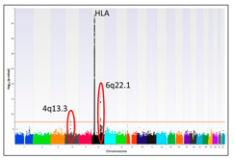
This Month's Highlights

BASIC RESEARCH

Tolerance Induction in a Mouse Model of Myeloperoxidase-ANCA–Associated GN

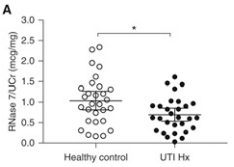
Treatment for the autoimmune disease myeloperoxidase (MPO)-ANCA–associated vasculitis (MPO-AAV), which causes rapidly progressive GN, is nonspecific and has considerable toxicities. Previous research in mice defined the nephritogenic immunodominant MPO CD4+ T cell peptide, MPO409-428. In this study, Gan *et al.* explored the therapeutic potential of generating endogenous MPO409-428-specific regulatory T cells to achieve tolerance to MPO and regulate the anti-MPO autoimmune response driving GN. They gave mice apoptotic MPO409-428-conjugated splenocytes before or after the animals had been immunized to MPO. The resultant generation of antigen-specific type 1 regulatory T cells significantly attenuated GN. Defining analogous MPO peptide(s) in human patients offers the potential to restore tolerance to MPO. *See Gan et al., pages 1365–1374.*

New Gene Loci for Steroid-Sensitive Nephrotic Syndrome



Although steroid-sensitive nephrotic syndrome (SSNS) is considered an autoimmune disease, its etiology is poorly understood. To date, genome-wide association studies (GWAS) have reported associations only in the classical HLA region for SSNS. In a GWAS of a large cohort of European ancestry comprising 422 ethnically homogeneous pediatric cases and 5642 ethnically matched controls, Dufek *et al.* found two loci associated with SSNS at genome-wide significance. The locus with strongest association contains the calcium homeostasis modulator family member 6 gene *CALHM6*, which has been implicated in the regulation of the immune system, suggesting that impaired down-regulation of the immune system may be a key mechanism in SSNS pathogenesis. *See Dufek et al., pages 1375–1384.*

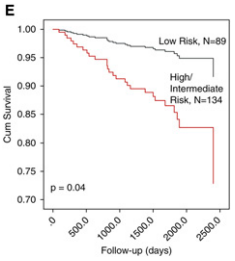
Ribonuclease 7 and UTIs



Evidence suggests that antimicrobial peptides protect the kidneys and bladder from bacterial challenge. In this study, Eichler *et al.*, who previously identified ribonuclease 7 (RNase 7) as an antibacterial peptide produced by human kidneys and bladder, found significantly lower urinary RNase 7 concentrations in girls and female adolescents with a urinary tract infection (UTI) history compared with controls. In human urothelial cultures and in humanized RNase 7–expressing transgenic mice, RNase 7 conferred protection compared with controls. These findings suggest that RNase 7 has potential as a UTI prognostic marker or a therapeutic target for protection against bacterial infection. *See Eichler et al., pages 1385–1397.*

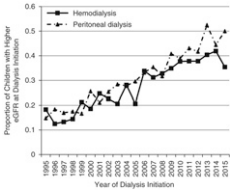
CLINICAL RESEARCH

Peripheral Blood Signature of Subacute Rejection



Biomarkers for noninvasive diagnosis of subclinical acute rejection in kidney transplant recipients are needed to enable risk-stratification and tailoring of immunosuppression. *Zhang et al.* used RNA sequencing analysis of whole blood collected from transplant recipients undergoing surveillance biopsy to identify a transcriptional signature based on 17 genes that detects ongoing subclinical rejection. In an independent cohort of 110 patients, a sequencing-based targeted expression assay based on this gene set identified subclinical rejection at 3 months posttransplant and increased risk of graft loss. This assay has potential as a useful tool to monitor kidney transplant recipients and optimize immunosuppressive therapy, although larger studies are needed to validate the assay's clinical utility. *See Zhang et al., pages 1481–1494.*

Early Dialysis Start in Children



In adults with ESRD, observational studies suggest that starting dialysis at higher levels of eGFR is not linked with survival benefit. In a retrospective cohort study in children, Winnicki *et al.* found a trend toward increased initiation of early dialysis at higher eGFR from 1995 to 2015. Higher eGFR at initiation was associated with an increased risk of death, particularly for children who initiated treatment with hemodialysis rather than peritoneal dialysis. The findings have important implications for the care of children with ESRD, and the authors note that a more concerted effort to delay dialysis initiation in asymptomatic children may reduce exposure to dialysis. A related editorial urges later initiation of dialysis except in the context of a trial. *See Winnicki et al., pages 1505–1513, and editorial by Larkins and Craig, pages 1344–1345.*

Automated Measurement of Kidney Size in PKD

Total kidney volume (TKV) is the most important biomarker of autosomal dominant polycystic kidney disease (ADPKD) severity and progression because renal function often remains stable in the early stages. In this study, van Gastel *et al.* describe the development and validation of a fully automated segmentation method that employs a deep learning network to measure TKV and total liver volume and their growth rates from magnetic resonance images, finding that the method's performance is equivalent to and requires far less time and skill than manual tracing. This approach may allow identification of patients with rapidly progressing ADPKD for emerging drug treatments and serve as a reliable alternative for assessing disease progression in clinical trials. *See van Gastel et al., pages 1514–1522.*