DIVISION OF NEPHROLOGY

BOSTON CHILDREN’S HOSPITAL
300 LONGWOOD AVENUE
BOSTON, MA 02115
Tel: 617-355-6129
Fax: 617-730-0569
COMMUNICATION WITH PROGRAM

Thank you for your interest in the Pediatric Nephrology fellowship training program at Boston Children’s Hospital. Enclosed is a brief summary of our current activities. It is strongly recommended that interested applicants visit our program so that we will have an opportunity to discuss all aspects of training with you. Most applicants have found this visit to be extremely helpful in clarifying training opportunities as well as our clinical and research facilities.

Please feel free to contact me if I can be of any assistance for further information at:

Arifa Kapadia, MS
Coordinator, Pediatric Nephrology Fellowship Program
Division Manager, Division of Nephrology
Boston Children’s Hospital
Email: arifa.kapadia@childrens.harvard.edu
Office: (617) 355-6129
Fax: (617) 730-0569

Page Metcalf
Administrative Associate, Division of Nephrology
Boston Children’s Hospital
Email: page.metcalf@childrens.harvard.edu
Office: (617) 919-7401
Fax: (617) 730-0365

PROGRAM DIRECTORS CONTACT INFORMATION

Michael A. Ferguson, M.D.
Director, Pediatric Nephrology Fellowship Training Program
Division of Nephrology, Boston Children’s Hospital
Assistant Professor of Pediatrics
Harvard Medical School
E-mail: michael.ferguson@childrens.harvard.edu
CURRENT STAFF

Friedhelm Hildebrandt, M.D.
Warren E. Grupe Professor of Pediatrics
Harvard Medical School
Chief, Division of Nephrology

Rannar Airik, Ph.D.
Instructor of Pediatrics

Michelle A. Baum, M.D.
Assistant Professor of Pediatrics

David M. Briscoe, M.D.
Associate Professor of Pediatrics

Ghaleb Daouk, M.D.
Director, Extramural Programs
Assistant Professor of Pediatrics

Paolo Fiorina, M.D., Ph.D.
Assistant Professor of Pediatrics

Michael Ferguson, M.D.
Instructor of Pediatrics
Co-Director, Pediatric Nephrology Training Program

Markus Frank, M.D.
Assistant Professor of Pediatrics

Heon Yung Gee, M.D., Ph.D.
Instructor of Pediatrics

William E. Harmon, M.D.
Professor of Pediatrics

Jordan Kreidberg, M.D., Ph.D.
Associate Professor of Pediatrics

Soumitro Pal, Ph.D.
Assistant Professor of Pediatrics

Nancy M. Rodig, M.D.
Assistant Professor of Pediatrics
Medical Director, Kidney Transplant Program

Valerie Schumacher, Ph.D.
Assistant Professor of Pediatrics

Michael J.G. Somers, M.D.
Director, Clinical Services
Associate Professor of Pediatrics

Deborah Stein, M.D.
Instructor of Pediatrics

Brian Wilson, Ph.D.
Instructor of Pediatrics
**Fellows**  
(Research and Clinical*)

<table>
<thead>
<tr>
<th>Name</th>
<th>Degree</th>
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<tbody>
<tr>
<td>Merlin Airik</td>
<td>M.D.</td>
<td>Tobias Hermle</td>
<td>M.D.</td>
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<tr>
<td>Murugabaskar Balan</td>
<td>Ph.D.</td>
<td>Tilman Jobst-Schwan</td>
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<td>Pallavi Banerjee</td>
<td>Ph.D.</td>
<td>Yun Joon Jung</td>
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<td>Roberto Bassi</td>
<td>M.D.</td>
<td>Nora M. Kochupurakkal</td>
<td>Ph.D.</td>
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<td>Moufida Ben Nasr</td>
<td>Ph.D.</td>
<td>Svjetlana Lovric</td>
<td>M.D.</td>
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<tr>
<td>Johan Boneschansker</td>
<td>M.D.</td>
<td>Oana Nicoara</td>
<td>M.D.*</td>
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<td>Daniela Braun</td>
<td>M.D.</td>
<td>Jia Rao</td>
<td>M.D.</td>
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<tr>
<td>Jing Chen</td>
<td>M.D., Ph.D.</td>
<td>Weizhen Tan</td>
<td>M.D.*</td>
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<tr>
<td>Won-Il Choi</td>
<td>Ph.D.</td>
<td>Sarah Twichell</td>
<td>M.D., M.P.H.*</td>
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<tr>
<td>Francesca D’Addio</td>
<td>M.D.</td>
<td>Asaf Vivante</td>
<td>M.D., Ph.D.*</td>
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<tr>
<td>Sandrine Ettou</td>
<td>Ph.D.</td>
<td>Jillian Warejko</td>
<td>M.D.*</td>
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<tr>
<td>Lakshmi Ganapathi</td>
<td>M.D.*</td>
<td>Johannes Wedel</td>
<td>M.D.</td>
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<tr>
<td>Qin Guo</td>
<td>Ph.D.</td>
<td>Eugen Widmeier</td>
<td>Ph.D.</td>
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<tr>
<td>Jessica Harris</td>
<td>Ph.D.</td>
<td>Le Zhang</td>
<td>Ph.D.</td>
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The central goal of the Pediatric Nephrology Fellowship Training Program at Boston Children’s Hospital has been to develop full-time academic Pediatric Nephrologists who establish independent investigative careers in areas relevant to the understanding of childhood Nephrological diseases. Our training program has expanded over the last 10 years and currently has two components. The first component is the training of academic pediatricians in the specialty of Pediatric Nephrology, including investigative biology and the basic science pertaining to the pathophysiology of pediatric kidney disease. The second component of our program is to train scientists in the specialty of Pediatric Nephrology. Trainees who enter our program are exposed to a wide variety of individuals, all dedicated to investigative Nephrology. Our faculty has expertise in many different specialties and our trainees include students, pre-doctoral and postdoctoral candidates as well as Ph.D.’s. Our program ensures that all trainees work side by side which enhances their mutual education and creates an environment for rigorous scientific investigation. Thus, our program is not only established for the training of Pediatric Nephrologists but also for the advancement of biomedical research in the specialty of Pediatric Nephrology.

Since its inception in 1974, our program has graduated over 75 fellows from the ACGME-accredited Pediatric Nephrology fellowship program. Graduating Pediatric Nephrology fellows fulfill the criteria for certification in Pediatric Nephrology by the American Board of Pediatrics and the specialty sections of the American Academy of Pediatrics. Graduates of our program include two Department Chairmen, 10 Directors of Pediatric Subspecialty Divisions and 12 Directors of major research laboratories. In total we have trained at least 20 independently funded Pediatric Nephrologists since the inception of the program and virtually all of our trainees are full-time faculty in academic pediatric hospitals or universities.

At the national and international level, several of our graduates are regarded as key innovators in the science of Pediatric Nephrology. Several are members of NIH study sections and are recognized as leaders in nephrology research. At least four of our graduates, Drs. A. Davis, A. Arnaout, A. Krensky and D. Briscoe, are members of the American Society of Clinical Investigation. Dr. L. Guay-Woodford is a leader in the field of inherited renal diseases. Dr. Ellis Avner, Director of the Children’s Research Institute of Wisconsin and Associate Dean for Research at the Medical College of Wisconsin, is internationally known for his work in polycystic kidney disease. Dr. Alan Krensky, is internationally known for his research in cellular and molecular immunology. Drs. Harmon and Briscoe are recognized experts in kidney transplantation and both have held leadership roles in the American Society of Transplantation. Dr. Norm Rosenblum of the Hospital for Sick Children in Toronto, Canada is regarded as an expert in the area of renal developmental disorders. In addition, some of our recent graduates have clearly identified themselves as future leaders. Dr. Stuart Goldstein of the Cincinnati Children’s Hospital is a leader in clinical and translational research, particularly in the areas of hemodialysis, acute kidney injury, and optimal renal management of critically ill children. Dr. Vikas Dharnidharka, Director of Pediatric Nephrology at Washington University School of Medicine, is increasingly recognized as an
expert in the area of post transplant lymphoproliferative disorder.

We believe that our program offers large and diverse training opportunities. Our Training Faculty are leaders in their fields and have significant experience in clinical and research mentorship. We strive to promote and offer our trainees access to opportunities for developing innovative concepts that have the potential to lead to a productive career in the understanding and treatment of childhood renal diseases. As a result of all of these endeavors, our program is currently recognized as a leading national and international resource for training in broad areas of renal diseases.
DESCRIPTION OF THE TRAINING PROGRAM

The Division of Nephrology at Boston Children’s Hospital is currently the largest Pediatric Nephrology division in the United States. One of the central goals of the Division is to develop academic Pediatric Nephrologists who will be able to establish independent investigative careers in areas relevant to the understanding of childhood renal diseases. The Fellowship Program provides broad training in all the major areas of Nephrology with opportunities to develop clinical and research skills. There are three years of training composed of one clinical year and two years of laboratory research. The Training Program meets the requirements for certification by the Sub-board of Nephrology of the American Board of Pediatrics.

The clinical training year provides the Fellow with extensive exposure to a wide variety of clinical problems in Pediatric Nephrology accomplished by full participation of fellows in all the patient care activities within the Division. This includes the direct care of Nephrology inpatients, serving as consultant to both inpatient and outpatient divisional programs; as well as the care of the transplant and pediatric dialysis outpatients and the general Nephrology outpatients clinic. Fellows become proficient in all of the technical aspects of Nephrology such as performing renal biopsies, hemodialysis and peritoneal dialysis. In addition, the Fellows acquire experience through the Department of Pathology in the interpretation of light, immunofluorescence and electron microscopy, and through the Department of Radiology in the interpretation of uroradiologic studies.

The Division has two clinical services: the End-Stage Renal Disease Service (dialysis and transplantation); and the General Renal Consult Service. Each Fellow spends approximately equivalent time on the End-Stage Disease and the Consult Services. The fellow is responsible for: 1) supervising the care of all inpatients who are followed by the Division of Nephrology; 2) providing consultant services for Boston Children’s Hospital and the neonatal intensive care unit at the Brigham and Women’s Hospital and Beth Israel Deaconess Medical Center, as well as affiliated community hospitals; and 3) performing acute dialysis and hemofiltration as well as all percutaneous renal biopsies.

The two research fellowship years are aimed at broadening the Fellow’s understanding of renal disease. One of the unique aspects of our training program is the ability to participate in one of the many ongoing research efforts in the Nephrology Research Laboratories and in our Transplant Research Program. The Director of Fellowship Training Program, Dr. David Briscoe meets with fellows and coordinates meetings with the research faculty approximately six months prior to initiating the research fellowship years. Our research faculty share a common interest and expertise in cellular and molecular biology, immunology, renal development, glomerular disease and transplantation biology. Research on the cell biology and transport mechanisms present in epithelia of the kidney, lung, and cell of the central nervous system are also interests within the faculty. Our renal development research program has a focused interest in the molecular regulation of organogenesis. We are expanding our program in glomerular disease, which currently is focused on the pathophysiology of glomerulosclerosis. Also, a specific interest of the clinical research faculty is the pathophysiology of chronic renal disease in children. Ongoing studies address growth abnormalities and defining risk factors influencing outcome of children undergoing chronic dialysis and transplantation therapies.
It is noteworthy that the clinical and basic research facilities of the Division of Nephrology are in close proximity to each other. Thus, the research and clinical faculty, as well as the fellows-in-training do truly have the ability to interact and share the resources listed below. The proximity of the clinical and research environments enables extensive interactions to occur among all members of the Nephrology staff. This mix and interactive environment among Clinicians, Physician-Scientists and Basic Science Researchers are the basis for innovation as a major Pediatric Nephrology Research Center.

Our Fellowship Program in Pediatric Nephrology has attracted aspiring trainees throughout the United States. In general, the schedule is designed to promote optimal exposure to all aspects of Pediatric Nephrology during the training years. Fellows are expected to prepare and present clinical conferences each month. In addition, Fellows actively participate in medical student teaching and house officer conferences. In subsequent years, the Fellow participates in research conferences and makes periodic presentations of his/her research efforts at individual laboratory as well as divisional research laboratory seminars and journal clubs. Lastly, all research fellows are encouraged to attend Harvard seminars specific to their research interest including the Harvard Medical School Seminars in Immunology and Vascular Biology.

Our program has purposefully maintained an emphasis on basic-science research training for several decades. As discussed earlier, this relates to the need as well as our success in the development of Physician-Scientists. Recently, with increasing attention paid to “translational research”, we have begun training our fellows to bridge the gap between bench and bedside. Our trainees have attended Clinical effectiveness training programs at the Harvard School of Public Health and the elite Clinical Investigator Training Program of the Massachusetts Institute of Technology to further expertise in translational research studies.

We expect that translational clinical research training will expand substantially as new programs and opportunities are expanding in the local Harvard Medical Area. Boston Children’s Hospital has initiated a Translational Research effort, directed by Dr. David Williams, and Harvard Medical School has recently recognized the need for formalization of Translational Research training. There are plans to initiate a new training-track in that discipline. Further, the recently awarded Harvard-wide Clinical and Translational Science Award (CTSA) will likely enhance the discipline of translational research within the local medical area, and provide exceptional opportunities for the education of Nephrology Fellows in translational research.

Fellows are introduced to translational research in a 3-step process. We initially plan for trainees who are interested in translational research to meet with our Program Faculty including Dr. Williams (Director of the Translational Research Program (TRP) at Boston Children’s Hospital) and/or Co-directors of the Program. Fellows will also meet with Dr Karumanchi who will introduce them to initiatives at the Howard Hughes Medical Institute. These initial meetings will serve to solidify the trainees’ interests and to ensure that they are aware of opportunities in the local Medical Area. The TRP initiative as well as the Harvard Catalyst are also available to trainees and their involvement will results in their participation in coursework, seminars and retreats. These center-specific activities will also introduce our trainees to their peers’ common interests. The second and third steps in the structure for training will involve the selection of courses as well as the selection of a translational research mentor. The research mentor is key, and will enable the trainee to learn appropriate skills for laboratory based techniques and assays to be performed on samples collected as an integral part of the translational research study. The choice of research mentor, and the project is discussed with Drs. Hildebrandt, Briscoe and Ferguson, and a Scholarship Oversight Committee is created for the trainee. Trainees will be expected to attend one course in translational research either at Harvard Medical School, the Harvard
School of Public Health, the Massachusetts General Hospital or the Clinical Investigator Training Program offered by the Massachusetts Institute of Technology. Enrollment in these courses is competitive and most demand a minimum of a 2-year commitment. Finally we wish to emphasize that the facilities for research training in our institution and in the local Harvard community are unparalleled and these opportunities have characterized our academic programs and our division. Recognizing that two years of research training is in most cases insufficient to develop an individual into a fully independent investigator, several nephrology fellows in our training program extend their initial two years of research training and continue research investigation for additional years of research training that are typically supported by other grants. We encourage this extended training for fellows who are dedicated to careers as Physician-Scientists.
OVERVIEW OF THE CLINICAL TRAINING YEAR

Yearly Schedule

<table>
<thead>
<tr>
<th>Service</th>
<th>Total Months</th>
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<tbody>
<tr>
<td>End-Stage</td>
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</tr>
<tr>
<td>Consult</td>
<td>6.0</td>
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Weekly Schedule

A. End-Stage Service: Transplant/Dialysis
   1. Inpatient rounds and outpatient dialysis rounds: daily
   2. Transplant clinic: twice weekly
   3. Dialysis review: weekly
   4. General Renal clinic: weekly
   5. Division research conference: weekly
   6. Division clinical conference: weekly

B. Consult Service
   1. Inpatient rounds: daily
   2. Renal biopsies: weekly
   3. General Renal clinic: weekly
   4. Transplant clinic: weekly
   5. Division research conference: weekly
   6. Clinical conference: weekly
   7. Firm Rounds

Call Schedule

A. First Year: every fourth week
B. Second Year: every seventh week
C. Third Year: every thirteenth week

Annual Number of procedures performed in the Division are as follows:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number</th>
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<tbody>
<tr>
<td>Renal Biopsies</td>
<td>45</td>
</tr>
<tr>
<td>Outpatient Visits</td>
<td>5000</td>
</tr>
<tr>
<td>Inpatient Consults (Plus Nephrology Patients)</td>
<td>5000</td>
</tr>
<tr>
<td>Renal Transplants</td>
<td>20-30</td>
</tr>
<tr>
<td>Acute Peritoneal Dialysis Treatments</td>
<td>10-20</td>
</tr>
<tr>
<td>Acute Hemodialysis Treatments</td>
<td>600</td>
</tr>
<tr>
<td>Chronic Hemodialysis Treatments</td>
<td>3000</td>
</tr>
<tr>
<td>CAPD-CCPD Patient-Months</td>
<td>50-100</td>
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DESCRIPTION OF BOSTON CHILDREN’S HOSPITAL AND THE HARVARD MEDICAL SCHOOL ENVIRONMENT

Boston Children's Hospital is one of the largest pediatric hospitals in the United States, and a major teaching facility of Harvard Medical School. Founded in 1869 as a 20-bed hospital for children, it is now a comprehensive medical center for pediatric and adolescent health care, dedicated to excellence in patient care, teaching and research. There are 196 inpatient beds in the main hospital building. The hospital houses two multidisciplinary intensive care units (41 beds), a neonatal intensive care unit (28 beds), a cardiac intensive care unit (24 beds), a bone marrow transplantation unit (12 beds), and a clinical research center. There are more than 100 outpatient programs ranging from primary care to a wide variety of specialty programs. Outpatient facilities include an 11-story building for ambulatory services. During the coming years, Children's plans to expand to almost 500 beds, adding another clinical building and an additional 21-story research building.

The Hospital is the primary pediatric teaching hospital of Harvard Medical School, where our staff have faculty appointments. The hospital's clinical staff includes approximately 960 active medical staff and 897 residents and fellows. Boston Children's Hospital has repeatedly been rated as one of the best hospital specializing in pediatric care in the nation.

As a major pediatric referral center, the mission of Boston Children's Hospital is to provide the highest quality health care. In support of this mission, Children's strives to be the leading source of research and discovery, seeking new approaches to the prevention, diagnosis and treatment of childhood diseases as well as education of the next generation of leaders in child health. Boston Children's Hospital consistently receives the highest amount of NIH grant support among independent pediatric institutions in the USA, and ranks 5th for NIH grant support to all independent domestic hospitals.

The research infrastructure for pediatric research at Boston Children’s Hospital is one of the largest in the world. Laboratory research is conducted in two buildings: the Enders Research building, which consists of approximately 184,000 square feet of space and the Karp Building, a 16-story facility, which was completed in 2004. The Karp research building is a 140,000 square foot facility, and has increased the total laboratory research space at Boston Children's Hospital to approx. 324,000 square foot. Of this, the Department of Medicine occupies approx. 200,000 square feet. This has allowed the expansion of all of the research programs within the Department of Medicine. An additional new research building is planned for completion in 2010, which will add another 100,000 square foot of research space. These expansions have resulted in the recruitment of new faculty, which is likely to continue over the next decade.

Approx. 30,000 square foot of space is devoted to clinical research. This is in addition to the space occupied by our NIH-funded General Clinical Research Center (GCRC) devoted solely to pediatric investigation. The inpatient GCRC is an 8-bed unit centrally located within the main building of Children’s and is organized to support the management of children participating in clinical research. Clinical research is also supported by the Clinical Research Program (CRP), which provides methodological expertise to the clinical research community.
The research facilities at Boston Children's Hospital are situated in the center of the Longwood Medical Area where Harvard Medical School and 3 other major teaching hospitals including Brigham and Women's, Beth Israel Deaconess Medical Center, and Dana Farber Cancer Institute are located. The hospital is within one block of the Joslin Diabetes Center, the Massachusetts College of Pharmacy, the Harvard School of Public Health, the Harvard Dental School, the Harvard Institutes of Medicine, the Channing Laboratory, and the Center for Blood Research Institute of Biomedical Research. We have taken advantage of our Division's location within this medical research area to provide a large number of educational opportunities for nephrology research trainees. We wish to emphasize that researchers at Boston Children’s Hospital greatly benefit from their location within the Harvard Medical community, and at the same time it should be recognized that the hospital is a free-standing world renowned research institution.

Our Nephrology Division is one of 14 divisions of the Department of Medicine at Boston Children's Hospital. The Division consists of 19 faculty. This includes 15 full time members (Drs. Airik, Briscoe, Daouk, Ferguson, Frank, Gee, Harmon, Hildebrandt, Kreidberg, Pal, Rodig, Schumacher, Somers, Stein, and Wilson). Dr. Hildebrandt is the Chief, Dr. Ferguson serves as Fellowship Training Program Director, Dr. Somers directs the clinical services, and Dr. Rodig directs the Renal Transplant Program. At present, there are 6 Pediatric Nephrology fellows and 26 post-doctoral research fellows receiving research training in the Division by our Faculty.

**Clinical Resources and Environment**

Drs. Rodig and Somers principally oversee the large number of clinical nephrology services offered by our Division. These services include a 7-bed pediatric dialysis unit providing acute and chronic hemodialysis, peritoneal dialysis, and continuous renal replacement therapy (CRRT) for infants, children, and adolescents with acute and chronic renal failure. The unit performs approximately 3,000 extracorporeal treatments annually. The dialysis unit and its accompanying renal transplantation program comprise the End Stage Renal Disease (ESRD) Program that has a staff of 13 dialysis nurses, 2 renal transplant coordinators, 2 social workers, a dietitian, a full-time research nurse and data coordinator, and 2 secretaries. Patients treated by this program who require hospitalization are routinely admitted to a dedicated 20-bed inpatient Solid Organ Transplant Unit located at the hospital. Dr. Harmon, the predecessor to Dr. Rodig, has developed most of the protocols used by the staff, who are specialized in the care of organ transplant recipients. The renal transplantation program performs approximately 20 – 30 renal transplants annually, and is among the larger pediatric renal transplant programs in the country. The clinical faculty also provides specialized dialysis services in the two pediatric intensive care units, the cardiac intensive care unit, the neonatal intensive care unit, and the bed bone marrow transplant unit.

The outpatient care of the division is administered through 2 ambulatory programs. The General Renal Program has approximately 3800 patient visits annually. The Renal Transplant Ambulatory Program has approximately 1200 visits annually, for a total of approximately 5000 outpatient visits annually. These programs are staffed by 5 ambulatory nurse coordinators as well by our Division’s professional and secretarial staff.
The nephrology office has 5 full time administrative staff and the research laboratory office has 4 administrative staff. In the research laboratories, every fellow has a personal computer, linked to the hospital wide electronic data network. At Boston Children's Hospital, all clinical information (including complete inpatient and outpatient medical records as well as laboratory data) is maintained in an integrated Electronic Medical Record. In addition, most medical journals are available in electronic form through a link with Harvard’s Countway Medical Library. Thus, the hospital network provides fellows with immediate access to patient material, research literature, databases and other Internet-based systems. In addition, each fellow is given an electronic mail box and can communicate with all hospital personnel and outside collaborators via this medium.

Research Resources and Environment

Research Space: The Division of Nephrology Research Laboratories consists of 7,500 square feet of research space including 38 benches and core facilities for tissue culture, molecular biology, protein assays, FACS analysis, immunohistochemistry and for radioactive work. Our research facilities and laboratories are housed on the 5th floor of the Enders Research Building. The divisional research space also includes several storage rooms that contain refrigerators, freezers, and large centrifuges. The Transplantation Research Center (TRC), directed by Dr. Sayegh, is a collaboration between our Division and the Brigham and Women’s Hospital, and Harvard University also has dedicated research space within our laboratories. The TRC houses 6 Principal Investigators and their laboratories at the Boston Children’s Hospital location. In addition, there are plans for the expansion of our research facility by the recruitment of 1-2 additional investigators into our laboratories. Each principal investigator has a personal office.

Research Equipment: Over the past five years the Division of Nephrology has evolved into one of the major research divisions at Boston Children’s Hospital. Each independent investigator has a well-equipped laboratory and independently acquires modern biomedical instrumentation as is necessary for their ongoing studies. As such, within the Division’s laboratories, there is equipment for cell culture, immunological assays, cell biology, molecular biology, and developmental biology research. For the most part, investigators share such instrumentation on an as needed basis.

Major Research Facilities at Boston Children’s Hospital

Animal Research Facilities: Boston Children’s Hospital operates ARCH (Animal Research at Children’s Hospital), a major ALAAC approved state-of-the-art modern virus-free animal facility housed in 4 floors the Enders and Karp research buildings, for the housing of animals in microisolator cages and for procedure rooms. In addition, there is also a large Zebrafish facility and facilities for large animal studies. All Nephrology Division investigators maintain their experimental animals in the Enders facility. Two full time veterinarians direct the ARCH facility. All experimentation by individual Principal Investigators involving animals is approved by the Institutional Animal Care and Use Committee (IACUC), and all personnel working with animals must attend animal use orientation and are required to gain appropriate training prior to approval on each investigators protocol.

Transgenic Core Facility: Drs. Briscoe and Kreidberg are members of the core transgenic facility. This facility is fully equipped and staffed to perform both pronuclear and blastocyst injections to obtain
transgenic and knockout mice. Generation of mice are guaranteed at a cost from this facility, and once generated, they are transferred to the investigators protocol within the ARCH animal housing facility.

**Histology cores:** Several Cores are available. One is located within the Department of Pathology at Boston Children’s Hospital; others are available locally at the Dana-Farber/Harvard Cancer Center, the Brigham and Women’s Hospital and Harvard Medical School. Facilities provide paraffin embedding and sectioning, frozen sections, in situ hybridization as well as laser capture microdissection and expression genomics. In addition, an electron microscope core facility is available at Harvard Medical School, a few minutes away from Boston Children’s Hospital. This facility is staffed two technicians, and provides the full array of electron microscopic analysis, including frozen sectioning for EM and immunogold staining.

**The Proteomics Center at Boston Children's Hospital:** Led by Hanno Steen, Ph.D., the Proteomics Center at Boston Children's Hospital offers the most up-to-date proteomics equipment currently available. This includes the latest equipment for protein separation and several state-of-the-art mass spectrometers, which detect and quantify proteins in a sample and measure them to determine their structure and characteristics. The Center draws on the capabilities of the Children's Hospital Informatics Program (CHIP, see below), whose powerful computational tools help reveal how groups of proteins interact and collaborate to do the work of the body. Proteomic Center projects involve both basic science and disease-related research. Investigators study the proteins encoded by an array of genes to better understand how diseases arise, while clinical researchers use the Center for screening application -- analyzing patients' blood and urine samples to find proteins that can serve as diagnostic and prognostic markers for a variety of diseases.

**Bioinformatics:** The Children’s Hospital Informatics Program (CHIP) is a multidisciplinary applied research and education program at Boston Children's Hospital. CHIP focuses on both bioinformatics and clinical informatics. CHIP bioinformatics research endeavors include development of statistical and computational techniques for analyzing gene expression data from microarrays under various experimental settings and for analyzing SNP (Single Nucleotide Polymorphism) data in performing large-scale association studies. CHIP staff also develop tools to integrate various databases effectively, and combine information from various genomic and proteomic data to gain insights into biological pathways. CHIP funding comes from multiple sources and collaborations, including NLM, NIHGR, NCI, NHLBI, NINDS, NIDDK, and NIAID. Web-based and downloadable bioinformatics resources created and maintained by CHIP (http://www.chip.org/).

**Computing Facilities at Boston Children’s Hospital:** There is a Research Computing Core Facility at Boston Children’s Hospital. Two user work areas are available: the Enders User Work Area located in Enders 151 and the Medical Library Work Area located in the Medical Library. The Enders User Work Area is open to all hospital employees Monday through Friday 8 a.m. to 5 p.m. Access is also available after hours, by pass-card, for the research community. The Medical Library User Work Area is open to all hospital employees 8 a.m. to 7 p.m. Monday through Friday. Access is also available after hours with approval from the hospital librarian. Both work areas have a variety of hardware and software running on PCs and Macs to meet the needs of the user community. Instruction is available on the use of any of the equipment and staff are available during normal working hours to respond to questions.

**Medical Literature Searching:** Medical literature searching is provided online to all trainees through the hospital library and access to the Countway library holdings. Access to most online journals is also available through this medium. Thus, on a 24 hour basis through the Hospital network, trainees can...
access literature searching and most internationally recognized online journals. Courses on the tools and how to construct searches are offered regularly through a NetLearning Program offered by the hospital.

**Genetics Sequence Analysis:** As mentioned above, sequencing cores are available to trainees within the Division of Genetics/Mental Retardation Research Center. In addition, Genetics Computer Group’s (GCG) genetics sequencing software is provided through Research Computing, and web-based GCG is available to all computers connected to the Hospital Network. Other tools are located in the user work area located through the hospital network. Software and training is available in the cores (discussed above) in GCG, Genbank, Primer (for PCR primers, Blast) through the National Library of Medicine Super Computer, MacVector, and Sequencher etc.

**Statistical Packages:** The department of Research Computing has a Ph.D. statistician who provides statistical consulting services to all researchers and clinicians at the hospital. The statistician is available to answer questions pertaining to research design and methodology, analysis of experimental data, and statistical computing. In addition, Boston Children’s Hospital has a Clinical Research Program (CRP) that provides assistance to investigators in trial design, data acquisition and management, statistical analysis and so forth. Statistical support is also available through the CHIP program and through interactions among dedicated Ph.D. level personnel who work with individual PI’s and their laboratories.

**Software and Hardware:** Research Computing offer a variety of hardware and complementary software to support graphics and drawing. Every possible commonly used software package is licensed through research computing.
Lecture Series on Introduction to Clinical Pediatric Nephrology: This year-long lecture series is staffed by Boston Children’s Hospital faculty, coordinated by Dr. Stein, and designed for clinical nephrology trainees, including rotating residents and medical students. Twice-weekly lectures follow an established curriculum that addresses essential concepts in pediatric nephrology, including principles of dialysis and transplantation, as well as subjects related renal physiology, developmental biology, inherited renal diseases, renal pathophysiology, immunology, pediatric urology, and uroradiology.

Nephrology Research Seminars: The Harvard Medical Area provides a rich source of seminars on a broad range of scientific and clinical subjects. Our Division sponsors a Renal Seminar Series involving invited outside speakers that occurs on average once per month from Oct-June each year. Outside seminars are organized by Drs. Kreidberg and Briscoe. In addition, Dr. Baum coordinates a special annual renal seminar series with the New England Pediatric Nephrology Group.

Individual Laboratory Conferences: Fellows also present their results, or recent relevant research, in the weekly lab meetings of their respective research laboratory.

Nephrology Laboratory Conferences: These are intra-divisional conferences where research fellows present their recent data for critical evaluation by members of the division. Each research fellow presents at this meeting at least once per year. Conferences are scheduled weekly but alternate with the research seminars, described above. This conference series is organized by Dr. Kreidberg and attendance at these conferences is required for both Pediatric Nephrology and post-doctoral research fellows in the division.

Clinical Conferences: All Pediatric Nephrology Fellows attend a weekly clinical conference organized by Dr. Baum. Conferences alternate between morbidity and mortality conference, biopsy pathology reviews, presentations by fellows and staff of pertinent clinical issues in pediatric nephrology, and presentations by invited speakers from the Longwood Medical area covering topics germane to clinical nephrology. Pediatric residents, medical students and any outside observer rotating through the division also attend these conferences.

Journal Clubs: There are two research journal clubs, each occurring twice monthly and involving local laboratories with common interests. Individual research fellows are encouraged to attend one journal club. In addition, there is a clinical journal club for Pediatric Nephrology fellows during their clinical training.

Shankman Library: Our Division maintains a library of approximately 100 textbooks and 20 journal subscriptions that provide fellows and faculty with immediate access to reference information on renal physiology, cell and molecular biology, and pediatric nephrology clinical care. Dr. Harmon provides oversight for the library and maintenance of its resources.

Clinical Research Office: The clinical research area is located within the ESRD program’s office suite. In this area, clinical research protocols are available for examination including those funded by the NIH such as the U01 Clinical Trials in Organ Transplantation in Children (CTOT-C) studies. Four dedicated
personal computers for research use, a research nurse-coordinator, and a research assistant are found in this office space.

**Biopsy slide library:** A collection of original biopsy specimens of cases from 1972 to present is maintained at Boston Children's Hospital. Moreover, a computer-based library has been created over the last 5 years containing representative electronic images from every renal biopsy performed in the Division.

**Computing:** The Division offers all trainees their own individual computer, as well as all the required software applications appropriate for their research training. These include access to the intranet of the hospital, as well as access to online journals through the hospital library and the Countway library at Harvard Medical School. In addition, trainees have access to networked research specific applications on computers distributed within offices and throughout the laboratory space.
OVERSIGHT OF TRAINING

Scholarship Oversight Committees (SOCs) are developed for each trainee and consist of three or more individuals including the research mentor, a clinical faculty member and a third individual from outside the subspecialty discipline. Each trainee is expected to meet with their outside SOC member at least yearly. Scholarship oversight is designed to ensure that each trainee is provided with sufficient feedback concerning his or her research progress and career development. For the purpose of programmatic oversight, the committee meets twice yearly. This ensures that each trainee can be discussed by all committee members as a whole and ensures that mentors and the program are maximizing opportunities to individual trainees.
1. **Friedhelm Hildebrandt, M.D.** is the *Warren E. Grupe Professor of Pediatrics* at Harvard Medical School and Chief of the Division of Nephrology of Boston Children's Hospital. Dr. Hildebrandt is also an Investigator of the *Howard Hughes Medical Institute (HHMI)*.

**Research Interests:** Dr. Hildebrandt's research work is concerned with the identification and functional characterization of recessive single-gene causes of kidney diseases in children, including nephrotic syndrome, cystic renal ciliopathies, and congenital anomalies of the kidney. His group has identified over 50 novel causative genes for chronic kidney disease and delineated the related pathogenesis. Dr. Hildebrandt’s lab studies the function of newly identified disease genes in disease models of mice and zebrafish as well as in cell-based systems. His work was involved in the early development of efficient methods for gene identification by combining homozygosity mapping with total human exome resequencing. Recently, his group discovered that DNA damage repair plays a role in the pathogenesis of ciliopathies (Chaki et al. *Cell* 150:533-48, 2012; Zhou et al. *Nat Genet* 44:910-15; editorial p. 836-8). His lab has recently shown that in a very high percentage of cases with chronic kidney disease of childhood a single gene may be identified using high-throughput sequencing technologies. The research work of his lab has been supported solely by peer-reviewed research grants, mostly from the NIH, the HHMI, the Doris Duke Charitable Foundation, the March of Dimes, the NephCure Foundation, the Thrasher Research Foundation, and the German Research Foundation. He has published over 240 original articles, many of them in high-ranking journals.

**Summary:** Dr. Hildebrandt received his M.D. from Heidelberg University, obtained his pediatric and nephrology subspecialty training at Marburg University Children's Hospital, and was a postdoctoral research fellow in the Department of Internal Medicine at Yale University Medical School. He received the *E. Mead Johnson Award* from the Society for Pediatric Research (2004), the *Franz Volhard Award* of the German Society of Nephrology (1997), and *Lillian Jean Kaplan Award for Polycystic Kidney Disease Research* (ISN, 2009). Dr. Hildebrandt was a *Heisenberg Scholar* of the German Research Foundation (DFG) and a *Doris Duke Distinguished Clinical Scientist* (2006-2014). He is an elected Member of the *Association of American Physicians* and of the *German National Academy of Sciences*.

2. **William E. Harmon, M.D.,** Professor of Pediatrics, Harvard Medical School

**Research Interests:** Pathophysiology and treatment of end-stage renal disease (ESRD) in children, Clinical Trials, Novel Immunosuppression, Tolerance induction.

**Summary:** Dr. Harmon is internationally recognized as a leader in pediatric organ transplantation. He serves on several NIH Study Sections evaluating and promoting transplant and dialysis research and is currently a permanent member of DDK-D. He is the President of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) organization. Dr. Harmon has served as the President of the American Society of Transplantation (AST), as well as serving as its Secretary-Treasurer and the Chairman of its Public Policy and Pediatrics Committees; the Board of Directors of the International Pediatric Transplant Association (IPTA); the Transplant Advisory Group and the Public Policy Board of the American Society of Nephrology; and the Public Policy and Advocacy Committee of the American Society for Pediatric Nephrology. Dr. Harmon’s prominence in pediatric transplantation led to his appointment as the first Chairman of the permanent Pediatric Committee of the United Network for Organ Sharing (UNOS) and he has served three terms on its Board of Directors. He has also served as the Chairman of the Board of the New England Organ Bank. He has been a member of the DHHS
Secretary’s Advisory Committee on Transplantation (ACOT) and was the pediatric consultant to the Scientific Registry of Transplant Recipients (SRTR). Dr. Harmon’s particular interest pertains to immunosuppression to optimize successes following pediatric renal transplantation. He developed the studies and protocols that were subsequently used as the basis for the development of the Cooperative Clinical Trials in Pediatric Transplantation (CCTPT) and its successor, Clinical Trials in Organ Transplantation in Children (CTOT-C), which have been sponsored by a U01 mechanism through NIAID. These trials have been extremely productive and have been the basis of new techniques for provision of renal transplantation to children. One of the most innovative components of these studies are mechanistic studies that are integral to all clinical trials, including the description and analysis of intragraft gene expression, effector and regulatory T cell responses, monitoring of alloantibody production, and blood and urine monitoring by gene arrays as biomarkers of ongoing rejection or tolerance. Dr. Harmon has been principal investigator on the consortiums that has been awarded positions in the CCTPT and CTOT-C and he has been Chair of studies’ Steering Committees. In addition to these scientific studies, Dr. Harmon is actively involved in issues concerning organ donation and allocation on which he has published multiple articles. He served as the Chairman of the Board of Trustees of the New England Organ Bank, one of the largest organ procurement organizations in the United States, has served several terms on the Board of Directors of UNOS and recently participated in the Istanbul Summit on Organ Trafficking and Transplant Tourism. Dr. Harmon also has extensive experience in the elements of pediatric dialysis, specifically urea kinetic modeling to monitor and prescribe hemodialysis treatments for children. He designed and directed the US multicenter trial of recombinant human erythropoietin in children undergoing chronic dialysis. Dr. Harmon has been one of the editors for the last three editions of *Pediatric Nephrology*, the internationally-recognized principal comprehensive textbook in the field. He has also been an editor of both editions of *Pediatric Solid Organ Transplantation*.

3. **Michael Somers, M.D.**, Director, Clinical Services, Assistant Professor of Pediatrics, Harvard Medical School.

**Research interests:** Focal and segmental glomerulosclerosis, renal replacement therapy in children.

**Summary:** As Clinical Director, Dr. Somers has significant interactions with pediatric renal fellows on our clinical service and has been involved in the training of many renal fellows and pediatric residents. Dr. Somers has initiated several mechanistic studies with members of our research training faculty. His active clinical research interests include the application of continuous renal replacement therapies in children with acute kidney injury as well as therapies in pediatric nephrotic syndrome. Dr. Somers is the local Principal Investigator on an NIH-sponsored multicenter trial for treatment of Focal Segmental Glomerulosclerosis in children as well as the Novel Therapies Trial in Pediatric FSGS. He is also a founding Principal Investigator of the Prospective Pediatric CRRT Registry. Dr. Somers also has participated in Harvard Medical School courses on renal physiology and pediatric physical diagnosis.

4. **Michelle Baum, M.D.**, Assistant Professor of Pediatrics, Harvard Medical School.

**Summary:** Dr. Baum’s major focus is the teaching and training of fellows in clinical nephrology. In addition, Dr. Baum has several clinical research interests pertaining to her involvement with the Myelodysplasia Program and Renal Stone Program at Boston Children's Hospital. She has also initiated clinical research studies in the pediatric nephrolithiasis population in collaboration with the Urology Department. She has an interest in how bladder abnormalities might affect renal function and she is designing a registry to follow patients with myelodysplasia and assess factors that will predict long-term renal dysfunction. Dr. Baum has participated in several projects with the North American Pediatric
Renal Transplant Cooperative Study (NAPRTCS) involving the effect of native renal diseases, particularly FSGS, on renal transplant outcome. She has also initiated clinical research program in pediatric nephrolithiasis in collaboration with the Urology Department.

5. Nancy Rodig, M.D., Medical Director, Kidney Transplant Program, Assistant Professor of Pediatrics, Harvard Medical School.

Summary: Dr. Rodig has developed clinical research studies involving translational mechanisms related to the outcome and treatment of pediatric patients with end-stage renal disease. She has a significant interest in transplantation and in immunosuppression. Dr. Rodig is the local Principal Investigator for an NIH-sponsored prospective multi-center study of Chronic Kidney Disease in Children. Through these activities she has significant interactions with all pediatric renal fellows while on the clinical service.

6. Ghaleb Daouk, M.D., Director, Extramural Programs, Assistant Professor of Pediatrics, Harvard Medical School.

Research Interests: Urinary tract infection, vesicoureteral reflux.

Summary: Dr. Daouk directs outpatient clinics in affiliated hospitals and at Boston Children’s Hospital outreach centers. He is significantly involved in the teaching of renal fellows while training on the clinical service. Dr. Daouk has an interest in pediatric urinary tract infection and vesicoureteral reflux and serves as center Principal Investigator on a NIH-sponsored multicenter trial of Randomized Intervention for Children with Vesicoureteral Reflux.

7. Michael A. Ferguson, M.D., Director, Pediatric Nephrology Fellowship Training Program, Director, Renal Hypertension Program, Assistant Professor of Pediatrics, Harvard Medical School.

Research Interests: Acute kidney injury, pediatric hypertension.

Summary: Dr. Ferguson joined the clinical faculty in July 2008. He has an interest in biomarker development for the prediction of acute kidney injury (AKI). He is the Principal Investigator for two studies evaluating novel biomarkers for the early prediction of AKI in pediatric patients following cardiac surgery. He is also collaborating with local and regional pulmonologists to evaluate the utility of biomarkers in cystic fibrosis patients receiving nephrotoxic medications. Dr. Ferguson is the Director of the Renal Hypertension Program and the Co-Director of the newly formed Midaortic Syndrome and Renovascular Hypertension Program. He is participating in a number of Quality Improvement initiatives related to pediatric blood pressure measurement. He is the local Principal Investigator for an industry-sponsored trial of a new antihypertensive medication. Dr. Ferguson supervises fellows in the General Renal outpatient clinic and has significant interactions with fellows on the inpatient service. Dr. Ferguson also has participated in Harvard Medical School courses on renal physiology.

8. Deborah Stein, M.D., Instructor of Pediatrics, Harvard Medical School

Summary: Dr. Stein is a clinician in the General Renal Program, the Hypertension Program and the multidisciplinary Midaortic Syndrome and Renovascular Hypertension Program. She recently completed a study of vitamin D status in children with chronic kidney disease as well as a comprehensive analysis of children with myelodyplasia and their risk factors for chronic kidney disease and bone disease. She is currently involved in a collaborative research project involving improvements
to current dialysis methodologies. Dr. Stein supervises fellows in outpatient clinic and on the inpatient service, and directs the Fellows Journal Club.

**Research Interests:** Dialysis Methodologies, Chronic Kidney Disease-Mineral and Bone Disorder, Hypertension

**EXTRAMURAL FACULTY**

1. **Joseph V. Bonventre, M.D., Ph.D.**, Professor of Medicine, Harvard Medical School; Director, Division of Health Sciences, Harvard Medical School-MIT; and the Director, Renal Division, Brigham and Women’s Hospital, Boston, Mass.

**Research interests:** Mechanisms of cell injury and repair, tissue regeneration, signal transduction, biomarkers of renal dysfunction.

**Summary:** Dr. Bonventre’s research focuses primarily on the study of kidney injury and repair and signal transduction, with a special emphasis on the role of inflammation, biomarkers and stem cells. The laboratory has three major areas of study: 1) **Pathophysiology of Kidney Tubular Injury and Chronic Fibrosis:** There are many parallels between repair and the normal development of the kidney. While repair is generally considered to be adaptive it can be maladaptive, especially when the acute injury is superimposed on chronic kidney disease. We have found two proteins, KIM-1, an epithelial protein and nmb, a macrophage protein, which we believe play critical roles in the response of the kidney. We have created a Kim-1 knockout/Gal4 knockin animal which will potentially allow us to use the characteristics of the promoter region of Kim-1 to express proteins specifically in the S3 segment of the proximal tubule, where most of the injury occurs. In addition we want to understand the factors determining the recovery of the kidney in order to design strategies to enhance and hasten the processes necessary for recovery. 2) **Kidney Stem Cells:** The kidney possesses the intrinsic capacity for repair after injury but whether adult kidney stem cells are responsible for epithelial regeneration is unresolved. During nephrogenesis, renal epithelia develop from precursors located in the metanephric mesenchyme that condense to form the nephron. Persistence of such cells in the adult could constitute a stem cell niche available for repair of damaged kidney. The laboratory is focused on the identification of intrarenal stem/precursor cells that may participate in repair. Genetic lineage approaches are in place and have provided a great deal of insight into the source of the cells. 3) **Biomarkers:** The insensitivity of commonly used biomarkers of renal dysfunction not only prevents timely diagnosis and estimation of injury severity, but also delays administration of putative therapeutic agents. Dr. Bonventre cloned and characterized Kidney Injury Molecule-1 (KIM-1) as a very sensitive and specific biomarker of proximal tubular injury. The laboratory is exploring the role of KIM-1 in the injured kidney using genetic and cell biological approaches and the role of this biomarker in a large number of kidney diseases in rodents and man is being evaluated. The laboratory has established a Biomarker Core facility to evaluate of urinary proteins that have the potential to serve as sensitive and specific biomarkers for kidney injury.

2. **David M. Briscoe, M.D.,** Associate Professor of Pediatrics, Harvard Medical School.

**Research interests:** Vascular Biology, Vascular Immunology, Endothelial cell Biology, Angiogenesis. Cell signaling, mechanisms of allorecognition, chronic allograft rejection.

**Summary:** Dr. Briscoe's research focuses on 3 broad areas of leukocyte-endothelial cell biology. These include 1) **Immune Mechanisms of Angiogenesis:** Lymphocytes and monocytes initiate angiogenesis in the process of their recruitment into allografts. Initial studies identified that cell surface molecule(s)
expressed on T cells may stimulate the production of Vascular Endothelial Cell Growth Factor (VEGF, an established potent angiogenesis factor). Dr. Briscoe further identified that cell surface interactions among CD40L (known to be expressed on activated platelets and T cells) and its receptor CD40 (expressed on endothelial cells and monocytes) mediate the transcription of VEGF. A focus of ongoing studies is to determine the signaling pathways in CD40-dependent activation of VEGF. 2) Vascular Endothelial Growth Factor (VEGF) in Allograft Rejection: VEGF, an established angiogenesis factor, is chemoattractant for monocytes via interactions with its receptor Flt-1 (VEGFR1). In addition, VEGF is functional in endothelial cells to promote leukocyte-endothelial cell interactions via its ability to induce endothelial cell adhesion molecule expression as well as the expression of the chemokine MCP-1. These observations imply mechanisms by which VEGF may be involved functionally in delayed type hypersensitivity responses and chronic inflammation. Ongoing studies in the laboratory have determined that VEGF has major proinflammatory properties in the development of chronic rejection and a focus of ongoing studies is to determine if VEGF functions as a proinflammatory cytokine independently of its effect on angiogenesis. 3) Post Transplant Monitoring of Humans Following Transplantation: The laboratory has had a long-standing interest in the evaluation and monitoring of endothelial cell activation responses in allografts post transplantation. Several longitudinal analyses of consecutive allografts identified a pattern to the expression of adhesion and activation molecules in the rejection process. These findings may have clinical implications for 1) the monitoring of patients for early predictors of rejection, 2) assessment of the efficacy of immunosuppression post transplantation; and 3) for the identification of patients at high risk for the development of chronic rejection.

3. Markus Frank, M.D., Assistant Professor of Medicine, Harvard Medical School.

Research Interests: stem cell therapeutics, cancer stem cell multidrug resistance, P-glycoprotein family of ATP-binding cassette (ABC) transporters

Summary: Dr. Frank’s laboratory research focuses on the physiological and pathological roles of the human P-glycoprotein family of ATP-binding cassette (ABC) transporters. His laboratory has cloned and characterized a novel human ATP-binding cassette (ABC) transporter, ABCB5, which marks mesenchymal stem cell (MSC) subpopulations in human and murine skin. Dr. Frank’s work has demonstrated a unique regulatory role of ABCB5 in the newly recognized phenomenon of stem cell fusion, and in cell fusion-dependent growth and differentiation. Current and future research efforts of Dr. Frank’s laboratory are geared towards using adult skin-derived ABCB5+ stem cells as a transplantable cell source for novel therapeutic applications in tissue engineering and regeneration, and for stem cell-based modulation of transplant allograft rejection and autoimmune disorders. Dr. Frank’s laboratory has also shown that ABCB5 serves as a multidrug resistance transporter in human malignant melanoma, conferring resistance to chemotherapy in vitro. Subsequent work has shown that ABCB5 expression marks melanoma cells of stem cell phenotype and function; and correlates with tumorigenic growth of melanoma cells in vivo (Nature, 2008 Jan 17; 451(7176):345-9). To further establish ABCB5 as an identifier of melanoma stem cells and to characterize the functional roles of ABCB5 in physiological and cancer stem cells, Dr. Frank’s laboratory is also exploring the clinical relevance of ABCB5 as a biomarker of melanoma progression, prognosis, and outcome, and he plans to investigate the therapeutic efficacy of ABCB5 targeting in preclinical animal models of human malignant melanoma.

4. Paolo Fiorina, M.D. Ph.D., Assistant Professor of Medicine, Harvard Medical School

Research Interests: treatment of autoimmune diabetes, islet-cell transplantation, treatment of diabetic nephropathy
**Summary:** Dr. Fiorina’s research focuses on diabetes. Particularly, 3 major areas of interest are studied:

1) The treatment of autoimmune diabetes: In type 1 diabetes (T1D) insulin producing beta cells are destroyed by the immune system provoking a sudden increase in blood glucose levels. The best animal model for T1D is the NOD mouse, which develops severe insulitis by 10 weeks of age. We are therefore studying and developing new immune-based strategies to prevent and reverse hyperglycemia in this mouse.

2) The replacement of beta cells through islet transplantation: Replacing beta cells is a fascinating task that could potentially cure diabetes in patients affected by longterm diabetes. Islet transplantation is a nice way to substitute beta cells with allogeneic insulin producing tissue. We are employing and searching new options to halt (possibly simultaneously) allo- and autoimmunity.

3) The treatment of diabetic nephropathy: The best cure for diabetic nephropathy is of course the cure of diabetes. We believe in a new line of investigation, which has its own core business in the use of immunological and cell-based approach to cure diabetic nephropathy. We use different cellular tools (podocytes cell line) to determine the effect of our therapeutic approach on a kidney relevant cell population.

5. **Benjamin Humphreys, M.D., Ph.D.** Assistant Professor of Medicine, Director, Harvard Stem Cell Institute Kidney group, Harvard Medical School

**Research Interests:** Renal injury and repair mechanisms, stem cells and regenerative medicine, kidney disease associated with cancer – “Onco-Nephrology.”

**Summary:** Dr. Humphreys’ laboratory investigates mechanisms of kidney injury and repair with a focus on stem cell and regenerative strategies to develop novel treatments for kidney disease. He uses mouse as a model system, and validates candidates with a human kidney biobank. Current projects make use of Next-Generation RNA sequencing to develop novel therapeutic targets in kidney disease. In addition, Dr. Humphreys basic research focuses on the role of the Hedgehog signaling pathway in kidney fibrosis. His clinical interests focus is kidney disease associated with cancer, and his laboratory has investigated mechanisms of chemotherapy-induced thrombotic microangiopathy. Currently, he has established translational studies in human subjects treated at the Dana Farber Cancer Institute for cancer to examine mechanisms of hypertension and proteinuria in patients receiving anti-VEGF chemotherapies. Fellows in the Humphreys lab receive intensive mentoring and training in state of the art techniques that advance their professional development and academic potential.

6. **Jordan A. Kreidberg, M.D., Ph.D.** Director, Office of Fellowship Training, Boston Children’s Hospital, Associate Professor of Pediatrics, Harvard Medical School.

**Research Interests:** inductive mechanisms of early organ development, regulatory interactions for normal glomerular function, stem cells and the developing kidney,

**Summary:** Dr. Kreidberg’s research focuses on how stem cell and progenitor populations in developing organs are regulated by signaling networks. Important areas of study include how integrin cell adhesion receptors and receptor tyrosine kinases integrate signals that control the gene expression of signaling molecules that regulate stem cell populations and that also regulate morphogenetic events during organogenesis. His laboratory is also studying how transcription factors and chromatin modification proteins are involved in organ development. Recently, Dr. Kreidberg’s laboratory determined that angioblasts, the precursors of endothelial cells in the vascular system, are involved in the early inductive events of the kidney. They are presently attempting to identify angioblast-derived signals mediating these
events, and whether signals derived from angioblasts are targeted to stem cell populations. It is also being determined whether stem-cell associated genes, such as Nanog and members of the Polycomb Group, whose expression we have defined in the developing kidney, are targets of the angioblast signals, or other signals known to be important in the induction of the kidney. Another project in the laboratory involves the Wilms’ tumor-1 tumor suppressor gene, that encodes a zinc finger transcription factor. Knockout of this gene completely blocks kidney and gonad development. Dr. Kreidberg’s laboratory is using approaches that include in vitro and in vivo RNAi, conditional gene knockout, and microarrays to identify Wt1 target genes within the stem cell population of the kidney. The Wilms’ Tumor gene is also expressed in podocytes, a key cell type in the kidney, that is damaged in several types of kidney disease including chronic renal failure. The laboratory is attempting to understand how this gene is involved in kidney disease. Finally, Dr. Kreidberg has an interest in Polycystic Kidney Disease (PKD), as a Project Head within a NIH Center of Excellence grant in PKD awarded to the Brigham and Women’s Hospital, (Dr. Jing Zhou, Principal Investigator). Dr. Kreidberg’s laboratory has demonstrated that coordinate signaling between integrins and receptor tyrosine kinases is disrupted in PKD, and they are presently testing a novel treatment for PKD based on this research in mice.

Dr. Kreidberg has significant experience in mentorship/training. He is Program Director of a Child Health Research Program K12 grant and a Pediatric Scientist Training Program T32 grant from the NIH to the Department of Medicine at Boston Children’s Hospital. In addition, he founded and directs the Office of Fellowship Training at Boston Children’s Hospital.

7. David M. Mount, M.D., Assistant Professor of Medicine, Harvard Medical School.

**Research Interests:** renal physiology, molecular and cellular physiology of salt and solute transport, molecular physiolology of transporters function, cloning of novel transporters.

**Summary:** Dr. Mount is the Director of the Laboratory of Molecular Transport Physiology. He has exploited genomic and cDNA databases to identify novel members of four transporter gene families and his laboratory has cloned several new members of the cation-chloride cotransporter gene family, most notably the K-Cl cotransporters KCC3 and KCC4. Dr. Mount also characterized five new members of the SLC26 gene family; these include SLC26A6, a multifunctional transporter that is the primary candidate for both the apical chloride-formate/oxalate exchanger in the renal proximal tubule and the CFTR-dependent chloride-bicarbonate exchanger in the pancreas, and SLC26A9, a lung-specific Cl-base exchanger. Apical chloride-formate/base/oxalate exchange mediated by SLC26A6 and basolateral K-Cl cotransport mediated by KCC3 and KCC4 play crucial roles in trans-epithelial salt transport by the renal proximal tubule, with implications for both essential hypertension and edema syndromes. Other gene families of interest include the sodium-solute (SLC5) and organic anion (SLC22) transporters, particularly novel family members with a potential or proven role in renal urate absorption. Basolateral and apical oxalate exchange in the proximal tubule, mediated by SLC26A1 AND SLC26A6, respectively, may also play a significant role in renal oxalate secretion. The transport function of cloned transporters is primarily studied by isotopic flux measurements, using heterologous expression in Xenopus laevis oocytes. In addition, the electrogenic properties of at least some of the SLC26 exchangers and other transporters leave them amenable to electrophysiological analysis. Isoform-specific functional properties provide a starting point for structure-function analysis, using chimeric and mutant cDNAs. Immunolocalization of transporter transcripts and proteins also provide important information on physiological roles in the kidney and brain, which have guided the laboratory on the physiological characterization of relevant knockout mice. Finally, Dr. Mount has developed collaborative investigations to address the role of multiple human transporters in both monogenic and polygenic renal disease(s). In particular, he is a project leader in an NIDDK program project grant on
the pathobiology of nephrolithiasis, assessing the contribution of several solute transporters to the genetics and pathophysiology of kidney stones.

8. **Martin Pollak, M.D.**, Associate Professor of Medicine, Harvard Medical School.

**Research interests**: genetics of FSGS, candidate genes in human kidney disease, mouse models of glomerular disease, cell signaling at the glomerular slit-diaphragm.

**Summary**: Dr. Pollak’s laboratory is working to identify genes involved in the development of focal segmental glomerulosclerosis (FSGS). FSGS is a common form of renal disease, seen both as an isolated entity and as a consequence of HIV infection, diabetes, obesity, and hypertension. Towards this goal, blood for DNA extraction and clinical analyses have been performed on members of approximately 90 families with an inherited form of this condition. The laboratory identified the first FSGS locus on chromosome 19q13. This locus was subsequently refined and demonstrated genetic heterogeneity of FSGS. Using careful analyses of genomic sequence databases, it was possible to identify a number of candidate genes. We identified the first of these genes, FSGS-1, or ACTN4 (alpha-actinin-4), a gene which encodes a protein which seems to be important in the structure in the cytoskeleton of certain kidney cells. When ACTN4 is mutated, it causes an autosomal dominant form of proteinuria, kidney failure, and FSGS. Dr. Pollak’s laboratory developed ACTN4 mutant (knockin) and knockout mice to help us understand the underlying disease mechanisms; and ongoing studies are exploring the role of mutations in the alpha-actinin-4 protein in altering the biomechanical properties of the actin cytoskeleton. In addition, the laboratory is studying the human genetics and biology of other inherited forms of FSGS, and is working to identify other FSGS genes. Dr. Pollak has a large collection of human DNA samples from subjects with kidney disease which forms the basis of many of these studies.

9. **Mohamed H. Sayegh, M.D.**, Faculty, Brigham and Women’s Hospital and Boston Children’s Hospital, Boston, MA.


**Summary**: Dr. Sayegh’s major research interests include the role and mechanisms of allore cognition in rejection and tolerance. Dr. Sayegh has studied the role of effector and regulatory cells activated by the so-called "direct" pathway, where T cells recognize intact allo-MHC molecules on the surface of donor cells. Peptides, derived from endogenous proteins including MHC molecules, bound into the groove of the MHC appear to play an important role in this mode of allore cognition. In the so-called "indirect" pathway T cells recognize processed alloantigen presented as allopeptides by self antigen-presenting cells (APCs). These allopeptides are derived from allo-MHC molecules or from minor histocompatibility or tissue specific antigens. Dr. Sayegh has demonstrated that the indirect pathway occurs during allograft and xenograft rejection and plays an important role in the rejection process, especially in chronic rejection. His laboratory is currently focusing on studying the contribution of indirect allore cognition to the rejection process including establishing a TCR transgenic animal which is specific to class II MHC allopeptides. In addition, human studies in his laboratory are focusing on developing novel assays to predict transplant outcome. Another major interest of Dr. Sayegh’s laboratory is investigating the role and mechanisms of T cell costimulation in transplantation and autoimmune diseases. Dr. Sayegh’s research studies focus on the role of costimulatory molecules CD28-B7 and ICOS-ICOSL as well as coinhibitory molecules such as PD-1-PDL-1 families of in allograft rejection and autoimmune diseases, including diabetes. In addition, his studies focus on dissecting the
mechanisms by which blockade of these pathways may prevent acute rejection and induce long term allograft survival and tolerance, and prevent and/or cure autoimmune diseases. Dr. Sayegh has an outstanding record of mentoring of trainees, several of his trainees have become NIH funded investigators and are leaders in the field of transplantation immunology. He supervises many post doctoral trainees within our program. He is the recipient of the 2008 Mentoring Award of the American Society of Transplantation.

10. **Terry B. Strom, M.D.**, Professor of Medicine and Surgery, Harvard Medical School.

**Research interests:** Immunology with an emphasis upon T cell immunobiology and immune tolerance.

**Summary:** Dr. Strom is the Director of the Transplant Research Center and the Division of Transplant Immunology at the Beth Israel Deaconess Medical Center in Boston, MA. He has a long-standing interest in mechanisms of allograft rejection, the regulation of cytokine gene expression and in tolerance induction. His laboratory has focused efforts on the understanding of the molecular aspects of T cell biology, transplantation rejection and tolerance. The ultimate goal of his research is to use molecular technology to 1) understand the mechanism of graft rejection, and, create tolerance, and 2) to develop new therapeutics and molecular diagnostic techniques to support the goal of creating immune tolerance. Ongoing studies in the laboratory involve an analysis of the fundamental basis of T cell tolerance; and the laboratory is significantly involved in the design of agents and the development of regimens that create T cell tolerance in vivo. In addition, the laboratory uses expression profiling and molecular diagnostic strategies to help achieve tolerance through analysis of the host and the allograft at the time of implantation and serially thereafter. Beginning with basic studies of lymphocyte growth and development, Dr. Strom has identified and characterized several T-cell growth factors involved in T cell activation responses, and he has studied them in vitro and evaluated them in experimental small animal models, in primates, and in clinical trials. Various forms of IL-2, CTLA4, CD2 and IL-15 fusion proteins have been developed in the laboratory for use as specific immunosuppressive agents. His most recent work has focused on the influence of inflammation on the texture of transplant rejection and autoimmunity and on investigation of a family of T-cell proteins known as TIM (T-cell Immunoglobulin Mucin domain), which serve as "checkpoints" for the survival or activation of T-cell subsets. To date, these findings have been published in the journals Nature, Nature Immunology and the Journal of Experimental Medicine. Other work has given insight into the effect of certain therapies on the inhibition or promotion of activation-induced T cell death, an event that is crucial for tolerance induction. Finally, studies have been performed on the basic biology governing the commitment of naïve or activated to distinctive T cell subset phenotypes, with new insights concerning the commitment to tissue protective Foxp3+ regulatory cells. The Strom laboratory places strong emphasis on the development of innovative biotherapeutics and some recent agents that have been developed and tested within the lab have shown great promise in the murine model of type1 diabetes and mouse and non-human primate models of islet and cardiac transplantation.

11. **Vishal S. Vaidya, Ph.D.**, Assistant Professor of Medicine and Environmental Health at Harvard Medical School and Harvard School of Public Health (HSPH). Associate faculty at the Harvard University’s Center for Environment, an affiliate member of Harvard Stem Cell Institute and HSPH NIEHS center.

**Research interests:** Translational Biomarkers, Kidney Toxicology, MicroRNAs, Kidney Tissue Repair.

**Summary:** Vishal directs the laboratory of kidney toxicology and regeneration with a goal of preventing, predicting and mitigating kidney disease by identifying better biomarkers and investigating
novel therapeutics to stimulate kidney regeneration. Projects that are being pursued in the laboratory involve: 1) characterizing fibrinogen signaling in kidney injury and tissue repair; 2) identifying and evaluating the role of microRNA’s as biomarkers and molecular regulators of kidney damage; 3) developing a high throughput, mechanistic and predictive platform for kidney toxicity and 4) identifying a molecular signature that governs progression of acute kidney injury to chronic kidney disease. Apart from research Vishal is also passionate about teaching and he directs a course on translational biomarkers titled “Understanding Biomarker Science” through Harvard Catalyst, The Harvard Clinical and Translational Science Center. Vishal also directs a 5-credit course on Principles of Toxicology-Molecular and Translational Toxicology at Harvard School of Public Health in the fall.

12. Sushrut Waikar, M.D., M.P.H., Director of Renal Ambulatory Services, Brigham and Women’s Hospital; Assistant Professor of Medicine, Harvard Medical School.

Research Interests: Acute kidney injury, chronic kidney disease, biomarkers of kidney disease, epidemiology, hyponatremia; renal replacement therapy

Summary: Dr. Waikar is a member of the BWH Renal Division and a clinician scientist with active research projects, including: 1) epidemiology of acute kidney injury: using large databases from BWH, BCH, and other institutions, Dr. Waikar and his research fellows explore the epidemiology of acute kidney injury; 2) biomarkers of kidney disease: Dr. Waikar is the PI of R01DK093574, Biomarkers of Kidney Pathology, in which patients undergoing kidney biopsy at BWH, BIDMC, and BCH are enrolled into a prospective observational study with biological sample collection in order to study novel biomarkers of kidney pathology; 3) biomarkers of nephrotoxicity: Dr. Waikar is a PI of the Kidney Safety Project, an F-NIH sponsored multicenter study that aims to identify new biomarkers of nephrotoxicity that may be superior to serum creatinine; 4) biomarkers of acute kidney injury: these studies focus on the identification and validation of novel biomarkers of acute kidney injury that may outperform traditional markers; 5) small solute clearance during CVVH/CRRT: Dr. Waikar has investigated potential adverse effects of CRRT related to excessive phosphate clearance by implementing a continuous partial effluent sample collection device, in which a small fraction of the effluent is continually collected to permit balance studies of small solutes including phosphate

13. Jing Zhou M.D., Ph.D., Associate Professor of Pediatrics, Harvard Medical School:

Research Interests: Genetics of human disease, Polycystic kidney disease, Pathophysiology of polycystins, Glomerular disease, Epithelial cell biology, Cell signaling and organ development

Summary: Dr. Zhou is the Director of the Harvard Center for Polycystic Kidney Disease Research. Her laboratory has three major areas of study: 1) Molecular mechanisms underlying polycystic kidney disease. Polycystic kidney disease (PKD), characterized by the growth of numerous, large epithelial-lined cysts from kidney tubules, is the most common lethal monogenic disease. Autosomal dominant polycystic kidney disease is the most common form of the disease and is caused by mutations in either of two genes, PKD1 and PKD2. Dr. Zhou’s laboratory has created four lines of mouse models for both dominant and recessive forms of PKD by gene targeting of Pkd1. The laboratory has shown that mice homozygous for a Pkd1 mutation develop severe embryonic PKD, cystic pancreas, polyhydramnios, hydrops fetalis, and defective skeletal development. These animals provide an entry point for research into pathways that lead to aberrant epithelial and chondrocyte development. More recently, Dr. Zhou has also demonstrated that full-length polycystin-1 acts as a G-protein coupled receptor and polycystin-2 suppresses its G-protein activation. 2) Molecular physiology and pathophysiology of polycystins. In addition to polycystins-1 and -2, the laboratory has identified four novel members of the polycystin
family and have shown that two polycystins, polycystin-2 and –L, are Ca\(^{2+}\)-permeable cation channels. Expression patterns of these polycystins indicate that they have a role in heart, brain function and in the male reproductive system. Dr. Zhou has developed polycystin-L and -2L2 knockout mice, and their phenotype is being characterized. 3) Molecular basis of glomerular disease: Dr. Zhou’s laboratory also studies Alport syndrome, which is a progressive hereditary nephropathy associated with deafness and ocular abnormalities. Over 90% of Alport syndrome cases are X-linked and affect the COL4A5 gene that encodes the alpha-5 chain of type IV collagen. The laboratory has demonstrated that deletions of the 5’ ends of COL4A5 and COL4A6 genes are associated with Alport syndrome. Dr. Zhou is interested in evaluating additional molecular components of the glomerular basement membrane and how they has found that they differ from those of the Bowman’s capsule and tubular basement membrane.

14. **David A. Williams M.D.**, Leland Fikes Professor of Pediatrics, Harvard Medical School; Director of Translational Research, Boston Children's Hospital; and Director, Division of Hematology/Oncology Boston Children's Hospital, Mass.

**Research interests:** Translational Research, hematopoietic stem cells, gene transfer methods

**Summary:** Dr Williams created the Translational Research Program (TRP) at Boston Children's Hospital in order to stimulate and facilitate the development of preclinical and ultimately, human translational trials seeking to improve the care of children with serious diseases. In order to accomplish this, the TRP provides support for faculty-initiated pre-clinical and clinical translational research projects, in addition to ensuring adequate infrastructure to facilitate the rapid completion of these trials. The TRP will fund a cadre of investigators and support them pursue successful translational research. The TRP also provides expertise and assistance with regulatory affairs issues for TRP-sponsored individuals/projects. TRP staff with significant experience and training in regulatory affairs provide expert analysis, planning, consultation, facilitation and project management for TRP-investigators for the development of investigational new drugs. Finally, the TRP is developing a curriculum that will be available to the entire BCH community, to broaden investigators’ knowledge base and ensure their success in Translational Research.

15. **Ananth Karumanchi, M.D.**, Associate Professor of Medicine, Harvard Medical School, Boston, MA, Investigator, Howard Hughes Medical Institute, Harvard Medical School, Boston, MA.

**Research Interests:** molecular basis for proteinuria, pregnancy-induced nephrological disorders, vascular biology, angiogenesis, renal cancer.

**Summary:** Dr. Karumanchi is a Nephrologist at the Beth Israel Deaconess Medical Center, Boston, and a clinical investigator in the Howard Hughes Medical Institute, located at Harvard Medical School. Dr. Karumanchi is known for his discovery of the cause of pre-eclampsia, and has a major interest in the role of angiogenic factors in the pathogenesis of proteinuric diseases. Dr. Karumanchi’s laboratory has three major areas of study: 1) Role of angiogenesis in the pathogenesis of preeclampsia (PE): Dr. Karumanchi’s laboratory identified that sFlt-1, an antagonist of circulating vascular endothelial growth factor (VEGF) and placental growth factor (PIGF), is released into the blood stream in vast excess in patients with preeclampsia. He also discovered that exogenous administration of sFlt-1 into pregnant rats reproduces the phenotype of preeclampsia, namely proteinuria, hypertension and glomerular endotheliosis (the classic lesion of preeclampsia). Further, the laboratory demonstrated that circulating sFlt-1 and PIGF levels can be used for the clinical diagnosis and the prediction of preeclampsia. Ongoing studies are testing the effects of antagonizing excess sFlt-1 with growth factors and small molecule compounds in an animal model of preeclampsia with the goal of finding novel treatment
options for this disease. Additionally, the laboratory is characterizing other gene products that are elevated in preeclampsia that may serve as biomarkers for the early diagnosis. 2), Molecular mechanisms of proteinuria: Dr. Karumanchi’s laboratory is evaluating mechanism(s) underlying proteinuria associated with diabetes. Preliminary microarray data generated from podocytes grown in high and normal glucose have revealed several novel targets and pathways. Urine proteomics data from diabetic patients with and without nephropathy are being analyzed in order to identify novel urine markers that predict worse renal outcomes. The laboratory is currently confirming in vitro cell culture data in diabetic rats by in-situ hybridization and is developing in vitro assays that may mimic in vivo proteinuria. 3), Renal Cancer and angiogenesis: Dr. Karumanchi discovered several novel targets that are regulated by the von Hippel-Lindau protein, including TGF beta1, TGF alpha, VEGF and AE2. Dramatic inhibition of renal tumor growth can be elicited following treatment with anti-TGF-b neutralizing antibodies, and the major mechanism appears to be an anti-angiogenic. In collaboration with the Sukhatme lab, Dr. Karumanchi is testing combination therapies with other anti-angiogenic molecules such as endostatin and restin to treat metastatic renal cancer; and he is characterizing two novel targets for VHL-associated renal cancer, identified by the laboratory.