3D imaging of Sox2 enhancer clusters in embryonic stem cells

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2015/01/23

Abstract:

Combinatorial *cis*-regulatory networks encoded in animal genomes represent the foundational gene expression mechanism for directing cell-fate commitment and maintenance of cell identity by transcription factors (TFs). However, the 3D spatial organization of *cis*-elements and how such sub-nuclear structures influence TF activity remain poorly understood. In this study, they combine lattice light-sheet imaging [1], single-molecule tracking [2], numerical simulations, and ChIP-exo mapping to localize and functionally probe Sox2 enhancer-organization in living embryonic stem cells [3]. Sox2 enhancers form 3D-clusters that are segregated from heterochromatin but overlap with a subset of Pol II enriched regions. Sox2 searches for specific binding targets via a 3D-diffusion dominant mode when shuttling long-distances between clusters while chromatin-bound states predominate within individual clusters. Thus, enhancer clustering may reduce global search efficiency but enables rapid local fine-tuning of TF search parameters. Our results suggest an integrated model linking *cis*-element 3D spatial distribution to local-versus-global target search modalities essential for regulating eukaryotic gene transcription.

References:

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3. Liu Z, Legant WR, Chen BC, Li L, Grimm JB, Lavis LD, Betzig E, Tjian R., 3D imaging of Sox2 enhancer clusters in embryonic stem cells. *Elife*, 2014, doi: 10.7554/eLife.04236.