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This Month in *AJP*

Cigarette Smoke and Alcohol Co-Exposure Decreases Airway Epithelial Cell Cilia Beating

Alcohol abuse disorders are associated with increased lung infections and exacerbations of chronic lung diseases. Although the effects of cigarette smoke are well recognized, the interplay of smoke and alcohol in modulating lung diseases is not clear. Because innate lung defense is mechanically maintained by airway cilia action and hindered by protein kinase C (PKC), Wyatt et al (**Am J Pathol 2012, 181:431–440**) examined the effects of combined exposure to smoke and alcohol on ciliary beat frequency (CBF) *in vitro*. Smoke and alcohol co-exposure activated PKCε and slowed both CBF and cilia beating, whereas a specific activator of PKCε, DCP-LA, slowed CBF following maximal PKCε activation. Further, PKCε activation by smoke and alcohol was only observed in ciliated cells, not basal bronchial epithelium. *In vivo*, no decreases in CBF were observed in PKCε knockout mice co-exposed to smoke and alcohol. These data identify PKCε as a key regulator of cilia slowing in response to combined smoke- and alcohol-induced lung injury.

α-7 nAchR Prevents Gut Barrier Failure after Severe Injury

Vagal nerve stimulation prevents intestinal barrier loss in a model of severe burn injury, which dysregulates intestinal tight junction proteins. The α-7 nicotinic acetylcholine receptor (α-7 nAchR) is necessary for the vagus nerve to modulate the systemic inflammatory response; however, the role of α-7 nAchR in mediating gut protection is unknown. Constantini et al (**Am J Pathol 2012, 181:478–486**) used *in vivo* mouse models as well as an *in vitro* model of intestinal epithelial cell and enteric glial cell (EGC) co-culture to define the ability of nicotine to improve barrier function. Nicotine injection following injury prevented burn-induced intestinal permeability and limited histological gut injury. Treatment also prevented the decreased expression and altered localization of tight junction proteins occludin and ZO-1. The barrier-protective effects of nicotine were lost in cytokine-stimulated intestinal epithelial cells when EGCs were removed from culture. Future studies of the interaction between the vagus nerve, EGCs, and the intestinal epithelium may lead to targeted therapeutics aimed at reducing gut barrier failure after severe injury.

Activated B Cells Found in Mycobacterium tuberculosis *Granulomas*

Host immune cells form a granuloma as a physical and immunological barrier that contains *Mycobacterium tuberculosis*. To understand the importance of humoral immunity in controlling *M. tuberculosis* infection, Phuah et al (**Am J Pathol 2012, 181:508–514**) characterized the B cell and plasma cell populations in infected animals. B cells were primarily present in clusters within the granuloma. These B cell clusters were found in close proximity to peripheral node addressin $(PNAd)^+$ cells, contained cells positive for the proliferation marker Ki-67, expressed CXCR5, and had elevated HLA-DR expression. Tissues containing *M. tuberculosis* bacilli had higher levels of *M. tuberculosis*-specific IgG, and plasma cells detected within the granuloma produced mycobacteria-specific antibodies. Thus, activated B cells, plasma cells, and antibodies are enriched within *M. tuberculosis* granulomas, having some characteristics of germinal centers and possibly the capacity to modulate local control of infection in tissues.

Classical BSE Prions Spread from the Gut to the Brain

Bovine spongiform encephalopathy (BSE) is a fatal neurodegenerative disease in cattle with similarities to Creutzfeldt-Jakob disease (CJD) in humans. Kaatz et al (**Am J Pathol 2012, 181:515–524**) examined the pathogenesis of BSE in the natural host on oral infection from early preclinical to terminal disease. Tissue samples collected from the gut, the central and the autonomic nervous system over the entire incubation period were examined for the presence of pathological prion protein PrP^{Sc}, followed by bioassay in cellular PrP^{C}-overexpressing transgenic mice (Tgbov XV), which lack the species barrier for bovine prions. PrP^{Sc} accumulated in the distal ileum in almost all animals, while PrP^{Sc} was found in the sympathetic nervous system starting at 16 months postinfection (mpi), and in the parasympathetic nervous system at 20 mpi. These findings decipher the centripetal spread of BSE prions along the autonomic to the central nervous system starting midway in the incubation time.

NANOG-Positive Stromal Cells Promote Human Cervical Cancer Progression

The embryonic stem cell gene *NANOG*, a divergent homeodomain transcription factor, is expressed in germ cells and several tumor types. Gu et al (**Am J Pathol 2012, 181:652–661**) examined the role of NANOG and its pseudogenes in cervical cancer. NANOG was expressed from the *NANOG* gene but was frequently localized to the cytoplasm, rather than the nucleus, in cervical cancer. Mesenchymal stem cells were identified as cytoplasmic NANOG-positive cells in cervical cancer stroma. Co-culture of cervical cancer-derived mesenchymal stem cells with SiHa human cervical cancer cells demonstrated increased proliferation characteristics *in vitro* as well as enhanced tumor growth *in vivo*. These findings provide evidence that NANOG is a cervical cancer progression marker, suggesting a starting point for a more extensive exploration of the cellular translocation of NANOG and the multifunctionality of the stromal microenvironment.