This Month in *AJP*

**Generating A Single Cell Atlas of Vestibular Schwannoma**
The mechanisms underlying tumor progression of vestibular schwannoma (VS) are unclear. Using single-cell RNA-seq on three clinically isolated VS samples and by performing bioinformatics analysis, Xu, Wang, and Jiang et al (*Am J Pathol, AJPA-D-22-00041*) studied these mechanisms. Analyses were performed to examine cell composition, cell type clustering, cell proliferation, and potential regulation and communication between cell types. Data suggest a microenvironmental mechanism underlying the development of VS. This preliminary cellular atlas of VS tissue may improve our understanding of VS tumor growth.

**Analyzing Gastric Foveolar-Type Adenoma**
The genomic features of sporadic foveolar-type adenoma (FGA) remain unclear. Using eight fresh-frozen sporadic FGA tissue samples from *Helicobacter pylori* (Hp)-naïve patients, Mishiro et al (*Am J Pathol, AJPA-D-21-00428*) studied these features. A common single nucleotide variation was observed within the DNA binding domain of the tumor suppressor gene Krüppel-like factor 4 (*KLF4*), KLF4 c.A1322C, in all cases. The transfection of mutant *KLF4* significantly suppressed the proliferation of gastric cancer cell lines compared to the wild type gene, in part through early apoptotic phase-related genes. This novel *KLF4* mutation may be responsible for the slow growth of FGA neoplasm in Hp-naïve patients.

**Understanding Liver Energy Homeostasis**
The miR-122 target SLC25A34 has been implicated in non-alcoholic fatty liver disease (NAFLD) and liver cancer; however, little is known about its function. Using cultured cells and by generating a hepatocyte-specific knockout (KO) mouse model, Roy et al (*Am J Pathol, AJPA-D-22-00143*) studied this role. Depletion of *Slc25a34* *in vitro* increased mitochondrial biogenesis, lipid synthesis, and ADP/ATP ratio whereas *Slc25a34* overexpression had the opposite effect. SLC25A34 KO mice showed exacerbated phenotypes of NAFLD after short-term fast-food diet (FFD) feeding and improved phenotype after long-term FFD feeding. This novel mouse model may help study the hepatic damage and mitochondrial changes associated with NAFLD.

**Detecting Nasopharyngeal Cancer**
Nasopharyngeal cancer (NPC) screening relies on detection of serum antibodies to Epstein-Barr virus (EBV) by immunofluorescence assay (IFA), which may suffer from observer variability. To further augment pathologist assessment as well as to scale NPC screening, Samanta and Swaminathan et al (*Am J Pathol, AJPA-D-22-00056*) used a machine learning algorithm to quantitatively characterize titers of EBV early antigen based on IF cellular staining. The hybrid
model—deep learning-fuzzy inference (DeLFI)—was clinically validated; it outperformed human evaluation and closely matched human performance. DeLFI may enable accurate and scalable population screening for NPC.

**Understanding Prostate Cancer Progression**

Toll-like receptor 3 (TLR3) is up-regulated in some castration-resistant prostate cancers (PCa); however, its role in PCa progression is unclear. Using prostate cell lines, Muresan et al (*Am J Pathol, AJPA-D-21-00639*) studied this role. *In vitro* activation of TLR3 resulted in secretion of some cytokines as well as an up-regulation of genes responsible for cell motility, migration, and invasion, which was also confirmed *in vivo* using an orthotopic xenograft model. Targeting TLR3 with an exogenous ligand led to apoptosis, with higher toxicity in TLR3-high chemoresistant PCa cells. TLR3 may be targeted to manage PCa progression and metastasis.