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IN BRIEF

GLOMERULAR DISEASE

Increased RAP1GAP expression implicated in podocyte injury

New research using a mutagenic screen of murine podocytes from disease models has revealed that an insertional mutation in the gene encoding the intrinsic Rap1 inhibitor Rap1gap increases expression of this protein. This increase in turn reduces the activity of Rap1, which has many functions—including roles in cell proliferation and adhesion—and might protect podocytes against injury. Inactivation of Rap1 induced glomerulosclerosis and premature death in mouse models, with haploinsufficiency also resulting in podocyte damage. In human biopsy samples of focal segmental glomerulosclerosis, diminished RAP1 activation was apparent, suggesting injury-induced RAP1GAP overexpression is a plausible target for future therapies.

Original article Potla, U. *et al.* Podocyte-specific RAP1GAP expression contributes to focal segmental glomerulosclerosis-associated glomerular injury. *J. Clin. Invest.* doi:10.1172/JCI67846

HYPERTENSION

Tick, tock goes the renal circadian clock

The master biological clock in the suprachiasmatic nucleus of the hypothalamus shares the same molecular machinery as peripheral clocks in various tissues, including the transcriptional activators BMAL1, CLOCK and NPAS2. New data suggest that expression of the circadian clock gene *Bmal1* in the murine kidney is critical for maintaining fluid and electrolyte balance and controlling blood pressure. Using *Bmal1^{lox/lox}/Ren1^d/Cre* mice, the researchers were able to show that a lack of *Bmal1* in the juxtaglomerular apparatus and collecting duct led to an abnormal phenotype—urine volume, glomerular filtration rate and plasma aldosterone were all increased, alongside a reduction in blood pressure. Additionally, urinary sodium excretion rhythms were disrupted. These findings suggest that BMAL1 loss in humans might have a role in misaligned circadian rhythms, which are a known risk factor for the development of hypertension and progression of chronic kidney disease.

Original article Tokonami, N. *et al.* Local renal circadian clocks control fluid–electrolyte homeostasis and BP. *J. Am. Soc. Nephrol.* doi:10.1681/ASN.2013060641

CHRONIC KIDNEY DISEASE

BMI of patients not on dialysis—still no clear ideal

Although obesity is associated with a raft of health conditions, the 'ideal' BMI for patients with chronic kidney disease (CKD) who are not on dialysis is an open question. A new analysis of >450,000 non-dialysis-dependent patients with CKD (estimated glomerular filtration rate [eGFR] <60 ml/min/1.73 m²) in the US Veterans system has shown that BMI has a U-shaped association with clinical outcomes. Using several definitions of progression (incidence of end-stage renal disease, doubling of serum creatinine levels and eGFR slopes), patients with BMI <25 kg/m² had the worst outcomes independent of CKD severity. In the early stages of CKD, high BMI (≥35 kg/m²) was associated with the worst outcomes. These results underline the need for prospective studies to understand the complexities of weight management in this population.

Original article Lu, J. L. *et al.* Association of body mass index with outcomes in patients with CKD. *J. Am. Soc. Nephrol.* doi:10.1681/ASN.2013070754