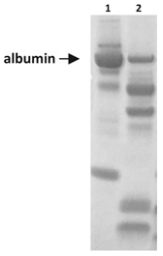
This Month's Highlights

BRIEF COMMUNICATION

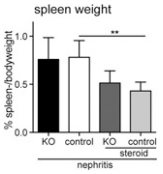
Degradation of Urine Protein by a Urine Preservative



A high rate of nonalbumin proteinuria was reported in participants of the African American Study of Kidney Disease and Hypertension (AASK), suggesting AASK nephropathy (AASK-N) could be a tubulopathy. Almaani *et al.* sought to investigate this possibility by further examination of stored 24-hour urine samples from patients with AASK-N. However, protein staining after SDS-PAGE indicated severe protein degradation in 34 of 37 samples. Notably, treatment of control urine samples with 0.5% acetic acid, the preservative in which AASK urine samples were stored, led to similar patterns of protein degradation. These findings may explain the unusually high rate of nonalbumin proteinuria detected in AASK participants and suggest acetic acid should not be used as a preservative for urine samples. *See Almaani et al., pages* 1394–1398.

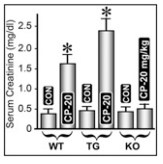
BASIC RESEARCH

Treating GN without Systemic Immunosuppression



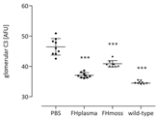
Clinical observations have suggested that glucocorticoids have a direct effect on renal cells, but this possibility remains unconfirmed. Using mouse models, Kuppe *et al.* found that genetic inactivation of the glucocorticoid receptor specifically in kidney epithelial cells attenuates crescentic GN as effectively as high-dose prednisolone does, but without the immunosuppressive effects. *In vitro* studies showed that prednisolone and a glucocorticoid receptor antagonist each act directly on parietal epithelial cells. Notably, pharmacologic antagonism of the glucocorticoid receptor in mice also effectively attenuates crescentic GN without systemic immunosuppression, suggesting this approach may have clinical utility in the treatment of GN. *See Kuppe et al., pages* 1408–1420.

Myo-inositol Oxygenase-Mediated Effects in AKI



The proximal tubular metabolic enzyme *myo*-inositol oxygenase (MIOX) has been implicated in diabetic tubulopathy, but the pathomechanisms involved remain undefined. In this issue, Dutta *et al.* report that, in cisplatin-treated mice, MIOX overexpression exacerbates renal function decline, enhances tubular cell apoptosis and reactive oxygen species generation, and promotes inflammation, whereas knockout of MIOX is renoprotective. Moreover, cisplatin treatment leads to demethylation of the MIOX promoter and upregulated expression of MIOX in proximal tubules. The therapeutic implications of these findings should be investigated. *See Dutta et al., pages* 1421–1436.

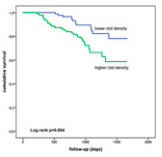
Moss-Derived Recombinant Human Factor H



Restoration of factor H (FH) function by administration of fresh frozen plasma can normalize complement activity in patients with atypical hemolytic uremic syndrome or C3 glomerulopathy (C3G), suggesting recombinant FH may have therapeutic value. Building on their previous study of recombinant FH production in the moss *Physcomitrella patens*, Michelfelder *et al.* developed and produced moss-derived recombinant human FH (FHmoss) with an optimized glycosylation pattern. FHmoss exhibits *in vitro* bioactivity comparable to that of plasma-derived human FH, and treatment of C3G mice with FHmoss increases serum levels and reduces glomerular deposition of C3. FHmoss warrants further evaluation as a candidate biopharmaceutical. *See Michelfelder et al., pages* 1462–1474.

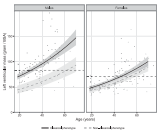
CLINICAL RESEARCH

Fibrin Clot Structure and Mortality in Hemodialysis Patients



Does fibrin clot structure affect outcome in patients receiving hemodialysis? To address this question, Schuett *et al.* conducted a prospective study in 171 patients on prevalent hemodialysis. In this cohort, increased clot density correlated with higher plasma levels of C-reactive protein and C3 and independently associated with greater risk of all-cause and cardiovascular mortality. Fibrinogen isolated from these patients exhibited an altered clot structure and post-translational modifications not found in fibrinogen from healthy controls. These findings require confirmation in diverse cohorts, but suggest that modifications in clot structure contribute to the higher mortality risk in hemodialysis patients. *See Schuett et al., pages* 1622–1630.

Natural Course of Fabry Disease



The natural course of disease has not been well defined for Fabry disease (FD), which is classified as classical or nonclassical by the degree of deficiency in α-galactosidase A. Here, Arends *et al.* report on their retrospective study of 541 patients with FD. When stratified by sex, men and women with classical FD had higher event rates than their counterparts with nonclassical FD had. Among all patients, men with classical FD had the highest rate of complications, the most severe cardiac and renal disease, and the highest plasma concentration of the α-galactosidase A substrate globotriaosylsphingosine. Women with nonclassical FD had the mildest disease course. These findings may inform the development of guidelines for patient treatment and counseling. *See Arends et al., pages* 1631–1641.