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# Genome-wide detection of gene co-expression domains showing linkage to regions enriched with polymorphic retrotransposons in recombinant inbred mouse strains

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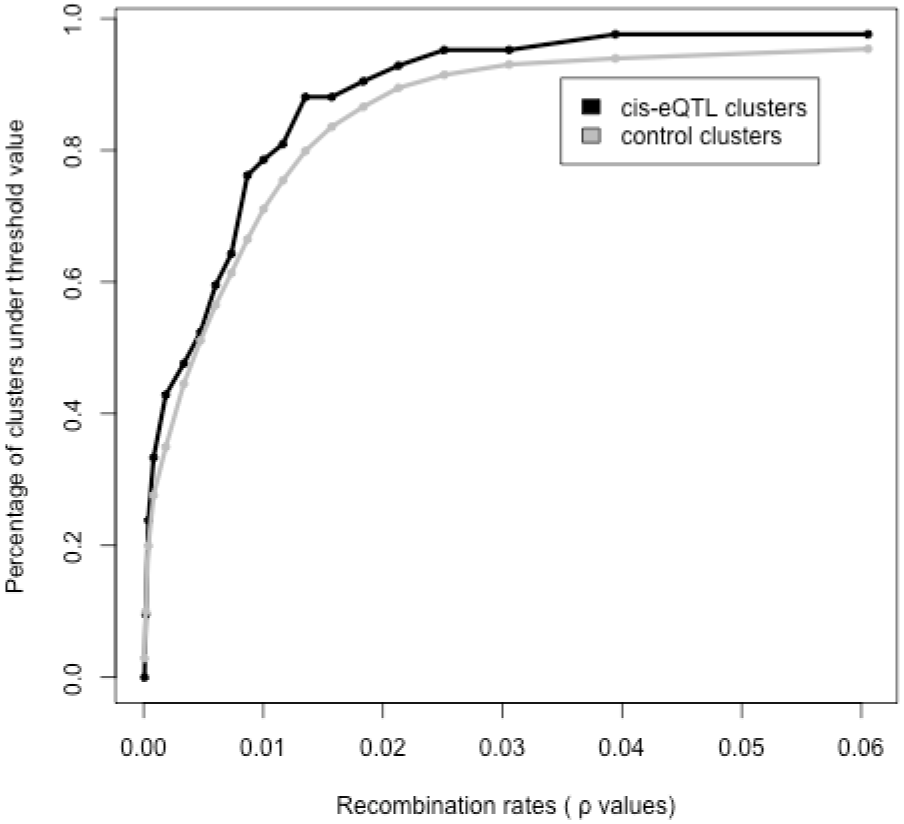

**Figure S1** Distribution of recombination rates in regions corresponding to either cis-eQTL or control clusters. The recombination rate values corresponded to the ρ values, as calculated and reported by Brunschwig H et al. (Genetics 191: 757–764, 2012). According to the Chi-square test, there was no significant difference in the distributions of recombination rates in the 2 types of regions ($P > 0.3$).

**Table S1 Abundance of polymorphic and total TEs in mouse genomes.** Lists of polymorphic TEs were obtained from either the publication of Nellåker et al (2012) or from the MouseIndelDB database. Lists of fixed TEs were obtained from the Transpogene database. n/a: non available.

| **Database** | **Genetic origin** | **full LINEs** | **LINE frag.** | **LTR-TEs** | **SINEs** |
|---|---|---|---|---|---|
| | | | | | |
| **Nellåker et al. (polymorphic TEs)** | Both strains | 1808 | 2969 | 4734 | 4303 |
| | C57(+) / A/J(-) | 606 | 1015 | 1901 | 2378 |
| | C57(-) / A/J(+) | 1202 | 1954 | 2833 | 1925 |
| | | | | | |
| **MouseIndelDB (polymorphic TEs)** | Both strains | | | 2413 | 1512 |
| | C57(+) / A/J(-) | | | 1436 | 1512 |
| | C57(-) / A/J(+) | | | 977 | 0 |
| | | | | | |
| **Transpogene (fixed TEs)** | | 78,002 | n/a | 84,724 | 190,057 |
| | | | | | |

**Table S2 Summary of gene expression datasets from mouse RIS.** Each line provides information about which tissue and which RIS panel was used for each gene expression dataset, as well as about the number of strains that were profiled and the nature of the microarray platform. The GN access numbers corresponds to the identification number of corresponding datasets in GeneNetwork.

| **Tissue** | **RIS panel** | **# of strains used** | **Microarray platform** | **GN access #** |
|---|---|---|---|---|
| Eye | AxB/BxA | 26 | Illumina MouseRef-6 | GN210 |
| Eye | BxD | 68 | Affymetrix Mouse Genome 430 | GN207 |
| Kidney | BxD | 54 | Affymetrix Mouse Genome 430 | GN240 |
| Hippocampus | BxD | 67 | Affymetrix Mouse Genome 430 | GN112 |
| Hypothalamus | BxD | 33 | Affymetrix MoGene 1.0 ST | GN281 |
| Cerebellum | BxD | 28 | Affymetrix Mouse Genome 430 | GN72 |

**Table S3 Properties of cis-eQTL and control clusters (defined using three different window sizes).** In addition to the sizes of the intervals between detected genes, some additional criteria were used in the selection of control clusters in order to have them match cis-eQTL clusters for size and density of total genes. For the 250 kB intervals, only clusters <400 kB and containing more than 3 genes were kept; for the 500 kB, only clusters <650 kB and containing at least 6 genes were kept; for the 750 kB intervals, only clusters of <800 kb and containing at least 8 genes were kept.

| **Maximum interval between cis-eQTLs or detected genes** | **250kB** | | | **500kB** | | | **750kB** | | |
|---|---|---|---|---|---|---|---|---|---|
| | Cis-eQTL clusters | Control cluters | p-val | Cis-eQTL clusters | Control cluters | p-val | Cis-eQTL clusters | Control cluters | p-val |
| Size of boxes (in kb) | 221.9 ±130 | 248± | 0.2 | 467.1 ±486 | 456±119 | 0.87 | 658.8 ±553 | 561±123 | 0.2 |
| Number of detected genes | 4.2 ±1.9 | 4.75± | 0.1 | 4.9 ±3.5 | 5.23±2.46 | 0.63 | 5.1 ±3.6 | 6.6±3.89 | 0.11 |
| Total number of genes | 7.2 ±6.6 | 6.30 ±2.9 | 0.38 | 12.3 ±16 | 10.1±3.45 | 0.35 | 15.70±17.6 | 14.9±11.1 | 0.81 |
| Number of clusters | 42 | 188 | | 53 | 59 | | 61 | 21 | |

**Table S4 Normalized abundance of polymorphic and fixed TEs in several sizes of genomic regions around "250 kB" clusters.** Normalized abundance of TEs was calculated by dividing the abundance of each element with that found in random regions. Test regions corresponded to those containing cis-eQTLs (either clustered or single) or control clusters, each region being augmented by flanking regions of either 250, 500, 1000 kb.

| | | Polymorphic | | | | Fixed | |
|---|---|---|---|---|---|---|---|
| | | **full LINEs** | **LINE frag.** | **LTR-TEs** | **SINEs** | **LTR-TEs** | **SINEs** |
| **Size of flanking regions** | 250 kB | | | | | | |
| **Normalized abundance of TEs / MB (mean ± SD)** | Cis-eqtl clusters (n=42) | 0.51 ± 1.39 | 0.77 ± 1.42 | 2.27 ± 1.75 | 4.78 ± 3.51 | 1.55 ± 2.17 | 2.85 ± 3.01 |
| | CTL clusters (n=188) | 0.46 ± 1.16 | 0.55 ± 1.01 | 1.28 ± 1.58 | 1.45 ± 2.07 | 1.53 ± 1.3 | 2.05 ± 1.62 |
| | Single cis-eQTL regions (n=232) | 0.59 ± 1.32 | 0.94 ± 1.33 | 1.8± 1.53 | 1.97±1.84 | 1.53±1.26 | 1.71±1.78 |
| | Random regions (n=500) | 1 ± 2.04 | 1 ± 1.72 | 1 ± 1.39 | 1 ± 1.72 | 1 ± 1.27 | 1 ± 1.42 |
| **Anova P values** | | 0.00039 | 0.0059 | 1.22E-13 | 1.11E-33 | 3.15E-08 | 4.40E-20 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | 0.99 | 0.83 | 0.00053 | <e-5 | 0.99 | 0.02306 |
| | Cis-eqtl clusters vs single cis-eQTL regions | 0.99 | 0.90 | 0.22 | <e-5 | 0.99 | 0.00023 |
| | Cis-eqtl clusters vs random | 0.28 | 0.77 | <e-5 | <e-5 | 0.048 | <e-5 |
| | Control and single cis-eQTL regions | 0.8 | 0.042 | 0.0019 | 0.029 | 0.99 | 0.15 |
| | CTL vs random | 0.001 | 0.003 | 0.12 | 0.03 | 2.00E-05 | <e-5 |
| | Random vs single cis-eQTL regions | 0.015 | 0.96 | <e-5 | <e-5 | <e-5 | <e-5 |

| | | Polymorphic | | | | Fixed | |
|---|---|---|---|---|---|---|---|
| | | **full LINEs** | **LINE frag.** | **LTR-TEs** | **SINEs** | **LTR-TEs** | **SINEs** |
| **Size of flanking regions** | 500 kB | | | | | | |
| **Normalized abundance of TEs / MB (mean ± SD)** | Cis-eqtl clusters (n=42) | 0.54 ± 1.42 | 0.98 ± 1.69 | 1.88 ± 1.43 | 4.14 ± 2.84 | 1.39 ± 1.22 | 2.46 ± 1.86 |
| | CTL clusters (n=188) | 0.61 ± 1.16 | 0.65 ± 1.05 | 1.10 ± 1.25 | 1.27 ± 1.59 | 1.41 ± 1.10 | 1.79 ± 1.39 |
| | Single cis-eQTL regions (n=232) | 0.75±1.24 | 0.93±1.07 | 1.62±1.21 | 1.7±1.45 | 1.39±1.1 | 1.53±1.48 |
| | Random regions (n=500) | 1 ± 1.77 | 1 ± 1.51 | 1 ± 1.20 | 1 ± 1.6 | 1 ± 1.10 | 1 ± 1.29 |
| **Anova P values** | | 0.0068 | 0.024 | 1.12E-11 | 2.22E-31 | 1.01E-06 | 6.32E-17 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | 0.99 | 0.47 | 0.001 | <e-5 | 0.99 | 0.024 |
| | Cis-eqtl clusters vs single cis-eQTL regions | 0.83 | 0.99 | 0.58 | <e-5 | 1 | 0.00041 |
| | Cis-eqtl clusters vs random | 0.23 | 0.99 | 5.00E-05 | <e-5 | 0.12352 | <e-5 |
| | Control and single cis-eQTL regions | 0.75 | 0.13 | 8.00E-05 | 0.03 | 0.99 | 0.22 |
| | CTL vs random | 0.014 | 0.013 | 0.79 | 0.21 | 1.00E-04 | <e-5 |
| | Random vs single cis-eQTL regions | 0.18 | 0.92 | <e-5 | <e-5 | 6.00E-05 | 1.00E-05 |

| | | Polymorphic | | | | Fixed | |
|---|---|---|---|---|---|---|---|
| | | **full LINEs** | **LINE frag.** | **LTR-TEs** | **SINEs** | **LTR-TEs** | **SINEs** |
| **Size of flanking regions** | 1 MB | | | | | | |
| **Normalized abundance of TEs / MB (mean ± SD** | Cis-eqtl clusters (n=42) | 0.59 ± 1.25 | 0.93 ± 1.27 | 1.71 ± 1.17 | 3.47 ± 2.36 | 1.26 ± 0.93 | 2.12 ± 1.54 |
| | CTL clusters (n=188) | 0.76 ± 1.26 | 0.72 ± 1.02 | 1.06 ± 0.92 | 1.14 ± 1.17 | 1.33 ± 0.99 | 1.53 ± 1.1 |
| | Single cis-eQTL regions (n=232) | 0.48±1.71 | 0.81±1.91 | 1.76±2.28 | 2.69±3.3 | 1.7±1.58 | 2.02±2.02 |
| | Random regions (n=500) | 1 ± 1.47 | 1 ± 1.39 | 1 ± 1.03 | 1 ± 1.39 | 1 ± 0.87 | 1 ± 1.11 |
| **Anova P values** | | 0.00013 | 0.1 | 4.95E-11 | 7.17E-31 | 1.75E-13 | 3.84E-20 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | 0.91 | 0.82 | 0.037 | <e-5 | 0.98 | 0.069 |
| | Cis-eqtl clusters vs single cis-eQTL regions | 0.96 | 0.96 | 0.99 | 0.1 | 0.083 | 0.97 |
| | Cis-eqtl clusters vs random | 0.32 | 0.99 | 0.011 | <e-5 | 0.46 | 1.00E-05 |
| | Control and single cis-eQTL regions | 0.22 | 0.91 | <e-5 | <e-5 | 0.0034 | 0.0024 |
| | CTL vs random | 0.22 | 0.11 | 0.96 | 0.86 | 0.0034 | 6.00E-05 |
| | Random vs single cis-eQTL regions | 7.00E-05 | 0.37 | <e-5 | <e-5 | <e-5 | <e-5 |

**Table S5 Normalized abundance of polymorphic and fixed TEs in several sizes of genomic regions around "500 kB" clusters.** Normalized abundance of TEs was calculated by dividing the abundance of each element with that found in random regions. Test regions corresponded to those containing cis-eQTLs (either clustered or single) or control clusters, each region being augmented by flanking regions of either 250, 500, 1000 kb.

| | | **Polymorphic** | | | | **Total** | |
|---|---|---|---|---|---|---|---|
| | | **full LINEs** | **LINE frag.** | **LTR-TEs** | **SINEs** | **LTR-TEs** | **SINEs** |
| **Size of flanking regions** | 250 kB | | | | | | |
| **Mean numbers of elements /MB (fold diff vs random mean)** | Cis-eqtl clusters (n=53) | 0.66 ± 1.33 | 0.96 ± 1.59 | 2.24 ± 1.73 | 4.00 ± 2.84 | 1.57 ± 1.99 | 2.85 ± 2.8 |
| | CTL clusters (n=59) | 0.89 ±1.71 | 0.72 ± 0.9 | 1.08 ± 1.1 | 1.29 ± 1.48 | 1.36 ± 1.17 | 1.91 ± 1.43 |
| | Single cis-eQTL regions (n=232) | 0.69±1.26 | 0.97±1.19 | 1.69±1.29 | 1.76±1.6 | 1.43±1.14 | 1.64±1.6 |
| | Random regions (n=500) | 1 ± 1.9 | 1 ± 1.56 | 1 ± 1.28 | 1 ± 1.6 | 1 ± 1.19 | 1 ± 1.33 |
| **Anova P values** | | 0.099 | 0.56 | 8.05E-16 | 3.05E-32 | 9.33E-06 | 1.16E-18 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | 0.88 | 0.8 | 2.00E-05 | <e-5 | 0.81 | 0.0078 |
| | Cis-eqtl clusters vs single cis-eQTL regions | 0.99 | 1 | 0.028 | <e-5 | 0.88 | <e-5 |
| | Cis-eqtl clusters vs random | 0.5 | 0.99 | <e-5 | <e-5 | 0.008 | <e-5 |
| | Control and single cis-eQTL regions | 0.84 | 0.63 | 0.0071 | 0.22 | 0.98 | 0.62 |
| | CTL vs random | 0.96 | 0.48 | 0.97 | 0.59 | 0.14 | 0.00012 |
| | Random vs single cis-eQTL regions | 0.09 | 0.99 | <e-5 | <e-5 | 8.00E-05 | <e-5 |

| | | **Polymorphic** | | | | **Total** | |
|---|---|---|---|---|---|---|---|
| | | **full LINEs** | **LINE frag.** | **LTR-TEs** | **SINEs** | **LTR-TEs** | **SINEs** |
| **Size of flanking regions** | 500 kB | | | | | | |
| **Mean numbers of elements /MB (fold diff vs random mean)** | Cis-eqtl clusters (n=53) | 0.69 ± 1.38 | 1.08 ± 1.73 | 1.80 ± 1.32 | 3.41 ± 2.19 | 1.36 ± 1.16 | 2.39 ± 1.77 |
| | CTL clusters (n=59) | 1.10 ± 1.9 | 0.88 ± 1.05 | 1.08 ± 1.07 | 1.14 ± 1.16 | 1.32 ± 1.1 | 1.60 ± 1.28 |
| | Single cis-eQTL regions (n=232) | 0.8±1.2 | 1±1.11 | 1.56±1.1 | 1.58±1.25 | 1.36±1.06 | 1.49±1.41 |
| | Random regions (n=500) | 1 ± 1.67 | 1 ± 1.49 | 1 ± 1.15 | 1 ± 1.54 | 1 ± 1.03 | 1 ± 1.22 |
| **Anova P values** | | 0.19 | 0.8 | 2.65E-11 | 5.09E-27 | 3.93E-05 | 2.80E-14 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | 0.49 | 0.86 | 0.0046 | <e-5 | 0.99 | 0.0092 |
| | Cis-eqtl clusters vs single cis-eQTL regions | 0.96 | 0.97 | 0.51 | <e-5 | 0.99 | 5.00E-05 |
| | Cis-eqtl clusters vs random | 0.50 | 0.97 | 1.00E-05 | <e-5 | 0.088 | <e-5 |
| | Control and single cis-eQTL regions | 0.52 | 0.93 | 0.019 | 0.17 | 0.99 | 0.93 |
| | CTL vs random | 0.96 | 0.91 | 0.96 | 0.9 | 0.117 | 0.0054 |
| | Random vs single cis-eQTL regions | 0.35 | 0.99 | <e-5 | 1.00E-05 | 9.00E-05 | 2.00E-05 |

| | | Polymorphic | | | | Total | |
|---|---|---|---|---|---|---|---|
| | | **full LINEs** | **LINE frag.** | **LTR-TEs** | **SINEs** | **LTR-TEs** | **SINEs** |
| **Size of flanking regions** | 1 MB | | | | | | |
| **Mean numbers of elements /MB (fold diff vs random mean)** | Cis-eqtl clusters (n=53) | 0.76 ± 1.21 | 1.06 ± 1.34 | 1.58 ± 1.04 | 2.93 ± 1.87 | 1.18 ± 0.86 | 2.02 ± 1.45 |
| | CTL clusters (n=59) | 1.01 ± 1.43 | 0.94 ± 1.08 | 1.03 ± 0.91 | 1.06 ± 1.02 | 1.16 ± 0.85 | 1.31 ± 0.95 |
| | Single cis-eQTL regions (n=232) | | | | | | |
| | Random regions (n=500) | 1 ± 1.4 | 1 ± 1.36 | 1 ± 0.99 | 1 ± 1.35 | 1 ± 0.84 | 1 ± 1.07 |
| **Anova P values** | | 1.97E-05 | 0.42 | 8.00E-10 | 3.84E-26 | 3.43E-13 | 4.94E-19 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | 0.78 | 0.97 | 0.16 | 1.00E-05 | 0.9 | 0.04 |
| | Cis-eqtl clusters vs single cis-eQTL regions | 0.47 | 0.7 | 0.9 | 0.75 | 0.012 | 0.99 |
| | Cis-eqtl clusters vs random | 0.65 | 0.99 | 0.022 | <e-5 | 0.65 | <e-5 |
| | Control and single cis-eQTL regions | 0.034 | 0.9 | 0.004 | 0 | 0.0047 | 0.0036 |
| | CTL vs random | 0.99 | 0.99 | 0.99 | 0.99 | 0.72 | 0.39 |
| | Random vs single cis-eQTL regions | 1.00E-05 | 0.39 | <e-5 | <e-5 | <e-5 | <e-5 |

**Table S6 Most significantly enriched binding sites in polymorphic SINEs**

| Motif Name (family) | CHIP-Seq cell line | Consensus | P-value | % of Target Sequences with Motif | % of Background Sequences with Motif |
|---|---|---|---|---|---|
| **CTCFL /BORIS (Zinc finger)** | K562 | CNNBRGCGCCCCCTGSTGGC | 1e-1283 | 63.96% | 3.33% |
| ZNF143 (Zinc finger) | CUTTL | ATTTCCCAGVAKSCY | 1e-1273 | 73.63% | 5.91% |
| c-Myc | mES | VVCCACGTGG | 1e-1213 | 75.98% | 7.34% |
| n-Myc (Helix-Loop-Helix) | mES | VRCCACGTGG | 1e-1116 | 76.39% | 8.77% |
| Max (Helix-Loop-Helix)) | K562 | RCCACGTGGYYN | 1e-1094 | 77.54% | 9.57% |
| RUNX (Runt) | HPC7 | SAAACCACAG | 1e-1000 | 76.44% | 10.61% |
| Gfi1b (Zinc finger) | HPC7 | MAATCACTGC | 1e-996 | 72.28% | 8.82% |
| RUNX2 (Runt) | PCa | NWAACCACADNN | 1e-906 | 76.44% | 12.37% |
| RUNX1 (Runt) | Jurkat | AAACCACARM | 1e-820 | 76.70% | 14.39% |
| Cdx2 (Homeobox) | mES | GYMATAAAAH | 1e-623 | 63.70% | 11.95% |
| Olig2 (Helix-Loop-Helix)) | Neuron | RCCATMTGTT | 1e-613 | 79.10% | 22.14% |
| HNF4a (Nuclear Receptors) | HpeG2 | CARRGKBCAAAGTYCA | 1e-359 | 33.54% | 4.58% |
| GATA3 (Zinc finger) | iTreg | AGATSTNDNNDSAGATAASN | 1e-322 | 23.19% | 1.97% |
| Erra( NR) | HepG2 | CAAAGGTCAG | 1.00E-304 | 62.35% | 22.53% |
| FOXA1 (Forkhead) | MCF7 | WAAGTAAACA | 1.00E-304 | 53.46% | 16.26% |
| Smad3 (MAD) | NPC | TWGTCTGV | 1.00E-265 | 68.28% | 29.69% |
| FOXA1 (Forkhead) | LNCaP | WAAGTAAACA | 1.00E-265 | 54.08% | 18.54% |
| AR-halfsite (Nuclear Receptors) | LNCaP | CCAGGAACAG | 1.00E-232 | 78.00% | 41.54% |
| Nkx2.5 (Homeobox) | HL1 | RRSCACTYAA | 1.00E-182 | 56.89% | 25.78% |
| Nanog (Homeobox) | mES | RGCCATTAAC | 1.00E-106 | 69.53% | 44.63% |
| NeuroD1 (Helix-Loop-Helix) | Islet | GCCATCTGTT | 1.00E-102 | 25.07% | 8.50% |
| **CTCF (Zinc finger)** | CD4+ | AYAGTGCCMYCTRGTGGCCA | 1.00E-67 | 9.26% | 1.82% |

**Table S7 Comparisons for respective normalized abundance of binding sites for regulatory factors in several sizes of genomic regions around "250 kB" clusters.** Normalized abundances of binding sites for regulatory factors was calculated in regions containing cis-eQTL cluster, control cluster, single cis-eQTL region or random regions, and augmented by flanking region of either 250, 500, 1000 kb.

| | | **CTSF** | **h3ac** | **gata4** | **MEF2A** | **NKX2_5** | **SRF** | **TBX5** | **P300** |
|---|---|---|---|---|---|---|---|---|---|
| **Size of flanking regions** | 250 kB | | | | | | | | |
| **Normalized abundance of TFs / MB (mean ± SD)** | Cis-eqtl clusters (n=42) | 2.81 ± 0.94 | 4.20 ± 2.89 | 2.10 ± 1.65 | 2.67 ± 4.8 | 2.11 ± 1.65 | 4.02 ± 2.92 | 3.65 ± 2.52 | 2.43 ± 2.22 |
| | CTL clusters (n=188) | 1.76 ±0.69 | 1.85 ± 1.19 | 1.72 ± 1.29 | 1.47 ± 3.27 | 1.86 ± 1.62 | 1.87 ± 1.51 | 1.91 ± 1.67 | 1.64 ± 1.8 |
| | Single cis-eQTL regions (n=232) | 1.63±0.73 | 1.81±1.6 | 1.68±1.4 | 1.34±2.53 | 1.64±1.41 | 1.9±1.85 | 1.85±1.73 | 1.7±1.89 |
| | Random regions (n=500) | 1 ± 0.89 | 1 ± 1.57 | 1 ± 1.46 | 1 ± 4.16 | 1 ± 1.63 | 1 ± 1.58 | 1 ± 1.57 | 1 ± 1.61 |
| **Anova P values** | | 4.4E-56 | 7.65E-37 | 6.20E-14 | 0.026 | 8.29E-13 | 5.89E-31 | 3.68E-27 | 1.48E-10 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.40684 | 0.22 | 0.77 | <e-5 | <e-5 | 0.039 |
| | Cis-eqtl clusters vs single cis-eQTL regions | <e-5 | <e-5 | 0.29376 | 0.140 | 0.27 | <e-5 | <e-5 | 0.059 |
| | Cis-eqtl clusters vs random | <e-5 | <e-5 | 1.00E-05 | 0.025 | 7.00E-05 | <e-5 | <e-5 | <e-5 |
| | Control and single cis-eQTL regions | 0.41 | 0.99 | 0.98 | 0.98 | 0.49 | 0.99 | 0.97 | 0.98 |
| | CTL vs random | <e-5 | <e-5 | <e-5 | 0.44 | <e-5 | <e-5 | <e-5 | 0.00014 |
| | Random vs single cis-eQTL regions | <e-5 | <e-5 | <e-5 | 0.65 | <e-5 | <e-5 | <e-5 | <e-5 |
| | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.4 | 0.22 | 0.77 | <e-5 | <e-5 | 0.039 |

| | | **CTSF** | **h3ac** | **gata4** | **MEF2A** | **NKX2_5** | **SRF** | **TBX5** | **P300** |
|---|---|---|---|---|---|---|---|---|---|
| **Size of flanking regions** | 500 kB | | | | | | | | |
| **Normalized abundance of TFs / MB (mean ± SD)** | Cis-eqtl clusters (n=42) | 2.43 ± 0.78 | 3.60 ± 2.36 | 2.06 ± 1.5 | 2.67 ± 4.69 | 2.06 ± 1.69 | 3.47 ± 2.58 | 3.24 ± 2.17 | 2.03 ± 1.64 |
| | CTL clusters (n=188) | 1.57 ± 0.59 | 1.63 ± 1.14 | 1.60 ± 1.07 | 1.42 ± 3.16 | 1.79 ± 1.56 | 1.69 ± 1.33 | 1.72 ± 1.54 | 1.33 ± 1.27 |
| | Single cis-eQTL regions (n=232) | 1.5±0.67 | 1.61±1.33 | 1.59±1.18 | 1.26±2.11 | 1.58±1.32 | 1.7±1.65 | 1.66±1.56 | 1.4±1.3 |
| | Random regions (n=500) | 1 ± 0.84 | 1 ± 1.42 | 1 ± 1.26 | 1 ± 3.44 | 1 ± 1.44 | 1 ± 1.47 | 1 ± 1.48 | 1 ± 1.31 |
| **Anova P values** | | 1.88E-41 | 1.06E-30 | 9.36E-15 | 0.0081 | 5.40E-13 | 6.99E-25 | 6.61E-22 | 1.34E-07 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.12 | 0.099 | 0.69 | <e-5 | <e-5 | 0.0094 |
| | Cis-eqtl clusters vs single cis-eQTL regions | <e-5 | <e-5 | 0.1 | 0.04 | 0.195 | <e-5 | <e-5 | 0.02 |
| | Cis-eqtl clusters vs random | <e-5 | <e-5 | <e-5 | 0.0063 | 4.00E-05 | <e-5 | <e-5 | 1.00E-05 |
| | Control and single cis-eQTL regions | 0.76 | 0.99 | 0.99 | 0.95 | 0.45 | 0.99 | 0.979 | 0.94 |
| | CTL vs random | <e-5 | <e-5 | <e-5 | 0.41 | 0<e-5 | <e-5 | <e-5 | 0.019 |
| | Random vs single cis-eQTL regions | <e-5 | <e-5 | <e-5 | 0.73 | <e-5 | <e-5 | <e-5 | 8.00E-04 |
| | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.12 | 0.099 | 0.690 | <e-5 | <e-5 | 0.009 |

|  |  | **CTSF** | **h3ac** | **gata4** | **MEF2A** | **NKX2_5** | **SRF** | **TBX5** | **P300** |
|---|---|---|---|---|---|---|---|---|---|
| **Size of flanking regions** | 1 MB |  |  |  |  |  |  |  |  |
| **Normalized abundance of TFs / MB (mean ± SD)** | Cis-eqtl clusters (n=42) | 2.15 ± 0.7 | 3.16 ± 1.98 | 1.87 ± 1.18 | 2.63 ± 5.5 | 1.82 ± 1.43 | 2.99 ± 2.2 | 2.90 ± 1.94 | 1.69 ± 1.11 |
|  | CTL clusters (n=188) | 1.45 ± 0.56 | 1.48 ± 0.97 | 1.45 ± 0.87 | 1.38 ± 3.2 | 1.59 ± 1.33 | 1.51 ± 1.19 | 1.53 ± 1.35 | 1.23 ± 0.96 |
|  | Single cis-eQTL regions (n=232) | 1.4±0.6 | 1.44±1.12 | 1.44±0.96 | 1.16±1.71 | 1.45±1.13 | 1.49±1.35 | 1.47±1.34 | 1.29±0.95 |
|  | Random regions (n=500) | 1 ± 0.76 | 1 ± 1.27 | 1 ± 1.01 | 1 ± 2.92 | 1 ± 1.17 | 1 ± 1.32 | 1 ± 1.34 | 1 ± 1.08 |
| **Anova P values** |  | 4.82E-33 | 4.59E-27 | 7.69E-14 | 0.004 | 6.77E-11 | 1.98E-20 | 2.12E-18 | 5.31E-06 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.05 | 0.05 | 0.65 | <e-5 | <e-5 | 0.038 |
|  | Cis-eqtl clusters vs single cis-eQTL regions | <e-5 | <e-5 | 0.04 | 0.013 | 0.25 | <e-5 | <e-5 | 0.087 |
|  | Cis-eqtl clusters vs random | <e-5 | <e-5 | <e-5 | 0.0028 | 0.00014 | <e-5 | <e-5 | 0.00017 |
|  | Control and single cis-eQTL regions | 0.82 | 0.97 | 0.99 | 0.86 | 0.65 | 0.99 | 0.97 | 0.92 |
|  | CTL vs random | <e-5 | 3.00E-05 | <e-5 | 0.42 | <e-5 | 6.00E-05 | 4.00E-05 | 0.05 |
|  | Random vs single cis-eQTL regions | <e-5 | 5.00E-05 | <e-5 | 0.9 | 2.00E-05 | 4.00E-05 | 9.00E-05 | 0.002 |
|  | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.059 | 0.056 | 0.65 | <e-5 | <e-5 | 0.038 |

**Table S8 Comparisons for respective normalized abundance of binding sites for regulatory factors in several sizes of genomic regions around "500 kB" clusters.** Normalized abundances of binding sites for regulatory factors was calculated in regions containing cis-eQTL cluster, control cluster, single cis-eQTL region or random regions, and augmented by flanking region of either 250, 500, 1000 kb.

| | | **CTSF** | **h3ac** | **gata4** | **MEF2A** | **NKX2_5** | **SRF** | **TBX5** | **P300** |
|---|---|---|---|---|---|---|---|---|---|
| **Size of flanking regions** | 250 kB | | | | | | | | |
| **Normalized abundance of TFs / MB (mean ± SD)** | Cis-eqtl clusters (n=53) | 2.50 ± 1.01 | 3.60 ± 2.53 | 1.96 ± 1.44 | 2.15 ± 4.14 | 1.91 ± 1.5 | 3.30 ± 2.59 | 3.18 ± 2.31 | 2.22 ± 1.81 |
| | CTL clusters (n=59) | 1.49 ± 0.56 | 1.53 ± 1.06 | 1.47 ± 1.37 | 1.30 ± 2.43 | 1.45 ± 1.27 | 1.37 ± 1.23 | 1.20 ± 0.94 | 1.31 ± 1.42 |
| | Single cis-eQTL regions (n=232) | 1.58±0.71 | 1.7±1.45 | 1.63±1.29 | 1.27±2.21 | 1.62±1.39 | 1.81±1.75 | 1.75±1.63 | 1.53±1.52 |
| | Random regions (n=500) | 1 ± 0.86 | 1 ± 1.47 | 1 ± 1.34 | 1 ± 3.71 | 1 ± 1.55 | 1 ± 1.51 | 1 ± 1.52 | 1 ± 1.41 |
| **Anova P values** | | 6.89E-41 | 2.25E-30 | 3.74E-11 | 0.1 | 1.80E-08 | 3.74E-23 | 2.03E-22 | 1.15E-09 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.21 | 0.53 | 0.35 | <e-5 | <e-5 | 0.0062 |
| | Cis-eqtl clusters vs single cis-eQTL regions | <e-5 | <e-5 | 0.37 | 0.30 | 0.56 | <e-5 | <e-5 | 0.011 |
| | Cis-eqtl clusters vs random | <e-5 | <e-5 | <e-5 | 0.079 | 0.00014 | <e-5 | <e-5 | <e-5 |
| | Control and single cis-eQTL regions | 0.86 | 0.86 | 0.83 | 0.99 | 0.86 | 0.25 | 0.08 | 0.73 |
| | CTL vs random | 1.00E-04 | 0.058 | 0.053 | 0.91 | 0.12 | 0.35 | 0.79 | 0.42 |
| | Random vs single cis-eQTL regions | <e-5 | <e-5 | <e-5 | 0.74 | <e-5 | <e-5 | <e-5 | 4.00E-05 |
| | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.21 | 0.53 | 0.35 | <e-5 | <e-5 | 0.0062 |

| | | **CTSF** | **h3ac** | **gata4** | **MEF2A** | **NKX2_5** | **SRF** | **TBX5** | **P300** |
|---|---|---|---|---|---|---|---|---|---|
| **Size of flanking regions** | 500 kB | | | | | | | | |
| **Normalized abundance of TFs / MB (mean ± SD)** | Cis-eqtl clusters (n=53) | 2.21 ± 0.78 | 3.08 ± 2.2 | 1.79 ± 1.34 | 2.19 ± 4.77 | 1.72 ± 1.35 | 2.82 ± 2.36 | 2.81 ± 2.03 | 1.87 ± 1.38 |
| | CTL clusters (n=59) | 1.26 ± 0.45 | 1.15 ± 0.75 | 1.30 ± 1.1 | 1.23 ± 2.17 | 1.30 ± 1.26 | 1.11 ± 0.95 | 0.99 ± 0.79 | 1.07 ± 1.05 |
| | Single cis-eQTL regions (n=232) | 1.46 ±0.66 | 1.56 ±1.26 | 1.54 ±1.1 | 1.25 ±1.99 | 1.52 ±1.24 | 1.62 ±1.54 | 1.59 ±1.49 | 1.33 ±1.12 |
| | Random regions (n=500) | 1 ± 0.81 | 1 ± 1.36 | 1 ± 1.16 | 1 ± 3.21 | 1 ± 1.33 | 1 ± 1.42 | 1 ± 1.44 | 1 ± 1.2 |
| **Anova P values** | | 2.53E-31 | 1.46E-24 | 2.40E-10 | 0.0467 | 1.93E-07 | 1.39E-17 | 2.76E-18 | 4.06E-07 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.10 | 0.32 | 0.33 | <e-5 | <e-5 | 0.0022 |
| | Cis-eqtl clusters vs single cis-eQTL regions | <e-5 | <e-5 | 0.45 | 0.165 | 0.76 | <e-5 | <e-5 | 0.016 |
| | Cis-eqtl clusters vs random | <e-5 | <e-5 | 1.00E-05 | 0.03 | 0.0008 | <e-5 | <e-5 | <e-5 |
| | Control and single cis-eQTL regions | 0.28507 | 0.18261 | 0.51 | 0.99 | 0.65 | 0.094 | 0.025 | 0.43 |
| | CTL vs random | 0.05502 | 0.84625 | 0.22 | 0.94 | 0.32 | 0.94 | 0.99 | 0.97 |
| | Random vs single cis-eQTL regions | <e-5 | <e-5 | <e-5 | 0.71 | <e-5 | <e-5 | <e-5 | 0.002 |
| | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.1 | 0.32 | 0.33 | <e-5 | <e-5 | 0.002 |

|  |  | CTSF | h3ac | gata4 | MEF2A | NKX2_5 | SRF | TBX5 | P300 |
|---|---|---|---|---|---|---|---|---|---|
| **Size of flanking regions** | 1 MB |  |  |  |  |  |  |  |  |
| **Normalized abundance of TFs / MB (mean ± SD)** | Cis-eqtl clusters (n=53) | 1.97 ± 0.65 | 2.61 ±1.79 | 1.64 ± 1.03 | 1.97 ± 4.7 | 1.53 ± 1.15 | 2.43 ± 1.9 | 2.48 ± 1.79 | 1.69 ± 1.06 |
|  | CTL clusters (n=59) | 1.14 ± 0.47 | 1.02 ± 0.66 | 1.16 ± 0.81 | 0.96 ± 1.59 | 1.16 ± 0.97 | 0.96 ± 0.77 | 0.88 ± 0.67 | 1.02 ± 0.2 |
|  | Single cis-eQTL regions (n=232) | 1.38±0.6 | 1.42±1.1 | 1.42±0.91 | 1.1±1.58 | 1.42±1.07 | 1.46±1.32 | 1.45±1.32 | 1.3±0.95 |
|  | Random regions (n=500) | 1 ± 0.74 | 1 ± 1.27 | 1 ± 0.97 | 1 ± 3.22 | 1 ± 1.15 | 1 ± 1.3 | 1 ± 1.32 | 1 ± 1.06 |
| **Anova P values** |  | 2.61E-25 | 1.28E-18 | 1.80E-09 | 0.13 | 3.93E-06 | 4.28E-14 | 3.91E-15 | 6.14E-07 |
| **Post-hoc Tukey P values** | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.042 | 0.25 | 0.28 | <e-5 | <e-5 | 0.0025 |
|  | Cis-eqtl clusters vs single cis-eQTL regions | <e-5 | <e-5 | 0.43 | 0.19 | 0.9 | 1.00E-05 | <e-5 | 0.055 |
|  | Cis-eqtl clusters vs random | <e-5 | <e-5 | 2.00E-05 | 0.092 | 0.0056 | <e-5 | <e-5 | 1.00E-05 |
|  | Control and single cis-eQTL regions | 0.087 | 0.12 | 0.25 | 0.98 | 0.38 | 0.04 | 0.016 | 0.21 |
|  | CTL vs random | 0.41 | 0.99 | 0.59 | 0.99 | 0.73 | 0.99 | 0.91 | 0.99 |
|  | Random vs single cis-eQTL regions | <e-5 | 0.00014 | <e-5 | 0.97 | 2.00E-05 | 9.00E-05 | 1.00E-04 | 0.0009 |
|  | Cis-eqtl clusters vs CTL | <e-5 | <e-5 | 0.04 | 0.25 | 0.28 | <e-5 | <e-5 | 0.0025 |

**Table S9 Descriptive information concerning the 42 "250 kB" cis-eQTL clusters**

| Chr | *Start* | end | Length | Number of cis-eQTsL | Symbols of cis-eQTL genes |
|---|---|---|---|---|---|
| 1 | *172981698* | 173434853 | 453155 | 11 | FCGR3,1700009P17RIK,SDHCAPOA2,<br>FCER1G,B4GALT3,PPOX,UFC1,KLHDC9,F11R,REFBP2 |
| 1 | *173934520* | 174206100 | 271580 | 5 | VANGL2,NCSTN,COPA,PEX19,ATP1A2 |
| 1 | *182837968* | 183096385 | 258417 | 4 | PYCR2,LEFTY1,TMEM63A,CNIH4 |
| 2 | *25207840* | 25354300 | 146460 | 4 | DPP7,UAP1L1,ENTPD2,C8G |
| 2 | *103921214* | 103964818 | 43604 | 3 | CD59B,CD59A,A930018P22RIK |
| 2 | *152590596* | 153048274 | 457678 | 6 | COX4I2,FKHL18,PDRG1,BC020535,TM9SF4,TSPYL3 |
| 3 | *35794225* | 35988326 | 194101 | 3 | LOC100046841,MCCC1,ACAD9 |
| 3 | *87719934* | 87861011 | 141077 | 3 | HDGF,NES,APOA1BP, |
| 4 | *41585069* | 41791875 | 206806 | 3 | DNAIC1,CCL27,CCL19, |
| 4 | *62160379* | 62363247 | 202868 | 3 | HDHD3,ALAD,RGS3, |
| 4 | *129193683* | 129525601 | 331918 | 4 | LOC100046039,X2510006D16RIK,CCDC28B,PTP4A2 |
| 4 | *132086525* | 132456695 | 370170 | 4 | ATPIF1,EYA3,XKR8,BC008163 |
| 4 | *132754041* | 133147532 | 393491 | 7 | WASF2,MAP3K6SLC9A1,4732473B16RIK,<br>2300002D11RIK,NUDCGPN2, |
| 4 | *133912418* | 134093953 | 181535 | 4 | EXTL1,STMN1,2410166I05RIK,SEPN1 |
| 4 | *155207073* | 155364772 | 157699 | 6 | AURKAIP1,DVL1,ACAP3,LOC545056,FAM132A,B3GALT6, |
| 5 | *147765528* | 147890516 | 124988 | 3 | GTF3A,MTIF3,POLR1D |
| 6 | *126875000* | 127079686 | 204686 | 3 | RAD51AP1,X9630033F20RIK,CCND2 |
| 6 | *145123111* | 145168681 | 45570 | 4 | LRMP,CASC1,LYRM5,KRAS |
| 7 | *19441998* | 19831693 | 389695 | 4 | MILL2,IRF2BP1,DMWD,D630048P19RIK |
| 7 | *30975506* | 31426230 | 450724 | 5 | CAPNS1,TBCB,TYROBP,HSPB6,RBM42 |
| 7 | *87461806* | 87505819 | 44013 | 4 | RCCD1,LOC675567,UNC45A,MAN2A2 |
| 8 | *32207411* | 32371718 | 164307 | 3 | DUSP26,RBM13,FUT10 |
| 8 | *87194527* | 87621384 | 426857 | 11 | NACC1,TRMT1,NFIX,FARSA,<br>GCDH,PRDX2,HOOK2,ASNA1,<br>DHPS,1500041N16RIK,MAN2B1 |
| 8 | *124990160* | 125154233 | 164073 | 3 | RNF166,TRAPPC2L,CBFA2T3H |
| 9 | *34933919* | 35024383 | 90464 | 3 | DCPS,FOXRED1,SRPR |
| 9 | *44199978* | 44212071 | 12093 | 3 | HYOU1,SLC37A4,TRAPPC4 |
| 9 | *44806893* | 44962140 | 155247 | 3 | CD3E,AMICA1,SCN4B |
| 9 | *106097518* | 106372827 | 275309 | 7 | PPM1M,TWF2,DUSP7,RPL29,ACY1,ABHD14A,PARP3 |
| 11 | *58804677* | 59235079 | 430402 | 4 | TRIM11,GJC2,MRPL55,1110031B06RIK |
| 11 | *59589470* | 59689992 | 100522 | 3 | MPRIP,COPS3,NT5M |
| 11 | *82619501* | 82756537 | 137036 | 3 | RFFL,LOC100044934,UNC45B |
| 11 | *94830377* | 95136060 | 305683 | 5 | SGCA,SAMD14,PDK2,ITGA3,MYST2 |
| 11 | *96799199* | 96910230 | 111031 | 3 | PNPO,SCRN2,MRPL10 |
| 11 | *114844007* | 115044431 | 200424 | 3 | 4732429D16RIK,SLC9A3R1,LOC100044159 |
| 13 | *64234749* | 64540754 | 306005 | 6 | ZFP367,HABP4,CDC14B,1110018J18RIK,<br>CTSL,CCRK |
| 13 | *113657734* | 114008245 | 350511 | 5 | PPAP2A,SKIV2L2,GPX8,2310016C16RIK,<br>ESM1 |
| 15 | *76545807* | 76682760 | 136953 | 3 | LRRC24,C030006K11RIK,ZFP251 |
| 15 | *85727285* | 85967913 | 240628 | 3 | TRMU,CELSR1,GRAMD4 |
| 16 | *20651876* | 20742404 | 90528 | 3 | PSMD2,EIF4G1,CHRD |
| 17 | *24645834* | 25029013 | 383179 | 5 | TRAF7,GFER,NDUFB10,FAHD1,SPSB3 |
| 17 | *34056177* | 34163052 | 106875 | 3 | ZBTB22,WDR46,H2.KE6 |
| 18 | *37847239* | 37909257 | 62018 | 3 | PCDHGA4,PCDHGB2,PCDHGA10 |

**Table S10 Descriptive information concerning “control clusters”**

**Table S11 Descriptive information concerning “random boxes”**

**Tables S10 and S11 are available for download at http://www.g3journal.org/lookup/suppl/doi:10.1534/g3.113.005546/-/DC1.**