This Month in AJP

Identifying Plasma Biomarkers for Alcoholic Hepatitis

Plasma biomarkers of hepatocyte function may help with diagnosis and prognosis of alcohol-associated hepatitis (AH). Using state-of-the-art in vitro analysis techniques, Argemi et al (Am J Pathol 2022, XXXX–XXXX) identified plasma protein signatures of hepatocyte function for mild and severe AH patients. These proteins were reduced in AH patients. Tested protein combinations differentiated between severe and nonsevere AH with high sensitivity and specificity. These plasma biomarkers may serve as a novel noninvasive molecular tool for research and clinical use in studying and managing AH.

Understanding Hypertension-Induced Glomerular Injury

In systemic arterial hypertension, mesangial injury may precede podocyte injury. Using two hypertensive rat models of focal and segmental glomerulosclerosis (FSGS) as well as biopsies of patients that suffered from arterial hypertension—derived nephrosclerosis, Kriz et al (Am J Pathol 2022, XXXX–XXXX) tested this hypothesis. Hypertension injures mesangial cells, resulting in ballooning of the glomerular capillaries. The increased stretch and stress on podocytes is a secondary effect that forces podocytes against Bowman’s capsule, leading to the formation of synechiae and FSGS. Hypertension may cause glomerular injury via direct effects on mesangial cells.

Understanding Skin Wound Healing

Hyaluronan synthesizing enzymes—hyaluronan synthases (HAS1, 2, 3)—have been implicated in wound healing. Using Has1/Has3 null mice and fibroblasts from these mice, Wang et al (Am J Pathol 2022, XXXX–XXXX) studied the underlying mechanisms. The healing skin of transgenic mice exhibited higher activity of transforming growth factor-beta (TGF-β) and increased dermal collagen maturation. In vitro, the TGF-β signal transduction related to the expression of alpha smooth muscle actin seems to be propagated via the p38 MAP kinase (p38 MAPK), myocardin-related transcription factor (MRTF), and serum response factor (SRF) pathways. HASs may regulate wound healing via p38 MAPK-MRTF-SRF axis.

Stratifying and Predicting Mantle Cell Lymphoma

Deep learning (DL) has sparingly been used for analyzing digital images of mantle cell lymphoma (MCL). Using a DL-based nuclear segmentation model, Chuang et al (Am J Pathol 2022, XXXX–XXXX) identified morphometry-based objective prognostic markers in MCL. The correlation of the various morphometric and clinicopathologic parameters was assessed with overall survival in univariate and multivariate analyses. The algorithmic results combined with clinical and pathologic features, may serve as a powerful tool for MCL prognostication and risk stratification.

Limiting Hyperglycemia-Induced Damage

An endogenous system may protect from diabetes-induced damage and delay disease manifestation. To test this hypothesis, Serikbaeva et al (Am J Pathol 2022, XXXX–XXXX) studied primary human retinal endothelial cells (HRECs) cultured in normal or high glucose (HG). Prolonged exposure to HG resulted in a reduction in oxidative stress—induced death and improved mitochondrial functionality. An endogenous system such as HG-induced mitochondrial adaptation may protect HRECs from the deleterious effects of HG.