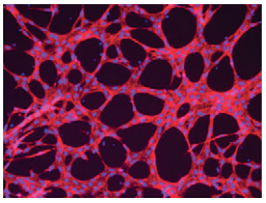
This Month's Highlights

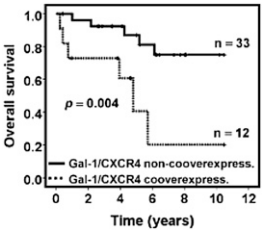
BASIC RESEARCH

Kidney-Targeted Inhibition of Hypoxia-Induced Damage



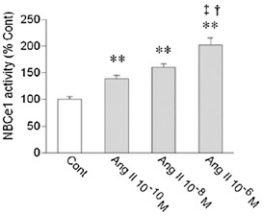
Activation of exchange protein activated by cAMP (Epac) protects proximal tubular epithelial cells from ischemic and toxic injury *in vitro* and *in vivo*. In this issue, Stokman *et al.* show that pharmacologic activation of Epac *in vitro* reduces mitochondrial production of reactive oxygen species after hypoxia. In mice, systemic administration of a proximal tubule-targeted activator of Epac before ischemia-reperfusion injury attenuates oxidative stress and prevents renal injury and failure. Such activation of Epac may have therapeutic potential for preventing renal damage induced by oxidative stress. *See Stokman et al., pages* 1474–1485.

Galectin-1 Promotes Tumorigenesis of Renal Cell Carcinoma



Upregulated expression of galectin-1 enhances tumor growth and progression in many tumor types, and galectin-1 may be a biomarker of renal cell carcinoma (RCC). Here, Huang *et al.* report the results of *in vitro* and *in vivo* studies that suggest galectin-1 promotes RCC tumorigenicity and angiogenesis through upregulation of CXCR4. In patients with RCC, galectin-1 expression levels correlated with CXCR4 expression levels and associated inversely with overall and disease-free survival times. These data support galectin-1 as a marker of RCC outcomes and indicate future studies should examine galectin-1 as a therapeutic target in RCC. *See Huang et al., pages* 1486–1495.

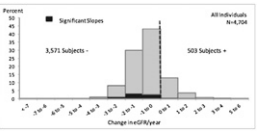
Species-Specific Effects of Angiotensin II



Does angiotensin II (Ang II) regulate renal proximal tubule sodium transport in a biphasic manner in humans as it does in other species? Here, Shirai *et al.* report that Ang II dose-dependently stimulates transport in isolated human proximal tubules through type 1 Ang II receptor-mediated signaling. Furthermore, the nitric oxide/cGMP pathway downstream of Ang II stimulates transport in human proximal tubules, but inhibits transport in murine proximal tubules, perhaps explaining the species-specific responses to Ang II. These results suggest the feasibility of targeting renal Ang II in human hypertension. *See Shirai et al., pages* 1523–1532.

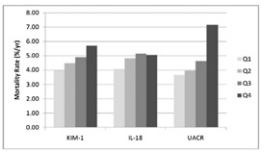
CLINICAL EPIDEMIOLOGY

Factors Associated with CKD in a Founder Population



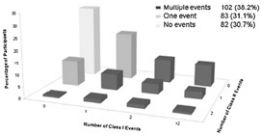
The clinical and genetic factors underlying geographic differences in the prevalence of CKD remain incompletely defined. Pani *et al.* examined the relationship between CKD prevalence and risk factors, including a novel genetic risk score, in a large Sardinian founder population. They found a high prevalence (15.5%) of CKD, and report that genetic risk score, increasing age, and sex each associated independently with CKD, change in eGFR, and fast eGFR decline in this population, whereas additional risk factors had varying associations with these outcomes. These results expand our understanding of the factors contributing to world-wide variations in CKD prevalence. *See Pani et al., pages* 1533–1544.

Urinary Biomarkers, Cardiovascular Disease, and Mortality



Can markers of tubular injury predict all-cause mortality or cardiovascular disease? Sarnak *et al.* analyzed data from an observational study of 3010 individuals with a median follow-up of >12 years to address this question. In adjusted models, albuminuria associated with both all-cause mortality and cardiovascular disease, urinary kidney injury molecule-1 associated with all-cause mortality, and urinary IL-18 did not associate with either outcome. Future studies should determine the bases for these differential associations and evaluate the prognostic potential of these markers in the context of CKD. *See Sarnak et al., pages* 1545–1553.

Adverse Safety Events in CKD



Whether the biology of CKD and CKD-specific medical treatments cause inadvertent injury in patients is largely unstudied. Ginsberg *et al.* have begun to assess the effects of such adverse safety events through cross-sectional analysis of data from the observational Safe Kidney Care study of patients with predialysis CKD. Using a data-mining technique, the authors determined the incidences and co-occurrences of patient-reported adverse safety events attributed to medicine and actionable adverse safety events detected at study evaluations. Overall, their results suggest ambulatory patients with CKD are vulnerable to harm associated with disease biology and treatment, and highlight the need to assess the effects of these events on patient outcomes. *See Ginsberg et al., pages* 1564–1573.