Deciphering the role of DNA compartmentalization in human diseases

Chromatin within the cell nucleus has a complex structure that is fundamental for genome function (1). The characteristic of the cells, their plasticity and the ability to respond to the environmental stimuli depend on the chromatin shape and remodelling properties. In recent years, what is emerging is that, besides the plasticity of the chromatin fundamental for fine-regulated process, the nuclear architecture can also influence important cellular processes. Alterations in chromatin and/or nuclear structures are associated with developmental defects, genetic diseases and cancer, while its proper conformation is a hallmark of healthy cells. My group is devoted in understanding how the genome folding occur in the nuclear space finding the right orientation and nuclear position and how this conformation is then maintained or regulated in dynamic physiological processes in health and in disease. We started studying epigenetic factors known to play a key role in genome folding and function, the Polycomb group (PcG) of proteins. We described for the first time a functional and evolutionary conserved crosstalk between the nuclear Lamin A/C and the PcG proteins (2, 3); this being required for the maintenance of the PcG repressive functions. In two recent works, we show how mutation of Lamin A can generate a dysfunctional Polycomb program leading to a defect in cell identity maintenance in laminopathies, human disorders caused by mutations in Lamin A/C gene (4, 5). We are now committed in understanding the role of PcG/LaminA interplay in aging and cancer. In parallel we developed a new high-throughput sequencing technique, the Sequential Analysis of MacroMolecule accessibilitY (SAMMY-seq) to study different levels of chromatin solubility (Nat Comm, in press). This technology, applied in several primary tissues and cell types, will be instrumental to investigate the role of chromatin conformation in pathology insurgence and/or progression

References:

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