Exploring long-range contacts between topological domains (TADs) in ES cells and neurons

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Abstract

Over the past decades the importance of specific chromatin folding in gene regulation has become evident and understanding chromosome organization is now a major focus of research. The development of molecular methods for chromosome conformation capture (3C), and associated approaches, allowed to identify important features of chromatin organization, namely the existence of topologically associated domains (or TADs). However, 3C-based methods provide only information about the average chromatin folding observed across populations of cells, whereas imaging by FISH can provide insights about the frequency and distance of chromatin contacts at the single cell level. Recent work from our lab and collaborators identifies long-range contacts between distant TADs that are cell type specific. Here, we investigate the spatial contacts of TADs that encompass important developmental loci and are separated by large genomic regions (¿ 1Mbp), in mouse ES cells and differentiated neurons with dopaminergic phenotype. We combine high-resolution confocal microscopy and FISH on ultrathin cryosections (180 nm) to measure distances between TADs and their radial positions within the nucleus on a single cell level, allowing us to measure both local and global features of 3D rearrangement during terminal differentiation.

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