | 7 | 2514.22 | 229.3524 |
| RP11-458D21.1 | 9 | 6 | 22924.47 | 52.9613 |
| ADAMTSL4-AS1 | 6 | 3 | 2249 | 50.9546 |
| FLJ37453 | 5 | 3 | 4126.5 | 7.1451 |
| RP1-212P9.3 | 4 | 1 | 397.41 | 0.5435 |
| RP11-337C18.8,RP11- | 3 | 1 | 250.67 | 0.044 |
| 337C18.10 | | | | |
| CH17-373J23.1 | 3 | 0 | 6056.3 | 35.8141 |
| SEC22B | 2 | 1 | 0 | 26.7178 |
| RP5-888M10.2 | 2 | 2 | 0 | 1.2264 |
| RP5-1092A3.5 | 2 | 1 | 0 | 2.3792 |
| RP4-798A10.2 | 2 | 1 | 501 | 14.2565 |
| RP1-37C10.3 | 2 | 2 | 0 | 0.1157 |
| RP11-474O21.5 | 2 | 2 | 0 | 111.6587 |
| RP11-337C18.10 | 2 | 0 | 249.33 | 0.0371 |

Table S2: Network properties of lincRNAs in the biggest connected component of chromosome 1

For each intergenic lncRNA we report its name (lncRNA), its degree centrality inside the connected component (degree), its degree centrality computed only from gene connections $(to-gene \ degree)$, its betweenness (betweenness) and its expression value (RPKM) in the K562 cell line (expression).

| Table S3: Network properties of lin | ncRNAs in | the | biggest | connecte | ed compo | nent of |
|-------------------------------------|-----------|--------|---------|----------|------------|---------|
| chromosome 17 | | | | | | |
| IncRNA | degree t | o gene | hetwee | enness | expression | |

| IncRNA | degree | to_gene | betweenness | expression |
|-------------------------|--------|---------|-------------|------------|
| | | degree | | |
| LINC00910 | 17 | 8 | 45314.76 | 37.0585 |
| SNHG16,RP11-666A8.8 | 9 | 5 | 8527.74 | 73.5648 |
| LINC00854 | 8 | 3 | 1776.27 | 70.9481 |
| RP13-516M14.1,RP13- | 6 | 2 | 1834.12 | 62.6496 |
| 516M14.4 | | | | |
| RP11-1055B8.9 | 6 | 4 | 513.68 | 9.3433 |
| RP11-400F19.8 | 5 | 5 | 7618.89 | 3.1249 |
| RP13-766D20.4 | 4 | 3 | 1130.2 | 1.2599 |
| LINC00482 | 4 | 2 | 348 | 15.868 |
| CTD-2020K17.1 | 4 | 4 | 423.66 | 8.9101 |
| RP11-285E9.6 | 3 | 2 | 1040 | 0.0321 |
| RP11-1055B8.3 | 3 | 1 | 695 | 0.5555 |
| RP11-1055B8.10,RP11- | 3 | 1 | 695 | 3.095 |
| 1055B8.4 | | | | |
| CTD-3014M21.1 | 3 | 0 | 35.83 | 6.4664 |
| RP11-666A8.8 | 2 | 0 | 0 | 2.8546 |
| RP11-392O1.4 | 2 | 1 | 10.47 | 0.0438 |
| RP11-358B23.1 | 2 | 1 | 173.5 | 0.9049 |
| RP11-1055B8.3,RP11- | 2 | 1 | 348 | 0.5555 |
| 1055B8.10,RP11-1055B8.4 | | | | |
| MAP3K14-AS1 | 2 | 1 | 348 | 12.5812 |
| CTD-2561B21.11 | 2 | 1 | 348 | 8.7781 |

For each lincRNA we report its name (lncRNA), its degree centrality inside the connected component (degree), its degree centrality computed only from gene connections $(to-gene \ degree)$, its betweenness (betweenness) and its expression value (RPKM) in the K562 cell line (expression).

Table S4: Network properties of lincRNAs in the biggest connected component of chromosome 11

| IncRNA | degree | to_gene degree | betweenness | rpkm |
|------------|--------|-------------------|-------------|------------|
| MALAT1 | 8 | 6 | 4023.77 | 10426.3926 |
| NEAT1 | 6 | 4 | 361.67 | 1685.197 |
| MIR194-2HG | 2 | 2 | 0 | 3.3122 |

For each lincRNA we report its name (lncRNA), its degree centrality inside the connected component (*degree*), its degree centrality computed only from gene connections (*to-gene degree*), its betweenness (*betweenness*) and its expression value (RPKM) in the K562 cell line (*expression*).

Table S5: Fuzzy clustering or inter-modular nodes

| IncRNA | chr | type | expr | degree |
|---------------|-------|----------------------|-------|--------|
| RP11-661A12.5 | chr8 | Inc_TSS | 11.36 | 2 |
| RP11-838N2.5 | chr18 | Inc_enhancer | 0.65 | 6 |
| AC073842.19 | chr7 | Inc_transcr_enhancer | 1.06 | 13 |
| RP11-400F19.8 | chr17 | Inc_transcr_enhancer | 3.13 | 5 |
| RP13-516M14.1 | chr17 | Inc_transcr_enhancer | 62.65 | 6 |
| RP11-388C12.5 | chr17 | Inc_TSS | 9.55 | 1 |
| RP4-798A10.2 | chr1 | Inc_transcribed | 14.26 | 1 |
| CH17-373J23.1 | chr1 | Inc_promoter | 35.81 | 3 |
| RP11-403I13.5 | chr1 | Inc_enhancer | 0.27 | 1 |
| CTD-2555K7.2 | chr14 | Inc_transcr_enhancer | 1.1 | 2 |
| RP11-298I3.4 | chr14 | Inc_CTCF | 0.74 | 3 |
| RP11-57206.1 | chr3 | Inc_transcribed | 35.16 | 2 |
| U91328.21 | chr6 | Inc_TSS | 0.15 | 2 |

For each lncRNA we report its name (lncRNA), the chromosomal location (chr), its genomic annotation (type), its expression value (RPKM) in the K562 cell line (expr) and degree centrality (degree)