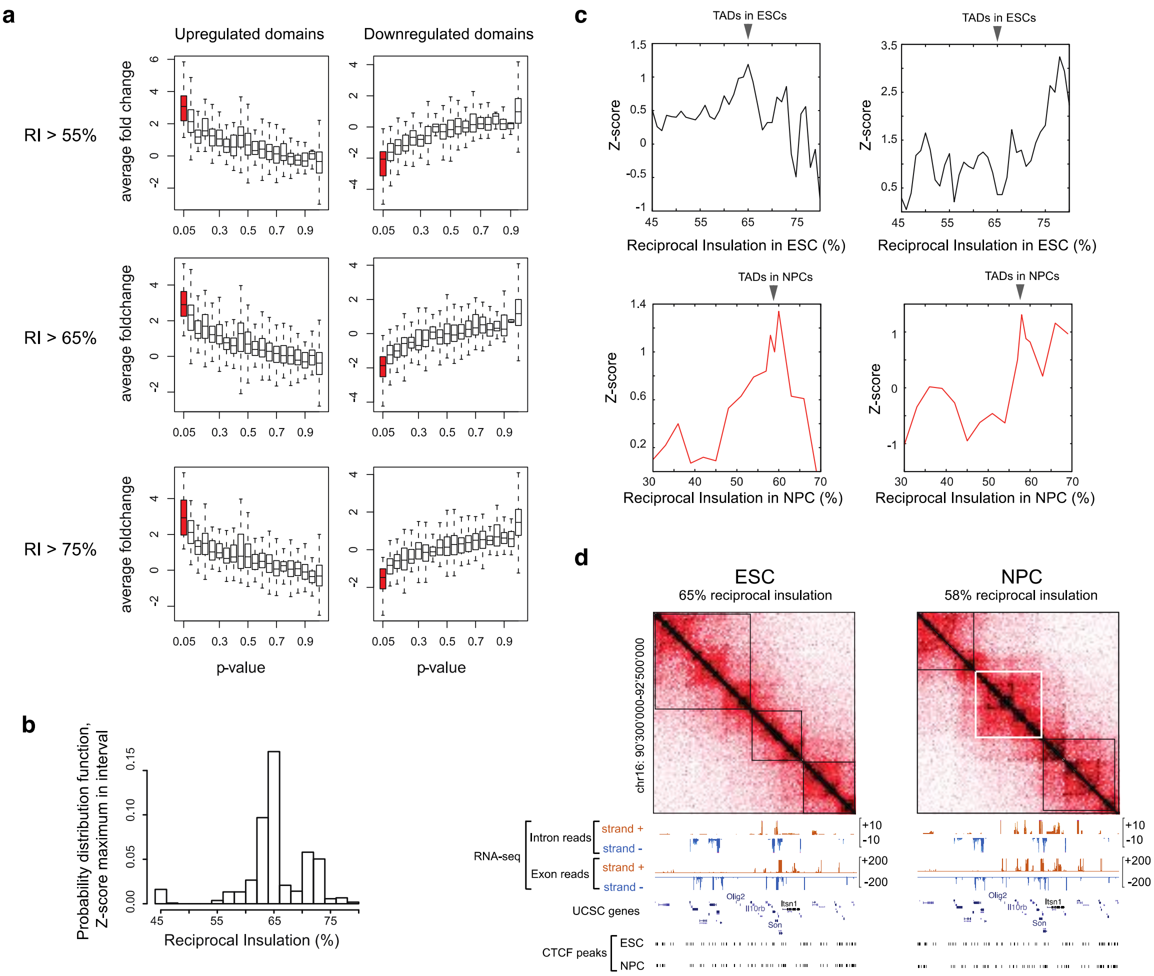

Supplemental Figure S3.

a. At all insulation levels, the subset of domains that we detected to be up- (left panels) or downregulated (right panels) at the p<=0.05 level (red rectangle) are those where the mean fold change of expression level within the domain is maximal. Shown for 3 RI value (55% top, 65% center, 75% bottom).

b. Density histogram showing the RI value where the maximum Z-score for coordinately down-regulated genes occurs when randomly reshuffling the fold-changes of 10% of genes. For 66% of the partially reshuffled genomes, the Z-score maximum was found to be located within a 4% interval around 65% reciprocal insulation (63%-66%).

c. Analysis of transcriptional co-regulation with a correction applied to genes on chrX to account for the inactive X in NPCs (see Supplemental Methods). Maximal transcriptional co-regulation consistently occurs at the scale of TADs.

d. Example of domains that were *de novo* created during differentiation and thus detected using domains based on Hi-C data in NPCs.