Published in final edited form as:

Curr Opin Cell Biol. 2016 June ; 40: iv–v. doi:10.1016/j.ceb.2016.05.007.

The cell nucleus: Plastic, elastic and fantastic

Orna Cohen-Fix and

The Laboratory of Cellular and Molecular Biology, National Institute of Diabetes and Digestive and Kidney Diseases, The National Institutes of Health, Bethesda, MD 20892, USA

Ulrike Kutay

Institute of Biochemistry, Department of Biology, ETH Zurich, 8093 Zurich, Switzerland

Within the Current Opinion in Cell Biology series, the nucleus has the distinct honor of being the only organelle to which an entire issue is dedicated. But with this privilege comes great responsibility; research in this field must advance rapidly to justify a new collection of reviews every year. Luckily, this is not a problem: technical advances, such as those that allow high-resolution imaging and measurements of chromosome organization (e.g. Hi-C), have led in recent years to an explosion of studies that uncovered fascinating new aspects of nuclear structure and function. In this issue on the Cell Nucleus we aimed to highlight the dynamic nature of the nucleus over a wide range of time scales: throughout the course of evolution, during the development and aging of an organism, as the cell traverses a single cell cycle, and even in very short time frames, such as during the response to mechanical pressure.

Currently, most studies on nuclear structure and function focus on a very small fraction of species, perhaps because of their perceived medical relevance or their proven suitability as model systems. Yet the diversity in nuclear shape, size and even number throughout all living organisms is immense. The usefulness of understanding processes in diverse life forms is undeniable; look no further than the impact that CRISPR-CAS9, discovered as part of a bacterial immune system, is having on today's research and therapeutics. For this reason we included reviews on the properties of the bacterial nucleoid (Dame and Tark-Dame), the diverse nature of nuclei in lower eukaryotes (Iwamoto *et al.*) and the broad array of nuclear shape and size in plants (Meier). These reviews illustrate the changes nuclei underwent throughout evolution. Surely, there are lessons to be learned from these and other diverse systems.

While textbooks often illustrate the nucleus (and, for that matter, all organelles) as a static structure suspended in the cell's milieu, the nucleus is highly responsive to external and cell internal forces. Take, for example, the deformation the nucleus must undergo during cell migration through tight spaces, reviewed by McGregor *et al.* Moreover, the nucleus is not impervious to mechanical forces experienced by the cell; rather, structures within the nuclear envelope, such as KASH and SUN domain proteins, help transduce mechanical signals that can ultimately affect nuclear processes such as gene expression (reviewed by Graham and Burridge). Thus, the nucleus is responsive to the environment outside it, and this affects processes that occur within it.

Components of the nucleus are also dynamic, and none more so than the nuclear envelope itself. During mitosis, the nuclear envelope disassembles to various degrees, depending on cell type. Vietri *et al.* describe interesting new findings on how the nuclear envelope reassembles, and in particular how the ESCRT complex remodels the membrane to seal the final gaps as the nuclear envelope reforms. The notion that the nucleus, once reformed, is merely a sac of randomly organized DNA has long been dispelled; two reviews (Rowley and Corces; Solovei *et al.*) summarize the vast literature describing the layers of organization of chromatin within the nucleus. While methodologies such as Hi-C take snapshots of chromosome conformation in a given cell at a given time, it has become clear that this organization is not static. Rather, chromosome organization can change during aging and development, thereby affecting gene expression and, in dividing cells replication timing (Chandra and Kirschner; Solovei *et al.*; Rivera-Mulia and Gilbert). Underlying this dynamic behavior is the existence of distinct nuclear environments that differ in their permissibility to certain processes (Ebrahimi and Promisel Cooper). By moving between different environments within the nucleus, such as between the nuclear interior versus the periphery, or into an environment that favors the expression of certain genes, such as histone locus bodies (reviewed by Romero and Schumperli), chromatin domains can be subjected to distinct types of regulation.

Key to the dynamic process of chromosome organization within the nucleus are interactions of the chromatin with components of the nuclear pore complexes (reviewed by Ptak and Wozniak) and the nuclear lamina (Ebrahimi and Promisel Cooper; Zheng). Chromosome organization changes even in the course of a single cell cycle: an obvious example is chromosome condensation and decondensation during mitosis, the mechanistic details of which are just starting to emerge (reviewed by Antonin and Neumann), but also during processes such as DNA repair (Ptak and Wozniak; Wild and Matos) and DNA damage tolerance (Branzei and Psakhye). Moreover, chromatin can be dynamic even within a single nuclear subdomain. A beautiful illustration of this is the behavior of telomeres, whose movement along the nuclear membrane is critical for the proper execution of meiosis (reviewed by Ebrahimi and Promisel Cooper).

This brings us to the organismal importance of nuclear organization as underscored by the ever-increasing number of diseases that are linked to abnormalities in nuclear components. It has long been known that mutations in certain nuclear lamina components are linked to cellular aging (e.g. progeria). Here, Yixian Zheng and colleagues present a new view of how defects in Lamin B can affect organismal aging by triggering systemic inflammation. Another component of the nuclear envelope, TorsinA, has also been linked to disease, although the exact function of Torsins in the nuclear envelope is yet unknown (reviewed by Laudermitch and Schlieker). The fact that the genome is not static bears with it considerable risks, especially in dividing cells during the processes of DNA replication and chromosome segregation. For example, replication stress can lead to the formation of common fragile sites that may underlie cellular transformation (reviewed by Sarni and Kerem). Likewise, errors in chromosome segregation might lead to aneuploidy, another hallmark of cancer cells (reviewed by Rutledge and Cimini), or to chromothripsis, which can wreak havoc on large chromosomal regions (reviewed by Storchová and Kloosterman). To avoid such defects and errors the cell has well-established repair mechanisms and checkpoint pathways that correct

mistakes in DNA and ensure accurate chromosome segregation. But not only DNA metabolism is under surveillance, also nuclear protein quality control mechanisms exist (reviewed by Jones and Gardner) that dispose of misfolded nuclear proteins. However, when these processes are defective, or perhaps overwhelmed, damage to nuclear components can accumulate. These too, can affect chromosome organization. For example, acute stress due to oncogene activation, or chronic stress due to aging, also result in changes in chromosome organization (Chandra and Kirschner). Whether these changes are a consequence of stress or contribute to the cellular response that deals with these stressors is an important yet unresolved question. What is certain, however, is that the nucleus is a dynamic structure, both in health and disease.

Biographies

Dr Orna Cohen-Fix received her PhD from the Weizmann Institute in Rehovot, Israel. She is currently a Senior Investigator at the NIH, where her lab studies the regulation of nuclear morphology using budding yeast and *C. elegans*. Ultimately, she would like to understand how nuclear morphology affects nuclear function.

Ulrike Kutay studied Biochemistry in Berlin and obtained her PhD on membrane integration of tail-anchored proteins. As a postdoc in Heidelberg, Ulrike investigated nucleo-cytoplasmic transport pathways. Currently, she is Professor of Biochemistry at ETH Zurich, where her lab studies nuclear structure, function and dynamics with special emphasis on nuclear envelope breakdown and ribosome synthesis in human cells.