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This Month in *AJP*

Diagnosing Bladder Cancer via Urinary Samples

Altered miRNA expression may occur early in bladder cancer, directing carcinogenesis and tumor behavior. Puerta-Gil et al (Am J Pathol 2012, 180:1808–1815) evaluated whether alterations in miRNA expression could improve disease stratification and outcome. Tumor miRNA expression correlated with tumor grade, size, and presence of carcinoma *in situ* (miR-222), recurrence (miR-222 and miR-143), progression (miR-222 and miR-143), disease-specific survival (miR-222), and overall survival (miR-222). Expression patterns of miRNA targets (BCL2, VEGF, ERBB3, and ERBB4) also correlated with tumor progression and/or several outcome endpoints. Furthermore, miR-452 and miR-222 detection in urine provided high accuracies for bladder cancer diagnosis, demonstrating the utility of examining miRNA expression in urinary specimens for noninvasive diagnosis.

Age Influences Injury and Repair in MS

Accumulating evidence suggests that age affects the course and prognosis of multiple sclerosis (MS). Hampton et al (Am J Pathol 2012, 180:1897–1905) used a novel MS model of focal immune-mediated demyelinating injury to show that aged adult mice exhibit both an increased vulnerability to axonal injury as well as a reduced efficiency of remyelination compared to younger animals. More importantly, remyelination in the aged animals was predominantly Schwann-cell mediated, in contrast to central oligodendrocyte-mediated remyelination in the younger rodents. Together, these findings establish an experimental platform to further study the influence of age on both injury and repair in a biologically relevant model of MS.

B-Cell Response Distinguishes Outcome in Leishmania *spp. Co-Infection*

Co-infection of C3HeB/FeJ (C3H) mice with both *Leishmania major* and *L. amazonensis* leads to a healed footpad lesion, whereas co-infection of C57Bl/6 (B6) mice leads to non-healing lesions, likely via deficient B cell responses. To clarify the mechanisms involved, Gibson-Corley et al (Am J Pathol 2012, 180:2009–2017) analyzed the draining lymph node germinal center B-cell response between co-infected C3H and B6 mice. C3H mice had more germinal center B cells, more antibody isotype-switched germinal center B cells, more memory B cells, and more antigen-specific antibody-producing cells following co-infection compared to B6 mice. These data establish a fundamental difference between these two mouse strains in the immune response to *Leishmania* infection, namely presence/absence of productive B-cell germinal center response.

CFTR *Mutation Impacts Bone Formation*

The cystic fibrosis transmembrane conductance regulator (*CFTR*) F508del mutation may be an independent risk factor for CF-related bone disease. Therefore, Le Henaff et al (Am J Pathol 2012, 180:2068–2075) evaluated bone formation and bone mass in F508del-Cftr homozygous mice (F508del $Cftr^{tm1Eur}$) and $Cftr^{+/+}$ littermate controls. F508del $Cftrt^{m1Eur}$ mice displayed reduced bone mineral density, lower femoral bone mass, and altered trabecular bone architecture, as well as decreased bone formation rate, compared to controls at all ages. Severe osteopenia and altered bone architecture were also found in young and mature adult F508del $Cftr^{tm1Eur}$ mice. These findings demonstrate that the F508del $Cftr^{tm1Eur}$ model may represent a valuable tool to examine emerging targets for the treatment of CF-related bone disease.

Redefining Glioblastoma Gene Expression Class

The Cancer Genome Atlas (TCGA) project assigns glioblastoma (GBM) to four transcriptional classes (proneural, neural, classical, and mesenchymal), but Cooper et al (Am J Pathol 2012, 180:2108–2119) hypothesized that the tumor microenvironment also has an impact. They found that the mesenchymal GBM class was enriched with samples displaying a high degree of necrosis, with transcriptional regulators of the mesenchymal transition tightly correlating with the extent of necrosis. Non-mesenchymal GBMs became more similar to the mesenchymal class with increasing levels of necrosis. In addition, C/EBP-β and C/EBP-δ were specifically expressed by hypoxic, perinecrotic pseudopalisading cells, accounting for their association with necrosis and poor prognosis and suggesting key signaling nodes for targeted therapies.