This Month in AJP

Understanding Polycystic Ovary Syndrome

The effect of the two common manifestations of polycystic ovary syndrome (PCOS)—hyperandrogenism and insulin resistance—on uterine spiral artery (SpA) remodeling is unclear. Using previously established rat models, Hu and Zhang et al (Am J Pathol 2023, 1916–1935) verified previous reports that the exposure to 5-dihydrotestosterone and insulin during pregnancy results in hyperandrogenism, insulin intolerance, and increased fetal mortality. Data confirmed previous findings and further suggest that perturbed uterine SpA remodeling, placental functionality, and placental senescence may result in higher pregnancy-related issues in women with PCOS.

Reversing Age-Related Kidney Dysfunction

Aging is linked to kidney dysfunction and disease. Using human cell cultures and mouse and human kidneys, Wang et al (Am J Pathol 2023, 1969–1987) studied the role of estrogen-related receptors (ERRs) in age-related kidney dysfunction. The expression of ERRs decreased in both the aging human and mouse kidneys and they were preserved in aging mice with lifelong caloric restriction. Treatment with a pan-ERR agonist improved age-related kidney injury and increased the expression of ERRs in mice. Modulating ERRs may help restore age-related kidney dysfunction and disease.

Mitigating Bronchopulmonary Dysplasia and Coincident Retinopathy

The mechanisms underlying severe bronchopulmonary dysplasia (BPD) and the associated retinopathy of prematurity (ROP) are unclear. Using an established neonatal hyperoxic mouse model of coincident BPD and retinopathy, Wickramasinghe et al (Am J Pathol 2023, 2001–2016) screened for candidate mediators. Higher expression of granulocyte colony-stimulating factor (G-CSF) was seen in response to hyperoxia, which was associated with more severe BPD. G-CSF–deficient neonatal pups had less severe symptoms and showed partial protection against ROP. G-CSF mediates BPD and ROP and may be targeted for treatment.

Protecting Against Carcinogen-Induced Oral Cancer

The role of autophagy in oral cancer is unclear. Using a carcinogen-inducible mouse model of oral squamous cell carcinoma (OSCC), Coeli-Lacchini and da Silva et al (Am J Pathol 2023, 2172–2181) studied this role. Autophagy was induced by spermidine treatment, which decreased the severity of lesions and the incidence of OSCC in mice exposed to the carcinogen. Spermidine-induced autophagy may protect against carcinogen-induced oral cancer.

Studying Hepatic Lymphangiogenesis

The mechanisms underlying lymphangiogenesis in liver are unclear. Using rat models, liver biopsies from portal hypertensive patients with portal-sinusoidal vascular disease (PSVD), and gene profile dataset from normal humans and idiopathic non-cirrhotic portal hypertension and cirrhotic patients, Tanaka and Jeong et al (Am J Pathol 2023, 2182–2202) studied the underlying mechanisms and their implication in liver fibrosis. Vascular endothelial growth factor-C, produced by Schwann cells of the sympathetic nervous system, promoted hepatic lymphangiogenesis in rat models and in PSVD and cirrhotic patients. Increasing liver lymphangiogenesis may protect against hepatic fibrosis.