This Month in AJP

Understanding Schwann Cell Remyelination

It remains unknown why and how Schwann cells contribute to remyelination in the central nervous system (CNS). Using a conditional astrocyte-specific phosphorylated Stat3-knockout mouse model, de Castro et al (Am J Pathol 2015, 185:2431—2440) studied the effect of abrogating astrocyte activation on remyelination in toxin-induced demyelination of spinal cord white matter. Preventing phosphorylation of Stat3 in astrocytes resulted in diminished demyelination-associated astrogliosis. The attenuated astrocyte response reduced remyelination due to oligodendrocytes and increased remyelination caused by Schwann cells in lesioned knockout mice compared with lesioned controls. Astrocyte activation via Stat3 signaling determines the balance of oligodendrocyte versus Schwann cell remyelination in the CNS.

Autophagy Links Ductular Reaction and Cirrhosis

The degradation and recycling of cellular components by lysosomes, or autophagy, regulates liver fibrosis, which may culminate in cirrhosis. Using a chemically induced cirrhotic rat model and human liver specimens from cirrhotic and non-cirrhotic individuals, Hung et al (Am J Pathol 2015, 185:2454—2467) examined the roles of autophagy in cirrhosis. Human cirrhotic livers showed increased autophagy and lysosomal activity. Increased autophagy in bile ductule cells in cirrhotic sections correlated with fibrosis severity and the degree of ductular reaction—typical responses to injury in human liver diseases. Increased autophagy in human cirrhotic livers of different etiologies and experimental cirrhotic livers of mice also correlated with ductular reaction. Modulating autophagy may aid in the management of liver cirrhosis.

Reversing Skeletal Muscle Damage

Retinoic acid receptor (RAR)γ agonist may reduce skeletal muscle damage. Using mouse models of muscle injury, Di Rocco et al (Am J Pathol 2015, 185:2495—2504) further tested this hypothesis. The effects on muscle repair were examined in the tibialis anterior (TA) muscle of 7-week-old female mice following injury and after treatment with RARγ agonist or corn oil vehicle. The muscle defects were partially repaired with newly regenerating muscle cells but were filled with adipose and fibrous scar tissue in both RARγ-treated and control groups. The fibrous or adipose area was smaller in RARγ-agonist–treated mice than in the control mice. Muscle repair was remarkably delayed in RARγ-null mice in both this critical defect model and a toxin injury model. After laceration of the TA muscle, a rapid increase in retinoid signaling was observed in retinoid signaling reporter mice. Selective RARγ agonists may aid in the repair of muscle injury and degeneration.

Jak2—Stat5a/b Signaling Promotes Prostate Cancer Metastasis

Stemness and epithelial-to-mesenchymal transition (EMT) are key issues in prostate cancer (PC) progression and resistance to therapy. Talati et al (Am J Pathol 2015, 185:2505—2522) therefore explored the role of Jak2-Stat5a/b signaling, which has been implicated in early recurrence and disease-specific death in PC, in EMT and cancer-initiating cells in PC. Experiments in PC cell lines, xenografted tumors in vivo, and patient-derived PCs ex vivo using organ explant cultures showed that Jak2-Stat5a/b signaling induced functional endpoints of EMT mediated by Twist1. Jak2-Stat5a/b signaling induced stem-like properties in PC cells such as sphere formation and expression of specific markers including BMI1. Activation of Jak2-Stat5a/b signaling promoted metastatic colonization of human PC cells delivered to mice i.v. Active Jak2-Stat5a/b signaling promotes metastatic progression of PCs by inducing EMT and stem-like properties in PC cells.

p62 Is a Novel Prognostic Marker of Endometrial Cancer

Despite high levels in several human cancers, the clinicopathological and functional contribution of SQSTM1/p62 expression is largely unknown in endometrial cancers (ECs). Iwadate et al (Am J Pathol 2015, 185:2533—2544) assessed the expression status of p62 in primary ECs and analyzed its clinical significance. Although p62 was expressed in the cytoplasm and/or nucleus in primary ECs, high level of cytoplasmic p62 and low level of nuclear p62 was associated with subtype exhibiting aggressive phenotype and poor clinical outcome, irrespective of histological type. p62 inhibition reduced invasive activity and resistance to oxidative stress of EC cells in vitro and suppressed tumor growth in vivo in an orthotopic mouse model of EC. p62 expression may be a useful prognostic biomarker of ECs.