
Division Data Summary

Research and Training Details

- Number of Faculty: 9
- Number of Joint Appointment Faculty: 1
- Number of Research Fellows: 6
- Number of Support Personnel: 15
- Direct Annual Grant Support: $1,012,587
- Direct Annual Industry Support: $115,487
- Peer Reviewed Publications: 29

Clinical Activities and Training

- Number of Clinical Staff: 27
- Number of Clinical Fellows: 6
- Number of Other Students: 6
- Inpatient Encounters: 4,614
- Outpatient Encounters: 4,190

Significant Publications

Dixon BP, Lu L, Chu A, Bissler JJ. RecQ and RecG helicases have distinct roles in maintaining the stability of polypurine.polypyrmidine sequences. Mutat Res 2008;643:20-8. This is the first study to reveal that helicase activity can greatly modify DNA replication fidelity and that such helicases may be involved in human diseases.

Weaver DJ, Kimball TR, Witt SA, Glascock BJ, Khoury PR, Kartal J, Mitsnefes MM. Sub-clinical systolic dysfunction in pediatric patients with chronic kidney disease. J Pediatrics 2008;153:565-9. This is the first study to demonstrate the presence of sub-clinical systolic dysfunction in children with chronic kidney

This is the first study to demonstrate the effects of changes in kidney allocation rules in the United States on pediatric transplant recipients.


This is the first study to describe a comprehensive gene expression atlas of the developing kidney.


This is the first study to demonstrate the utility of sodium bicarbonate as a reno-protective agent after cardiac surgery, and the utility of the novel biomarker NGAL to assess early responses to treatment of acute kidney injury.

**Division Highlights**

**Bradley Dixon, MD**

**Understanding the risk of cancer after bladder reconstruction surgeries:**
Children born with abnormal urinary tracts often also develop chronic kidney damage early in life. These children may require reconstructive surgery of their small, stiff-walled bladders before they can receive a kidney transplant to prevent damage to the new kidney. Bladders that have been reconstructed are at a higher risk for developing cancer later in a patient’s life. Dr. Bradley Dixon, Assistant Professor of Nephrology at CCHMC, is studying the possible reasons for this increased risk of cancer. His research has shown that high concentrations of waste products such as urea in the urine may prevent the reconstructed bladder from recognizing that its genetic code may have been damaged, leading to cancer development.

**Kimberly Czech, MD, PhD**

**Understanding the mechanisms of kidney failure in children with nephrotic syndrome:**
Children with nephrotic syndrome caused by a disease called focal segmental glomerulosclerosis (FSGS) are at high risk for developing kidney failure. To better understand this disease, Dr. Kimberley Czech, Assistant Professor of Nephrology at CCHMC, is exploring the mechanisms of disease progression. Using microarray methods, she has determined which genes are turned on or off in FSGS. Currently, she is employing proteomic techniques to determine what specific proteins are lost in the urine of children with FSGS. The results will lead to improved diagnostic tools and treatments.

**Larry Patterson, MD**

**A new understanding of how a kidney stops growing:**
The kidney develops by branching and growth at the tips of the branches. The length of time that branching continues before it ends determines ultimate kidney size and function. A research team lead by Larry Patterson, MD, Associate Professor of Nephrology at CCHMC, has shown that a shift in the balance of cell fates causes the end of kidney development. This shift in fates favors differentiation over maintenance of kidney stem cells leading to exhaustion of the stem cell pool and loss of any potential for further renal growth. Dr. Patterson is exploring how to manipulate this shift in balance, which could enable us to promote kidney growth and function when its development goes awry.

**John Bissler, MD**

**A transplant drug stops the growth of kidney tumors:**
The basic cellular pathway that is disrupted in kidney and lung tumors of the tuberous sclerosis complex and a sporadic disease called lymphangioleiomyomatosis is the same pathway that is suppressed by the transplant drugs sirolimus and everolimus. A research team led by Dr. John Bissler, the Clark D. West Endowed Chair and Professor of Nephrology at CCHMC, demonstrated that sirolimus reduced the volume of renal tumors and improved the lung manifestations in patients with lymphangioleiomyomatosis. Following up on these studies, Dr. Bissler has an ongoing clinical trial examining different dosing regimes of sirolimus to optimize the effectiveness while reducing side effects. Dr. Bissler has also partnered with industry to launch a placebo controlled clinical trial that, if successful, will be used to support the FDA approval of everolimus in tuberous sclerosis patients. At the bench, the Bissler Laboratory is
conducting pre-clinical trials using human angiomyolipoma cells to see if there are better combination drug approaches to treat this devastating disease, and working with different tuberous sclerosis complex-related renal cystic disease models to understand better how cells go from normal renal structures to cysts and cancers.

**Division Collaboration**

**Collaboration with Developmental Biology;**

Collaborating Faculty: A. Kuan;
- Co-investigator for study entitled "Global gene expression atlas of the developing kidney"
- Co-investigator for study entitled "Glomerulosclerosis in human FSAs and mouse models"
- Co-investigator for study entitled "Implications of JNK pathways in renal IRI"

**Collaboration with Clinical Pharmacology**

Collaborating Faculty: A. Vinks
- Co-investigator for study entitled "Pharmacogenetics of mycophenolic acid in kidney transplant patients"

**Collaboration with Rheumatology**

Collaborating Faculty: H. Brunner
- Co-investigator for study "Early prediction of Lupus Nephritis using advanced proteomics"

**Collaboration with Cardiology**

Collaborating Faculty: C. Krawczeski
- Co-investigator for study entitled "Novel biomarkers for acute renal failure"
- Co-investigator for study entitled "Adiponectin and Cardiovascular disease in the CKID children"

**Collaboration with Epidemiology and Biostats**

Collaborating Faculty: S. Salsbury; L. Martin
- Co-investigator on Tuberous Sclerosis Complex natural history study
- Co-investigator for study entitled "Adiponectin and Cardiovascular disease in the CKID children"

**Collaboration with Interventional Radiology**

Collaborating Faculty: J. Wansapura
- Co-investigator on Tuberous Sclerosis Complex natural history study

**Collaboration with Bioinformatics**

Collaborating Faculty: M. Wagner
- Co-investigator for study entitled "Early prediction of Lupus Nephritis using advanced proteomics"

**Collaboration with Preventive Cardiology**

Collaborating Faculty: E. Urbina
- Co-investigator for study entitled "Modifying dietary behavior in adolescents with elevated blood pressure"

**Faculty Members**

- Prasad Devarajan, MD, Professor
- John J. Bissler, MD, Professor
- Kimberly Czech, MD, PhD, Instructor
- Bradley P. Dixon, MD, Assistant Professor
- Jens Goebel, MD, Associate Professor Clinical
- Elizabeth Jackson, MD, Associate Professor Clinical
- Paul McEnery, MD, Professor Emeritus
- Mark Mitsnefes, MD, Associate Professor Clinical
- Larry Patterson, MD, Research Associate Professor
- C. Frederic Strife, MD, Professor
Trainees

- Donald Weaver, MD, PL-3,
- Amy Wilson, MD, PL-3,
- David Hooper, MD, PL-2,
- Elizabeth Abraham, MD, PL-2,
- Benjamin Laskin, MD, PL-1,
- Megan Lo, MD, PL-1,

Significant Accomplishments

A simple new lab test predicts acute kidney failure and its clinical consequences

About 4 million people die of acute kidney failure each year. They die primarily because the current diagnosis of acute kidney failure is woefully delayed, crippling our ability to institute potentially effective therapies in a timely manner. A research team led by Dr. Prasad Devarajan, the Louise M. Williams Endowed Chair, Professor and Director of Nephrology at CCHMC, has identified a new biomarker called neutrophil gelatinase-associated lipocalin (NGAL), which appears in the urine and blood of patients up to three days before the current tests for acute kidney failure become positive. Dr. Devarajan’s team has validated the biomarker in a wide variety of pediatric and adult patient populations, including those undergoing heart surgery, kidney transplantation, sepsis, nephrotoxic agents, subjects admitted to intensive care units, and even patients randomly presenting to the emergency room. In these patients, early NGAL measurements also predict long-term clinical outcomes such as dialysis requirement, length of hospital stay, and death.

In addition, Dr. Devarajan has partnered with industry collaborators to design standardized clinical laboratory-based point-of-care kits that can measure NGAL in a drop of urine or blood and provide quantitative results in 30 minutes or less. These simple new tests have already been launched worldwide, and will also become available in the US within the next year. The availability of an early biomarker like NGAL could revolutionize medical care and save lives, by providing clinicians with a desperately needed tool for predicting acute kidney failure in hospitalized and ambulatory subjects, allowing for accurate risk assessment, optimizing resource utilization, providing timely therapies, monitoring the response to therapies, and providing a kidney safety marker for future drug development.

A new way to personalize immunosuppression management

Mycophenolate mofetil (MMF), a commonly used anti-rejection medication, is associated with gastrointestinal and hematological toxicity. Reducing the dosage may minimize toxicity but can also increase the risk of transplant rejection. To understand how to use MMF more effectively, Jens Goebel, MD, medical director of kidney transplantation, is leading a multi-center collaborative project that builds on pilot work demonstrating an association between genetic variants in the main MMF-metabolizing enzyme uridine glucuronyl transferase and the risk of MMF-associated toxicity. Ultimately, researchers expect these efforts to allow prediction of individual patients’ responses to MMF and prospective personalization of drug dosing to avoid toxicity.

Getting to the heart of the matter in chronic kidney disease

Heart disease is the 2nd leading cause of death among children with kidney failure. A research team led by Mark Mitsnefes, MD, Associate Professor of Nephrology at CCHMC, has shown that early markers of cardiovascular disease such as left ventricular hypertrophy and increased thickness of carotid artery, are already apparent at early stages of kidney insufficiency in children. Currently, Dr. Mitsnefes is leading a multi-center effort to better understand the development of cardiovascular abnormalities in children with chronic kidney disease. Ultimately, researchers expect that identifying risk factors associated with cardiac and vascular problems will allow them to treat and prevent these conditions in children with chronic kidney disease.

Division Publications


### Grants, Contracts, and Industry Agreements

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<td>Altered Gene Expression using Microarray in Focal Segmental Glomerulosclerosis</td>
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### Industry Contracts

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**Current Year Direct Receipts**  
$115,487

**Total**  
$1,128,074