Repeated DNA sequences and nuclear architecture : new approaches

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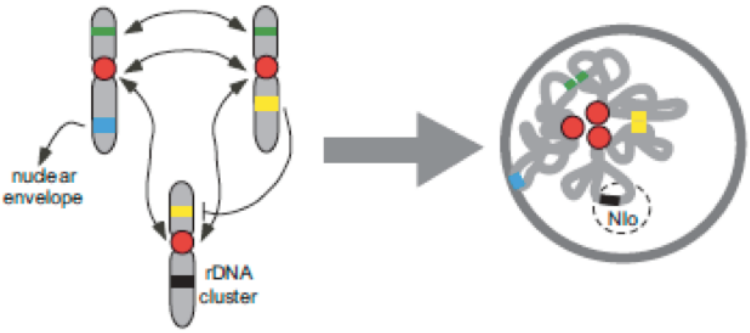
There is now numerous evidence for a role of nuclear architecture on gene regulation during cell differentiation. The mechanisms that are responsible for the highly organized structure adopted by mammalian genomes in the interphase nucleus are not known. One proposed model raises the interesting proposal of a role of repeated DNA sequences located in the centromeric regions of mammalian chromosomes (see figure). In accordance with this model, it is known that in mouse cells, pericentromeric repeats from different chromosomes cluster to form a heterochromatic nuclear structure called the chromocenter[1]. The observation that organization of chromocenters and centromeres vary between different cell types further supports an important role of centromeric repeats in gene regulation.

FISH and immunochemistry represent attractive techniques for studying nuclear organization. We are using high resolution fluorescence microscopy coupled to automated image analysis[2] for studying the nuclear organization and dynamics of centromeric regions in mouse and human cells. These studies benefit from the development of new oligonucleotide probes for the efficient and specific detection of centromeric repeats.

Recent experimental data have provided evidence for a role of non-coding RNAs in heterochromatin assembly[3] and for a transcriptional activity of pericentromeric DNA sequences[4]. The nature of the transcripts often remains elusive due to technical challenges. Our new probes can provide informations regarding transcripts that emanate from repeated DNA sequences. In order to understand the role of repeated DNA sequences in the assembly of chromatin structure and regulation of cellular functions, we are investigating how both the nuclear organization and the transcription pattern of repeated DNA sequences are modified upon various stimuli or addition of various inhibitors.



Self-organization in the genome (from T. Misteli, Proc Natl Acad Sci *106*, 6885-6886). Functional interactions between different chromosomes constrain the chromosome's motion and determine the position of a chromosome relative to all others. Interactions include association of centromeres (red), clustering of coregulated genes (green), association of a regulatory element and its target genes (yellow), interaction of a genome region with the nuclear envelope (blue) or clusters of rDNA (black) genes. Nlo, nucleolus.

References :

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