This Month in AJP

Modeling Streptococcal Necrotizing Fasciitis

The lack of appropriate animal models has limited the study of pathogenesis as well as optimization of therapeutic regimens for streptococcal necrotizing fasciitis (NF). To this effect, Keller et al (Am J Pathol 2018, 188:1517–1523) characterized a murine NF model. For the first time, the pathology in Streptococcus-infected mice was compared to the pathology of human NF patient tissues. The streptococcal mouse NF model mimicked all histological characteristics observed in human streptococcal NF. This streptococcal NF mouse model may help improve our understanding of NF pathogenesis and facilitate study of new therapeutic regimens.

Visualizing Pancreatic Anatomy and Pathology in Three Dimensions

Visualizing pathologies in three dimensions can significantly improve our understanding of the biology of human diseases. Noë et al (Am J Pathol 2018, 188:1530–1535) chemically cleared thick sections of fresh and archived surgically resected human pancreatic parenchyma. The sections were immunolabeled with antibody to CK19, a marker for the pancreatic ductal system, and analyzed microscopically to generate three dimensional (3D) images of normal pancreatic tissue as well as various tumors. 3D imaging highlighted changes in physiological structures in cancer samples that are hard to conceptualize otherwise. 3D visualization of archived tissues may provide new insights into the anatomy and pathophysiology of the normal as well as diseased pancreas.

Mapping Entry of Cryptococci to the Brain

Poor understanding of the pathogenesis of neurocryptococcosis limits measures to improve clinical outcomes. To understand dissemination of Cryptococcus to the central nervous system (CNS), Kaufman-Francis et al (Am J Pathol 2018, 188:1653–1665) studied the innate immune response to Cryptococcus neoformans (Cn) infection in CNS of mice. Normal, chimeric, GFP-phagocyte–positive and phagocyte-depleted mice were infected with Cn. Predominantly circulating monocytes effected Cn translocation and immune cell infiltration into the perivascular space (PVS) of post-capillary venules. Free Cn crossed the protective barrier between the PVS and the cerebral parenchyma, and they established cryptococcomas in the adjacent cerebral parenchyma. Phagocyte depletion prevented cryptococcoma formation and PVS infiltrates. The PVS of post-capillary venules provides a niche for Cn to enter the brain for further dissemination.

Understanding Cavitation in Tuberculosis

Our understanding of the pathogenesis of cavity formation (cavitation) in tuberculosis (TB) is limited by the lack of available animal models. To study TB cavitation, Ihms et al (Am J Pathol 2018, 188:1666–1675) characterized a rabbit model. Rabbits were repeatedly infected with low-dose Mycobacterium tuberculosis aerosol to generate cavities. Cavitation was monitored for over 14 weeks using serial computed tomography and four-dimensional cavity mapping at several time points, followed by eventual histopathological analysis of cavities. Cavity formation, growth, and characteristics were studied. The dynamic cavitation process was guided by mechanical stress. This novel rabbit TB cavitation model may help prevent TB transmission by improving insight into the evolution of this disease.

Exploring Retinal Detachment

Though the mitochondria-mediated apoptotic pathway has been implicated in photoreceptor degeneration after retinal detachment, responsible upstream events are unclear. Using rats, She et al (Am J Pathol 2018, 188:1713–1722) studied the role of dynamin-related protein 1 (Drp1), a mediator of mitochondrial fission, in retinal photoreceptor degeneration. Induction of retinal detachment in rats activated Drp1–dependent mitochondrial fission pathway and consequent apoptotic cascades in photoreceptor cells; these processes were reactive oxygen species (ROS) dependent. In vitro, exogenous ROS insult was sufficient to activate Drp1–dependent mitochondrial fission. Inhibiting Drp1 activity restored mitochondrial integrity and rescued photoreceptors. The ROS–Drp1–mitochondria axis may be targeted to manage photoreceptor degeneration–related blindness in retinal diseases.