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Functional structure of the cell nucleus

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The nucleus is delimited by the nuclear envelope and contains a number of compartments. Contrary to the cytoplasm, the intranuclear compartments are not delimited by membranes. After four decades of extensive research, many nuclear domains have been morphologically characterized and the role of some of them in nuclear functions could be identified. The nucleus harbors major nuclear functions such as the replication of cellular genetic material, its repair and transcription. The aim of this special issue is to offer the reader either original observations on different aspects of functional nuclear architecture or overviews of data related to it.

The most investigated and probably also the best understood nuclear compartment is the nucleolus. It is known as the site of ribosomal RNA synthesis and processing, as well as of ribosomal subunit assembly. Its possible involvement in other nuclear functions under special physiological conditions has been suggested in the past and remains presently a subject of further investigations. The nucleoplasmic domains have been morphologically defined, especially by ultrastructural cytochemistry. The nuclear constituent containing genetic material is chromatin. Although DNA plays a major role in its functioning, there is growing evidence about histone modifications and chromatin remodeling as epigenetic factors influencing gene expression. Most chromatin is present in the nucleus in the form of condensed chromatin, which essentially determines chromatin

domains. Ultrastructural investigations allowed one to reveal dispersed chromatin fibers on the periphery of such chromatin domains, which has been named the perichromatin region. It represents sites of the DNA replication and transcription. Interphase chromosome territories are observed as an assembly of chromatin domains, intermingled with interchromatin space or compartment largely devoid of DNA. In addition to transcribing DNA sequences, the perichromatin region contains perichromatin fibrils representing in situ forms of nascent transcripts, and perichromatin granules involved in mRNA storage and/or transport. The interchromatin space compartment contains a number of nuclear domains, such as interchromatin granule clusters (speckles), Cajal (coiled) bodies, PML bodies, interchromatin granule-associated zones or gems. Some of these domains have been shown to be involved in storage of factors playing a role in important nuclear functions.

The nucleus is therefore not only structurally compartmentalized, but many functions take also place in defined domains. Thus, histone methylation, an essential epigenetic mechanism of gene regulation, is confined to certain nuclear regions. In the HeLa cell model, DNA replication, transcription as well as storage of RNA polymerase II also appear to frequently occur in distinct nuclear domains. Interestingly, in vitrified ultrathin sections some nuclear domains are clearly visualized while others are not recognizable compared to resin-embedded and heavy metal-contrasted preparations. Nuclear lamina with its building elements, lamins, plays a vital role in some physiological functions. Moreover, intranuclear lamin complexes appear to be critically involved in regulation of gene expression. Consequently, lamin mutations can give rise to serious pathological states. Intranuclear lectins and carbohydrates also participate in some nuclear functions. Chromatin organization and remodeling is an extremely complex process crucial for DNA packaging, gene expression, silencing, heterochromatinization, or DNA repair. The supra-organization of a native chromatin fiber is still little understood although

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it is of a great importance for the formation of intranuclear order and is connected with replication timing in various nuclear compartments. The nucleolus acquires various morphology reflecting different physiological or pathological conditions. Plant and animal cell nucleoli share some similarities, but also have little understood differences. Besides ribosome subunit production, the nucleolus can be critically involved in the cell cycle regulation, protein sequestering, and snRNP metabolism. In addition, the functional nuclear architecture is related to special states of the cell such as apoptosis or hibernation, and can exhibit unusual nuclear features.

There are many questions concerning the nucleus that need to be answered. The relationship between the architecture and specific nuclear functions is still poorly understood. For example, we do not understand the molecular mechanism of assembly of functional nuclear domains and interphase chromosome territories. A self-organizing mechanism (Mistelli 2001), molecular crowding effects (Hancock 2004), and structural role of polymerases (Oakes et al. 1993; Jackson and Cook 1995) can be considered important for the building and maintenance of nuclear compartments. Obviously, coordination between such mechanisms will be necessary, and their contribution can vary depending on the molecular environment, complexity of the structure and the degree of assembly. Nuclear matrix has been proposed as a supporting structure in the nucleus. While the existence and functional significance of the lamina has been well established (Gruenbaum et al. 2005), we lack clear information about the occurrence of the internal, mostly protein network in the intact nucleus in situ (Pederson 2000; Hancock 2004). We also lack information about regulatory mechanisms at different levels of genome organization and its involvement in functional nuclear architecture (van Driel et al. 2003). As to nuclear RNA metabolism, recent studies indicate that many RNAs synthesized in the nucleus are not coding for proteins even though many of them seem to be polyadenylated (Mattick 2003). The way in which various RNA types migrate throughout the nucleus is not yet elucidated. Whether it is a random movement (Daneholt 2001), channeled diffusion (Kramer et al. 1994) or another yet unidentified transport mode remains unclear.

Future investigations of the functional nuclear architecture will largely depend on the methods used. Live cell microscopy which has become a routine tool is improving, thanks to the introduction of new vital markers, in parallel with perfecting optical system detection and resolution. Together with a subsequent ultrastructural analysis using modern techniques of sample preparation making the specimen closer to its native state, and completed with tomography, this combination represents a powerful approach. We look forward to these developments that promise a multitude of exciting news.

We hope that this special issue will contribute to our knowledge about functional nuclear architecture and will become a valuable source of information.

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