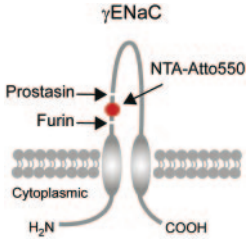
This Month's Highlights

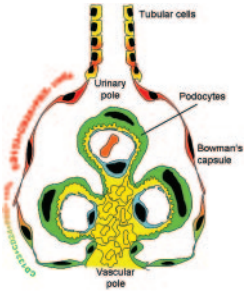
BASIC RESEARCH

Plasmin Modulates Sodium Retention in Nephrotic Syndrome



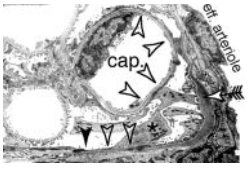
Renal sodium retention accompanies nephrotic syndrome, but the underlying mechanisms are incompletely understood. Here, Svenningsen *et al.* report that urine from humans and animals with nephrosis activate the epithelial sodium channel (ENaC) and that this activation depends on the serine protease plasmin. They suggest that tubular urokinase-type plasminogen activator converts filtered plasminogen to plasmin, which in turn cleaves an inhibitory peptide from the γENaC subunit. These data provide a novel mechanism by which proteinuria leads to sodium retention *via* ENaC activation. *See Svenningsen et al., pages 299–310.*

Podocyte Progenitors in Bowman's Capsule



Loss of podocytes plays a role in the pathogenesis of glomerulosclerosis. Ronconi *et al.* identified an organized hierarchy of progenitor cells within Bowman's capsule that have regenerative potential. Specific cells localized to the urinary pole can regenerate both tubular cells and podocytes, cells localized between the urinary pole and vascular pole can regenerate only podocytes, and cells localized to the vascular pole exhibit features of differentiated podocytes. They found that the cells at the urinary pole can be injected as a cell-based therapy for adriamycin-induced nephropathy in mice, suggesting therapeutic possibilities for these progenitor cells. *See Ronconi et al., pages 322–332.*

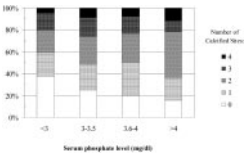
Podocytes Are Recruited from Parietal Epithelial Cells



Even in the absence of renal disease, podocytes are continuously shed into the urine at low numbers. Without a mechanism for podocyte replacement, everyone would likely progress to ESRD within the usual human lifespan. In this issue, Appel *et al.* demonstrate that cells at the vascular stalk of the glomerulus exhibit features of both parietal epithelial cells (PECs) and podocytes. Using transgenic mice to follow PECs over time, they established that podocytes are recruited from PECs in juvenile mice. Determining the signals involved in this recruitment may stimulate novel approaches to the treatment of renal disease. *See Appel et al., pages 333–343.*

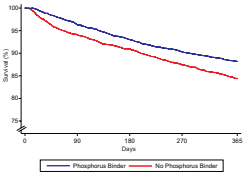
CLINICAL EPIDEMIOLOGY

"Normal" Phosphate Promotes Calcification



Higher serum phosphate concentrations, even within the normal range, associate with cardiovascular morbidity, possibly by promoting vascular calcification. In a community-based cohort of 439 individuals with moderate chronic kidney disease but no known cardiovascular disease, Adeney *et al.* identified an association between serum phosphate levels, 95% of which were within the normal range, and the presence of vascular and valvular calcification. Adjusting for traditional cardiovascular risk factors, parathyroid hormone, and 1,25-dihydroxyvitamin D did not modify this association. These data suggest that even mild elevations in serum phosphate may promote calcification in individuals with moderate chronic kidney disease. *See Adeney et al., pages 381–387.*

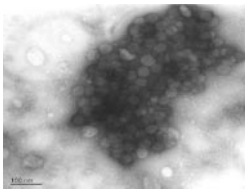
Phosphorus Binders Improve Survival



Hyperphosphatemia increases mortality risk, but does the use of phosphorus binders improve survival? Isakova *et al.* addressed this question in the Accelerated Mortality on Renal Replacement (ArMORR) prospective cohort of >10,000 incident hemodialysis patients. Analyzing their data several different ways (intention-to-treat, as-treated, or by using propensity scores) produced similar results: Treatment with phosphorus binders associates with a 20 to 30% reduction in risk for mortality, independent of serum phosphate levels. This suggests that phosphorus binders may confer benefits beyond reduction of serum phosphate levels, raising the question of whether a similar mortality benefit may be observed among predialysis patients, many of whom have normal phosphate levels. *See Isakova et al., pages 388–396.*

CLINICAL RESEARCH

Haufen Diagnose BK Nephropathy



Polyoma BK virus nephropathy is a common infectious complication after renal transplantation, but current noninvasive diagnostic tests are inaccurate. In this issue, Singh *et al.* report that polyoma BK virus nephropathy is accompanied by the presence of urinary Haufen, which are aggregates of polyomavirus detected by electron microscopy. Furthermore, over time, the presence or absence of Haufen in an individual patient closely mirrors the course of renal disease. These results suggest that detection of urinary Haufen may serve as a noninvasive means to diagnose polyoma BK virus nephropathy. *See Singh et al., pages 416–427.*