Regional Colonic Wnt Gene Expression Patterns

Wnt genes play a central role in regulating intestinal development and homeostasis. To understand further the impact of Wnt signaling, Neumann et al (Am J Pathol 2014, 184:592–599) investigated the regional heterogeneity of Wnt signaling in the proximal versus distal colon of mice raised under germ-free conditions. Analysis of 84 Wnt-mediated signal transduction genes identified differential expression signature of Wnt-related genes in the proximal versus distal murine colon. Data also showed reduced Wnt/β-catenin activity and decreased Wnt5a and Wnt11 expression in mice lacking commensal bacteria, an effect that was reversed by conventionalization of germ-free mice. Findings also suggested a role for Toll-like receptor signaling in regulating Wnt5a expression. Therefore, the morphological and physiological heterogeneity within the colon is in part facilitated by differential Wnt expression and influenced by bacterial colonization.

Novel Biomarkers for Primary Effusion Lymphoma

Primary effusion lymphoma (PEL) is a rare B-cell neoplasm characterized by Kaposi’s sarcoma-associated herpesvirus (KSHV) infection and by growth in body cavities without tumor mass formation. To identify new proteins related to PEL pathogenesis, Gloghini et al (Am J Pathol 2014, 184:618–630) performed an in-depth proteomics analysis of the secretomes of four PEL cell lines. Functional classification showed that PEL cell secretomes were enriched in proteins specifically involved in growth, development, and maintenance of the tumor microenvironment (angiogenesis and inflammation). These data provide an important resource to study PEL biology and/or facilitate the discovery of novel PEL biomarkers with potential pathogenetic significance.

Enterovirus 71 Infects the Palatine Tonsil

Enterovirus 71 (EV71), a major causative agent of hand, foot, and mouth disease, may rarely be complicated by fatal encephalomyelitis. Using autopsy tissues from seven fatal EV71 cases, He et al (Am J Pathol 2014, 184:714–720) investigated viral localization in the central nervous system (CNS) and extra-CNS organs. The CNS showed stereotypical distribution of inflammation and neuronal localization of viral antigens and RNA in all cases. In six cases for which tonsillar tissues were available, viral antigens and/or RNA localized to squamous epithelium lining the tonsillar crypts. A more significant correlation existed between viral infection and scavenger receptor B2 expression than for P-selectin glycoprotein ligand-1 expression. The tonsillar crypt epithelium may represent an important viral replication site for viral transmission.

Overload-Induced Intervertebral Disc Degeneration

Intervertebral disc (IVD) degeneration is characterized by apoptosis of nucleus pulposus cells occurring early in the disease process. Using in vitro and in vivo models of compressive loading, Yamada et al (Am J Pathol 2014, 184:753–764) elucidated the underlying mechanism of IVD degeneration and investigated apoptosis as a potential therapeutic target. In vitro nucleus pulposus cell-agarose 3D composite cultures subjected to uniaxial unconfined static compressive loading exhibited a time-dependent increase in apoptosis. Caspase 3 siRNA protected rabbits against IVD degeneration during long-term sustained compressive overload, and the imbalance in matrix-degrading enzyme production was largely dependent on caspase 3 activation. Therefore, the manipulation of local apoptotic events may constitute a simple and effective means to prevent and/or reduce IVD degeneration.

Understanding Osteoblast Recruitment in Bone Remodeling

Bone remodeling is critical for maintaining healthy and functional bones throughout life, but the origin of osteoblast (OB) progenitors in the context of diseases such as osteoporosis is unknown. By quantifying cell densities, cell proliferation, OB differentiation markers, and capillaries in iliac crest biopsies, Kristensen et al (Am J Pathol 2014, 184:778–789) assessed OB recruitment during adult cancellous bone remodeling. Recruitment took place on both reversal and bone-forming surfaces, bone formation occurred only above a given cell density, and bone remodeling compartment canopies were an important source of osteoprogenitors. Thus, canopies and nearby capillaries are likely critical for reaching the OB density required for bone formation.