Characterizing iPSC-Derived Kidney Cells and Organoids

The relative accuracy with which kidney organoids generated from human induced pluripotent stem cells (iPSCs) model normal morphogenesis, and the maturity and identity of the renal cell types they comprise, remain to be fully investigated. Vanslambrouck et al. describe the generation and validation of 10 fluorescent CRISPR/Cas9 gene-edited iPSC reporter lines specifically designed for the visualization, isolation, and characterization of cell types and states within kidney organoids, and demonstrate the use of these lines for cellular isolation, time-lapse imaging, protocol optimization, and lineage-tracing applications. These tools offer promise for better understanding this model system. See Vanslambrouck et al., pages 1811–1823.

Machine Learning and Kidney Pathology

Advances in machine learning, particularly the development of deep neural networks, offer the potential to automate and enhance histopathological assessment of kidney tissue and discern patterns and novel features pertinent to disease progression and prognosis. In this issue of JASN, two articles describe use of convolutional neural networks as a tool for such assessment. In one study, Ginley et al. used image analysis and machine-learning algorithms to digitally classify biopsy samples from 54 patients with diabetic nephropathy, finding substantial agreement between digital classifications and those made by three different pathologists. Their findings demonstrate that digital processing of renal tissue may augment traditional clinical diagnostics. In the second study, Hermsen et al. trained and validated a convolutional neural network for histological analysis in kidney tissue sections stained by periodic acid–Schiff. They assessed segmentation performance for multiple tissue classes on 10 transplant biopsies, as well as on 10 biopsies from an external center for validation. Their findings demonstrate applicability of such networks for tissue from multiple centers, for biopsies and nephrectomy samples, and for the analysis of both healthy and pathologic tissues. In addition, they validated the network’s results with components from the Banff classification system. Their convolutional neural network may have utility for quantitative studies involving kidney histopathology across centers and potential for application in routine diagnostics. See Ginley et al., pages 1953–1967, and Hermsen et al., pages 1968–1979. Also see related editorial by Lemley, pages 1780–1781.

GWAS Loci and Diabetic Kidney Disease

Searches for genetic determinants of diabetic kidney disease have had limited success. In this study, a new international genomics consortium assembled nearly 20,000 samples from participants with type 1 diabetes, with and without kidney disease. Salem et al. found 16 new diabetic kidney disease–associated loci at genome-wide significance. The strongest signal centers on a protective missense coding variant at COL4A3, a gene that encodes a component of the glomerular basement membrane that, when mutated, causes the progressive inherited nephropathy Alport syndrome. These GWAS-identified risk loci may provide insights into the pathogenesis of diabetic kidney disease and help identify potential biologic targets for prevention and treatment. See Salem et al., pages 2000–2016.

Transplant and Outcomes for HCV-Viremic Kidneys

After the advent of direct-acting hepatitis C virus (HCV) treatments, small trials demonstrated good outcomes for transplanting HCV-viremic kidneys into recipients without HCV, who were then treated for the infection. Using registry data, Potluri et al. show that transplantation of HCV-viremic kidneys into recipients without HCV infection has increased dramatically since 2015, and that HCV-viremic kidney recipients have excellent kidney function at 12 months posttransplant. Kidneys from donors with HCV viremia function well and are a valuable resource for transplant candidates with or without HCV. See Potluri et al., pages 1939–1951.

Selonsertib in Diabetic Kidney Disease

In a randomized placebo-controlled phase 2 trial in patients with moderate-to-advanced diabetic kidney disease, Chertow et al. found that selonsertib, a selective inhibitor of apoptosis signal-regulating kinase 1 (ASK1), had no dose-dependent adverse effects over 48 weeks. Although the trial did not meet its primary efficacy end point (eGFR change from baseline to week 48), acute effects related to inhibition of creatinine secretion by selonsertib confounded differences in eGFR. Exploratory post hoc analyses accounting for these effects suggest that selonsertib resulted in a dose-dependent reduction in kidney function decline and merits further study. See Chertow et al., pages 1980–1990.