

Guided nuclear exploration increases CTCF target search efficiency.

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Public Summary:

The enormous size of mammalian genomes means that for a DNA-binding protein the number of nonspecific, off-target sites vastly exceeds the number of specific, cognate sites. How mammalian DNA-binding proteins overcome this challenge to efficiently locate their target sites is not known. Here, through live-cell single-molecule tracking, we show that CCCTC-binding factor, CTCF, is repeatedly trapped in small zones that likely correspond to CTCF clusters, in a manner that is largely dependent on an internal RNA-binding region (RBRI). We develop a new theoretical model called anisotropic diffusion through transient trapping in zones to explain CTCF dynamics. Functionally, transient RBRI-mediated trapping increases the efficiency of CTCF target search by ~2.5-fold. Overall, our results suggest a 'guided' mechanism where CTCF clusters concentrate diffusing CTCF proteins near cognate binding sites, thus increasing the local ON-rate. We suggest that local guiding may allow DNA-binding proteins to more efficiently locate their target sites.

Scientific Abstract:

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