

Nuclear structure and function

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The Minisymposium on Nuclear Structure and Function featured new strategies and approaches for understanding how the vast amount of information in the nucleus is parsed out in individual cells. The field faces the problem of deducing the structure of a dynamic polymer (chromatin) in a living cell. Classical structural biology approaches have not been as forthcoming for dissecting the structure of this highly flexible and dynamic polymer. From a statistical mechanics perspective, the number of states that chromatin can adopt provides a rich source of conformational energy. Extrapolating to nuclear domains, we appreciate these are statistical definitions for regions within the nucleus that are on average differentiated from adjacent regions. Nuclear domains are not confined by membranes; rather, they are more like eddies in a highly viscous environment that provide chemistry favoring one chromatin state over another. The question is how we probe subtle features in such a fragile environment as the cell.

Domain targeting

Jason Brickner (Northwestern University) has cracked the code for clustering of active genes at the nuclear periphery in yeast. Gene promoters contain “DNA zip codes” that target genes to nuclear pores as one mechanism to enhance expression. The positional information is epigenetically propagated through several cell cycles, providing a mechanism of transcriptional memory. Aspects of this mechanism are conserved to humans, suggesting

that the interaction of genes with nuclear pore proteins plays an important, conserved role in regulating transcription and chromatin structure.

Gatekeeping function of the nuclear pore

Weidong Yang (Temple University) is interested in the mechanism of RNA transport through the nuclear pore and has developed a new method called SPEED (single-point edge excitation subdiffusion) microscopy. SPEED microscopy enabled him to beat the loss of spatial resolution in z and visualize single RNA molecules as they traverse a nuclear pore with an unprecedented spatiotemporal superaccuracy of 8 nm and 2 ms. The three-dimensional mapping of export routes indicates that mRNAs primarily interact with the periphery on the nucleoplasmic side and in the center of the NPC (nuclear pore complex) without entering the central conduit utilized for passive diffusion of small molecules. These are important findings that enable discrimination of various models in the field.

Gene and chromosome pairing

Megan Bodnar (David Spector’s laboratory, Cold Spring Harbor Laboratory) investigated the organization of pluripotency genes during early embryonic stem cell differentiation. She reported that a DNA element mediates allelic pairing at the *Oct4* gene locus during the onset of *Oct4* gene repression. Thus, just as active genes may be corralled for maximum expression, inactive genes may also rely on positional cues. On a larger scale, **Ofer Rog** (Abby Dernberg’s laboratory, University of California–Berkeley) showed us chromosome synapsis in live meiosis. These remarkable images revealed a rapid and processive event that initiates from previously identified pairing sites and elongates the length of the chromosome. This study opens up a new understanding of the intimate contacts and exchange that occur between homologous chromosomes.

Finally, we heard two talks on mechanisms of chromosome segregation. **Ajit Joglekar** (University of Michigan) updated his nanometer localization mapping of kinetochore protein position in live cells to address mechanisms of force transduction. Using a sensitive fluorescence resonance energy transfer (FRET) assay and statistical analysis of the data, Joglekar demonstrated that the microtubule (mt)-binding complex (Ndc80) is responsible for attachment to shortening mt-plus ends, while the homologue of XMAP215 (Stu2) seems to be required for corraling growing mt-plus ends. **Kerry Bloom** (University of North Carolina–Chapel Hill) discussed the structure of the chromatin spring that is required for tension sensing and distribution of forces between sister kinetochores. The spring is most likely a cross-linked polymer network. The cluster of 16 kinetochores in budding yeast is analogous in structure to one mammalian kinetochore that makes multiple microtubule attachments in mitosis.

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