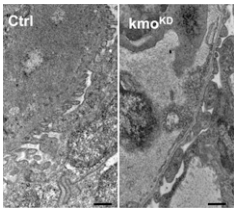
This Month's Highlights

BRIEF COMMUNICATION

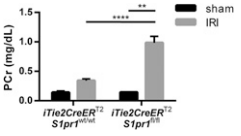
A Functional Role for Kynurenine-3-Mono-oxygenase



The significance of abnormalities in the kynurenine pathway observed in CKD is unclear. Korstanje *et al.* investigated the potential role of the kynurenine-3-mono-oxygenase gene (*Kmo*), which they previously identified as a candidate gene associated with proteinuria. Compared with healthy renal tissue from mice and humans, diabetic renal tissue expresses lower levels of KMO in glomerular cells, particularly in podocytes. Knockdown of *kmo* in zebrafish or genetic knockout of *Kmo* in mice causes proteinuria and foot process effacement. Further studies are needed to understand the pathways regulated by KMO. *See Korstanje et al., pages* 3271–3277.

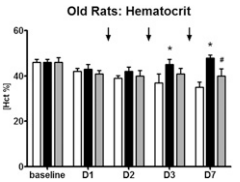
BASIC RESEARCH

Sphingosine 1-Phosphate Receptor 1 Protects against AKI



Sphingosine 1-phosphate receptor 1 (S1P1) is required for endothelial barrier integrity and vascular development, but its role in AKI prevention and recovery is not well understood. In this issue, Perry *et al.* report that induced genetic deletion of endothelial S1P1 in mice before ischemia-reperfusion injury increases renal injury and inflammation, whereas S1P1 deletion during recovery after injury prolongs inflammation, endothelial activation of leukocyte adhesion molecules, fibrosis progression, and reduced kidney function. These results suggest S1P1 activation as a possible prophylactic or therapeutic approach in AKI. *See Perry et al., pages* 3383–3393.

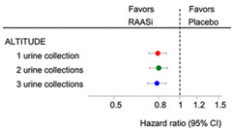
Carbamylated Erythropoietin for AKI



Carbamylated erythropoietin (CEPO) may improve renal function without increasing hemoglobin levels as erythropoietin (EPO) does, but studies in clinically relevant animal models are needed. Tögel *et al.* compared the effects of EPO and CEPO in several models of AKI, examining outcomes in male and female rats, old rats, and in rats with AKI superimposed on CKD. In these models, both drugs are renoprotective, improve survival, and enhance renal function recovery and tissue repair. Compared with CEPO, however, EPO leads to significantly higher systolic BP and hematocrit levels, providing further evidence that CEPO may be a more favorable therapeutic option. *See Tögel et al., pages* 3394–3404.

CLINICAL EPIDEMIOLOGY

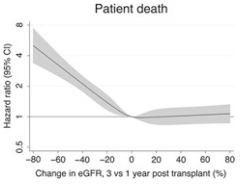
Measuring Albuminuria Class Transition in Diabetic Kidney Disease



Transition in albuminuria class is assessed as an intermediate end point in drug intervention trials in diabetic nephropathy, but protocols vary. Here, Kröpelin *et al.* performed a *post hoc* analysis of four completed clinical trials and found that the following variations do not alter the average drug effect: including a class change confirmation visit, adjusting the timing of the confirmation visit, increasing the number of urine samples collected per visit, or adding a minimal required albuminuria change. The authors conclude that one urine sample collected per study visit is sufficient for assessing albuminuria in such trials. Prospective studies are needed to confirm these findings. *See Kröpelin et al., pages* 3405–3412.

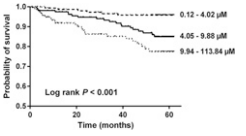
CLINICAL RESEARCH

eGFR Decline as a Surrogate Outcome after Kidney Transplant



The use of surrogate outcomes may overcome barriers to clinical trials designed to evaluate long-term outcomes after kidney transplants. Clayton *et al.* investigated the association between eGFR decline and hard outcomes in 7949 kidney transplants over a median follow-up of 8.5 years and found that a ≥30% decline in eGFR between years 1 and 3 after transplant strongly associates with increased risks of graft loss and recipient death. If these findings are confirmed in diverse cohorts, assigning such a clinically plausible decline in eGFR as a surrogate end point would allow shorter trials enrolling smaller numbers of patients. *See Clayton et al., pages* 3440–3446.

Phenylacetylglutamine and Adverse Outcomes in CKD



Do adverse outcomes associated with high levels of *p*-cresyl sulfate and indoxyl sulfate in CKD result solely from the high protein-binding affinity of these solutes? In 488 patients with CKD not on dialysis, Poesen *et al.* investigated the behavior of phenylacetylglutamine (PAG), another colonic microbial metabolite cleared by tubular secretion but with low protein-binding affinity. Patients with more advanced CKD had higher serum PAG levels, and serum levels of PAG predicted overall mortality and cardiovascular disease, highlighting the importance of microbial metabolism and renal tubular function in these outcomes. *See Poesen et al., pages* 3479–3487.