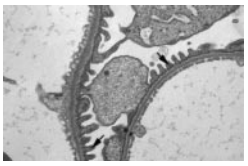
This Month's Highlights

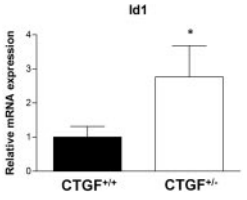
BASIC RESEARCH

Stressed Podocytes Promote Diabetic Nephropathy



Excessive production of reactive oxygen species (ROS) seems to play a role in the pathogenesis of diabetic nephropathy, but the specific sites of ROS-mediated damage are not completely understood. Zheng *et al.* used a double-transgenic strategy to show that podocyte-specific overexpression of the antioxidant metallothionein reduces podocyte damage, lessens the expansion of glomerular and mesangial volume, and delays the onset of proteinuria in the setting of diabetes. These data suggest that antioxidant protection of podocytes may delay or prevent diabetic nephropathy. *See Zheng et al., pages 2077–2085.*

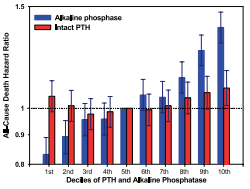
CTGF Inhibits BMP Signaling in Diabetic Kidneys



How connective tissue growth factor (CTGF) contributes to the development of diabetic nephropathy is unknown. Nguyen *et al.* report that CTGF inhibits signaling activity of the renoprotective molecule bone morphogenetic protein 7 (BMP-7). *In vivo*, upregulation of CTGF in the diabetic kidney reduces BMP-7–induced gene transcription, matrix metalloprotease activity, thickening of the glomerular basement membrane, and proteinuria. These data suggest that CTGF modulation of BMP-7 contributes to the pathogenesis of several characteristic features of diabetic nephropathy. *See Nguyen et al., pages 2098–2107.*

CLINICAL EPIDEMIOLOGY

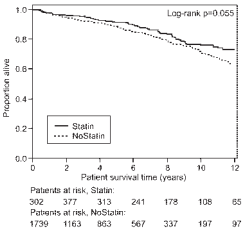
Alkaline Phosphatase Predicts Mortality



Practice guidelines recommend a target range for serum calcium, phosphorus, and parathyroid hormone (PTH) but not for serum alkaline phosphatase, which is a biochemical marker of bone turnover. Regidor *et al.* studied a cohort of 74,000 hemodialysis patients and found that serum alkaline phosphatase levels ≥120 U/L are associated with a 25% increased risk for death, even after adjusting for multiple confounders. Furthermore, rising alkaline phosphatase levels within the first 6 mo of dialysis are associated with increased mortality during the subsequent 2.5 yr. These results call for prospective trials to evaluate the incorporation of alkaline phosphatase measurement into treatment algorithms. *See Regidor et al., pages 2193–2203.*

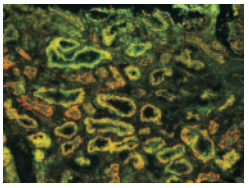
CLINICAL RESEARCH

Statins Benefit Kidney Transplant Recipients



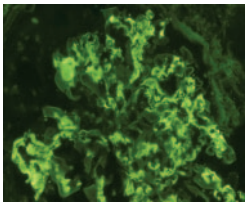
Hyperlipidemia predicts cardiovascular morbidity and mortality among recipients of kidney transplants, but whether lipid-lowering therapy benefits this population has not been established. Wiesbauer *et al.* retrospectively studied more than 2000 recipients of a first kidney transplant and found that statin use is associated with a significantly reduced risk for all-cause mortality. The authors did not identify a significant improvement in graft survival among users of statins. In the absence of randomized, controlled trials, these observational data support the use of statins after renal transplantation. *See Wiesbauer et al., pages 2211–2218.*

ER Stress in Diabetic Nephropathy



The endoplasmic reticulum (ER) gets "stressed" when its capacity to fold proteins is overwhelmed. The induction of "unfolded protein response" genes to handle the extra workload occurs, but apoptosis ensues when the response is inadequate. Lindenmeyer *et al.* report upregulation of these genes in kidney biopsy specimens from patients with mild diabetic nephropathy compared with control kidneys and their corresponding products localize to the tubular epithelia. *In vitro*, exposure of tubular epithelial cells to albumin and high concentrations of glucose increases expression of genes involved in ER stress. These results suggest that proteinuria and hyperglycemia induce ER stress, which triggers an adaptive response, but continued exposure drives tubular cells toward apoptosis. *See Lindenmeyer et al., pages 2225–2236.*

Spotlight on C1q Nephropathy



In 1985, Jennette and Hipp originally described the clinicopathologic entity C1q nephropathy. In this issue, Vizjak *et al.* report that this disease comprises two predominant subsets: A disorder of podocytes, which typically presents clinically as nephrotic syndrome with biopsy findings of minimal change disease or FSGS, or an immune-complex disease, which typically presents as chronic kidney disease. Clinical outcomes are heterogeneous, but these clinicopathologic data should help predict prognosis for patients with this uncommon disease. *See Vizjak et al., pages 2237–2244.*