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Review

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François Le Dily, Miguel Beato

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TADs as modular and dynamic units for gene regulation by hormones

François Le Dily^{1,2} and Miguel Beato^{1,2,*}.

¹ Gene Regulation, Stem Cells and Cancer Program, Centre de Regulació Genòmica [CRG], Barcelona, Spain ; ² Universitat Pompeu Fabra [UPF], Barcelona, Spain.

*: Correspondence: Miguel Beato

E-mail: miguel.beato@crg.es

Centre de Regulació Genòmica (CRG)

Dr. Aiguader 88,

E-08003, Barcelona, Spain.

Tel +34 93 316 0119

Fax +34 93 316 0099

Abstract:

During cell differentiation epigenetic processes permit the establishment of a cell type specific transcriptome by limiting the fraction of the genome that will be expressed. Based upon steady-state requirements and transcription factor expression, differentiated cells respond transiently to external cues by modulating the expression levels of subsets of genes. Increasing evidence demonstrates that the genome is organized non-randomly in a hierarchy of structures within the nuclear space, where chromosome territories are segmented into Topologically Associating Domains (TADs) and sub-domains. It remains poorly understood how three-dimensional organization of the genome participates in the acquisition of a cell-specific program of gene expression. Furthermore, it is unknown whether this spatial framework influences the dynamic changes of gene expression that accompany alterations in the cell environment. In this review, we will discuss the impact of genome topology on the response of breast cancer cells to steroid hormones. We will cover steroid nuclear receptor mechanisms of action and discuss how topological organization of the genome, including segmentation into TADs, acts as a combinatorial platform to integrate signals whilst ultimately ensuring coordinate regulation of gene expression.

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