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Title: Evolutionary dynamics of CTCF binding sites in mammalian genomes

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Effect of CTCF binding sites on gene expression Obtaining CTCF binding sites in human CTCF and the three dimensional genome

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Abstract:

CTCF is a ubiquitously expressed protein, which over the years, has been associated with several functions, initially that of a transcriptional repressor and activator. Subsequently, it was identified as an insulator protein with enhancer-blocking functions. Research on the three-dimensional genome revealed its involvement in genome organization, mainly through the formation of chromatin loops, leading to long-range communication between genes and regulatory elements and also blocking interactions, aligning with its role as an insulator. Evidence for these functions of CTCF has come from Hi-C maps and experiments showing the enrichment of TAD boundaries with CTCF binding sites. Studies have shown changes in gene expression at specific loci as a result of changes in chromatin loops and disruption of TAD structure. However, the mechanism and extent of this effect is not understood. In this thesis, we study the evolutionary dynamics of CTCF binding, focussing on the CTCF binding sites in human that are lost in other species. We hypothesize that evolutionary differences in CTCF binding could reflect in changes in gene expression and lineage or species specific phenotypes We also do a more detailed analysis of the sites that are lost in mouse. We look at the effect of the presence of CTCF binding sites on the expression of the gene nearest to it. While small changes are seen in gene expression across developmental stages, differences in chromatin states of these sites do not show enough difference to validate these changes.

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