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Nucleus and gene regulation

Editorial overview

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At the close of a 1973 meeting on Chromosome Structure and Function, an observer commented that chromosomes resembled ''a bad day at a macaroni factory'' [1]. But things change. Only a few months later nucleosomes were discovered and within just a few more years it began to be appreciated that the nucleus is organized as functionally distinct domains. Even the regions between the chromosomes started to become interesting. Today, we see the nucleus as among the most dynamic centers of the cell, and the extant parts list has reached mind-numbing levels. Many current descriptions of the molecular events underlying a particular nuclear process require the use of so many protein acronyms per sentence as to hardly leave room for verbs and conjunctions. This is, of course, a good thing for cell biology (if not language).

This issue of *Current Opinion in Cell Biology* presents an array of articles commissioned to cover at least the great majority of key nuclear functions in today's terms, by some of the top authorities. There are, to be sure, variations in the authors' styles and points of emphasis within their general subject, but we are pleased with the overall lively tone and especially the focus on unresolved issues that many of the authors have underscored. We trust readers will find this issue as engaging and informative as we have during our editorial efforts.

As is traditional in works on the nucleus, the present series of articles starts with DNA. The molecular machinery that licenses (even 'pre-licenses') DNA replication in metazoan cells is discussed by DePamphilis and colleagues, with particular emphasis on regulation. The parallel subject of how the DNA repair machinery dynamically congresses at sites of damage is reviewed by Houtsmuller and colleagues, and in the third article in this group Bertuch and Lundblad discuss the mechanisms by which telomeres are protected and maintained. Readers may note a degree of homology among certain aspects of these three processes and their machineries, suggesting that at least some aspects may have descended from common ancestral mechanisms. In the fourth article in this group, Blasco and colleagues discuss telomerase and its regulation, a subject that has come a long way from its initial 'all-or-none' framework.

The presence of actin and myosin in non-muscle cells was discovered 40 years ago but only in the past few years have the existence and functions of actin and myosin in the nucleus come into sharp view. Miralles and Visa summarize the current thinking on how actin might be involved in transcription, and Percipalle and Farrants discuss how a component of the chromatin remodeling machinery interacts with myosin and might couple this process to transcriptional activation.

A major advance in the past five years or so has been the realization of just how pervasively and extensively chromatin is transcriptionally regulated by epigenetic mechanisms that stably mark these sites on a developmental timetable. Bantignies and Cavalli discuss one of the best-studied of these mechanisms, involving the polycomb group proteins. Misteli and colleagues review the tremendous advances that have been made in recent years in understanding the dynamics of nuclear proteins and RNA, consisting of wide-roaming paths combined with rapid shuttling in and out of concentrated sites, often interspersed with glancing visits elsewhere.

However fascinating these foregoing subjects, one cannot talk about the nucleus long before coming to RNA. Barrera and Ren discuss new technologies for studying transcriptional regulation on a genome-wide basis and in the context of chromatin structure. Cole and Scarcelli review the complex process of mRNA export from the nucleus, with particular emphasis on a relatively new player. How the interphase chromosomes are arranged with respect to one another and in relation to their transcriptional activity is next addressed in exhaustive detail by Cremer and colleagues. The roles of nucleoplasmic structures in gene expression has been a fertile area in the past decade and Matera and Shpargel review the Cajal body, which has seen a complete renaissance of interest since its discovery a century ago. Raska and coauthors comprehensively review the nucleolus (the first intra-nuclear structure to be discovered) with emphasis on its growing proteomics tally and functions beyond ribosome synthesis.

As transcripts prepare to leave their first home, and as nucleocytoplasmic traffic bustles, we come finally to the nuclear lamins and nuclear pores. Gruenbaum and coauthors update us on the growing evidence for roles of lamin protein mutations in aging and disease, now bringing more attention to the lamina than ever before. Lim and Fahrenkrog review the structural details of the nuclear pore complex afforded by new methods that reveal clues to the cargo translocation mechanism.

Given the laudable efforts of the authors, we hope this issue of *Current Opinion in Cell Biology* will not be out of date for quite some time. But these aspects of the nucleus are moving very fast now and if the need arises to review the subject again in only two years, we suspect all of us in this field will not be displeased.

Reference

1. Swift H: **Chromosome Structure and Function**. *Cold Spring Harbor Symp Quant Biol* 1974, **38**:963.