This Month in AJP

Understanding Blast-Induced Trauma

The majority of individuals with traumatic brain injury due to blast exposure suffer from visual dysfunction; however, long-lasting ocular blast injuries remain unstudied. Using a compressed air–driven shock tube system, Mammadova et al (Am J Pathol 2017, 187:1459–1472) studied the retinal and neurological effects of blast injury. Adult mice were exposed to blast wave pressure of 300 kPa/day for three successive days and euthanized 30 days post injury. Examination of retinal tissue showed activation of glial cells and microglia, loss of photoreceptor cells, and an increase in phosphorylated tau in retinal neurons and glia. The proximity of the eye to the blast wave pressure correlated with the severity of retinal responses. There were no detectable cognitive or motor deficits or damage to striatal or cortical neurons. The blast wave pressure model may improve our understanding of long-lasting ocular blast injuries.

Modeling Lymphomagenesis

APRIL, a tumor necrosis factor family member, regulates B cell immunity. Using transgenic mice expressing human APRIL, Floch et al (Am J Pathol 2017, 187:1473–1484) studied the role of APRIL during Helicobacter infection. Wild-type and transgenic mice were infected with H. pylori and H. felis, euthanized 18-month post-infection, and analyzed for inflammatory responses and histopathology. In wild-type mice, the infiltrates comprised T cells, mainly CD4+ for H. pylori and CD8+ for H. felis; whereas, in APRIL transgenic mice, infiltrates were composed of B cells with few CD4+ T cells for both species. B cells were particularly involved in lymphoepithelial lesions, a hallmark of gastric MALT lymphoma. APRIL transgenic mice infected by Helicobacter species may help model gastric lymphomagenesis.

Managing Hepatic Fibrosis in Primary Sclerosing Cholangitis

Gonadotropin–releasing hormone (GnRH) and microRNA (miR)-200b promote hepatic fibrosis; however, their role in the context of primary sclerosing cholangitis (PSC) is unknown. Kyritos et al (Am J Pathol 2017, 187:1551–1565) studied this role by using a PSC mouse model (Mdr2−/−) and patient samples. Expression of receptor subtype GnRHR1 was absent in normal bile duct, but was up-regulated in a late-stage PSC patient. GnRH treatment up-regulated GnRHR1 expression in cultured cholangiocytes. GnRHR1 expression increased in Mdr2−/− mice. GnRH and GnRHR1 expression levels correlated with increased intrahepatic biliary mass and fibrosis. GnRH or GnRHR1 suppression significantly inhibited biliary hyperplasia and fibrosis in Mdr2−/− mice. Inhibition of miR-200b, a down-stream target of GnRH/GnRHR1, also reduced hepatic fibrosis. Targeting the GnRH/GnRHR1/miR200b axis may help manage hepatic fibrosis during PSC progression.

Semaphorin 3E Alleviates Experimental Allergic Asthma

The role of semaphorin 3E in allergic asthma is poorly understood. Movassagh et al (Am J Pathol 2017, 187:1566–1576) studied this role in a house dust mite (HDM) challenge model of airway inflammation/asthma in the mouse. HDM exposure significantly reduced semaphorin 3E expression in mouse airways. Administration of exogenous semaphorin 3E protected mice from allergic asthma, in part by the regulation of cytokine response and pulmonary dendritic cell recruitment and function. Targeting semaphorin 3E may help manage airway hyperresponsiveness and airway inflammation.

Improving Hormonal Treatments for Multiple Sclerosis

Epidemiological sex differentials observed in multiple sclerosis (MS) incidence and course are poorly studied. Using a mouse experimental autoimmune encephalomyelitis (EAE) model, Massa et al (Am J Pathol 2017, 187:1613–1622) dissected hormonal effects on the chronic neurodegenerative and acute neuroinflammatory processes of MS. Subcutaneous injection of testosterone and aromatase inhibitor (to prevent endogenous estradiol conversion) into female EAE mice ameliorated the acute but exacerbated the chronic disease course. In vitro, testosterone decreased Th1 and Th17 cell differentiation in an aromatase-independent manner and worsened neuronal cell death under oxidative stress conditions in an aromatase inhibitor–dependent manner. Therefore, androgens aggravated neurodegeneration in EAE and oxidative stress environments. Further mechanistic insights may prove vital when considering hormonal treatments for MS patients.