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This Month in *AJP*

Protecting Podocyte Injury

Though repulsive guidance cue receptor ROBO2 is important for early kidney development, its role during kidney injury, especially in mature podocytes, is unclear. Using conditional *Robo2* knockout mice, Pisarek-Horowitz, Fan, and Kumar et al (**Am J Pathol 2020, 799–816**) studied this role. Podocyte injury resulted in increased Robo2 expression and podocyte-specific knockout of Robo2 decreased podocyte injury. ROBO2 expression also increases in humans with membranous nephropathy. Increased expression of Robo2 caused podocyte detachment *in vitro*. ROBO2 may be targeted to manage podocyte injuries and podocytopathies.

Understanding Liver Regeneration

The functional roles of mammalian target of rapamycin complex 2 (mTORC2) during liver regeneration are unclear. By performing partial hepatectomy (PHx) in mice, Xu and Wang et al (**Am J Pathol 2020, 817–829**) studied these roles. Wild-type mice as well as mice with liver-specific knock out of *Rictor*—encoding the pivotal unit of mTORC2 complex—were used. *Rictor* deficient mice were more intolerant to PHx and exhibited higher mortality after PHx. Akt phosphorylation decreased upon Rictor loss, delaying hepatocyte proliferation and lipid biosynthesis along liver regeneration. mTORC2 signaling is necessary for liver regeneration.

Managing Zika Virus–Related Neuroinflammation

Hippo signaling pathway regulates proliferation and differentiation of neural progenitor cells; however, its role in neuronal pathogenesis of Zika virus (ZIKV) is unclear. Using a mouse model and human retinal pigment epithelial cells, Garcia and Paul et al (**Am J Pathol 2020, 844–861**) studied this role. ZIKV infection activated Hippo pathway and silencing downstream components of Hippo signaling reduced ZIKV replication *in vitro*. ZIKV infection activated Hippo pathway in the blood brain barrier in the mouse model. The Hippo signaling pathway may be targeted to manage ZIKV-associated ocular and neuronal inflammation.

Exploring Group A *Streptococcus* Infections

The lack of suitable animal models has limited our understanding of the Group A *Streptococcus* (GAS) genes responsible for colonization in the primate female genital tract. Using genome-wide transposon mutagenesis screens, Zhu and Olsen et al (**Am J Pathol 2020, 862–873**) identified potential candidate genes. From the array of genes essential for colonization of the primate vaginal mucosa and infection of the uterine wall identified *in vivo* and *ex vivo*, respectively, 39 overlapping genes were identified to be responsible for GAS fitness. Two genes encoding bacterial surface proteins SpyAD and Isp2 were identified to be critical for GAS vaginal colonization, myometrium infection, and necrotizing myositis. These findings open avenues to explore treatments for female GAS genital tract infections.

Understanding Head and Neck Cancer

The mechanisms underlying tumor metastasis to the draining lymph nodes in head and neck squamous cell carcinoma (HNSCC) are unclear. Using HNSCC cells and lymphatic endothelial cells (LECs) as well as a potent anticancer agent, CF_3DODA-Me, Kumaravel et al (**Am J Pathol 2020, 900–915**) explored these mechanisms. The crosstalk between the LECs and HNSCC tumors is mediated via the CXCR3–CXCL11 chemokine axis, which activates many tumor promoting pathways that are abrogated by CF_3DODA-Me. CF_3DODA-Me may effectively target tumor cells at sites of metastasis and prevent tumor progression via lymphatics.

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