NEPHROLOGY

Martin Pollak, MD, Chief — The Division of Nephrology is committed to providing the best possible patient care, educating the next generation of academic nephrologists, and moving the field of nephrology forward through its clinical, translation and basic research efforts. We are committed to providing leading-edge diagnosis and treatment for the entire spectrum of renal disease, with expertise in chronic kidney disease, polycystic kidney disease, renal transplantation, hemodialysis and peritoneal dialysis. We are dedicated to ensuring compassionate, high-quality care to patients with end-stage renal disease.

We are committed to training nephrologists for both academic careers and clinical practice. We are dedicated to education on all levels of the medical curriculum, teaching medical student, residents and our own Nephrology fellows. Many graduates of our program have gone on to become leaders in their respective areas.

Martin Pollak, MD

Our faculty members perform cutting-edge research in a wide variety of areas related to renal physiology and kidney disease. These activities encompass both laboratory, translational and clinical investigations. The range of topics under investigation includes the pathophysiology and treatment of acute renal failure, the molecular mechanisms of cell injury and cell metabolism, regulation of ion transport and water excretion, mechanisms of muscle wasting and intracellular protein breakdown, preeclampsia, glomerular pathology, vascular leak, diabetic nephropathy, kidney fibrosis and the genetic basis of kidney disease.

Highlights

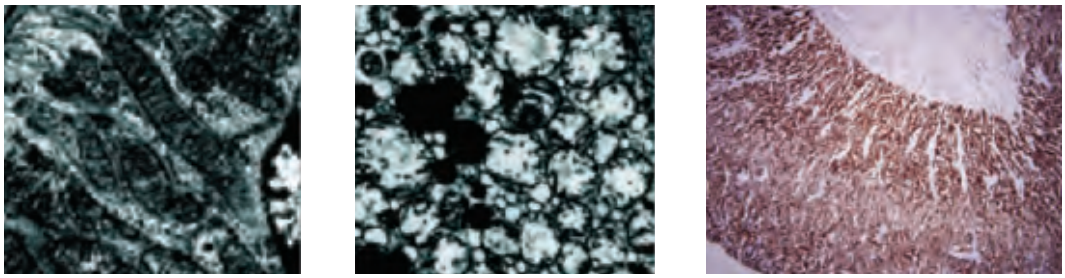
Acute kidney injury (AKI) is a common and morbid condition that compounds the mortality of sepsis and related critical illnesses. Recent large clinical trials designed to optimize renal outcomes in AKI have yielded disappointingly equivocal results. With the rising societal burden of AKI and the lack of clinical advances, there is an unprecedented need for discovery of new disease-causing pathways that can be manipulated to benefit AKI sufferers.

Dr. Samir Parikh's laboratory has identified a critical role for a molecular pathway, the Tie-2 signaling axis. In the septic kidney, Tie-2 function is markedly impaired. As a result, renal blood vessels become leaky and inflamed with sluggish blood flow. Restoration of Tie-2 function prevents AKI in experimental models of sepsis. The ongoing clinical development of therapies to enhance Tie-2 function may enable us to translate these findings for patients afflicted with AKI.

Using complementary screening approaches, we have identified a second pathway in the septic kidney that governs the ability of the kidney

Top: Genevieve Moreault Moin, RN, CRC, with a patient

to generate the energy necessary to filter blood and balance electrolytes throughout the body. Its master regulator, PGC1-alpha, is a protein that accelerates the production of mitochondria, the energy factory of cells. In septic AKI, kidney levels of PGC1-alpha rapidly plummet. In turn, this prevents the kidney from recovering after a bout of sepsis. Pharmaceutical approaches to enhance the expression of PGC1-alpha or its downstream targets may therefore shorten or even prevent the often-prolonged course of AKI in patients.



The healthy kidney contains abundant mitochondria, the energy powerhouses of the cell, visible here as elongated tubes in left image. In acute kidney injury related to sepsis, these mitochondria become swollen, seen as clear circular structures in middle image. The activity of a critical mitochondrial enzyme, cytochrome c oxidase, is markedly diminished in the septic kidney, evident in the right hand image as reduced brown staining in the upper right and lower left of this low-power kidney photomicrograph. Courtesy of Samir Parikh, MD.

Selected Publications

Khankin EV, Mutter W, Tamez W, Yuan HT, Karumanchi SA, Thadhani R. Soluble erythropoietin receptor contributes to erythropoietin resistance in end stage renal disease. *PLOS One* 2010; 5:e9246.

Hristova M, van Beek C, Schurgers LJ, Lanske B, Danziger J. Rapidly progressive severe vascular calcification sparing the kidney allograft following warfarin initiation. *Am J Kidney Dis* 2010; 56:1158-62.

Genovese G, Friedman DJ, Ross MD, Lecordier L, Uzureau P, Freedman BI, Bowden DW, Langefeld CD, Oleksyk TK, Knob AU, Bernhardy AJ, Hicks PJ, Nelson GW, Vanhollebeke B, Winkler CA, Kopp JB, Pays E, Pollak MR. Association of trypanolytic apol1 variants with kidney disease in African Americans. *Science* 2010; 329:841-5.

Tran M, Tam D, Bardia A, Bhasin M, Rowe GC, Kher A, Zsengeller ZK, Akhavan-Sharif MR, Khankin EV, Saintgeniez M, David S, Burstein D, Karumanchi SA, Stillman IE, Arany Z, Parikh SM. PGC-1alpha promotes recovery after acute kidney injury during systemic inflammation in mice. *J Clin Invest* 2011; 121:4003-14.

Yu W, Hill WG, Apodaca G, Zeidel ML. Expression and distribution of transient receptor potential (TRP) channels in bladder epithelium. *Am J Physiol Renal Physiol* 2011; 300:F49-59.

Stewart AK, Kedar PS, Shmukler BE, Vandorpe DH, Hsu A, Glader B, Rivera A, Brugnara C, Alper SL. Functional characterization and modified rescue of novel AE1 mutation R730C associated with overhydrated cation leak stomatocytosis. *Am J Physiol Cell Physiol* 2011; 300:C1034-46.

Christov M, Koren S, Yuan Q, Baron R, Lanske B. Genetic ablation of sfrp4 in mice does not affect serum phosphate homeostasis. *Endocrinology* 2011; 152:2031-6.

Faculty

Seth L. Alper, MD, PhD
Robert S. Brown, MD
Marta Christov, MD, PhD
Robert A. Cohen, MD
John Danziger, MD
John A. D'Elia, MD
Bradley M. Denker, MD
David J. Friedman, MD
Alexander Goldfarb, MD, PhD
Junichi Hanai, MD, PhD
Warren Hill, PhD
Melanie Hoenig, MD
Antoine Kaldany, MD
S. Ananth Karumanchi, MD
Stewart H. Lecker, MD, PhD
Didier A. Mandelbrot, MD
C. John Mathai, PhD
Bryce MacIver, PhD
Walter P. Mutter, MD
Samir M. Parikh, MD
Martha Pavlakis, MD
Martin R. Pollak, MD
Michael D. Ross, MD, PhD
Burton Rose, MD
Bijan Roshan, MD
Terry B. Strom, MD
Johannes Schlondorff, MD, PhD
Robert C. Stanton, MD
Theodore I. Steinman, MD
Isaac Stillman, MD
Vikas P. Sukhatme, MD, PhD
Mark E. Williams, MD
Hai-Tao Yuan, MD, PhD
Mark L. Zeidel, MD