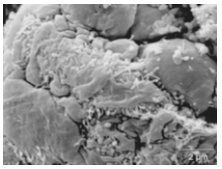
This Month's Highlights

BRIEF COMMUNICATION

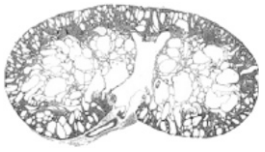
Cdc42 Critical to Podocyte Structure



Rho family GTPases modulate cytoskeletal dynamics, but whether they are required for normal podocyte physiology is unknown. In this issue, Scott *et al.* report that mice with podocytes deficient in the Rho GTPase Cdc42 develop congenital nephropathy with deranged slit diaphragms and die soon after birth from ESRD, but mice with podocytes deficient in Rac1 or RhoA have a normal phenotype. The authors found that Cdc42 deficiency impairs actin polymerization at sites of nephrin aggregates and disturbs cell polarity. These data suggest that the Rho GTPase Cdc42 is critical for normal podocyte structure and function. See *Scott et al., pages* 1149–1154.

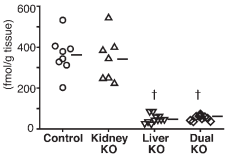
BASIC RESEARCH

AKI Provides Clues to Cystogenesis



AKI promotes cystogenesis, suggesting that biological processes associated with AKI may provide clues regarding the pathogenesis of polycystic kidney disease (PKD). In this issue, Zhou *et al.* report that inducing or inhibiting the activity of the renoprotective enzyme heme oxygenase slows or promotes cystogenesis, respectively, in a mouse model of ARPKD. Expression of the complement component C3, which heme oxygenase modulates, strongly correlates with cystogenesis. These data suggest that inhibiting C3 or promoting the activity of heme oxygenase may have therapeutic potential in PKD. See *Zhou et al., pages* 1161–1171.

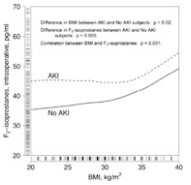
Liver Supplies Source of Renal Angiotensin II



Where does renal angiotensin II (AngII) come from? Matsusaka *et al.* observed that mice with kidney-specific knockout of angiotensinogen have levels of both renal angiotensinogen and AngII that are similar to controls, suggesting an extra-renal source. Liver-specific knockout of angiotensinogen, however, nearly eliminates these proteins from the plasma and kidney. Furthermore, they found that the generation of renal AngII depends on the reabsorption of filtered angiotensinogen by the proximal tubule. These data suggest that liver-derived angiotensinogen is the primary source of renal angiotensinogen and AngII and that proteinuria could increase renal AngII by delivering excess angiotensinogen to the proximal tubule. See *Matsusaka et al., pages* 1181–1189.

CLINICAL EPIDEMIOLOGY

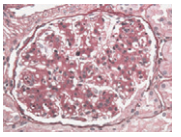
Obesity Increases Risk for Postoperative AKI



Obesity associates with increased oxidative stress, endothelial dysfunction, and inflammation, which could contribute to postoperative AKI. Billings *et al.* investigated the relationship between body mass index (BMI) and postoperative AKI among 445 patients who underwent cardiac surgery, 25% of whom developed AKI. The authors report that each BMI increment of 5 kg/m^2 independently associated with 27% higher odds of AKI. Adjusting for biomarkers of oxidative stress eliminated this association, but adjusting for biomarkers of inflammation or anti-fibrinolysis did not. These data suggest that obesity does increase the risk for postoperative AKI and that oxidative stress may partially mediate this association. See *Billings et al., pages* 1221–1228.

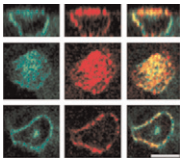
CLINICAL RESEARCH

Histologic Changes Following Eculizumab Therapy



Eculizumab is a humanized monoclonal antibody that inhibits the terminal complement pathway, suggesting that it may benefit C3 glomerulopathies. In this issue, Herlitz *et al.* describe renal histology before and after 1 year of eculizumab therapy among five patients with these disorders. Three patients exhibited a reduction in disease activity, one did not significantly change, and one had persistent activity and worsening chronic changes. Furthermore, *de novo* appearance of IgG-κ in the distribution of C3 and C5b-9 mimicked monoclonal immunoglobulin deposition disease. The efficacy and safety of this therapy requires further investigation for these glomerulopathies. See *Herlitz et al., pages* 1229–1237.

Mutation Elucidates AE1 Trafficking



Mutations that mislocalize the basolateral chloride-bicarbonate exchanger AE1 cause autosomal dominant distal renal tubular acidosis (ddRTA), but the molecular characteristics that govern AE1 trafficking are incompletely understood. Fry *et al.* identified a family with ddRTA resulting from a mutation in the C terminus of AE1. In polarized cells, the mutant AE1 retains its anion-exchange function but targets both the apical and basolateral membranes. The mutation introduces a class 1 PDZ ligand domain, which may be responsible for this abnormal localization. In addition to providing a mechanistic basis for disease, these observations provide insight into the control of AE1 trafficking. See *Fry et al., pages* 1238–1249.