



This Month in *AJP*

MyD88 Restricts *F. tularensis* Pathogenesis

Inhalation of *Francisella tularensis* results in pneumonic tularemia, an infection associated with high mortality rates. Using mice deficient in myeloid differentiation primary response gene 88 (MyD88), a key innate immunity signaling molecule, Russo et al (*Am J Pathol* 2013, 183:1223–1232) investigated the pathological consequences of the innate immune response following *F. tularensis* infection. MyD88 knockout mice succumbed to infection faster than wild-type mice due to greater bacterial burdens in lungs and distal organs as well as the absence of IFN- γ in the lungs, spleens, and sera. Despite the absence of cellular infiltration, cell death in the lungs of MyD88 knockout mice was higher than in wild-type mice. These results highlight a previously unappreciated role for the host response during infection with virulent *F. tularensis*.

HSV-1 Targets Lymphatic Vessels in *CD118*^{-/-} Mice

Herpes simplex virus type-1 (HSV-1) induces lymphangiogenesis in the infected cornea. Bryant-Hudson et al (*Am J Pathol* 2013, 183:1233–1242) examined the impact of HSV-1 replication on lymphangiogenesis and angiogenesis using immunocompetent type I interferon (IFN) receptor-deficient (*CD118*^{-/-}) mice. Impairment of type I IFN signaling resulted in transient lymphatic vessel growth, stable blood vessel growth, extensive corneal edema, and loss of epithelial layers due to robust viral replication and skewed leukocyte recruitment. HSV-1 selectively targeted lymphatic vessels, but not blood vessels, during acute infection, underscoring the key role of the type I IFN pathway in maintaining corneal structural integrity in addition to its antiviral role.

Revisiting the Pandemic H1N1 Virus of 2009

Fatal cases of 2009 pandemic influenza H1N1 virus (2009 pH1N1) infection differ from seasonal influenza virus infections, and the host immune response to 2009 pH1N1 is poorly understood. Gao et al (*Am J Pathol* 2013, 183:1258–1268) analyzed autopsied lung tissues from fatal 2009 pH1N1 cases. Pathogenesis of the viral infection was

associated with both viral replication and production of proinflammatory mediators. In addition, FasL and caspase-3 were involved in the apoptotic process frequently observed in lung and airway tissues of 2009 pH1N1 fatal cases. The disequilibrium between Fas and FasL levels in the lung may contribute to delayed clearance of virus and subsequent pathological damage, having implications on clinical treatment strategies.

Mesangial Invasion of Alport Glomerular Capillaries

Alport syndrome results from mutations in type IV collagen genes, but the mechanism for delayed glomerular disease onset is unknown. Zallocchi et al (*Am J Pathol* 2013, 183:1269–1280) examined two mouse models and human kidney tissue to explore disease progression. Laminin accumulated in the glomerular basement membrane (GBM) in the mice. Mesangial processes invading the capillary loops of both mouse models, as well as in human Alport glomeruli, were the likely source of this laminin. Mesangial cell process invasion was enhanced by L-NAME salt-induced hypertension *in vivo*, reduced by treatment with Rac1 inhibitor or deletion of integrin $\alpha 1$ *in vitro*, and ameliorated on laminin deletion in Alport mice. These data define a role for biomechanical strain-mediated induction of mesangial cell process invasion as a key aspect of Alport glomerular disease initiation, setting the stage for novel therapeutic targets aimed at blocking this process.

OLFM4 Suppresses Prostate Cancer Progression

The olfactomedin 4 (*OLFM4*) gene is located on chromosome 13q14.3, which is frequently deleted in prostate cancer. Using various molecular techniques, Li et al (*Am J Pathol* 2013, 183:1329–1338) investigated the genetics, protein expression, and functions of *OLFM4* in prostate cancer. Patient sample and tissue array data correlated *OLFM4* deletion with prostate cancer, whereas tissue array and *in vitro* data inversely correlated *OLFM4* protein expression with advanced prostate cancer. *OLFM4* may play an important tumor suppressor role in the progression of prostate cancer and may serve as a molecular target for improving prostate cancer prognostic and therapeutic approaches.