



This Month in *AJP*

Understanding Idiopathic Subglottic Stenosis

The mechanisms underlying idiopathic subglottic stenosis (iSGS) are unclear. Using next-generation sequencing on tissue sections from patients with iSGS, individuals with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), and controls, Zhang et al (**Am J Pathol**, XXXX–XXXX) studied these mechanisms. Epithelial-mesenchymal transition (EMT) emerged as a vital pathogenetic mechanism of subglottic stenosis in iSGS and AAV. High expression of the EMT regulator PMEPA1 in iSGS patients was related to a shorter recurrence interval. Further understanding the profibrotic roles of PMEPA1 may confirm its biomarker potential to predict disease recurrence in iSGS.

Managing Renal Lipotoxicity

Approaches to manage renal lipotoxicity are limited. Using scavenger receptor class B type I-deficient (*SR-BI*^{-/-}) transgenic mice, Liu et al (**Am J Pathol**, XXXX–XXXX) studied the protective effects of paraoxonase 1 (PON1) enzyme against high-fat diet-induced renal toxicity. The transgenic mice exhibited a reduction in plasma and renal Pon1 and increased renal injury, which was attenuated by PON1 overexpression. Mechanistic data implicate reactive oxygen species, AKT/mTOR pathway, and Nod-like receptor family protein 3 inflammasome. Modulating PON1 may help treat diseases related to renal lipotoxicity.

Modeling Nanomaterial-Induced Peritonitis

The link between long-term exposure to carbon nanotubes (CNTs) and chronic inflammation is unclear. Tsunematsu et al (**Am J Pathol**, XXXX–XXXX) generated a mouse

model of chronic peritonitis to study this link. Chronic peritonitis was achieved by intraperitoneal injection of Taquann-treated multiwalled CNTs (T-CNT). T-CNT caused organ fibrosis by activating NFκB signaling in macrophages resulting in an up-regulation of matrix metalloproteinase-12 and release of profibrotic activity. This novel mouse model may help improve our understanding of the immunotoxicology of nanomaterials.

Managing Ear Cholesteatoma Formation

The mechanisms underlying keratinocyte growth factor (KGF)-induced cholesteatoma are unclear. Using an established mouse model of cholesteatoma to trace neural crest cell lineage, Yamamoto-Fukuda et al (**Am J Pathol**, XXXX–XXXX) studied potential molecular triggers resulting in middle ear cholesteatoma. p75 was expressed with a high proliferative activity in mice, depleting p75 *in vivo* reduced cholesteatoma. Higher expression of p75-positive cells was also observed in human cholesteatoma tissues. p75 signaling may be targeted to manage cholesteatoma.

Understanding Distal Colon Contractility

The mechanisms underlying aberrant colonic motility are unclear. Using transgenic mice, Lambrinos and Cristofaro et al (**Am J Pathol**, XXXX–XXXX) studied the role of the transmembrane receptor, neuropilin 2 (*Nrp2*), in regulating colonic smooth muscle contractility. Chemical induced colonic contractility was higher in smooth muscle-specific knockout of *Nrp2* mice or *Nrp2*-deficient mice compared to control mice. *Nrp2* knockout mice exhibited increased colon motility. *Nrp2* may be targeted to manage colonic smooth muscle contractility and dysmotility.