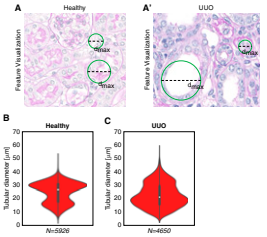
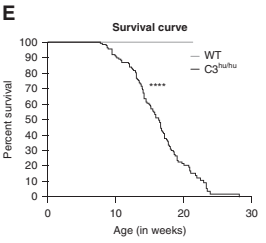
This Month's Highlights

Deep Learning Algorithms for Animal Pathology



Analyses of kidney pathology provide important outcomes-related data in animal model studies that are essential to understanding disease pathophysiology. The authors used a deep learning technique, the convolutional neural network, as a multiclass histology segmentation tool to evaluate kidney disease in animal models. This enabled rapid, automated segmentation of digital whole-slide images of periodic acid–Schiff–stained kidney tissues, allowing high-throughput analyses in multiple disease models. The network also performed well in evaluating patient samples, bridging preclinical and clinical research. Extracted quantitative morphologic features closely correlated with standard morphometric measurements. These findings indicate that deep learning–based segmentation in experimental renal pathology is a promising step toward reproducible, unbiased, and high-throughput quantitative digital pathology of the kidney. *See Bouteldja et al., pages 52–68.*

Humanized Mouse Model of C3 Glomerulopathy

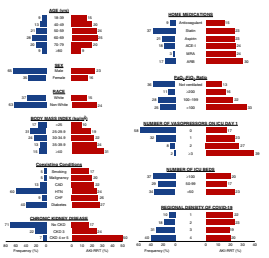


Animal models are valuable to explore factors that modulate progression of C3 glomerulopathy (C3G), which is characterized by alternative pathway hyperactivation and glomerular complement deposition. When the authors replaced the mouse *C3* gene with the human equivalent, the humanized C3 mice rapidly mimicked pathologic features of C3G patients, potentially due to dysregulated interaction of human C3 protein with mouse complement regulators. C3b and CFB blocking antibodies provide benefit, indicating that alternative pathway hyperactivation drives pathology in these mice. This model allows genetic and pharmacologic dissection of critical contributors to complement-driven renal pathology. *See Devalaraja-Narashimha et al., pages 99–114.*

Adiposity and CKD

Although diabetes and high BP explain half of the association that conventional epidemiology has found between increased body mass index (BMI) and higher risk of CKD, residual confounding factors preclude causal inferences and impede mediation assessments. A genetic approach (Mendelian randomization) may overcome these limitations. Analyses of 281,228 genotyped individuals suggest that conventional associations between central and general adiposity with CKD are largely causal. However, conventional approaches underestimate mediating roles of diabetes, BP, and their correlates. Genetic approaches suggest that these mediators explain most of adiposity-CKD–associated risk. *See Zhu et al., pages 127–137.*

AKI and Renal Replacement in COVID-19

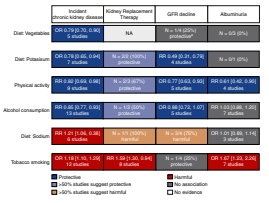


Although AKI is an important sequela of COVID-19, data on AKI treated with RRT (AKI-RRT) in patients with COVID-19 are limited. This study of 3099 adults with COVID-19 in intensive care units in the United States found that AKI-RRT is common among critically ill patients with COVID-19 and is associated with high mortality; one in five patients developed AKI-RRT, 63% of whom died during hospitalization. AKI-RRT also was associated with high mortality and persistent RRT dependence. The study also identified patient- and hospital-level risk factors for AKI-RRT and death. *See Gupta et al., pages 161–176. Also see related editorial by Wald and Bagshaw, pages 4–6.*

Phosphate Removal During Dialysis

The origin of most phosphate removed during hemodialysis has been uncertain. The authors used phosphorus (^{31}P) magnetic resonance spectroscopy to quantify intracellular inorganic phosphate (Pi), phosphocreatine, and ATP kinetics in 11 patients with ESKD during a 4-hour hemodialysis treatment. They confirmed that Pi is, at least partially, released by the intracellular compartment, which raises the possibility that excessive dialytic removal of phosphate might adversely affect the intracellular availability of high-energy phosphates and ultimately, cellular metabolism. *See Chazot et al., pages 229–237.*

Lifestyle Factors and CKD



Although CKD incidence is increasing, there are no evidence-based lifestyle recommendations for CKD primary prevention. In a systematic review and meta-analysis that included 104 observational studies of 2,755,719 participants, the authors found consistency of evidence for a number of measures associated with preventing CKD onset, including increasing dietary intake of vegetables and potassium, increasing physical activity, moderating alcohol consumption, lowering sodium intake, and stopping tobacco smoking. In the absence of clinical trial evidence, these findings can help inform public health recommendations and patient-centered discussions in clinical practice about lifestyle measures to prevent CKD. *See Kelly et al., pages 239–253.*