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This Month in *AJP*

CMV Infection Exacerbates IBD

Active CMV infection in the colon exacerbates inflammatory bowel disease (IBD). To determine whether latent CMV infection affects the development and/or severity of IBD, Onyeagocha et al (Am J Pathol 2009, 175: 2034-2042) examined mice with latent murine CMV (MCMV) infection, ie, mice infected at low viral levels only detectable by PCR. Latent CMV infection did not induce IBD in either wild-type mice or a colitis-prone mouse model, but it did exacerbate the severity of colitis induced by another mechanism. MCMV infection resulted in increased numbers of intestinal lymphocytes and heightened antibody responses to commensal microbial antigens, which are associated with IBD severity. Therefore, modulation of mucosal immunity by latent CMV may contribute to the pathogenesis of IBD.

Eosinophils in Allergy and Asthma

Asthma and allergic disease are associated with an improper Th2 immune response. Although eosinophils have long been considered the terminal effectors in allergic and asthmatic Th2 immune responses, they are also capable of modulating the adaptive immune response by interacting with T cells to promote Th2 polarization. Moreover, eosinophils in the thymus may contribute to immune development; therefore, Tulic et al (Am J Pathol 2009, 175: 2043-2052) examined the ontogeny of thymic eosinophils in children. They observed an age-dependent decrease in the number of eosinophils in the thymus, suggesting an early role of eosinophils in Th2 bias. These eosinophils expressed indoleamine 2,3-dioxygenase, which depletes tryptophan, resulting in activation of kynurenines and subsequent apoptosis in Th1 but not Th2 cells. Taken together, these results suggest an early immunomodulatory role for eosinophils, which may play a pivotal role in Th2 immune development.

GAGs in Bone Pathology

Mucopolysaccharidoses (MPSs) are a group of lysosomal storage diseases that result in decreased breakdown and thus increased accumulation of glycosaminoglycans (GAGs) in various tissues. GAGs have been shown to inhibit the collagenolytic activity of cathepsin K in osteoclasts; the resultant collagen accumulation leads to insufficient space for bone formation and consequent bone pathology. As MPS patients have severe deficiencies in bone growth and development, Wilson et al (Am J Pathol 2009, 175: 2053-2062) hypothesized that cathepsin K inhibition may contribute to bone pathology in MPS patients. They found that GAG expression colocalized with cathepsin K in the growth plates of a mouse model of MPS type I and that higher levels of cartilage accumulated in bone growth plates of MPS I mice than in their wild-type counterparts. In addition, cathepsin K-mediated collagen degradation was significantly reduced in osteoclasts from MPS I mice. These data suggest that increased GAG expression in MPS inhibits cathepsin K function, resulting in collagen accumulation in the bone growth plate and subsequent bone pathology.

CpG DNA Therapy for Alzheimer's Disease

Accumulation of soluble oligomeric amyloid β (oAβ) peptide leads to neurological dysfunction in Alzheimer's disease patients. Microglia cluster around senile Aβ plaques in Alzheimer's disease patients; however, the role of microglia in oAβ toxicity remains unclear. Doi et al (Am J Pathol 2009, 175: 2121-2132) discovered that microglial activation with unmethylated CpG DNA, a ligand for Toll-like receptor 9, prevented oAβ toxicity and enhanced oAβ peptide clearance in culture. Furthermore, intracerebroventricular injection of class B and C CpG DNA mitigated both cognitive impairment and learning defects in a mouse model of Alzheimer's disease. CpG DNA may therefore be a therapeutic candidate for treatment of Alzheimer's disease.

Vitronectin Receptor Inhibits Ovarian Cancer Progression

Vitronectin receptor ($\alpha_v\beta_3$-integrin) expression plays a key role in tumor progression in breast cancer and melanoma as well as in tumor angiogenesis in endothelial cells. Kaur et al (Am J Pathol 2009, 175: 2184-2196) therefore examined the function of $\alpha_v\beta_3$-integrin in ovarian cancer. In contrast to other tumor models, ovarian cancer cells that overexpressed $\alpha_v\beta_3$-integrin showed impaired invasion, protease expression, and colony formation *in vitro*; proliferated at a slower rate; and produced fewer metastatic nodules *in vivo* than control cells. Conversely, inhibiting β_3-integrin increased ovarian cancer cell invasion and proliferation, whereas high β_3-integrin expression significantly improved ovarian cancer patient prognosis. $\alpha_v\beta_3$-Integrin is therefore not an appropriate therapeutic target for ovarian cancer.