This Month in AJP

Monocyte Contribution to Liver Fibrosis

The temporal cellular interplay driving liver fibrosis remains unclear. Using a mouse model of hepatotoxin-induced liver fibrosis, Melino et al (Am J Pathol 2016, 186:524–538) studied the time course of liver pathology. Two phases of liver fibrosis were observed: an early phase of steady collagen deposition and a late phase of accelerated progressive fibrosis with a fivefold increase in collagen deposition. The early phase was characterized by pericentral monocyte infiltration associated with myofibroblast activation, and the late phase by tissue-resident macrophage turnover and the development of a mature ductular reaction. Colony stimulating factor (CSF)-1 was identified as the key mediator of fibrosis. Blocking CSF-1 may reduce fibrosis in chronic liver diseases.

Modeling Repeat Mild Traumatic Brain Injury

Study of repeat mild traumatic brain injury (rmTBI) in contact sports is limited by the lack of proper rodent models. Winston et al (Am J Pathol 2016, 186:552–567) modeled the acute effects of a single mTBI and the chronic effects of up to 30 rmTBIs on neuronal structure and brain pathology in mice. Single mTBI resulted in rapid transient loss of excitatory synapses. Thirty rmTBIs caused dendritic spine loss when there was a 7-day interinjury interval (but not with a 1-day interval) between each mTBI. Thirty rmTBIs caused chronic white matter inflammation, which continued to develop through 60 days and was still apparent 1 year after injury. This model of repetitive head trauma will be useful for the study of synaptic loss after mTBI as a trigger of white matter pathology.

Exploring Pathology of Fatal MERS-CoV

The pathological changes and viral distribution of fatal severe Middle East respiratory syndrome coronavirus (MERS-CoV) infection in humans remains unknown. Ng et al (Am J Pathol 2016, 186:652–658) describe findings from the first autopsy of a fatal case of MERS-CoV. Histopathology showed diffuse alveolar damage in the lungs, severe peripheral vascular disease, patchy cardiac fibrosis, and hepatic steatosis. Immunohistochemical and ultrastructural analyses identified type 2 pneumocytes and epithelial syncytial cells as important targets of MERS-CoV antigen with no evidence of extrapulmonary MERS-CoV antigens. These and future insights will improve our understanding of MERS-CoV pathogenesis to develop appropriate animal models as well as treatment strategies.

Linking Ovarian Brenner and Mucinous Tumors

Benign ovarian Brenner tumors and mucinous cystic neoplasms may share a histogenic origin and progression, but molecular evidence is limited. Using molecular genetic analysis, Tafe et al (Am J Pathol 2016, 186:671–677) examined the molecular mechanisms of such a relationship. Somatic mutation profiles were assessed using a 358-gene panel and DNA from archival samples of Brenner tumors (with or without associated mucinous neoplasm) as well as atypical proliferative (borderline) Brenner tumors. Comparison of variants suggests a shared origin or progression for Brenner and mucinous tumors. However, differences in affected genes point to possible mechanisms of divergent phenotype and progression of these tumors.

FBP Regulates MYC in Embryonic Development

The fundamental biology and pathology of the transcription factor far upstream element binding protein (FBP) is complex. To study FBP functions, Zhou et al (Am J Pathol 2016, 186:701–715) generated an FBP-knockout mouse. FBP loss led to embryonic lethality, with embryos displaying a range of pathologies including cerebral and pulmonary hyperplasia. Hematopoietic stem cell dysfunction resulted in irregular trilineage anemia, as confirmed by immunophenotyping. The levels of MYC, a key FBP target, were misregulated in the knockout mice. FBP acts as a molecular cruise control, regulating MYC expression for the maintenance of multiple embryonic physiological processes.