This Month in AJP

Urinary miRNAs in Diabetic Nephropathy

Urinary microRNAs (miRNAs) have been proposed as biomarkers for diabetic kidney disease (DKD). Beltrami et al (Am J Pathol 2018, 188:1982–1992) therefore profiled 754 miRNAs in pooled urine samples from DKD patients and non-diabetic controls. miR-126, -155, and -29b were found to be significantly increased in DKD patients. This result was verified in an independent cohort of DKD patients, non-DKD diabetic patients, and non-diabetic controls. DKD-related cytokines triggered the release of these three miRNAs from glomerular endothelial cells. Urinary miR-126, -155, and -29b may serve as biomarkers for DKD.

Imaging Drug-Induced Kidney Damage

The relationship between drug accumulation and phospholipid localization in drug-induced phospholipidosis (DIPL), a lysosomal storage disorder, is poorly understood. Using imaging mass microscopy (IMM), Sakurai et al (Am J Pathol 2018, 188:1993–2003) examined this association. The macrolide antibiotic azithromycin—which can induce DIPL—was orally administered to rats for a week. IMM revealed correlations between areas of kidney damage and the accumulation of azithromycin, its metabolites, and specific phospholipids associated with DIPL. IMM may help explore drug-induced toxicity mechanisms and identify potential biomarkers for DIPL.

Improving Corneal Transplant Outcomes

The neuropeptide vasoactive intestinal peptide (VIP) improves corneal endothelial cell (CEnC) integrity during donor cornea tissue storage and protects CEnCs against oxidative stress-induced apoptosis. Using monolayers of immortalized human CEnCs subjected to scratch injury and syngeneic mice subjected to penetrating keratoplasty, Satitpitakul et al (Am J Pathol 2018, 188:2016–2024) studied the effect of exogenous VIP administration on corneal transplant outcomes. VIP administration enhanced endothelial cell migration and cytoprotection against proinflammatory cytokines in vitro and increased CEnC density, decreased graft opacity scores, and improved corneal allograft survival in vivo. VIP administration may help improve corneal transplant outcomes.

Understanding Sorafenib Sensitivity in Hepatocellular Carcinoma

Copy number variations in the gene encoding lymphocyte-specific protein-1 (LSP1)—an f-actin-binding protein—are associated with human hepatocellular carcinoma (HCC). Using animal models and cell cultures, Koral et al (Am J Pathol 2018, 188:2074–2086) examined the role of LSP1 in liver regeneration after partial hepatectomy (PHx) and sensitivity to the FDA-approved drug Sorafenib in normal and neoplastic hepatocytes. Loss of LSP1 increased proliferation and ERK activation after 2/3 PHx in Lsp1 knockout mice. Inhibition of LSP1 function increased sensitivity to Sorafenib treatment in human and rat cultured hepatoma cells. LSP1 may serve as a biomarker for Sorafenib sensitivity in HCC patients.

Managing Osteoarthritic Cartilage Damage

The function of hyaluronan-binding protein involved in hyaluronan depolymerization (HYBID) in osteoarthritic (OA) cartilage remains unclear. Shimizu et al (Am J Pathol 2018, 188:2109–2119) therefore studied HYBID expression and its roles in human OA cartilage. HYBID is highly expressed in OA chondrocytes and its production is further enhanced with tumor necrosis factor-α (TNF-α). Inhibiting TNF-α or HYBID may help manage OA cartilage damage.