ID de Contribution: **16** Type: **Non spécifié**

Poster: Role of the Nuclear Periphery in Epithelial to Mesenchymal Transition

The positioning of genomic loci on the center-to-periphery nuclear radius, called radial nuclear positioning, is neither fixed nor random. In particular, association of genomic loci with the nuclear lamina is usually associated with cell-type specific gene repression, while association with the nuclear pores has been proposed to facilitate super-enhancers activation of cell-type specific genes. In addition to these direct interactions with chromatin, the nuclear pores are also the only gateways between the nucleus and the cytosol, and have been shown to regulate the nuclear translocation of transcription factors upon specific signals, such as translocation of the NF-kB transcription factor upon pro-inflammatory signals. Taken together, these results have therefore positioned the nuclear periphery as a major player in the regulation of gene expression. Whether and how this nuclear periphery-mediated regulation of gene expression might be hijacked in cancer is however poorly understood.

Here, we aim to study the role of the nuclear periphery compartments in gene regulation during the epithelial-to-mesenchymal transition (EMT), a crucial process in metastasis formation. Using a combination of multi-omics profiling, we mapped genome-wide changes in chromatin accessibility and histone modifications at different time points in a cell line model of EMT. Our preliminary data reveal differential expression of putative enhancers, including mesenchymal-specific regulatory elements that acquire active chromatin marks, while epithelial-specific enhancers are progressively silenced. We now aim to map nuclear periphery associations (with the nuclear lamina or the nuclear pores) during EMT and to correlate putative genomic loci positioning changes with regulation of their expression. We will then further perform forced repositioning of genomic loci assays to directly test the influence of genomic association with the lamina or the nuclear pores on the regulation of EMT associated genes.

Several transcription factors have been suggested to be translocated from the cytosol to the nucleus during the EMT. Whether and how this translocation is orchestrated is however not known. Notably, while the expression of most of the nuclear pore components remain unchanged during the EMT, we identified a striking downregulation of NUP210—a transmembrane nuclear pore protein—in mesenchymal cells, suggesting its potential involvement in the nuclear transport of EMT-related transcription factors. We therefore aim to determine whether the loss of NUP210 during the EMT might regulate nuclear import of EMT-specific transcription factors.

Taken together, our project will therefore determine the role of the nuclear periphery in the EMT, from the regulation of gene positioning to the control of transcription factors cellular localization.

Author: LAABAS, Nouhaila (CNRS-IGH)

Co-auteurs: OLDFIELD, Andrew (CNRS-IGH); BOUMENDIL, Charlène (CNRS-IGH)

Orateur: LAABAS, Nouhaila (CNRS-IGH)