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This Month in *AJP*

Using Fluorescent Q-Dots to 3D-Reconstruct Pick Bodies

The smooth, spherical shape of Pick bodies differs from Alzheimer disease neurofibrillary tangles. Uematsu et al (Am J Pathol 2012, 180:1394–1397) immunofluorescently labeled tau-positive Pick bodies with quantum dot (QD) nanocrystals for 3D reconstruction via electron microscopy (EM) to identify QD immunolabeling on the same Pick body for comparison in detail. The identity of the QD nanocrystals, which are detectable both by fluorescence light microscopy and by EM, was confirmed via super-resolution scanning transmission EM. The exact comparison of the same structure by EM and 3D light microscopy demonstrated relevance between ultrastructural details and surrounding structures on a 3D basis. This method provides further insights into how molecules woven into specific pathological ultrastructures are at work *in situ*.

Full-Genome Dissection of an Epidemic Group A Streptococcus

An epidemic of severe invasive human infections caused by type *emm59* group A *Streptococcus* (GAS) spread across Canada from 2006 to 2008. By sequencing the genomes of 601 epidemic, historic, and other *emm59* organisms, Fittipaldi et al (Am J Pathol 2012, 180:1522–1534) identified a recently emerged, genetically distinct *emm59* clone as being responsible for this epidemic, as well as its spread into the United States. Mouse and nonhuman primate models demonstrated that the emerged clone is unusually virulent, with transmission occurring primarily by skin contact. In addition, the *emm59* strains had a significantly impaired ability to persist in human saliva, colonized the oropharynx of mice, and seldom caused human pharyngitis. This analysis illustrates how full-genome data can be used to precisely illuminate the landscape of strain dissemination during a bacterial epidemic.

FTY720 Aids Recovery after Spinal Cord Injury

Levels of the lysophospholipid mediator sphingosine-1-phosphate (S1P) increase in the spinal cord after contusion injury. To apply S1P receptor modulation to the treatment of spinal cord injury (SCI), Norimatsu et al (Am J Pathol 2012, 180:1625–1635) examined the therapeutic effects of FTY720, an S1P receptor agonist, on locomotor recovery after SCI in mice. FTY720 administered orally shortly after contusion SCI significantly improved motor function recovery, induced lymphopenia, and reduced T-cell infiltration in the spinal cord, but it did not affect early neutrophil infiltration, microglial activation, or expression of inflammatory cytokines. Vascular permeability and astrocyte accumulation were both decreased by FTY720 in the injured spinal cord. FTY720 also ameliorated motor function after SCI in mice with severe combined immunodeficiency. These data highlight the importance of immune-independent functions of FTY720 in promoting locomotor function recovery after SCI.

APP Is a Biomarker for Transformed Stem Cells

An important function of the β-amyloid precursor protein (APP) may exist in malignant disease, but its biological basis is unclear. To understand the role of APP in transformed pluripotent stem cells, Venkataraman et al (Am J Pathol 2012, 180:1636–1652) studied its expression levels in human testicular germ cell tumors. The cooperative expression of APP aligned with prominent pluripotency-related genes (*Sox2*, *NANOG*, and *Oct3/4*); however, the closest homologue family member, APLP2, showed no correlation. In addition, treatment with histone deacetylase (HDAC) inhibitors suppressed the levels of APP and stem cell markers. Loss of pluripotency was accompanied by decreased APP protein levels both *in vitro* and *in vivo*. Thus, APP represents a novel and specific biomarker in human transformed pluripotent stem cells that can be selectively modulated by HDAC inhibitors.

EPO Protects Neuroretinal Function in Ischemic Retinopathy

Retinal ischemia is a common feature of vision loss caused by diabetes, retinal vascular occlusion, and retinopathy of prematurity. Mowat et al (Am J Pathol 2012, 180:1726–1739) investigated the effects of ischemia in murine oxygen-induced retinopathy (OIR) on retinal function and neurodegeneration. OIR was associated with significant neuroretinal dysfunction as well as significantly increased apoptosis and atrophy of the inner retina. Erythropoietin (EPO) deficiency in heterozygous Epo-Tag transgenic mice led to more profound retinal dysfunction after OIR but had no measurable effect on the extent of retinal ischemia, preretinal neovascularization, or neuroretinal degeneration. Systemic administration of recombinant EPO protected EPO-deficient mice, but EPO supplementation in wild-type animals with OIR did not rescue neuroretinal dysfunction or degeneration. Therefore, endogenous EPO can protect neuroretinal function in ischemic retinopathy.