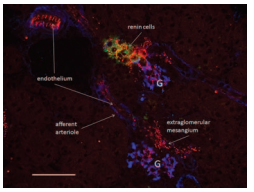
This Month's Highlights

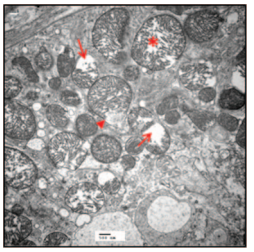
BASIC RESEARCH

Connexin 40 Mutant Causes Renin-Dependent Hypertension



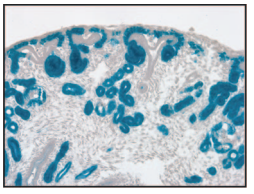
Polymorphisms in the human gene encoding the gap-junction-forming protein connexin 40 (Cx40) associate with hypertension, but the underlying mechanism is unknown. Lubkemeier *et al.* generated mice homozygous for one of these mutations (A96S) and found that they are hypertensive and have sixfold higher concentrations of plasma renin. The renin-expressing cells are located outside of their normal location in the media layer of the afferent arterioles, resulting in continued renin secretion despite any increases in renal perfusion pressure. These results suggest that the A96S mutation in Cx40 leads to renin-dependent hypertension as a result of aberrantly localized renin-secreting cells. *See Lübkemeier et al., pages 1031–1040.*

Mitochondria-targeted Peptide Protects Against Ischemic Injury



Reperfusion of tissues after ischemic injury can open mitochondrial permeability transition pores, increasing production of damaging reactive oxygen species and decreasing ATP synthesis. In this issue, Szeto *et al.* explored whether SS-31, a peptide that can inhibit these processes by specifically targeting the inner mitochondrial membrane, protects against ischemic renal injury. They report that SS-31 has many renoprotective effects in a rat model of ischemia-reperfusion injury, including improved mitochondrial function, accelerated recovery of ATP, reduced apoptosis of tubular cells, and decreased oxidative stress and inflammation. Their data suggest that SS-31 has therapeutic potential for acute kidney injury. *See Szeto et al., pages 1041–1052.*

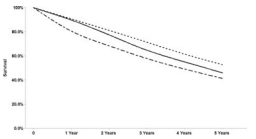
MicroRNAs Modulate Kidney Development



Nephrogenesis requires an orchestrated sequence of events, which includes upregulation and downregulation of specific genes at precise times. Because microRNAs (miRNAs) can modulate gene expression, Ho *et al.* studied their role in kidney development. In this issue, they report that several highly expressed miRNAs target the pro-apoptotic protein Bim during nephrogenesis. Furthermore, loss of miRNAs in nephron progenitors increases apoptosis and the early depletion of this population of cells. These data suggest that miRNAs may control apoptosis during kidney development, likely through the modulation of Bim expression in nephron progenitors. *See Ho et al., pages 1053–1063.*

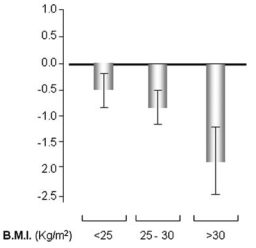
CLINICAL EPIDEMIOLOGY

Catheters Explain Mortality Difference Between Dialysis Modalities



Several studies suggest superior survival for patients treated with peritoneal dialysis (PD) compared with hemodialysis (HD) during the first 1 to 2 years after reaching ESRD, but the reasons for this are unknown. Analyzing data from >40,000 incident dialysis patients, Perl *et al.* found that 1-year morality is similar between PD patients and HD patients who initiate dialysis with an arteriovenous fistula or graft, but mortality is 80% higher for HD patients with a central venous catheter. These data suggest that the use of catheters in incident HD patients may largely explain the survival benefit previously attributed to PD. *See Perl et al., pages 1113–1121.*

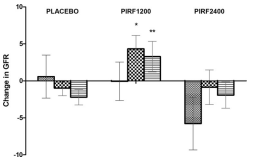
Ramipril is Renoprotective in Obesity



Obesity may increase the risk for CKD and its progression, but whether inhibitors of the renin-angiotensin system (RAS) are renoprotective in this population is unknown. In a post hoc analysis of the Ramipril Efficacy in Nephropathy (REIN) trial, Mallamaci et al. found that the incidence rate of ESRD is highest among obese patients compared with both overweight patients and those with normal body mass index (BMI). Ramipril reduces proteinuria and the rate of renal events in all BMI subgroups, but the magnitude of renoprotection is highest among the obese. These data suggest that obese patients are at greater risk for adverse renal events but RAS inhibitors may abrogate this risk. *See Mallamaci et al., pages 1122–1128.*

CLINICAL RESEARCH

Pirfenidone May Benefit Diabetic Nephropathy



Animal models suggest that the antifibrotic compound pirfenidone may benefit diabetic nephropathy, but human data are lacking. Here, Sharma *et al.* report results from a randomized, double-blind, placebo-controlled pilot study involving 77 subjects with diabetic nephropathy and albuminuria. Among the 52 subjects who completed the 54-week trial, the mean estimated GFR was significantly higher in the group receiving pirfenidone 1200 mg/d compared with placebo. Gastrointestinal effects and fatigue were the most common symptoms leading to discontinuation of the drug. Although larger trials are necessary to confirm this apparent renoprotective effect, pirfenidone may hold promise as a new therapy for diabetic nephropathy. *See Sharma et al., pages 1144–1151.*