Nuclear biology: making sense of complex processes

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The session on Nuclear Organization and Control of Gene Expression brought together researchers who are interested in a wide range of questions related to nuclear cell biology and who use a variety of experimental approaches to tackle the biological questions at hand.

Recruiting factors to active genes

Nuclear factors involved in transcription and RNA processing are dynamically roaming the nucleus. Yaron Shav-Tal (Bar-Ilan University, Israel) presented measurements of splicing-factor intracellular kinetics using fluorescence recovery after photobleaching, fluorescence loss after photobleaching, and fluorescence correlation spectroscopy. Kinetics were probed in the nucleoplasm and nuclear speckles and on an actively transcribing gene. Further analysis showed that ongoing pre-mRNA splicing does not impede the release of RNA polymerase after transcription termination (Brody et al., 2011).

Development and the epigenome

The three-dimensional context of the epigenome is likely to play a major role in gene expression. Jennifer Phillips-Cremins (Victor Corces’s laboratory, Emory University) and colleagues examined the geometric configurations of chromatin architecture during development. They used chromosome conformation capture capture carbon copy technology in combination with high-throughput sequencing to generate structure maps for pluripotent embryonic stem (ES) cells, multipotent ES-derived neural progenitor cells, and mouse embryonic fibroblasts. Their kb-resolution analysis revealed a complex chromatin interaction network in ES cells that undergoes extensive reorganization during neural lineage commitment.

DNA repair: who’s on first?

DNA mismatch repair corrects mistakes made during DNA replication that otherwise could lead to mutations. Chris Campbell (Arshad Desai’s laboratory, Ludwig Institute for Cancer Research) and colleagues in the Kolodner laboratory developed new assays for visualizing different stages of mismatch repair in live cells, allowing them to determine when and how various components of the mismatch machinery contribute to the repair process. These assays are powerful tools for the analysis of mutants that disrupt the mismatch repair pathway, including disease mutants identified from cancer patients.

Nuclear shape: all dressed up and nowhere to go

The yeast nuclear envelope does not break down during mitosis but instead increases in size before dividing. But what happens when cells delay in mitosis? Work from Orna Cohen-Fix’s laboratory (National Institutes of Health) showed that under these conditions, membrane is still added to the nucleus, but rather than increasing in size, the nucleus forms a single, long extension. Cohen-Fix and colleagues hypothesize that this allows cells to maintain intranuclear organization during a prolonged mitotic delay.

Sperm nuclei thrive on PIPs

Nuclear morphogenesis during sperm head formation is critical for sperm development and male fertility. Lacrimoara Fabian (Julie Brill’s laboratory, Hospital for Sick Children, Toronto, Canada) showed that phosphatidylinositol (4,5)-bisphosphate (PIP2) is critical for shaping the sperm head and for nuclear elongation and chromatin condensation during spermiogenesis in flies. PIP2 may regulate these events directly or by affecting levels of other phosphoinositides or inositol polyphosphates. This establishes a novel role for PIPs in nuclear morphogenesis and spermatogenesis.

mRNP export: recycling of the dead (box protein)

The regulation of the DEAD-box protein 5 (Dbp5) nucleotide-binding activity of Dbp5 by stimulating ATP loading, while the nuclear pore complex protein Nup159 directly stimulates Dbp5 release of ADP to complete the cycle (Noble et al., 2011). This is the first report of a nucleotide release factor for a DEAD-box protein, serving as a novel paradigm for DEAD-box protein regulation.

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