

# **Nephrology and Hypertension**

#### **Division Details**

#### RESEARCH AND TRAINING DETAILS

Faculty	11
Research Fellows and Post Docs	2
Total Annual Grant Award Dollars	\$2,021,344
Total Annual Industry Award Dollars	\$178,425
CLINICAL ACTIVITIES AND TRAINING	
Clinical Fellows	11
Inpatient Encounters	4,298
Outpatient Encounters	4,959



Row 1: V Taylor, D Claes, E Erkan, M Schuh, E Ciccia

Row 2: H Stone, R Hjorten-Kohlberg, H Woollen, S Goldstein, S Benoit, M Mitsnefes, B Siroky

Row 3: F Flores, E Nehus, R Bignall, G Hamdani, D Hooper, C Varnell, M Bennett, P Devaraian

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### **Division Highlights**

#### Prasad Devarajan, MD

Dr. Devarajan's research includes a wide spectrum of approaches to kidney health and disease processes, spanning from molecular, genomic and proteomic approaches to human observational and clinical trials. Dr. Devarajan is the director of the National Institutes of Health (NIH)-funded P50 Pediatric Nephrology Center of Excellence, a unique multi-disciplinary research program designed to support basic, translational, and clinical research on critical pediatric kidney diseases that have major unmet needs. The proposal includes several research projects in the areas of acute kidney injury, proteinuric kidney disease, cardio-renal syndromes, and lupus nephritis, with participation from recognized teams of investigators from multiple disciplines. Also included are high-resource Gene Expression, Proteomics, Biomarker, Enhancement, and Training Cores with core leaders of international repute. Dr. Devarajan is also the nephrology lead investigator for several NIH-funded prospective clinical studies. He has also established a unique Kidney Biomarker Laboratory which now performs more than 50 distinct assays for acute and chronic kidney disease biomarkers. Dr. Devarajan is also the director and principal investigator of the NIH T32-funded Fellowship in Nephrology. Dr. Devarajan's research on biomarkers and new therapeutic targets in kidney diseases has yielded over 25 publications and new patent applications during the last fiscal year. He is currently the PI or Co-PI on eight NIH grants.

#### Stuart L. Goldstein, MD

Dr. Stuart Goldstein, MD, FAAP, FNKF, is the director of the Center for Acute Care Nephrology (CACN), and has had a very productive research year, with achievements that spanned the scope of the Center's research missions. The nephrotoxic medication acute kidney injury (AKI) reduction project, NINJA, results show a five year sustained reduction in AKI, preventing AKI in more than 600 children. NINJA is now used in 13 U.S. pediatric centers. This collaborative observed sustained decreases in nephrotoxic medication exposure and

associated AKI. Based on these results, it is the next hospital acquired condition the 100 hospital Solutions for Patient Safety Collaborative will address. The CACN reported the initial epidemiological results from the prospective pediatric AKI study ever undertaken in the *New England Journal of Medicine*: "Assessment of Worldwide AKI, Renal angina and Epidemiology in Children (AWARE)". The CACN successfully integrated its real-time AKI risk stratification system, the Renal Angina Index, to guide novel AKI biomarker testing in critically ill patients in the PICU. The CACN pioneered applications of specialized techniques, such as aquapheresis and the Molecular Adsorbent Recirculating System, for liver support. The CACN also launched an LDL-apheresis program to treat patients with refractory FSGS. The CACN remains the only single center in the U.S. to offer all of these specialized novel extracorporeal techniques. In addition, the CACN demonstrated unparalleled commitment to education via the CRRT University Simulation course, offered to more than 300 RNs and MDs from all over the world during the past three years, and received a commitment for a fourth and fifth year of extramural funding this year.

#### Mark Mitsnefes, MD MS

Dr. Mitsnefes' research interest has been to define biologic targets for interventions to prevent progression of cardiovascular disease in children with chronic kidney disease, through epidemiological and translational studies. Dr. Mitsnefes is a co-investigator and co-chair of the Cardiovascular Subcommittee in the multicenter National Institutes of Health (NIH)-funded study of chronic kidney disease in children, the CKiD study. In one published study, his group showed that greater cystatin C level independently associates with increasing cardiac size and worsening diastolic function. This serum marker was also able to predict decline in diastolic function, even after adjusting for kidney function. This suggests that cystatin C may have an independent role in cardiovascular disease risk stratification among children and adolescents with chronic kidney disease. In another published study utilizing longitudinal data from Midwest Pediatric Nephrology Consortium to evaluate trends in ambulatory blood pressure control over time in the pediatric and young adult kidney transplant recipient population, he showed that regular ambulatory blood pressure (BP) monitoring led to overall improved BP over time, attributable to improved control of BP by using antihypertensive medications.

#### **Division Publications**

- Kaddourah A; Basu RK; Bagshaw SM; Goldstein SL; Investigators AWARE. Epidemiology of Acute Kidney Injury in Critically III
   Children and Young Adults. The New England journal of medicine. 2017; 376:11-20.
- Bagshaw SM; Darmon M; Ostermann M; Finkelstein FO; Wald R; Tolwani AJ; Goldstein SL; Gattas DJ; Uchino S; Hoste EA. Current state of the art for renal replacement therapy in critically ill patients with acute kidney injury. Intensive Care Medicine. 2017; 43:841-854.
- Kwiatkowski DM; Goldstein SL; Cooper DS; Nelson DP; Morales DLS; Krawczeski CD. Peritoneal Dialysis vs Furosemide for Prevention of Fluid Overload in Infants After Cardiac Surgery A Randomized Clinical Trial. JAMA Pediatrics. 2017; 171:357-364.
- Greenberg JH; Zappitelli M; Devarajan P; Thiessen-Philbrook HR; Krawczeski C; Li S; Garg AX; Coca S; Parikh CR; TRIBE-AKI
  Consortium. Kidney Outcomes 5 Years After Pediatric Cardiac Surgery The TRIBE-AKI Study. JAMA Pediatrics. 2016;
  170:1071-1078.
- 5. Chawla LS; Bellomo R; Bihorac A; Goldstein SL; Siew ED; Bagshaw SM; Bittleman D; Cruz D; Endre Z; Fitzgerald RL. Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup. Nature Reviews Nephrology. 2017; 13:241-257.
- 6. Devarajan P. Acute kidney injury: still misunderstood and misdiagnosed. Nature Reviews Nephrology. 2017; 13:137-138.
- 7. Kamal FA; Travers JG; Schafer AE; Ma Q; Devarajan P; Blaxall BC. **G Protein-Coupled Receptor-G-Protein beta gamma-Subunit Signaling Mediates Renal Dysfunction and Fibrosis in Heart Failure.** *Journal of the American Society of Nephrology : JASN*. 2017; 28:197-208.

- 8. Bansal N; Carpenter MA; Weiner DE; Levey AS; Pfeffer M; Kusek JW; Cai J; Hunsicker LG; Park M; Bennett M. **Urine Injury Biomarkers and Risk of Adverse Outcomes in Recipients of Prevalent Kidney Transplants: The Folic Acid for Vascular Outcome Reduction in Transplantation Trial.** *Journal of the American Society of Nephrology: JASN.* 2016; 27:2109-2121.
- López-Juárez A; Titus HE; Silbak SH; Pressler JW; Rizvi TA; Bogard M; Bennett MR; Ciraolo G; Williams MT; Vorhees CV.
   Oligodendrocyte Nf1 Controls Aberrant Notch Activation and Regulates Myelin Structure and Behavior. Cell Reports. 2017; 19:545-557.
- 10. Nehus EJ; Khoury JC; Inge TH; Xiao N; Jenkins TM; Moxey-Mims MM; Mitsnefes MM. **Kidney outcomes three years after bariatric** surgery in severely obese adolescents. *Kidney international*. 2017; 91:451-458.
- 11. Soto K; Campos P; Pinto I; Rodrigues B; Frade F; Papoila AL; Devarajan P. **The risk of chronic kidney disease and mortality are increased after community-acquired acute kidney injury.** *Kidney international.* 2016; 90:1090-1099.
- 12. Goldstein SL; Mottes T; Simpson K; Barclay C; Muething S; Haslam DB; Kirkendall ES. **A sustained quality improvement program** reduces nephrotoxic medication-associated acute kidney injury. *Kidney international*. 2016; 90:212-221.
- Savant JD; Betoko A; Meyers KEC; Mitsnefes M; Flynn JT; Townsend RR; Greenbaum LA; Dart A; Warady B; Furth SL. Vascular Stiffness in Children With Chronic Kidney Disease. Hypertension. 2017; 69:863-869.
- 14. Ascher SB; Scherzer R; Peralta CA; Tien PC; Grunfeld C; Estrella MM; Abraham A; Gustafson DR; Nowicki M; Sharma A.
  Association of Kidney Function and Early Kidney Injury With Incident Hypertension in HIV-Infected Women. Hypertension.
  2017; 69:304-313.
- 15. Garimella PS; Bartz TM; Ix JH; Chonchol M; Shlipak MG; Devarajan P; Bennett MR; Sarnak MJ. **Urinary Uromodulin and Risk of Urinary Tract Infections: The Cardiovascular Health Study.** *American Journal of Kidney Diseases*. 2017; 69:744-751.
- 16. Brady TM; Townsend K; Schneider MF; Cox C; Kimball T; Madueme P; Warady B; Furth S; Mitsnefes M. Cystatin C and Cardiac Measures in Children and Adolescents With CKD. American Journal of Kidney Diseases. 2017; 69:247-256.
- 17. Jotwani V; Scherzer R; Estrella MM; Jacobson LP; Witt MD; Palella FJ; Macatangay B; Bennett M; Parikh CR; Ix JH. HIV Infection, Tenofovir, and Urine alpha(1)-Microglobulin: A Cross-sectional Analysis in the Multicenter AIDS Cohort Study. American Journal of Kidney Diseases. 2016; 68:571-581.
- 18. Neri M; Villa G; Garzotto F; Bagshaw S; Bellomo R; Cerda J; Ferrari F; Guggia S; Joannidis M; Kellum J. **Nomenclature for renal replacement therapy in acute kidney injury: Basic principles.** *Critical Care (UK)*. 2016; 20.
- 19. Villa G; Neri M; Bellomo R; Cerda J; De Gaudio AR; De Rosa S; Garzotto F; Honore PM; Kellum J; Lorenzin A. Nomenclature for renal replacement therapy and blood purification techniques in critically ill patients: Practical applications. *Critical Care (UK)*. 2016; 20.
- 20. Downes KJ; Dong M; Fukuda T; Clancy JP; Haffner C; Bennett MR; Vinks AA; Goldstein SL. **Urinary kidney injury biomarkers and tobramycin clearance among children and young adults with cystic fibrosis: a population pharmacokinetic analysis.** *Journal of Antimicrobial Chemotherapy.* 2017; 72:254-260.
- 21. Garimella PS; Jaber BL; Tighiouart H; Liangos O; Bennett MR; Devarajan P; El-Achkar TM; Sarnak MJ. Association of Preoperative Urinary Uromodulin with AKI after Cardiac Surgery. Clinical journal of the American Society of Nephrology: CJASN. 2017; 12:10-18.
- 22. Ruebner RL; Ng D; Mitsnefes M; Foster BJ; Meyers K; Warady B; Furth SL. Cardiovascular Disease Risk Factors and Left Ventricular Hypertrophy in Girls and Boys With CKD. Clinical journal of the American Society of Nephrology: CJASN. 2016; 11:1962-1968.
- 23. Wang Z; Ma S; Zappitelli M; Parikh C; Wang C-Y; Devarajan P. **Penalized count data regression with application to hospital stay after pediatric cardiac surgery.** *Statistical Methods in Medical Research.* 2016; 25:2685-2703.

- 24. Scherzer R; Lin H; Abraham A; Thiessen-Philbrook H; Parikh CR; Bennett M; Cohen MH; Nowicki M; Gustafson DR; Sharma A. Use of urine biomarker-derived clusters to predict the risk of chronic kidney disease and all-cause mortality in HIV-infected women. Nephrology Dialysis Transplantation. 2016; 31:1478-1485.
- 25. Wikenheiser-Brokamp KA; Klein M; Hershey GKK; Devarajan P; DeWitt TG; Loch J; Strauss AW; Muglia LJ; Hostetter MK. Evaluation of Fellows' CrossTalk Effectiveness in Promoting Transdisciplinary Networking and Research. *The Journal of Pediatrics*. 2017; 181:5-6.e3.

### Grants, Contracts, and Industry Agreements

#### **Annual Grant Award Dollars**

Investigator	Title	Sponsor	ID	Dates	Amount
Mark M Mitsnefes, MD	Chronic Kidney Disease in Children (CKiD III)	National Institutes of Health (Children's Mercy Hospital)	U01 DK066143	08/01/2013 - 07/31/2018	\$64,853
Prasad Devarajan, MD	Progression of Acute Kidney Injury to Chronic Kidney Disease	National Institutes of Health (Yale University School of Medicine)	U01 DK082185	09/19/2013 - 06/30/2018	\$30,599
Prasad Devarajan, MD	Research Training in Pediatric Nephrology	National Institutes of Health	T32 DK007695	07/01/2014 - 06/30/2019	\$127,247
Stuart Goldstein, MD	Recombinant Erythropoietin Protects Against Kidney Disease (REPAKD)	National Institutes of Health (Children's Hosp & Reg Med Ct-Seattle)	R01 DK103608	09/17/2014 - 08/31/2019	\$34,823
Stuart Goldstein, MD	Reduction of Nephrotoxic Medication-Associated Acute Kidney Injury in Children	Agcy for Healthcare Research and Quality	R18 HS023763	04/01/2015 - 03/31/2018	\$497,585
Mark M Mitsnefes, MD	Chronic Kidney Disease in Children (CKiD III)	National Institutes of Health (Children's Mercy Hospital)	U01 DK066143	08/01/2013 - 07/31/2018	\$171,365
Prasad Devarajan, MD	Novel Serum and Urinary Biomarkers of Diabetic Kidney Disease	National Institutes of Health (Mount Sinai Hospital)	R01 DK096549	10/01/2014 - 06/30/2017	\$12,007
Mark M Mitsnefes, MD	Phosphate Binders in Children with Chronic Kidney Disease-Mineral Bone Disorder	National Institutes of Health (Univ of California Los Angeles)	U34 DK104619	08/01/2015 - 07/31/2016	\$14,215
Donna Claes, MD	Integrative Proteomics &  Metabolomics for Pediatric  Glomerula Disease Biomarkers	National Institutes of Health (Nationwide Children's Hospital)	UM1 DK100866	06/01/2014 - 05/31/2018	\$14,958
Prasad Devarajan, MD	Novel Biomarkers in Cardiac Surgery to Detect Acute Kidney	National Institutes of Health (Yale University School of Medicine)	R01 HL085757	07/01/2016 - 04/30/2020	\$37,440
Prasad Devarajan, MD	Critical Translational Studies in	National Institutes of Health	P50	09/21/2012	\$43,680

	Pediatric Nephrology		DK096418	-	
				08/31/2017	
Prasad Devarajan, MD	Critical Translational Studies in	National Institutes of Health	P50	09/01/2016	\$730,772
	Pediatric Nephrology		DK096418	-	
				08/31/2017	
Burns C Blaxall, PhD	Targeting Pathologic G-protein	National Institutes of Health	R01	09/01/2016	\$241,800
Prasad Devarajan, MD	Signaling in Cardiac and		HL133695	-	
	Kidney Fibrosis			07/31/2020	

Total Annual Grant Award Dollars \$2,021,344

## **Annual Industry Award Dollars**

Investigator	Industry Sponsor	Amount
Donna Claes, MD	Mallinckrodt Pharmaceuticals (Children's Hospital of Philadelphia)	\$9,000
Stuart Goldstein, MD	Bristol -Myers Squibb	\$169,425
Total Annual Industry Award Dollars		\$178,425