Differential chromosome conformations and dynamics in living cells

Kerstin Bystricky*[1]

[1]University of Toulouse – Centre National de la Recherche Scientifique - CNRS – France

Abstract

Variations in the three-dimensional organization of chromosomes guide genome function from gene expression to DNA repair and recombination. Models of chromosome organization obtained from genome-wide chromosome conformation data or biophysical simulations provide important insights into the average behavior. To reveal features from dynamic or transient events that are only visible in a fraction of cells at any given moment, we develop new fluorescent DNA labelling tools and quantitative image analysis methods to analyze chromosome folding and motion. In a first application using three distinct DNA tags, we demonstrated that conformation of yeast chromosome 3 is mating type specific(1). Folding properties could be attributed to a small sequence element and chromatin structural properties dependent on the Asf1 histone chaperone. To determine how 3D folding of chromatin is related to gene regulation, we have also set out to study estrogen inducible loci in human mammary tumour cells. Here, histone variants and chromatin looping are required to remodel the chromatin environment to allow priming of transcription activation(2). Furthermore, we map chromatin folding over several hundreds of kb around estrogen responsive genes using 3D DNA and RNA FISH and confront these data it with 5C data to establish models of domain organization which are cell type specific. These initial studies indicate that rapid estradiol induction of gene expression occurs in the context of pre-existing chromosomal architectures that become stabilized in response to estradiol signalling.Transient decondensation is only visible during mRNA production. In addition, a real time analysis of the dynamic behavior of single gene loci in living human cells using new, non-intrusive methodology for visualizing DNA loci will be presented(3). We discovered that DNA motion of estrogen target genes dramatically decreases within 30min of transcription activation.

1.LassadiI,KamgouéA,GoiffonI,Tanguy−le−GacN,BystrickyK.Differentialchromosomeconformationsashallmarksofcellularidentityrevealedbymathematicalp

*Speaker