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Spatiotemporal Dynamics of 3D Genome Architecture and Gene Expression during Lactogenic Differentiation of Murine Mammary Epithelial Cells

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Abstract

Orchestration of differential gene expression program during cellular development and differentiation is tightly coordinated in each and every cell type. Cell-type specific gene expression is primarily regulated by the spatial arrangement of genome within the 3-dimensional space of the cell nucleus. Recent evidences suggest that interphase chromosome territories are non-randomly organized in a cell-type specific manner and their neighbourhood are interlinked with cell-type specific gene expression patterns. In this study we made an attempt to study chromosomal dynamics and gene expression in the context of mammary epithelial cells lactogenic differentiation under the influence of lactogenic hormones. We derived genome-wide chromosome conformation capture HiC based chromosome interactions and gene expression by RNA-seq in undifferentiated murine mammary epithelial cells and hydrocortisone and Prolactin hormone treated cells. We found that chromosome territories are non-randomly organized in HC11 cells undifferentiated as well as differentiated cells-types. There seems to be increased and decreased interactions within and in between chromosomes upon differentiation. We derived A & B compartments within each chromosome and their relationship with gene expression. We also studied topologically associated domain reorganization during differentiation which indicates that majority of the TADs are highly conserved and minor or less TADs are highly reorganized during signalling. From these studies, we concluded that differentiation signals promote subtle shift of chromosomal territories neighbourhood but promotes extensive reorganization within or between chromosomes.

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