This Month in AJP

Modeling Age-Related Macular Degeneration

Functional alternations in P2X7 scavenger receptors are associated with age-related macular degeneration (AMD). Using P2X7 null and wild-type (WT) mice, Vessey et al (Am J Pathol 2017, 187:1670–1685) explored the effects of these functional alterations during aging. Macrophage phagocytosis activity, ocular histological changes, and retinal function were studied in mice at different ages. Phagocytosis decreased at 18 months in the WT mouse, whereas lack of P2X7 receptor function reduced phagocytosis at all ages compared to WT mice. By 18 months of age, P2X7 null mice exhibited retinal structural and functional defects that mimicked defects in early AMD. P2X7 null mice may help improve our understanding of the mechanisms underlying AMD.

Understanding AKT Activation in Diffuse Large B-Cell Lymphoma

The clinical significance of AKT activation in diffuse large B-cell lymphoma (DLBCL) remains poorly studied. Wang et al (Am J Pathol 2017, 187:1700–1716) studied the role of AKT activation in a large cohort of DLBCL patients. Patients with high phospho-AKT (p-AKT) expression had a significantly lower progression-free survival than patients with low expression. High p-AKT expression was associated with Bcl-2 and Myc overexpression, but it was not an independent risk factor. A subset of DLBCL patients may benefit from combining therapy that targets AKT with other treatments.

Modeling Esophagitis

Our understanding of esophagitis and the associated complications is limited by the lack of appropriate models. Laczkó et al (Am J Pathol 2017, 187:1787–1799) tested the efficacy of three-dimensional (3D) organotypic tissue culture (OTC) that recapitulates normal esophageal epithelial stratification and differentiation, in modeling esophagitis. Human peripheral blood mononuclear cells were added to OTC and stimulated to induce an acute inflammatory response; the human immune cells were viable and responsive to cytokines under OTC conditions. Acute inflammation in epithelium induced a regenerative response whereas the resulting oxidative stress induced DNA damage and strand breaks, which could be chemically reversed. OTC may help identify underlying mechanisms in esophagitis.

PDGF-BB Improves Muscle Regeneration

The role of platelet-derived growth factor BB (PDGF-BB) in muscle regeneration in humans is poorly understood. Piñol-Jurado et al (Am J Pathol 2017, 187:1814–1827) studied this role using human biopsies, cultured human myoblasts, and the mdx mouse model of Duchenne muscular dystrophy (DMD). PDGF-BB is expressed in regenerating and necrotic muscle fibers in biopsies of patients with DMD. PDGF-BB attracted myoblasts and stimulated their proliferation. Muscles from mice treated with PDGF-BB showed a higher population of satellite cells, an increase in the number of regenerative fibers, and a reduction in inflammatory infiltrates compared to vehicle-treated mice. PDGF-BB may improve muscle regeneration in muscular dystrophies through activation of satellite cell proliferation and migration.

Linking Cigarette Smoke and Breast Cancer

Smoking has been linked with the development and progression of breast cancer; however, the underlying mechanisms remain unclear. Using human breast cancer cells and human tumor tissue, Kispert et al (Am J Pathol 2017, 187:1855–1866) studied the effect of cigarette smoking in calcium-independent phospholipase A2 (iPLA2)-initiated metabolic pathways in breast cancer. Cigarette smoke triggered platelet activating factor (PAF) accumulation, prostaglandin E2 release, PAF receptor and COX-2 expression, and decreased the expression of 15-hydroxyprostaglandin dehydrogenase. iPLA2-dependent metabolic pathways can be targeted in breast cancer patients who smoke.