

CTCF and cohesin regulate chromatin loop stability with distinct dynamics.

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Authors: Anders S Hansen, Iryna Pustova, Claudia Cattoglio, Robert Tjian, Xavier Darzacq

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Public Summary:

Folding of mammalian genomes into spatial domains is critical for gene regulation. The insulator protein CTCF and cohesin control domain location by folding domains into loop structures, which are widely thought to be stable. Combining genomic and biochemical approaches we show that CTCF and cohesin co-occupy the same sites and physically interact as a biochemically stable complex. However, using single-molecule imaging we find that CTCF binds chromatin much more dynamically than cohesin (~1-2 min vs. ~22 min residence time). Moreover, after unbinding, CTCF quickly rebinds another cognate site unlike cohesin for which the search process is long (~1 min vs. ~33 min). Thus, CTCF and cohesin form a rapidly exchanging 'dynamic complex' rather than a typical stable complex. Since CTCF and cohesin are required for loop domain formation, our results suggest that chromatin loops are dynamic and frequently break and reform throughout the cell cycle.

Scientific Abstract:

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