Cytoskeletal and nuclear ("nucleoskeletal") intermediate filaments and disease

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Why did so many scientists attend the Intermediate Filaments (IFs) Minisymposium on December 15? Two reasons are new connections (IFs can connect to one or both sides of nuclear envelope–spanning LINC complexes) and new evidence that IFs are active players in cell regulation and signaling. **Omar Skalli** (University of Memphis) discussed synemin, which is highly expressed in astrocyte precursor cells and in astrocytoma cancers. Synemin binds α-actinin and colocalizes with α-actinin at the leading edge of astrocytoma cells. Synemin also associates with the cell cycle regulator Akt. In synemin–down-regulated cells, there is less F-actin at the leading edge, and Akt becomes mislocalized and underactive. **Ryan Hobbs** (Northwestern University, Chicago) showed evidence that desmoplakin, which links keratin IFs to desmosomes, is aberrantly sequestered on keratin IFs in cells deficient for the SERCA2 calcium pump, which is often defective in Darier's disease keratinocytes. Stimulation of protein kinase Cα (PKCα) signaling restored proper desmoplakin–keratin association and rescued the weakened intercellular adhesion caused by SERCA2-deficiency, raising the possibility that PKC agonists might be used to treat skin blisters in Darier's disease patients. **Harald Herrmann** (German Cancer Research Center, Heidelberg) is using TIRF microscopy to follow the rapid assembly of long keratin filaments in vitro and monitoring the assembly and localization of normal keratins versus disease variants in keratinocytes from mice lacking the entire keratin family. **Elisabeth Booth-Gauthier** (Carnegie Mellon University) reported that shear forces on cells caused a dramatic shift in the organization of lamin A filaments and widespread changes in chromatin organization within the nucleus as measured by the positions of fiducial marks. These effects were not detected in nuclei made abnormally stiff by expression of progerin, the dominant mutated lamin A protein that causes Hutchinson–Gilford progeria syndrome. This failure to remodel chromatin organization in response to force is proposed as a new mechanotransduction deficiency in accelerated aging. **George Dialynas** (University of Iowa) discussed a new partnership with University of Iowa clinicians in which novel *LMNA* mutations that cause Emery–Dreifuss muscular dystrophy are studied in *Drosophila* muscle to understand how A-type lamins function in vivo. They detect many tissue-specific nuclear defects that provide a potential basis for therapeutic screens. The final speaker, **Jason Berk** (Johns Hopkins School of Medicine), discussed the posttranslational regulation of both cytoskeletal and nucleoskeletal IFs and a conserved lamin-binding nuclear membrane protein named emerin, by a small sugar, *O*-GlcNAc, which is added to Ser/Thr residues. Even though *O*-GlcNAc levels generally decrease during mitosis, emerin is heavily modified by both *O*-GlcNAcylation and phosphorylation at different stages of mitosis, suggesting emerin is specifically regulated and may have active roles during mitosis. Cochair **Katherine Wilson** made a plea to recognize the term "nucleoskeleton" as a concept and use nucleoskeleton as a keyword, to enable proper annotation of findings about lamin IFs and other components (e.g., actin, myosins, spectrin, and titin) that contribute to nuclear structure.

DOI: 10.1091/mbc.E10-12-0960
Molecular Biology of the Cell Volume 22 Page 725
MBoC is pleased to publish this summary of the Minisymposium "Cytoskeletal and Nuclear Intermediate Filaments and Disease" held at the American Society for Cell Biology 2010 Annual Meeting, Philadelphia, PA, December 15, 2010.
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