HIC SEQ

MAIN APPLICATIONS

EASI-Genomics facilities perform high-throughput chromosome conformation capture approaches such as HiC to analyze spatial genome organization and map higher-order chromosome folding and topological associated domains (TADs) (see figure 1). Analysis of spatial chromatin organization highlights regulatory networks governing transcriptional programs which could have a critical role in physiological and pathological conditions. We also use HiC data at low resolution to help analyzing structural variation (Dixon et *al*., Nat. genet. 2018)

METHODOLOGICAL AND SCIENTIFIC BACKGROUND:

In HIC methods, cells are cross-linked with formaldehyde to link DNA regions covalently that are in close spatial proximity in nucleus. Next, DNA is cleaved by restriction digestion and DNA ends are filled in with biotinylated nucleotides. DNA is then ligated to form hybrid DNA molecules, each corresponding to an interaction event of a pair of loci. Biotinylated DNA is finally purified by using streptavidin-coated magnetic beads. This step facilitates selective purification of ligation junctions that are then sequenced.

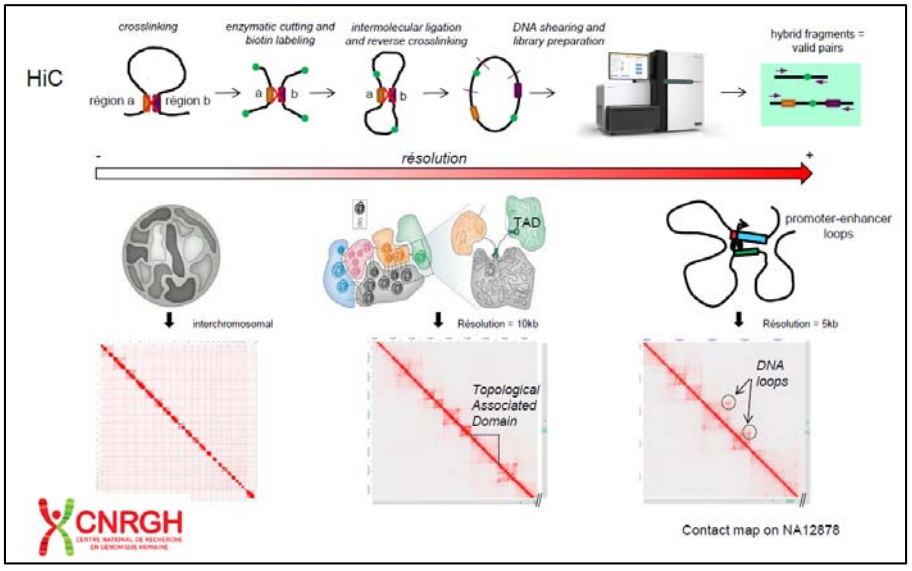

Figure 1: Top: Principle of HIC approach. Bottom: HIC normalized interaction maps of all chromosomes, focused on a chromosome at a resolution of 10 kb, and (c) of a locus on this chromosome at a resolution of 5kb. In (c), region delimited by a black dashed line corresponds to a topological associated domain (TADs).

EXPECTED RESULTS

When performed at high sequencing depth, these approaches can also capture point interactions between localized genomic elements such as promoters and enhancers, which represent functional and biological regulatory interactions. Such information is particularly useful because enhancers are often located far away from their target promoters. EASI-Genomics facilities also offers Hi-ChIP experiments (Hi-C protocol coupled with ChIP immunoprecipitation). This coupling increases the yield of conformation informative reads and therefore improves resolution and specificity while reducing sequencing depth.