



#### Supplementary Figure 4.

a. Enrichment in interactions between pairs of loci bound by CTCF and belonging to the same domain or across the boundary with the neighboring domain, as a function of reciprocal insulation in ESCs. Pairs of CTCF sites occur at convergent, divergent or parallel CTCF DNA binding motifs are plotted separately.

b. Enrichment in interactions between pairs of loci belonging to the same domain or across the boundary with the neighboring domain, as a function of reciprocal insulation in NPCs. Colors refer to random loci within active TADs (blue), enhancer-promoter pairs (red), random loci with the same distance distribution as enhancer-promoter pairs (green) and CTCF-containing loci (black). Median enrichments over all pairs of considered loci are plotted.

c. Same as in panel b, for CH12 cells.

d. Scaling of contact probabilities as a function of genomic distance. Genome-wide average Hi-C contacts are plotted for the three cell types analyzed in this work. Zeroes were not included in the averages to highlight the regime where random sequencing noise sets in at large genomic distances. Black lines indicate the cutoff distance used in the analysis for Figure 4 (2 Mb for ESCs and NPCs, 1 Mb for CH12).