This Month in AJP

Protecting Renal Tubules in Chronic Kidney Disease

Transmembrane and immunoglobulin domain-containing 1 (TMIGD1) is renoprotective; however, the role of TMIGD1 in chronic kidney disease (CKD) is unclear. Using Tmigd1 knockout mice models and CKD rodent models, Belghasem and Yin et al (Am J Pathol 2023, 1501–1516) studied this role. Tryptophan-derived uremic toxins were found to cause tubulotoxicity. TMIGD1 specifically protected renal tubular cells from renal injury in various CKD models. TMIGD1 may be targeted to protect renal tubules in CKD.

Understanding Nemaline Myopathy

The processes underlying the pathogenesis of the congenital myopathy, nemaline myopathy (NM), are unclear. By combining proteomic analysis and structural/functional analyses in a mouse model of severe NM, Slick et al (Am J Pathol 2023, 1528–1547) studied these processes. Aberrations in energetic metabolism and stress-related pathways contributed to pathophysiology of NM. Mitochondrial dysfunction may be a novel contributor of muscle weakness in NM.

Studying the Age-Dependent Effects of High-Fat Diet on Brain Dysfunction

Chronic exposure to high-fat diet (HFD) from a young age exacerbates severe neurobehavioral disturbances; however, the underlying mechanisms are unknown. Using mice, Yao et al (Am J Pathol 2023, 1568–1586) studied these mechanisms. Mice aged 4 or 8 weeks were either fed a control diet or HFD for 6 months and effects on metabolism, neurobehavior, and brain plasticity were studied. The detrimental effects were stronger when the HFD began at 4 weeks of age compared to 8 weeks of age and were modulated by microglial insulin signaling pathway. Microglial insulin signaling pathway may be targeted to manage HFD-induced brain dysfunction.

Dissecting Ferroptosis Resistance in Lung Cancer

Loss or mutation of TP53 affects sensitivity to ferroptosis, a novel iron-dependent type of cell death. Using in vivo and in vitro gain- and loss-of-function approaches and clinical tissue for mutation analysis and pathological research, Peng et al (Am J Pathol 2023, 1587–1602) studied the mechanism by which mutant TP53 becomes resistant to ferroptosis. TP53 mutation in lung cancer cells leads to ferroptosis insensitivity, which is regulated by the TP53—forkhead box M1 (FOXM1)—myocyte-specific enhancer factor 2C (MEF2C) axis. TP53-FOXM1-MEF2C axis may be targeted to manage lung cancer.

Studying the Role of RNF152 in Lung Adenocarcinoma

Ring finger protein 152 (RNF152) has been implicated in hepatocellular and colorectal carcinoma; however, its role in lung adenocarcinoma (LUAD) is unclear. Using publicly available gene expression profiling data, cultured cells, and mouse xenograft models, Zhu et al (Am J Pathol 2023, 1603–1617) studied this role. RNF152 is down-regulated in LUAD, and low RNF152 expression correlates with a poor prognosis. Increasing the expression of RNF152 inhibited the growth and metastasis of LUAD mediated by the RNF152—interleukin-1 receptor-associated kinase 1 (IRAK1)—AKR1B10 axis. Targeting the RNF152-IRAK1-AKR1B10 axis may help manage LUAD.