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EDITORIAL

In focus in HCB

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In this issue, several review articles which cover various structural and functional aspects of diverse nuclear structures and constituents are published as part of the 60th anniversary of *Histochemistry and Cell Biology*.

The review by Schöfer and Weipoltshammer (2018) on Nucleolus and chromatin summarizes the current understanding of mammalian nucleolar chromatin organization as seen mainly from a microscopist's perspective. It starts with a historical synopsis which is followed by an in-depth analysis of the structure of human rDNA, the morphology and positioning of the nucleolus and perinucleolar chromatin, and aspects of the organization and epigenetic regulation of rRNA transcription.

The review by Masiello et al. (2018) concentrates on the perichromatin region, a 200-nm-thin area which is located at the periphery of the condensed chromatin areas and in which the majority of the functions of DNA in interphase occur. This includes fundamental processes such as replication, DNA repair and transcription, RNA processing and splicing, as well as some epigenetic modifications, including methylation of DNA and RNA on cytosine and adenosine.

In their review on Nuclear actin, Bajusz et al. (2018) analyze the aspects of the evolutionary history and ancient functions of actin as they relate to the development of the nucleus, and critically evaluate the diverse biological functions of nuclear actin and their underlying molecular mechanisms. The function of monomeric actin in transcription and its association with different chromatin-remodeling complexes is highlighted. Furthermore, the existence and particular conformation of nuclear F-actin and its involvement, for instance, in the movement of chromosomes and segments of some genes as well as chromatin decondensation is discussed. Finally, the aspects of the exchange between cytoplasmic and nuclear actin pools are considered.

The regulation of gene expression and chromatin by nuclear phospholipids is well established. The review by Uličná et al. (2018) covers less known roles which nuclear phospholipids and inositol phosphates have in the epigenetic regulation. The regulation of histone acetylation and deacetylation by sphingosine-1-phosphate and inositol phosphates, respectively, is discussed. Furthermore, the influence the different inositol pyrophosphates has on histone demethylation, as well as DNA and histone methylation is described in detail. Together, this review provides a detailed account on the importance of nuclear phospholipids and inositol phosphates for diverse cellular processes through the regulation of the epigenome.

Fibrillin localization in murine myocardium

Close interactions between cardiac myocytes and the extracellular matrix (ECM) are required for proper function and morphology of cardiac tissue (Borg et al. 1996). Moreover, derangements in myocardial ECM proteins can result in various pathologic conditions. One such condition, Marfan Syndrome is caused by pathogenic variants in the fibrillin-1 gene, resulting in an autosomal dominant connective tissue disorder affecting the cardiovascular system (De Backer 2009). Fibrillins are main components of ECM microfibrils with a diameter of 10–12 nm (Sherratt et al. 2001), playing a role in determining the mechanical properties of the myocardium. Since there is limited information on the distribution of fibrillin proteins across the entirety of the myocardium, as well as how this distribution may differ between males and females and during development, Steijns and colleagues (2018) performed an extensive immunohistochemical analysis of fibrillin-1 and -2 arrangement in the mouse myocardium. Fibrillin-1 immunostaining was detected in patterns of long fibers with a wide distribution across the myocardium, including the apex, mid-ventricles, and atria (see cover image). No difference in immunostaining intensity was

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observed between the sexes, or during development (animals 1, 3, and 6 months of age). In contrast, only limited amounts of fibrillin-2 immunofluorescence were detected in the heart. Their results representing the detection of fibrillins in the entire myocardium suggest that these proteins are involved in maintaining the structural arrangement of the myocardium. They conclude their manuscript with a section on potential "limitations" of their study based on immunohistochemical methods. Importantly, they emphasize that although only one antibody against each fibrillin class was used, these antibodies had already been well validated for specificity against their intended antigens.

Neomycin ototoxicity in the mouse cochlear

Many compounds and drugs are responsible for producing ototoxicity; prevalent amongst these is the aminoglycoside family of antibiotics. Animal studies with this family of antibiotics, which includes familiar compounds such as neomycin, gentamycin, kanamycin, and tobramycin, have revealed that their ototoxicity is resulting from damage to the sensory hair cells located in the cochlear (Forge and Schacht 2000). This damage most likely results from the local formation of reactive oxygen species (ROS), resulting in hair cell death via apoptotic mechanisms (Poirrier et al. 2010). Due to inherent limitations and variabilities in the in vivo response of rodent species to treatment with aminoglycoside compounds, cochlear explants utilized for organotypic cultures have become important model systems. Lin and colleagues (2018), expanding upon their recent observation of an atypical pattern of neomycin toxicity in cultured 3-day postnatal C57BL/6 mouse cochlear, have now used an organ of corti culture model to further characterize this interesting finding. Cultured cochlear explants were incubated with neomycin conjugated to Texas red (NTR) fluorophore, and uptake into sensory hair cells was determined. Survival of both inner and outer hair cells was reduced upon exposure to NTR, but with regional differences noted. For instance, inner hair cell survival was much greater in the apical segment than in the basal segment. Likewise, outer hair cell survival was greatest in the apical and hook regions of the cochlear, and much lower in the basal region. Semi-quantitative analysis of fluorescence intensities demonstrated that uptake of NTR was inversely correlated with sensory hair cell survival. Interestingly, since C57Bl/6 mice develop age-onset hearing loss by 3–6 months of age, the authors speculate that a known mutation in the *Cdh23* gene affecting the functioning of mechanoelectrical transducer channels in the cochlear may be the underlying cause for the regional sensitivity to neomycin exposure described in the manuscript. They caution that the regional sensitivity of sensory hair cells in the mouse cochlear to aminoglycoside treatment should be taken into account when using this animal model of accelerated hearing loss.

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