This Month in AJP

Understanding Diabetic Gastroparesis

The role of transient receptor potential vanilloid 1 (TRPV1) ion channels in diabetic gastroparesis (DGP) is unclear. Using high-fat diet—induced DGP mice, Xu and Liang et al (Am J Pathol 2023, 548–557) studied this role. TRPV1 activation facilitated gastric fundus relaxation by regulating neuronal nitric oxide synthase and promoting nitric oxide release in normal mice. However, these effects and associated mechanisms disappeared in high-fat diet—induced DGP mice. TRPV1 dysfunction may contribute toward dysfunction of DGP gastric nitrergic neuromuscular relaxation.

Mapping Wnt Receptors

The anatomic expression of Wnt signaling components—key drivers in establishing and maintaining liver zonation—remains to be characterized. Using multiplex fluorescent in situ hybridization, Gayden et al (Am J Pathol 2023, 558–566) quantitatively mapped the spatial expression of Frizzled (Fzd) receptors in adult mouse liver. This atlas shares definitive mRNA expression, especially of Fzds, and confirms that the expression of Fzds and Wnts varies in different hepatic cell types. This spatial atlas of Wnt receptors may facilitate their functional characterization in healthy and disease liver states.

Predicting Rectal Cancer

The role of RhoB in rectal cancer is unknown. Using tensor decomposition and deep-learning—based methods, Pham et al (Am J Pathol 2023, 579–590) studied this role. The predictive factors of RhoB were studied in two cohorts of rectal cancer patients with survival rates of less and more than 5 years. Differences were observed in the tensor decomposition factors of the two cohorts. RhoB may have utility as a predictive factor for rectal cancer.

Managing Prostate Cancer

The role of protein kinase D (PKD) family of proteins in prostate cancer metastasis is unclear. Using human cultured cells and a mouse model of bone metastasis, Roy et al (Am J Pathol 2023, 624–637) studied the role of PKD2 and 3 (PKD2/3) in prostate cancer bone metastasis. Reducing PKD2/3 strongly inhibited colony formation and cell migration, significantly inhibited tumor cell invasion, and repressed the expression of genes related to bone metastasis. PKD2/3 depletion was in part mediated by the Runx2–MEK–ERK1/2 pathways. Targeting PKD may help treat metastatic prostate cancer.

Studying Vascular Proliferative Diseases

Fragile-X related protein-1 (FXR1) negatively regulates inflammation; however, its role in vascular disease is unknown. Using cultured cells and a targeted knockout mouse for FXR1, Corbett et al (Am J Pathol 2023, 638–653) studied this role. Modulating expression of FXR1 in smooth muscle cells modified several genes and proteins. FXR1 stabilized cell cycle related genes in vascular smooth muscle cells and deletion of FXR1 induced a senescent phenotype in vivo. Targeting FXR1 expression and/or activity may help manage vascular proliferative diseases.