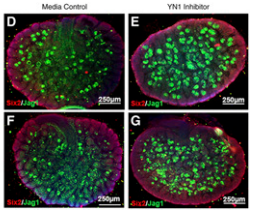
This Month's Highlights

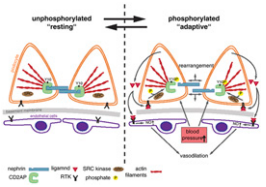
BASIC RESEARCH

Von Hippel-Lindau Protein in Nephron Development



Nephron progenitors are particularly metabolically active; as development progresses, they undergo differentiation after switching from relying primarily on glycolysis to mitochondrial respiration for energy. To study the potential role in this metabolic shift of von Hippel-Lindau (VHL), a protein component of a ubiquitin ligase complex, Cargill *et al.* generated nephron progenitor cell–specific VHL knockout mice. In addition to identifying VHL as a critical regulator of nephron progenitors' metabolic switching, they demonstrate that this switch also plays a large role in the differentiation process and suggest that VHL is required for normal kidney development. *See Cargill et al., pages 1192–1205.*

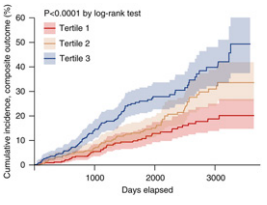
Slit Diaphragm Stability and Scaffolding Protein CD2AP



The connection between the slit diaphragm and actin network of podocyte foot processes involves signaling between slit diaphragm proteins and multiple signaling pathways of the actin machinery. Tossidou *et al.* define CD2AP, a slit diaphragm–associated scaffolding protein, as a phosphorylation target of receptor tyrosine kinases stimulated by VEGF-A in podocytes. They demonstrated that phosphorylation of tyrosine at position Y10 of the SH3-1 domain of CD2AP can change CD2AP's affinity to nephrin, and is indispensable for CD2AP function and slit diaphragm functionality *in vivo*, findings that implicate CD2AP phosphorylation as a molecular target in proteinuric kidney diseases. *See Tossidou et al., pages 1220–1237.*

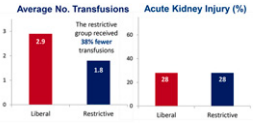
CLINICAL RESEARCH

Impaired Osmoregulation and Kidney Transplant Outcome



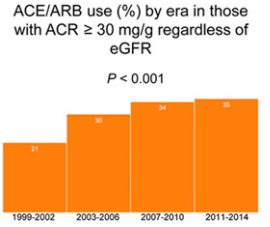
Kidney transplant recipients may have impaired urine dilution capability, but it is unclear what effects alterations in osmoregulation (changes that are subtler than hyponatremia) may have on outcomes. In a large single-center prospective cohort of kidney transplant recipients, Mazloum *et al.* found that most transplant recipients (unlike healthy controls) did not maintain constant plasma sodium during sustained water loading. The magnitude of this osmoregulation defect independently predicted deterioration of kidney function and allograft loss. Understanding the basis of defective osmoregulation may point to therapeutic targets to prevent kidney allograft dysfunction. *See Mazloum et al., pages 1282–1293, and related editorial by Bichet, pages 1141–1143.*

Red Blood Cell Transfusion and AKI



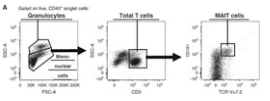
Safely reducing red blood cell transfusions could prevent transfusion-related adverse effects. Both anemia and transfusion may harm the kidney, but how reducing transfusions might affect AKI risk is unknown. In a substudy by Garg *et al.* of 4531 patients undergoing cardiac surgery with cardiopulmonary bypass, patients were randomized to a restrictive approach for receiving red blood cell transfusion (transfuse if hemoglobin <7.5 g/dL) or a more liberal approach (transfuse if hemoglobin <9.5 g/dL). Patients in the restrictive group received 38% fewer transfusions compared with the liberal group (1.8 versus 2.9 transfusions, on average, respectively). Both approaches were equally safe with respect to AKI risk. Results were similar in patients with preoperative CKD. *See Garg et al., pages 1294–1304, and related editorial by Macdougall and Richards, pages 1143–1144.*

ACE Inhibitor/ARB Use in CKD Stagnant in Recent Years



Despite being mainstays of treatment in CKD, frequency of use of angiotensin-converting enzyme (ACE) inhibitor and angiotensin II receptor blocker (ARB) medications has not been well characterized in this population. Murphy *et al.* report that nationally representative data from 1999 to 2014 show that overall ACE/ARB use during this period was only 34.9% among those with CKD; use rose from 25.5% to 40.1% during that time, but appeared to level off after the early 2000s. ACE/ARB use in CKD was consistently the exception unless concomitant illnesses like diabetes mellitus were present. This suggests that a significant opportunity exists for improving care in community-based CKD. *See Murphy et al., pages 1314–1321.*

Mucosal-Associated Invariant T Cells in CKD Fibrosis



Mucosal-associated invariant T (MAIT) cells are emerging as key players in chronic inflammatory diseases; their role in CKD's hallmark fibrosis is unclear. Law *et al.* identified tissue-resident MAIT cells in healthy kidneys and demonstrated that absolute numbers of activated tissue-resident MAIT cells within the tubulointerstitial compartment of fibrotic human kidneys correlate with severity of interstitial fibrosis. In an *in vitro* mechanistic model of human renal fibrosis, hypoxia-damaged proximal tubular epithelial cells were potent drivers of MAIT cell activation and cytotoxicity within the inflammatory and fibrotic microenvironment. These findings suggest that kidney MAIT cells are a potential therapeutic target in CKD. *See Law et al., pages 1322–1335, and related editorial by Sawitzki, pages 1145–1146.*