Nuclear architecture and gene expression

Romain Solinhac, Florence Mompart, Yvette lahbib-Mansais, Hervé Acloque, Eddie Iannuccelli, David Robelin and Martine Yerle-Bouissou
INRA, UMR444, Laboratoire de Génétique Cellulaire, 31326 Castanet Tolosan, France

Numerous studies have supported the concept of a three-dimensional remodelling of chromatin as determinant for genomic regulation, pinpointing the major role of 3D nuclear organisation on gene regulation (reviewed in Lanctôt et al. 2007; Misteli 2007; Pai and Engelke 2010). In this context, we focussed our interest on several models to study the role of nuclear architecture on gene regulation.

One of these models concerns an important biological process, the development of an immune response, involving an extensive regulation of cells that are central to the inflammatory process. The first actors are phagocytic cells (macrophages and neutrophils) which are essential for building and modulating the innate response due to their ability to destroy infectious agents. While some data are available on the 3D organisation of the genome in lymphocytes, little information is available for phagocytes which play a key role in this process. In this context, we chose porcine monocyte-derived macrophages as model and lypopolysaccharide (LPS)/interferon gamma (IFNγ) activation to study the relation between nuclear position and gene activity status. Using a transcriptomic approach, we first determined which genes are differentially expressed when the macrophages are activated. We then selected 4 up- and 4 down-regulated genes and one non-expressed gene to investigate the relationship between nuclear positions and expression levels. The spatial arrangements of differentially expressed genes were then compared in control and activated macrophages using three-dimensional fluorescence in situ hybridization (3D-FISH), confocal microscopy and three-dimensional image analyses (Iannuccelli et al., 2010). In order to estimate whether the type of repositioning observed is gene-specific and/or cell-specific, similar analyses were also performed on neutrophils subjected to LPS stimulation as another type of immune cells and finally on fibroblasts not related to immune response.

References:

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