This Month in AJP

New Mouse Model for Systemic Autoimmune Disease

The lack of successful mouse models for mutation-activated JAK1-induced diseases hampers the understanding of disease pathology related to signaling downstream of cytokine receptor activation. Sabrautzki et al (Am J Pathol 2013, 183:352–368) isolated a dominant Jak1 mouse line carrying a new nonsynonymous point mutation (Jak1 S645P+/−). The morphological, histological, clinical chemical, and hematological phenotypes of Jak1 S645P+/− mice correlate with systemic autoimmune diseases. This new model may be useful for the development of JAK kinase inhibitors to treat arthritis, psoriasis, lupus, colitis, and multiple types of cancer.

DMA Prevents Preterm Birth

Preterm birth (PTB) causes more than 70% of perinatal morbidity and mortality in the United States. Using an established mouse model, Sundaram et al (Am J Pathol 2013, 183:422–430) investigated the effect of pro-inflammatory cytokines in inflammation-associated PTB pathogenesis. In vitro and in vivo analyses showed that the common organic solvent N,N-dimethylacetamide (DMA) can prevent endotoxin-induced preterm birth in timed pregnant mice and rescue their pups from spontaneous abortion at doses many-fold lower than those currently used clinically and in a dose-dependent fashion. DMA may be a promising novel anti-inflammatory agent not only in PTB but also in a broad spectrum of inflammatory disorders.

C3 Protects the Retina in Age-Related Macular Degeneration

Complement component C3 is a key inflammatory protein activated in age-related macular degeneration (AMD), a leading cause of blindness in the elderly in the Western world. Kam et al (Am J Pathol 2013, 183:480–492) examined retinal integrity in aged mice deficient in various complement pathway components. Data show that both uncontrolled C3 activation (via complement factor H deletion) and complete absence of C3 negatively impact aged retinas. Data are consistent with a major role for C3 in maintaining retinal health and also indicate an additional role for complement factor H in this process that is not related to its role in C3 regulation.

Human Oligodendrocyte Progenitor Injury in MS

Remyelination in multiple sclerosis (MS) is often incomplete, and the source of cells and the basis for their limited effectiveness remains unclear. Cui et al (Am J Pathol 2013, 183:516–525) compared the relative susceptibility of adult human oligodendrocyte progenitor cells (OPCs) and mature oligodendrocytes (OLs) to injury in actively demyelinating MS lesions and under in vitro stress conditions. Results suggest that vulnerability of human OPCs to conditions that induce injury of mature OLs in MS lesions contribute to the limited remyelination observed in both acute and chronic stages of MS.

Ovarian Cancer Colonizes Milky Spots

Omental adipose, which contains milky spots—structures consisting of immune cells—is a site of prodigious metastasis in ovarian cancer models and in clinical disease. Clark et al (Am J Pathol 2013, 183:576–591) examined the milky spot-driven model of omental colonization using both in vivo and in vitro assays. Their findings support a two-step model wherein the localization of disseminated cancer cells is first dependent upon milky spots, and then adipocytes are required for progressive growth and subsequent spread to other sites within the peritoneal cavity.