Nephrology and Hypertension

Division Photo

Back Row: L Patterson, J Goebel, B Dixon, C.F. Strife, J Bissler; Front Row: M Mitsnefes, E Jackson, K Czech, P Devarajan

Division Data Summary

Research and Training Details

Number of Faculty                              9  
Number of Research Fellows                     2  
Number of Research Students                    5  
Number of Support Personnel                    13 
Direct Annual Grant Support                    $1,206,219 
Direct Annual Industry Support                 $89,941   
Peer Reviewed Publications                     37

Clinical Activities and Training

Number of Clinical Staff                       3  
Number of Clinical Fellows                     6  
Inpatient Encounters                          2766 
Outpatient Encounters                         3350

Faculty Members

Prasad Devarajan, MD,  Professor
John J. Bissler, MD,  Associate Professor
Bradley P. Dixon, MD,  Research Instructor
Jens Goebel, MD,  Associate Professor Clinical
Elizabeth Jackson, MD,  Associate Professor Clinical
Mark Mitsnefes, MD,  Associate Professor Clinical
Significant Accomplishments in FY08

Nephrology and Hypertension -- Research Highlights

A simple new lab test predicts acute kidney failure: 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, radio-contrast administration, sepsis, nephrotoxic medications, subjects admitted to intensive care units, and even patients randomly presenting to the emergency room. Their results have recently been published in prestigious medical journals such as *Lancet* and *Annals of Internal Medicine*. 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. It is anticipated that these simple new tests will become widely accessible to the medical community 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 transplant drug proves effective in treating kidney tumors: One goal of medical research is to understand disease mechanisms in order to develop new and more effective treatments. This was true for the kidney and lung manifestations of tuberous sclerosis complex and a sporadic disease called lymphangioleiomyomatosis. The cell-signaling pathway that is disrupted in both these diseases is the same pathway that is suppressed by the transplant drug called sirolimus. A research team led by Dr. John Bissler, the Clark D. West Endowed Chair in Nephrology at CCHMC, conducted a study to determine whether sirolimus had any effect on the kidney tumors called angiomyolipomas and the lung manifestation called lymphangioleiomyomatosis found in both diseases. After one year of treatment with sirolimus, the average size of angiomyolipomas was reduced by nearly 50 percent in patients. Sirolimus also improved lung function in the lymphangioleiomyomatosis patients. These results have recently been published in *New England Journal of Medicine*. Dr. Bissler is now conducting a study to identify an optimum dosing schedule for this strategy, to understand the mechanisms of this response, and to identify biomarkers that predict the best response. Research in Dr. Bissler's laboratory is also looking at drug combinations to further optimize the treatment of these patients.

Significant Publications in FY08


This is the first study to validate a standardized laboratory platform for the measurement of a novel sensitive biomarker of acute kidney injury.
   This is the first study to demonstrate the efficacy of a new treatment regimen for angiomyolipomas.

   This is the first elucidation of a novel concept of using emerging biomarkers for the diagnosis and outcomes of acute kidney injury.

   This is the first demonstration of the utility of a novel biomarker for the prediction of acute kidney injury in a heterogeneous population.

   This is the first demonstration of decreased exercise tolerance in children with chronic kidney disease.

**Division Collaboration**

**Collaboration with Developmental Biology**
**Collaborating Faculty: S. Potter**
   Co-investigator for study entitled "Global gene expression atlas of the developing kidney"

**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: K. Dent; T. Kimball**
   Co-investigator for study entitled" Novel biomarkers for acute renal failure"
   Co-investigator for study entitled "Adioponectin 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 (DOD)
   Co-investigator for study entitled "Adioponectin and Cardiovascular disease in the CKID children"

**Collaboration with Interventional Radiology**
**Collaborating Faculty: J. Wansapura**
   Co-investigator on Tuberous Sclerosis Complex natural history study (DOD)

**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"

Mentions in Consumer Media

Division Publications


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**Grants, Contracts, and Industry Agreements**

**Grant and Contract Awards**

<table>
<thead>
<tr>
<th>Grant and Contract Awards</th>
<th>Annual Direct / Project Period Direct</th>
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<tbody>
<tr>
<td><strong>Bissler, J</strong></td>
<td></td>
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<tr>
<td><strong>DNA Replication Fork: Pausing, Recombination &amp; Disease</strong></td>
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<td>National Institutes of Health</td>
<td>05/01/03 - 02/28/09</td>
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<tr>
<td>R01 DK 061458</td>
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<td><strong>Tuberous Sclerosis Complex Natural History Study</strong></td>
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<td>Department of Defense - Army</td>
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<td>W81XWH-06-1-0538</td>
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<tr>
<td><strong>Czech, K</strong></td>
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<td><strong>Altered Gene Expression Using Microarray in Focal Segmental Glomerulosclerosis</strong></td>
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<td>National Institutes of Health</td>
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<td>F32 DK 079545</td>
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<tr>
<td>Devarajan, P</td>
<td>Implications of the ASK1/JNK Pathway in ARF</td>
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<td>Early Prediction of Lupus Nephritis Using Advanced Proteins</td>
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<td>Lai, H</td>
<td>Mechanism of Termination of Kidney Development</td>
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<td>Mitsnefes, M</td>
<td>Adiponectin and Cardiovascular Disease in the CKiD Children</td>
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<tr>
<td>Strife, C</td>
<td>Chronic Renal Insufficiency in NAPRTCS Patients</td>
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**Total Current Year Direct** | $1,206,219

**Industry Contracts**

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<thead>
<tr>
<th>Name</th>
<th>Company</th>
<th>Direct Costs</th>
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<tr>
<td>Bissler, J</td>
<td>Novartis Pharmaceuticals</td>
<td>$ 11,550</td>
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<tr>
<td>Devarajan, P</td>
<td>Ross Products Divisions, Abbott Labs</td>
<td>$ 22,715</td>
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<td>Mitsnefes, M</td>
<td>Kings Pharmaceuticals Res &amp; Dev, Inc</td>
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<td>Strife, F</td>
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<td></td>
<td>Liutpold Pharmaceuticals</td>
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**Current Year Direct Receipts** | $89,941

**Total** | $1,296,160