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This Month in *AJP*

Understanding Alcohol-Exacerbated COVID-19

Chronic alcohol use complicates the course of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—related acute respiratory distress syndrome (ARDS). To further study this link, Solopov et al **(Am J Pathol 2022, 990–1000)** developed a combined ARDS and chronic alcohol abuse mouse model. A subunit of SARS-CoV-2 spike protein was intratracheally introduced in an ethanol-fed transgenic mouse model expressing the human angiotensinconverting enzyme 2 (ACE2) receptor for SARS-CoV-2. This combinatorial model may help understand the underlying mechanisms as well as explore therapeutic interventions for alcohol-exacerbated COVID-19.

Managing Cardiac Fibrosis

The role of the key subunit of the Mediator complex—mediator 1 (MED1)—in cardiac remodeling is unclear. Fatima et al **(Am J Pathol 2022, 1016–1027)** generated a macrophage-specific *Med1* conditional deletion mouse model to understand this role. Cardiac fibrosis was chemically induced in the transgenic mice. Macrophage Med1 deficiency increased chemical-induced cardiac fibrosis via transforming growth factor-β–Smad2/3 pathway. MED1 may be targeted to manage cardiac fibrosis.

Studying Antibody-Mediated Allograft Vasculopathy

Our understanding of cardiac allograft vasculopathy (CAV) is limited by the lack of appropriate animal models. Tsuda et al **(Am J Pathol 2022, 1053–1065)** generated a novel mouse model of CAV to understand underlying mechanisms. This model allowed studying contributions of different cell types to vasculopathy and performing molecular analysis on graft specimens. This novel mouse model may help study the role of allograft- and recipient-derived cells in the development of arterial CAV lesions.

Diagnosing Chronic Myeloid Leukemia

Morphological evaluation is a key step in diagnosing chronic myeloid leukemia (CML). Using hematoxylin and eosin–stained bone marrow biopsies, Zhang and Huang et al **(Am J Pathol 2022, 1083–1091)** developed a conditional generative adversarial network (cGAN)–based model, CMLcGAN, to segment megakaryocytes from myeloid cells. The performance of CMLcGAN was compared to the existing deep learning–based segmentation models. The model was validated on whole slide images. CMLcGAN may outperform existing deep learning–based segmentation models for multiclass segmentation of bone marrow cells.

Linking Atherosclerosis and Hypercholesterolemia

Though low density lipoprotein receptor adaptor protein-1 (LDLRAP1) has been implicated in hypercholesteremia and atherosclerosis, direct causality remains unclear. Using *Ldlrap1*$^{-/-}$ mice, Leigh et al **(Am J Pathol 2022, 1092–1108)** studied the role of Ldlrap1 in atherosclerosis and insulin resistance. Loss of Ldlrap1 caused a significant increase in serum cholesterol, promoted the development of atherosclerosis, increased insulin resistance and weight gain, and deceased glucose uptake in adipocytes. LDLRAP1 may be targeted to treat diseases that jointly drive metabolic syndrome.

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