Major reorganization of chromosome conformation during late muscle development

Maria Marti-Marimon¹, Nathalie Vialaneix², Hervé Acloque³, Martine Bouissou-Matet⁴, Diane Esquerré⁴, Sarah Djebali⁴, Yvette Lahbib-Mansais⁴, David Robelin⁴, Matthias Zytnicki², Sylvain Foissac⁴.

¹CNAG-CRG, Centre for Genomic Regulation (CRG), Barcelona Institute of Science and Technology (BIST), Dr. Aiguader 88, 08003 Barcelona, Spain. ²MIAT, Université de Toulouse, INRA, Auzeville-Tolosane, 31320, France.

³GABI, AgroParisTech, INRA, Université Paris Saclay, F-78350 Jouy-en-Josas, France. ⁴GenPhySE, Université de Toulouse, INRA, ENVT, Auzeville-Tolosane, 31320, France.

The three dimensional organization of the genome plays a major role in the regulation of gene expression. Chromosome territories, compartments, topological domains, and loops, are the main features of the genome topology. Most of these features are quite stable ensuring a suitable niche for maintaining either transcriptional activation or repression. However, the structural plasticity of the chromatin also permits conformational changes that may lead to alterations in the transcriptional activity. These dynamic changes are particularly remarkable during gene expression reprograming occurring in early development (*i.e.* zygote genome activation, transition from pluripotent to lineage-committed cells, and cell differentiation). However, these dynamic events remain poorly understood, especially those concerning late development and tissue maturity processes. Our study offers new insights into the 3D genome organization dynamics at late gestation in mammals. More precisely, we addressed the global genome organization of porcine muscle nuclei at 90 and 110 days of gestation by performing in situ Hi-C experiments. This stage of gestation is a relevant period for porcine muscle development and maturity, as already shown in a previous transcriptome study. We obtained evidence of important topological changes in the 3D genome structure at this period that are associated to variations in gene expression. This dynamic changes correspond to a global fragmentation of the genome, switches of compartment type, differential chromatin interactions and dynamics of the telomeric regions. Overall, our study shows that extensive conformational changes occur in late development even though the gene expression program does not change as much as during early development.