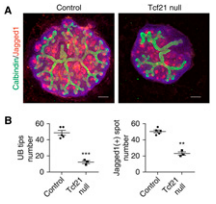
This Month's Highlights

BASIC RESEARCH

Transcription Factor 21 and Kidney Development

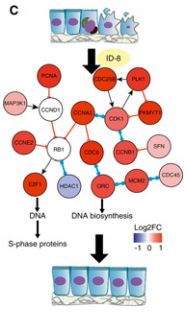


Branching morphogenesis of the ureteric bud is central to forming a normal kidney, and the most severe forms of congenital anomalies of the kidney and urinary tract (CAKUT) arise from mutations in genes involved in branching. Ide *et al.* report that deletion in mice of *transcription factor 21* (*Tcf21*) results in a spectrum of renal developmental phenotypes that resemble human CAKUT. Germline or specific deletion of *Tcf21* from the stromal mesenchyme results in branching defects and reduced expression of *Gdnf-Ret-Wnt11* (a key pathway for branching morphogenesis). *Tcf21* deletion from the cap mesenchyme results in glomerular defects and no *Gdnf-Ret-Wnt11* downregulation. These findings point to a central role for Tcf21 in regulating the Gdnf axis and renal stromal factors crucial for branching. *See Ide et al., pages 2795–2808.*

Genetics of Atypical Hemolytic Uremic Syndrome

Atypical hemolytic uremic syndrome (aHUS) is caused by complement dysregulation; however, mutations are not identified in complement genes in half of patients. After screening aHUS patients and controls for variation in 93 complement and coagulation genes, Bu *et al.* identified six genes with rare variants that are more likely in aHUS patients than in controls, including *VTN* (a gene not previously identified as relevant to aHUS). They also highlighted specific protein domains in three of these variants as aHUS-related. They propose a minor allele frequency threshold of 0.1% for a variant to be considered as possibly disease relevant. These data may help in directing clinical management of aHUS patients. *See Bu et al., pages 2809–2819.*

ID-8 Stimulates Tubular Proliferation



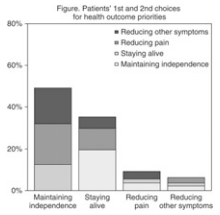
One potential strategy for treating AKI is stimulating proximal tubular epithelial cell proliferation. Monteiro *et al.* used high-throughput screening to identify ID-8, an inhibitor of dual specificity tyrosine-phosphorylation-regulated kinase 1A (DYRK1A), a first-in-class compound that stimulates kidney tubular epithelial cell proliferation after different types of acute damage in two- and three-dimensional *in vitro* models. They also provide *in vitro* evidence that ID-8 also can bind DYRK1A in human proximal tubular epithelial cells and stimulate proliferation after injury by upregulating cell cycle mediators. This early-stage discovery study identifies ID-8 as a potential therapeutic candidate to stimulate kidney epithelial cell regeneration and repair following AKI. *See Monteiro et al, pages 2820–2833.*

CLINICAL RESEARCH

CVD and Atrial Fibrillation in CKD Patients

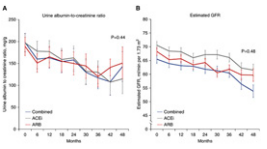
Atrial fibrillation is linked with an increased risk of ischemic stroke and death in patients with dialysis-treated ESRD; less is known about outcomes associated with atrial fibrillation among CKD patients who do not require dialysis. To evaluate whether development of this arrhythmia is linked with other important cardiovascular outcomes among adult nondialysis patients with CKD, Bansal *et al.* studied a large, well-characterized, longitudinal cohort of such patients, finding that incident atrial fibrillation was independently associated with two-fold to five-fold increased risks of developing subsequent heart failure, myocardial infarction, stroke, or death. These findings have important implications for cardiovascular risk reduction in patients with CKD. *See Bansal et al., pages 2859–2869.*

Health Outcome Priorities in CKD



Although older adults with advanced CKD carry a substantial burden from disease-related symptoms and disability and often have to accept trade-offs in their treatment, little is known about these patients' health outcome priorities or their nephrology providers' perceptions of these priorities. Ramer *et al.* found that more of these patients prioritize maintaining independence over staying alive, and that these priorities are associated with what patients would find acceptable toward the end of life. Nephrology providers, however, tend to show limited awareness of which health outcomes their individual patients value most. The gap in understanding is a barrier to effective participation of nephrology providers in more patient-centered decision making about initiation of maintenance dialysis and other interventions. *See Ramer et al., pages 2870–2878.*

RAS Inhibition in Albuminuria and Cardiovascular Risk



Whether use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) alone or together prevents mortality or ESRD in people with albuminuria and cardiovascular risk factors is uncertain. Saglimbene *et al.* describe findings from a multicenter randomized clinical trial involving 1243 evaluable patients with moderate or severe albuminuria and cardiovascular risk. Although the trial was stopped early with low power due to slow enrollment, it found that ACE inhibitors or ARBs used alone or in combination appear to result in similar cardiovascular and renal outcomes. ACE inhibitor and ARB treatment may yield similar outcomes in people with albuminuria and cardiovascular risk factors, although ARB monotherapy may be better tolerated. *See Saglimbene et al., pages 2890–2899.*