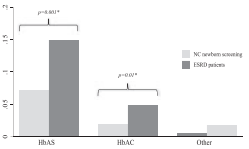
This Month's Highlights

BRIEF COMMUNICATION

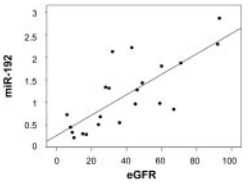
Sickle Cell Trait More Prevalent in ESRD



Sickle cell trait is a potential risk factor for kidney disease. Here, Derebail *et al.* investigated the prevalence of sickle cell trait among black patients with ESRD compared with the general population. In this cross-sectional study, sickle cell trait (HbAS) and hemoglobin C trait (HbAC) both were twice as common among those with ESRD compared with the general population. Although this study cannot address cause, these results suggest that being heterozygous for these hemoglobinopathies may not be benign and call for further study. *See Derebail et al., pages 413–417.*

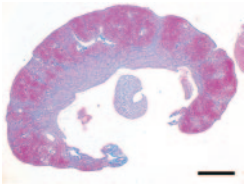
BASIC RESEARCH

MicroRNA Modulates Fibrosis in Diabetic Nephropathy



MicroRNAs are endogenous RNA oligonucleotides that regulate gene expression. Here, through microRNA profiling, Krupa *et al.* report that low levels of a specific microRNA (miR-192) correlate with more extensive tubulointerstitial fibrosis in biopsies of human diabetic nephropathy and with lower estimated GFR. *In vitro*, treatment of proximal tubular cells with the profibrotic cytokine TGF-β decreases miR-192; conversely, overexpression of miR-192 counteracts TGF-β–induced downregulation of E-cadherin. These observations suggest that microRNAs modulate renal fibrosis in diabetic nephropathy. *See Krupa et al., pages 438–447.*

MicroRNAs Maintain JG Cells



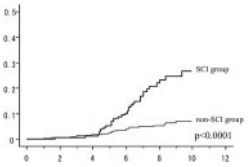
How do the renin-secreting juxtaglomerular (JG) cells maintain their unique identity and precise location in the glomerular afferent arterioles? Sequeira-Lopez *et al.* hypothesized that microRNAs may play a role, because these oligonucleotides can regulate gene expression in a spatiotemporal manner. They found that conditional knockout of *Dicer*, which produces mature microRNAs, reduces the number of JG cells and decreases both renin expression and BP. Furthermore, the resultant kidneys exhibit abnormal vasculature and striped fibrosis. These observations demonstrate that microRNAs maintain JG cells, which in turn support normal kidney structure and function. *See Sequeira-Lopez et al., pages 460–467.*

ZONAB Flips the Proliferation Switch

The signals that regulate epithelial proliferation and differentiation are important to renal development, tissue repair, and carcinogenesis. Here, Lima *et al.* identify the transcription factor ZONAB as a regulator of the transition between epithelial proliferation and differentiation in the kidney and demonstrate that megalin and cubulin are target genes. Furthermore, ZONAB seems to be a component of the system that modulates cellular events on the basis of sensing of epithelial density. These data improve our understanding of fundamental cellular processes with broad application, potentially opening new avenues to study nephrogenesis and tubular regeneration after injury. *See Lima et al., pages 478–488.*

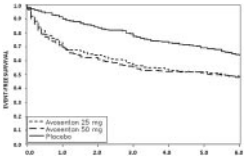
CLINICAL RESEARCH

A Brain–Kidney Connection in Diabetic Nephropathy



Diseased small arteries may contribute to the progression of diabetic nephropathy, but how to assess the vascular beds of the kidney is not well established. Uzu *et al.* hypothesized that evidence of vascular abnormalities in the brain may predict renal morbidity. Among 608 patients who had type 2 diabetes and did not have evidence of overt nephropathy, evidence of silent cerebral infarction on baseline magnetic resonance imaging associated with a nearly 2.5-fold greater risk for ESRD or death during an average of 7.5 years of follow-up. These data suggest that screening for extrarenal vascular disease may help to risk-stratify patients with diabetic nephropathy. *See Uzu et al., pages 520–526.*

Cardiovascular Events Stop ASCEND



Avosentan, an endothelin receptor antagonist, reduces proteinuria without affecting BP in the short term. In this issue, Mann *et al.* report the results of a multicenter, randomized, double-blind, placebo-controlled trial (ASCEND) designed to assess the efficacy of avosentan with regard to renal morbidity and mortality among nearly 1400 patients who had type 2 diabetes and were already treated with renin-angiotensin system blockade. Despite its effective reduction of proteinuria, an excess of cardiovascular events (congestive heart failure and fluid overload) with a trend toward increased mortality led to premature termination of the trial. At least at the dosages studied in this trial, avosentan is not a therapeutic option for diabetic nephropathy. *See Mann et al., pages 527–535.*