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The role of histone acetylation in sub-megabase chromatin folding

Genome 3D organization is highly complex, made of several layers of organization from nucleosome to chromosome territory. At the Megabase scale, the genome is partitioned into Topologically Associating Domains (TADs), that may define functional genomic units. TADs are mostly revealed by cell population-based assays such Hi-C and their organization is defined by the extrusion action of cohesin complexes delimited by CTCF at TAD borders.

To better understand this level of genome organization, we addressed TAD structure at the single cell level using a combination of FISH with Oligopaint and Structured Illumination Microscopy (3D-SIM). Super-resolution microscopy revealed the heterogeneous properties of TADs in mammals as well as the presence of subdomains that we dubbed Chromatin NanoDomains or CNDs. Their formation is independent of Cohesin or CTCF function but appears to depend on the level of histone acetylation. Moreover, their genomic size (in the range of 100-150 kb) is compatible with Enhancer-Promoter communication. Using a combination of genomics approaches and super-resolution microscopy, we are trying to decipher the relationship between acetylation, chromatin folding and genome function, as well as the role of specific histone acetyl transferase (HAT) complexes.

Auteur principal: BANTIGNIES, Frédéric (CNRS)

Co-auteurs: CAVALLI, Giacomo (CNRS); REBOUL, Henri (LUPM UMR 5299)

Orateur: BANTIGNIES, Frédéric (CNRS)

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