Table 2. Participating Faculty Members (Alphabetically by Faculty Member)

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Abboud, Francois, MD	Professor	Internal Medicine (Cardiology)	Mentor	Research interests are directed toward the integrated neurobiology of the circulation. Specific studies examine the cellular and molecular mechanisms of mechanical activation of baroreceptors and chemical activation of chemoreceptors in isolated neurons and glomus cells, and in transgenic mice. A more recent focus is on the autonomic regulation of the immune system in cardiovascular disease. Human studies have focused on the integrated control of sympathetic activity in physiologic and pathologic states (e.g., sleep apnea and hypertension).

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Anderson, Mark MD	Professor	Internal Medicine (Physiology & Biophysics)	Internal Advisor/Mentor	Dr. Anderson's research is dedicated to understanding myocardial biology of arrhythmias in structural heart disease. He and his laboratory have focused on the multifunctional Ca2+/calmodulin dependent protein kinase II (CaMKII). Dr Anderson was the first to hypothesize that CaMKII is a proarrhythmic signal and defined the biophysical mechanism for CaMKII regulation of L-type Ca2+ channels in heart. More recently, Dr Anderson's laboratory developed a genetic mouse model of CaMKII inhibition they used to demonstrate that CaMKII is a key signal element for causing proarrhythmic electrical, intracellular Ca2+ and adverse structural remodeling in the setting of catecholamine toxicity and after myocardial infarction. Present areas of active investigation include: 1. electrophysiological mechanisms of CaMKII signaling in heart; 2. cellular signaling in the biology of cardiac hypertrophy; 3. signaling mechanisms of impulse formation in specialized conduction cells; 4. the role of CaMKII in myocardial oxidation and inflammation.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Apicella, Michael MD	Professor	Microbiology (Internal Medicine)	Internal Advisor/Mentor	Dr. Apicella's lab has had almost forty years' experience in working on bacterial surface glycolipids in pathogenic *Neisseria*, *Haemophilus* and more recently *Vibrio fischeri* and *Francisella tularensis*. The majority of the work has focused on the role of these glycolipids in pathogenesis and survival within their host species. Their efforts combine molecular, structural and biological approaches. In the pathogenic *Neisseria* and *Haemophilus* studies, they have demonstrated the role of the lipooligosaccharide structures in mimicry of human antigens, their role in co-opting epithelial cell receptors to allow entry into epithelial cells and the introduction of sialic acid into their structure as a molecular mask to enable the bacteria to evade host innate defenses. They have demonstrated that both *Neisseria* and *Haemophilus* can form biofilms and have identified biosynthetic and metabolic pathways important in biofilm formation. The recent studies of *Francisella tularensis* have resulted in the purification, characterization of the biosynthetic pathway and composition of the capsular polysaccharide of this species. Dr. Apicella's lab has shown that this antigen has a potential role as a protective immunogen against infection with this agent. Their studies of *V. fischeri* have helped to characterize an important model of symbiosis in a novel bacterial-host system. The laboratory has been continually funded from NIH since 1971 and published over 230 peer-reviewed publications dealing with different aspects of pathogenic bacteriology.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Baldwin, H. Scott MD	Professor	Pediatrics (Cardiology) Vanderbilt University	External Advisor	Dr. Baldwins's laboratory has concentrated on delineating the molecular basis of vascular development in the mammalian embryo as an approach to understanding the etiology of congenital heart diseases with a particularly focused on semilunar valve development. The ultimate goal is to use developmental biology to inform the development of tissue engineered heart valves and to exploit developmental mechanisms to enhance myocardial repair following injury. Studies in the laboratory are based on the hypothesis understanding the molecular basis of endothelial heterogeneity is essential in defining the mechanisms and treatment of congenital cardiac disease. The laboratory utilizes in vitro cell culture, in situ whole mouse embryo culture, and BAC transgenesis, model systems and has pioneered the analysis of the first endocardial specific transcription factor identified to date, Nuclear Factor of Activated T cells (NFATc1). Dr. Baldwin's laboratory has served as a venue for training several graduate students and post-doctoral fellows, most of which have remained in academic medicine. Dr. Baldwin has maintained continuous NIH funding for almost 20 years and I have participated as a member of the NIH CVA /CDD study section. He has served as Chair of the National and Southeast Regional Cardiovascular Development Study Sections for the AHA; and has also participated in numerous special program project review panels and was PI of the SCOR in Pediatric Cardiovascular Disease at the Children's Hospital of Philadelphia.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Baldwin, H. Scott MD (cont.)				Dr. Baldwin is currently a member of the National AHA Research Committee. In addition, he has maintained an active clinical practice in Pediatric Cardiology and been heavily involved in the development of Physician / Scientists for a large part of his career. He has served as the Co-Director of Cardiovascular Research at the Children's Hospital and as Vice Chair for Research at Vanderbilt. Dr. Baldwin is currently a member of the Faculty Advisory Committee for the MSTP training program at Vanderbilt and Chair of the Scientific Board of the Sarnoff Foundation, and organization dedicated to providing medical students with an in-depth research experience by supporting a 1-2 year hiatus from medical school to participate in a basic laboratory investigation. He has also served as the primary thesis advisor for 5 Ph.D. candidates and as a committee member for 18 graduate students in Cell and Developmental Biology, Pharmacology, and Genetics. Finally, Dr. Baldwin is the PI of the recently funded NIH/NHLBI T32 focused on development of both MD and PhD training in disease processes relevant to congenital and acquired heart diseases.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Barnard, John PhD	Section Head	Quantitative Health Sciences (The Cleveland Clinic Foundation)	External Advisor	Dr. Barnard has committed much of his career to fellow and faculty development as an academic pediatric gastroenterologist. He has served as PI or co-PI on two T32 training grants, one devoted to training pediatric and adult investigative gastroenterologists at Vanderbilt University Medical Center, and the other an institutional training grant for pediatricians awarded during his tenure at Nationwide Children's Hospital. In addition, Dr. Barnard is program director of an NICHD K12 training grant for junior pediatric faculty. Thus, he has extensive experience in training, especially physician scientists. The Barnard laboratory group has a longstanding interest in the biology of transforming growth factor beta, especially in epithelial systems. His R01-funded laboratory has a variety of unique reagents and mouse model systems related to TGF-beta biology. Since this growth factor has relevance to pathophysiology of fibrosis, growth regulation, apoptosis and tumor suppression in a variety of organ systems, his laboratory is uniquely positioned to be of value as a training laboratory for a variety of trainee interests. Finally, as president of The Research Institute at Nationwide Children's Hospital, Dr. Barnard is able to focus attention and resources to the individual and collective needs of trainees in this program.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Bassuk, Alexander MD, PhD	Associate Professor	Pediatrics (Neurology)	Recruitment Officer	Dr. Bassuk's laboratory focuses on the molecular and genetic mechanisms of epilepsy, and he is a practicing pediatric neurologist. With a wide-array of collaborators both at the University of Iowa and internationally, the use of multiple model organisms (including mutant mice, zebrafish and fruit flies) and multiple techniques (including immunohistochemistry, mouse EEG, mouse behavioral studies, zebrafish calcium imaging, zebrafish behavioral analysis, fruit fly behavioral analysis, electrophysiology in the fruit fly, and electrophysiology of cultured hippocampal cells) to elucidate mechanisms underlying epilepsy, and other neurological disorders. Dr. Bassuk is currently the PI on an NINDS R01 examining the role of the *PRICKLE* genes in human disease, and evaluating animal models of *Prickle* dysfunction, and on recently completed supplemental Collaborative Activities to Promote Translational Research (CAPTR) award specifically geared toward Translating human PRICKLE-epilepsy discoveries to therapies using a fruit fly model.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Bishop, Gail PhD	Professor	Microbiology (Internal Medicine)	Mentor	The Bishop lab studies molecular mechanisms of lymphocyte activation. By working to understand how cells communicate with one another and their environment, we address questions of how normal immunity, autoimmunity and malignancy are regulated. A major focus of our work is understanding signals delivered to cells by members of the Tumor Necrosis Factor Receptor (TNFR) superfamily of molecules. This large family of receptors is expressed on many cell types, but is of special importance to regulating the activities of cells of the immune system. One of the family members that we study, CD40, is expressed primarily on immune cells that present antigen to T lymphocytes, including B lymphocytes, the immune cells that produce antibodies. CD40 plays a critical role in B cell function. In parallel, we study a protein produced by Epstein-Barr virus, called latent membrane protein 1 (LMP1), which plays important roles in the development of EBV-associated lymphomas that can arise in immunosuppressed patients, and also contributes to disease flares in Lupus and arthritis.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Bishop, Gail PhD (cont.)				LMP1 is a remarkable mimic of CD40 signals, but in an amplified and dysregulated manner. Using combined approaches of cell line studies, freshly isolated cells (mouse and human) and genetically altered mice, we are investigating how signaling by CD40 and LMP1 differ. A key difference is how the two receptors regulate the function of a family of cytoplasmic proteins called TNFR associated factors (TRAFs). We are also studying how TRAF function and regulation contributes to cell signaling by TNFR family members, including CD95, TNFR2, CD27, BAFFR and TACI, as well as the innate immune TLR receptors. Some of the molecules we have begun to study regulate T cell activating and apoptotic signals delivered by the T cell antigen receptor. We have developed a method using gene targeting by homologous recombination in somatic cells to produce cell lines specifically and completely deficient in single of multiple types of TRAF molecules, as well as mice that lack particular TRAFs in certain cell types. Another line of investigation in the lab involves understanding how innate immune receptor signals interact with signals via adaptive receptors, such as antigen receptors. We are examining such signals and their roles in optimizing the use of immune cells in cellular vaccines to protect from infectious organisms and malignant cells.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Campbell, Kevin PhD	Professor	Physiology & Biophysics (Internal Medicine)	Mentor	Dr. Campbell is a Howard Hughes Medical Institute Investigator. Research in Dr. Campbell's laboratory is focused on two topics: the Dystrophin-Glycoprotein Complex and Muscular Dystrophy Pathogenesis and Therapeutic Strategies. Alterations in the dystrophin-glycoprotein complex cause several forms of muscular dystrophy, including those with abnormal central nervous system development and function. We are investigating the structure and function of the dystrophin-glycoprotein complex in skeletal, cardiac, and smooth muscle as well as non-muscle tissues including brain and peripheral nerve. In particular, we are interested in the following projects: 1) the post-translational processing of dystroglycan required for its functional activity and steps in this process targeted in muscular dystrophy, (2) the functional role of members of the sarcoglycan-sarcospan complex, (3) the function of dystroglycan within the central and peripheral nervous system including neuronal migration, peripheral nerve conduction, and synaptic plasticity. Muscular dystrophy research in my lab utilizes a variety of biochemical tools and modern genetic approaches, including human patient samples, spontaneous mutant or gene targeted mice, viral gene transfer and stem cell therapy. These approaches are geared to understanding disease mechanisms and forming the basis of therapeutic studies in vivo. We have also uncovered a pathway for muscle membrane repair that is responsible for at least two different forms muscular dystrophy not associated with the dystrophin-glycoprotein complex. Current investigations include: (1) the function of dysferlin in membrane repair; (2) the membrane repair machinery in skeletal muscle; and (3) the role of membrane repair in other forms of muscular dystrophy.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Casavant, Thomas PhD	Professor	Bioinformatics (Computational Biology)	Mentor	Dr. Casavant is the Director of the Center for Bioinformatics and Computational Biology at the University of Iowa. Dr. Casavant's research is divided among two areas: 1. High-Performance Parallel and Distributed Computing; and 2. Gene Discovery, Mapping, and Disease Linkage. Since 1986, my work in High-Performance Parallel and Distributed Computing has involved the theory, design, and prototyping of computer systems to solve the largest and most computationally demanding problems. This work involves the design of hardware, software, and the networking/communications to interconnect them. The two patents he holds are for the design of a parallel computing systems, and languages, that allow large numbers of microprocessors to be interconnected to cooperate in the solution of large, complex, computational problems. Since late 1994, he has been involved in the application of these high-performance computing technologies to the specific problem domain of the Human Genome Project. His efforts, in collaboration of members of the College of Medicine, have involved the design of networked systems of computers to analyze large amounts of genetic sequence data taken from mixed tissue libraries of variably expressed mRNA transcripts. Further, processing of this data has required extensive computation to construct genetically anchored maps showing relative locations of all genes. Finally, they have constructed web-based tools to collect, organize, and analyze genetic marker data, pedigree and clinical data to identify linkage between gene candidates and specific diseases including hypertension, obesity, glaucoma, and autism.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Davidson, Beverly PhD	Professor	Internal Medicine (Physiology & Biophysics))	Internal Advisor	Research in Dr. Davidson's laboratory is focused on inherited genetic diseases that cause central nervous system dysfunction, with a focus on (1) recessive, childhood onset neurodegenerative disease, in particular the lysosomal storage diseases such as the mucopolysaccharidoses and Battens disease; and (2) dominant genetic diseases for example the CAG repeat disorders, Huntington's disease and spinal cerebellar ataxia type I. Their research on childhood onset neurodegenerative diseases is focused on experiments to better understand the biochemistry and cellular trafficking of proteins deficient in these disorders, and to develop gene and cell-based medicines for therapy. These gene therapy studies are focused on vector development, emphasizing the study of novel envelopes for cellular targeting of lentivirus vectors, or non-traditional capsid proteins for encapsidated vectors (AAV and adenovirus). In recent work Dr. Davidson's lab has demonstrated that the application of these vectors to animal models of storage disease could reverse CNS deficits. Molecular correlates, examined using gene chip arrays, corroborated the beneficial effects of gene therapy. For cell based therapies, experiments are directed towards understanding the early signaling events required for differentiation of progenitor cell populations using microarray studies coupled with bioinformatics. The proteins revealed are then studied for their roles in development, and for their ability to induce differentiation of endogenous progenitor populations. Therapies for dominant disorders are an exciting challenge and require that the dominant disease allele be silenced.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Davidson, Beverly PhD (cont.)				To approach this, they have developed vectors expressing small inhibitory RNA, or siRNA. These small RNAs lead to the degradation of the targeted sequence. This has shown that siRNA reduces expression of the target in cell culture models of CAG repeat diseases, leading to an improved phenotype. Current studies are determining the effectiveness of in vivo delivered siRNA to correct disease manifestations in relevant models.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Di Paola, Jorge MD	Associate Professor	Pediatrics (Hematology/Oncology) University of Colorado at Denver	External Advisor	The Di Paola laboratory dedicates all efforts to scientific and clinical problems related to the effect that critical components of the hemostatic system, such as platelets and coagulation factors, have on human disease. In the past we have explored the genetics of hemophilia B, the signaling pathways that contribute to the procoagulant response in platelets, including novel roles for mitochondria; the genetic variation of platelet receptors and some of the most common clinical problems caused by defects in these biological systems. Taking advantage of recent advances in genomics we continue to investigate the genetic basis for hemostatic disorders. We have recently identified that mutations in *NBEAL2* cause the rare autosomal recessive platelet disorder Gray Platelet Syndrome, a disease characterized by thrombocytopenia and large platelets that lack alpha granules. The discovery of *NBEAL2* will likely give new insights into platelet alpha granule biogenesis. Additionally using large pedigrees and nuclear families we study the genetic basis for the phenotypic variability observed in the bleeding disorder von Willebrand disease. Our ultimate hope is that through research we can contribute to the improvement of lives of individuals with bleeding and thrombotic disorders.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Engelhardt, John PhD	Professor	Anatomy & Cell Biology (Internal Medicine)	Mentor	Research in the Engelhardt laboratory focuses on the molecular basis of inherited and environmentally induced diseases, and on the development of gene therapies for these disorders. Included are two major research areas: 1) the study of lung molecular and cellular biology as it relates to the pathogenesis and treatment of cystic fibrosis (CF) lung disease and associated diabetes, and 2) the molecular mechanism underlying redox-mediated injury and the development of molecular therapies for ischemia/reperfusion injury, sepsis, and the neurodegenerative disease amyotrophic lateral sclerosis (ALS). Research on lung biology includes the study of adult epithelial stem cells and their niches in the airway, and dissecting the pathogenesis of lung disease in animal models of cystic fibrosis. The laboratory is currently elucidating transcriptional signals important for early establishment of the airway glandular stem cell niche, and for mobilization of stem cells from this niche following airway injury. The newly generated ferret and pig models of cystic fibrosis are being used to understand how stem cells in the adult airway respond to injury resulting from dysfunction of CFTR (the chloride channel that is defective in cystic fibrosis). These new genetic models of CF are also being used to dissect pathophysiologic mechanisms of disease and to develop gene therapies that target the lung with recombinant adeno-associated virus. A second area of interest is the dissection of pro-inflammatory, redox-dependent, signaling pathways in the liver and central nervous system.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Engelhardt, John PhD (cont.)				Such studies are aimed at the treatment of environmentally induced liver injuries—those resulting from sepsis, ischemia/reperfusion, and (in the case of ALS) motor neuron injury. We are using rodent transgenic and knockout models to better understand the mechanisms that are involved in inflammation and injury and are controlled by reactive oxygen species. Of particular interest in this area are mechanisms of redox-regulated NFκB activation via several NADPH oxidase complexes (Nox1, Nox2 and Nox4), whose roles include generating intracellular superoxides in response to extracellular pro-inflammatory cytokine signals (IL-1beta and TNFalpha pathways are a major focus). This redox-signaling program heavily utilizes recombinant viral vectors, transgenic/knockout mice, and proteomic approaches to address basic aspects of pathophysiology, and also to generate new therapies capable of promoting organ regeneration and repair while also minimizing the deleterious inflammatory responses to injury.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Felder, Robert MD	Professor	Internal Medicine (Cardiology)	Mentor	Dr. Felder's laboratory utilizes electrophysiological, immunohistochemical and molecular techniques to explore the contribution of the brain to the pathophysiology of cardiovascular disease states. The primary focus is upon central neural mechanisms contributing to heart failure and hypertension in rodent models, with an emphasis on the forebrain influences of pro-inflammatory cytokines and the renin-angiotensin-aldosterone system on volume regulation and sympathetic drive.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Ferguson, Polly MD	Associate Professor	Pediatrics (Rheumatology)	Program Director	Research in the Ferguson laboratory is aimed at defining the immunologic and genetic basis of chronic recurrent multifocal osteomyelitis (CRMO). CRMO is a genetically determined immunologic disorder and frequently occurs together with psoriasis or Crohn disease implicating a shared pathophysiology. Dr. Ferguson's lab has studied CRMO for the past 7 years and is recognized as a leader in the field. Her laboratory offers expertise in murine and human genetics, autoinflammatory disorders, innate immunity and inflammatory bone disorders. Immunologic studies in her laboratory currently include establishing the role of interleukin-1 in murine CRMO and on defining the immunologic pathways that lead to sterile bone inflammation in children.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Geyer, Pamela PhD	Professor	Biochemistry (Obstetrics & Gynecology)	Mentor	The focus of the Geyer laboratory is on chromosome organization and regulation of gene expression. Eukaryotes contain thousands of genes whose unique patterns of expression establish distinct cellular identities. These processes require coordinate transcriptional regulation of hundreds of genes. Within the nucleus, genes reside within chromosomes that are arranged in the nucleus to facilitate gene expression. Emerging evidence suggests that nuclear organization of chromosomes is a fundamental to transcription regulatory processes. We address mechanisms involved in these processes using molecular and genetic investigations in Drosophila. We are actively engaged in two lines of investigation. First, we are studying a class of DNA regulatory elements, known as insulators. Insulators define independent transcriptional domains by restricting the action of enhancers and silencers. Models suggest that insulator establish loop domains within chromosomes and contribute to the formation of higher order chromatin structures. Insulators play a critical role in many developmental processes, such as imprinting and mammalian dosage compensation and a loss of insulator function is associated with congenital forms of myotonic dystrophy. Second, we are investigating the role of the nuclear lamina in nuclear organization. Mutations in the nuclear envelope proteins are associated with several human diseases, including muscular dystrophy and bone density disorders. Models suggest that these diseases are caused by mis-expression of genes due to changes in nuclear positioning. Our studies will provide insights into mechanisms of transcriptional regulation and its relationship to human disease.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Grose, Charles MD	Professor	Pediatrics	Mentor	Research in Dr. Grose's laboratory is focused on various aspects of varicella-zoster virus (VZV). VZV is the virus that causes varicella in children and herpes zoster (shingles) in late adulthood. In 1995, the live attenuated varicella vaccine was approved for administration to children in the United States. Research in Dr. Grose's laboratory has evolved over the past years. The initial focus involved the identification and characterization of the major immunogenic glycoproteins on the surface of the varicella virion. As part of these endeavors, we identified the following major glycoproteins called gE, gI, gB, gH, gL, and gC. As an unexpected consequence of these investigations, we discovered the first mutant varicella strain in a community varicella outbreak. We characterized the mutant virus further and identified a missense mutation within an immunodominant B-cell epitope on glycoprotein gE, the major VZV surface protein. We subsequently formed collaboration with the National Microbiology Laboratory of Canada and completed the sequencing of a total of 11 VZV genomes. Our most recent VZV research emphasis is directed towards the role of autophagy during infection. We chose to study autophagy after we discovered that the characteristic skin vesicles found during both varicella and zoster infections are filled with autophagosomes. This result was not predictable. It is well known that the closely related herpes simplex virus contains an inhibitor of autophagy within its genome. Without this inhibitor, herpes simplex infection is quickly eliminated. Yet, the VZV genome, which contains no inhibitor of autophagy, is able to replicate in skin vesicles in the presence of autophagosomes. In our current laboratory experiments, we seek to resolve this apparent paradox between VZV and HSV infections and thereby elucidate the role of autophagy during VZV infection.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Grose, Charles MD (cont.)				Since the currently approved varicella vaccine is a live attenuated virus, the autophagy results have direct relevance to one of the vaccines recommended for all children living in the United States.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Hirsch, Raphael MD	Professor	Pediatrics (Chair effective 7/1/2012)	Mentor	Dr. Hirsch spent five years as a Medical Staff Fellow at the National Cancer Institute, Bethesda, MD, where his research focused on modulation of T cell function in transplantation and autoimmunity. He continued this area of investigation during the first decade of his faculty career at the University of Cincinnati College of Medicine, Children's Hospital Medical Center. This work led to the demonstration that non-mitogenic anti-T cell receptor antibodies suppress Th1 responses and could ameliorate autoimmunity. He also developed a research program on the biology of gene transfer to the synovium and is internationally recognized as a pioneer in this field. After arriving in Pittsburgh in 2002 he developed a major focus on understanding the pathophysiology of arthritis. This effort led to identification of Follistatin-like protein 1 (FSTL-1) as a novel inflammatory mediator and he has received two RO1 grants to pursue this research. In Pittsburgh, he also began a collaboration with other rheumatologists and with robotic engineers at Carnegie Mellon University that lead to development of a novel approach to measuring outcomes in children and adults with arthritis using thermal and 3D surface imaging. This effort has been funded by the NIH and also led to a commercial start-up venture to use surface imaging to improve outcome measures in arthritis. Dr. Hirsch has been a funded investigator since 1992. His research has been supported by the NIH, the Arthritis Foundation, and the American College of Rheumatology (ACR). He has published over eighty articles and holds six patents.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Hirsch, Raphael MD (cont.)				He has served on numerous NIH study sections. Beginning July 1, 2012 he will head the Department of Pediatrics at the University of Iowa where he will continue his research. Dr. Hirsch has devoted a great deal of attention to the training of students and fellows in rheumatic disease research and has been the primary research mentor for 32 students and fellows. Many of these have received national awards and grants, including the ACR Senior Scholar Award and Arthritis Foundation Physician Scientist Development Award (Michael Henrickson, M.D.), the ACR Medical Student Summer Research Fellowship (Catherine Hughes), the Arthritis Foundation Post-doctoral Fellowship Award (Constance Cullen, Ph.D.), an NIH post-doctoral fellowship and an Arthritis Foundation Arthritis Investigator Award for junior faculty (Sherry Thornton, Ph.D.). He is the Director of the only NIAMS-funded T32 training grant program dedicated to the training of academic pediatric rheumatologists, which was renewed in 2010.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Kwitek, Ann PhD	Associate Professor	Internal Medicine (Pharmacology)	Mentor	Dr. Kwitek's laboratory uses genetics as well as physiological and comparative genomic approaches to identify genes and mechanisms leading to complex disease - hypertension, diabetes and obesity in particular - using both rat models and human populations. Dr. Kwitek' s lab uses genetic linkage strategies to map genes, develop genetically unique rat strains to positionally clone and/or test candidate genes within a specific region of the genome. They then compare the genomes between the species, via comparative genomics, to translate the data from the rat to human and back again. Genes underlying these loci are being examined for their role in hypertension, dyslipidemia, obesity, and end stage organ damage. Because the rat and human genes are 90% identical, it is likely the same genes or pathways will also play a role in many diseases. Dr. Kwitek is an active mentor and involved in teaching and committee activities related to education. I currently mentor one K award fellow (whom has been promoted to Associate Professor), two graduate level students and an undergraduate student. Past mentees include one additional graduate student and two post-doctoral fellows, all of whom have pursued careers in academic medical research. My lab also had three graduate research rotations and seven undergraduate trainees, several of whom have entered medical school training. I have been director of two graduate level courses, and have lectured in courses including (but not limited to) Medical Physiology, Physiological Genomics, Genetic Analyses of Biological Systems. Finally, Dr. Kwitek currently several on thesis committees of seven graduate students (not including those in her laboratory).

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Lentz, Steve MD	Professor	Internal Medicine	Mentor	Dr. Lentz's laboratory utilizes molecular and cellular techniques, along with transgenic and gene targeted animals, to investigate the mechanisms of regulation of hemostasis by vascular cells such as endothelium, vascular muscle, and platelets. The long-term goals of the laboratory are to define the molecular and cellular interactions that regulate vascular function and to identify the key mechanisms of impairment of vascular function in disease states such as hyperhomocysteinemia and atherosclerosis. Current areas of investigation in the Lentz lab include the following: Vascular Function in Hyperhomocysteinemia and Atherosclerosis. A high blood level of the sulfur-containing amino acid, homocysteine, is a risk factor for cardiovascular disease, stroke, and vascular dementia. This condition is called hyperhomocysteinemia. Our laboratory was among the first to demonstrate abnormal vascular structure and function in moderate hyperhomocysteinemia. We are now using molecular genetic approaches to define the mechanisms of vascular dysfunction and accelerated thrombosis in hyperhomocysteinemia. Current projects are investigating the role of reactive oxygen species ROS), endoplasmic reticulum (ER) stress, the inducible form of nitric oxide synthase (iNOS), and the vascular NAD(P)H oxidases. We are using similar genetic approaches to investigate mechanisms of altered endothelial regulation of hemostatic function during atherosclerosis and regression of atherosclerosis. Platelet procoagulant activity. We have developed methods to study platelet procoagulant activity in mice. We have demonstrated that the adapter protein SLP-76 is essential for platelet signal transduction in response to collagen. We are currently are using genetic approaches in mice to further define the signal transduction pathways responsible for platelet procoagulant activity.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Lentz, Steve MD (cont.)				Current projects are examining the role of platelet transglutaminases (factor XIIIA and tissue transglutaminase) and platelet-derived ROS in the generation of a unique subpopulation of highly procoagulant “coated” platelets.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
McCray, Paul MD	Professor	Pediatrics (Microbiology)	Mentor	Dr. McCray is a pediatric pulmonologist with a long-standing interest in airway epithelial cell biology, innate immaturity, and the applications of gene transfer for lung diseases. His group is using molecular, genomics, and bioinformatic approaches to discover novel host host defense functions in airway epithelia. This includes microRNA regulation of epithelial cell gene expression and the impact of disease on gene expression. A major interest is the pathogenesis and treatment of cystic fibrosis. Dr. McCray's group is also developing non-primate FIV lentiviral and transposon based vectors for gene therapy applications, focusing on cystic fibrosis and hemophilia A. Ongoing studies are aimed at improving gene transfer efficiency, and targeting vector integration using designed zinc finger proteins.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Moreland, Jessica MD	Associate Professor	Pediatrics	Mentor	Dr. Moreland is a physician-scientist with clinical practice in the Pediatric Intensive Care Unit. Her research program is centrally focused around the theme of neutrophilic inflammation, in the context of human disease, with a specific interest in the neutrophil NADPH oxidase. For a number of years, the laboratory has sought to define the role of the neutrophil NADPH oxidase (Nox2) in neutrophil priming by infectious and inflammatory stimuli. Focusing specifically on mechanisms of neutrophil priming by TNF-α and endotoxin, the Moreland lab has identified proteins involved in the regulation of the NADPH oxidase. Most recently, the laboratory has become interested in how pro-inflammatory stimuli and cellular outputs are balanced by anti-inflammatory responses to restore host homeostasis. Using an animal model of generalized sterile inflammation to study the systemic inflammatory response syndrome, new data suggest innate and adaptive immune crosstalk. In her clinical practice, Dr. Moreland cares for patients with a wide range of systemic inflammatory processes, including sepsis, and her clinical interests have further focused her laboratory interests. In the last 18 months, the laboratory has initiated several ongoing translational projects using patient samples from the ICU and the clinic. One of these projects focuses on the role of TNF-α in inflammatory bowel disease, and a second project explores neutrophil priming during cardiopulmonary bypass in infants undergoing congenital heart repair. Dr. Moreland has mentored multiple trainees in the laboratory as the current program director for the Fellowship training program in Pediatric Critical Care, and now serves as the primary scientific mentor to two K08 funded junior faculty members in the Department of Pediatrics, 2 fellows in the Department of Pediatrics, as well as undergraduates and PhD students.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Murray, Jeff MD	Professor	Pediatrics (Biological Sciences)	Internal Advisor	Dr. Murray is Vice-Chair for Research in the Department of Pediatrics, Program Director for the University of Iowa CHRCDA, and Director of the Craniofacial Anomalies Research Center at the University of Iowa. The Murray Laboratory has focused on using genetic/genomic tools to investigate the underlying etiology of complex pediatric disorders. Building on our previous experience in developing comprehensive human genetic maps, current projects include strategies to identify and characterize genes and environmental contributors to birth defects, language delays and prematurity. In one example, the Van der Woude syndrome, we have identified the etiologic gene for this rare form of cleft lip and palate in collaboration with Brian Schutte in our Department. We have recently defined its role in facial development in the more common non syndromic forms of clefting and demonstrated that it confers about 15% of the risk for this common, complex birth defect. In parallel studies, we have demonstrated critical roles for four additional genes in human clefting (MSX1, FGFR1, BMP4 and FGF8) using high throughput DNA sequencing and animal model correlates. Many of our studies are carried out using large population and epidemiologic studies of children with craniofacial anomalies, particularly from the Philippines, Japan, Denmark and Brazil, and we work in close collaboration with investigators in these countries. In 1999 we created the Perinatal Research DNA Bank in Iowa that now contains epidemiological information and DNA samples from over 1000 infants (including 700 preterm infants) and their parents. These samples and the accompanying data are being used for research examining the genetic influences on neonatal disease.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Murray, Jeff MD (cont.)				This innovative program provides a resource for analyzing the role of pharmacogenetic variation as a modulator of neonatal disease and therapeutic response. Combining our molecular and developmental expertise with studies of epidemiology and environmental causes, has allowed us to initiate two clinical trial programs to complete a bench to bedside approach to Pediatric Diseases. In one we are using a Pediatric Care intervention in a trial to decrease mortality in children born with clefts in indigent populations in developing countries. In the second we are determining if high dose folic acid (4mg/day) can decrease the rate of clefting in families at increased risk for a second child to be born with a cleft. Our overall goals are to understand the primary causes of pediatric disorders with a genetic component, to implement primary prevention programs and to improve outcomes by targeting therapies more effectively using a personalized medicine approach.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Nauseef, William MD	Professor	Internal Medicine (Microbiology)	Mentor	Dr. Nauseef is Director of the Interdisciplinary Iowa Inflammation Program on campus. Ongoing projects in Dr. Nauseef's laboratory are designed to address several questions pertinent to the cell biology of human polymorphonuclear neutrophil (PMN)-mediated responses during inflammation and host response to infection. We have a longstanding interest in two important aspects of the neutrophil response, namely the NADPH-dependent phagocyte oxidase and the granule hemeprotein myeloperoxidase (MPO), and have active projects examining various aspects of each of these important elements in a variety of clinically relevant settings. Ongoing studies related to the NADPH-dependent oxidase seek to define biochemical events and molecular determinants that dictate the outcome of vents after human PMN ingest *Staphylococcus aureus* (SA). We focus our attention not only on the synergistic toxicity of host-derived oxidants and granule proteins that are released into the phagosome, but also on the transcriptional responses of SA that promote its survival within phagosomes. We are also examining the consequences of these events on the fates of PMN that have ingested the SA and of macrophages, cells downstream in the innate immune response to infection. In related host-pathogen studies, we are characterizing the functional changes in human PMN that transmigrate across endothelial and epithelial monolayers stimulated by *Francisella tularensis*.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Nauseef, William MD (cont.)				Studies related to our interest in MPO include characterization of MPO biosynthesis and the identification of various genotypes of hereditary MPO deficiency. Studies on MPO biosynthesis currently focus on defining the mechanism by which heme is incorporated into MPO, as very little is currently known regarding heme acquisition by peroxidases. The impact of heme insertion on the subsequent proteolytic processing and intracellular targeting of MPO to the lysosome is also under study. Studies of hereditary MPO deficiency include identification of the genotype underlying the specific phenotype and then characterization of the impact of that mutation on the synthesis of MPO. For these studies we used transfected HEK cells to stably express mutant MPO cDNA and characterize the biosynthesis. Related to our interests in the phagocyte NADPH oxidase, we are studying two recently described members of the NADPH oxidase (NOX) protein family, dual oxidase 1 and 2 (Duox1 and Duox2). Characterization of the putative peroxidase domain and the regulation of oxidase activity are the aspects of Duox biology currently under study.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Norris, Andrew MD, PhD	Assistant Professor	Pediatrics (Endocrinology)	Mentor	Research in Dr. Norris's laboratory is focused on two main topics: metabolic control in skeletal muscle and fetal consequences of hyperglycemic exposure. (i) Dysregulation of fuel metabolism and insulin signaling in skeletal muscle contributes to the pathogenesis of type 2 diabetes. The Norris lab currently is investigating the mechanisms by which the transcription factor PPARgamma modulates skeletal muscle metabolism and alters insulin signaling. (ii) During pregnancy, fetal exposure to maternal diabetes leads to short and long term health consequences. To better understand the underlying mechanisms, the Norris lab has created a novel model of fetal diabetes exposure in the pregnant rat. This is accomplished by infusing glucose into the left uterine artery at rates that create hyperglycemia in the left uterine horn but not in the mother or the right uterine horn. This allows dissection of the contributions of hyperglycemia alone to the short and long term consequences of diabetes during pregnancy in a precisely time-controlled manner. Current projects are aimed at understanding the mechanisms by which fetal hyperglycemia alter insulin secretion and insulin sensitivity.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Perlman, Stanley MD, PhD	Professor	Microbiology (Pediatrics)	Mentor	The overall theme of Dr. Perlman's research is to study coronavirus-induced immunopathogenesis, using a murine coronavirus, mouse hepatitis virus and the coronavirus that caused the severe acute respiratory syndrome (SARS).Mice infected with mouse hepatitis virus develop a demyelinating disease with many similarities to the human disease, multiple sclerosis. Research in my laboratory is aimed at determining the immunological and viral factors involved in the demyelinating process. Previously, we determined the CD4 and CD8 T cell epitopes recognized in the central nervous system (CNS) of infected mice. We showed that in mice infected chronically with the virus, cytotoxic T cell escape mutants arise. These mutations completely abrogate recognition by CD8 T cells and thereby facilitate persistence. Dr. Perlman's lab has developed a reverse genetics system for introducing mutations into the murine coronavirus genome. We have developed a model to determine the role of individual effector molecules in demyelination, using immunodeficient mice infected with the virus. Dr. Perlman's lab has recently spent much of their effort studying the anti-inflammatory response in infected mice, which is necessary for disease resolution and prevention of immunopathological disease. The ultimate goal of these experiments is to develop a system whereby we can introduce changes into immunologically important epitopes within the virus and study the effects of these changes on virus replication and persistence in the infected CNS.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Perlman, Stanley MD, PhD (cont.)				The SARS-coronavirus causes the most significant disease of any of the human coronaviruses. Our goal is to understand the mechanism of disease, especially in aged individuals and mice. For this purpose we use a mouse-adapted strain of sars-cov that causes disease largely in old mice. We are especially interested in the environment in the lung in old mice and humans, since this appears to impact immune responses.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Potash, James MD, MPH	Professor	Psychiatry	Mentor	Dr. Potash holds the Paul W. Penningroth Chair at the University of Iowa, where he is Professor and Head of the Psychiatry Department. His research focus is on the genetic and epigenetic basis of mood disorders. His research focus is on the genetic and epigenetic basis of mood disorders. One particular emphasis has been on the genetic vulnerability to the psychotic form of bipolar disorder, and on its overlap with the vulnerability to schizophrenia. He has principally explored this issue using phenotypic dissection, and genomic methods, the latter being linkage and genome-wide association. Currently he has an R01 grant from the NIMH to perform next-generation exome sequencing in about 3,000 bipolar disorder cases and controls, and examine the data, searching for rare variants associated with this illness. Work on this project in the lab involves DNA sequencing, bioinformatic annotation of sequence variation, and statistical genetic analysis to determine whether rare variation seen in cases is likely to be associated with illness. Rare variation seen in bipolar will be assessed in relation to comparable variation seen in schizophrenia samples. Another focus is on the potential role that stress has in triggering depression. He hypothesizes that stress confers risk through its impact on epigenetic control of depression-related genes. He has an R01grant from the NIMH to assess genome-wide variation in one epigenetic mark, DNA methylation, in a mouse model of stress and depression. In the model, animals are exposed to social defeat stress for two weeks. Following this, the defeated animals behave in ways that model aspects of human depression. The defeated animals are sacrificed and DNA from their hippocampus is studied using a genome-wide DNA methylation platform.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Potash, James MD, MPH (cont.)				of DNA methylation variation. Bioinformatic annotation of the implicated chromosomal regions, and statistical genetics analysis of these large data sets are also required.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Richerson, George MD, PhD	Professor	Neurology (Physiology & Biophysics)	Mentor	Dr. Richerson is an adult neurologist and physician-neuroscientist with expertise in basic neurobiology, cellular electrophysiology, neuroanatomy and *in vivo* physiology. My lab studies, at the single cell and systems levels, chemosensitivity of serotonin neurons and their role in respiratory control and arousal. We have shown that a subset of 5-HT neurons are central CO_2 chemoreceptors. Those in the medullary raphe are critical for the ventilatory response that occurs *in vivo* in response to inhalation of CO_2. Those in the midbrain raphe are also chemosensitive, and initiate arousal in response to the increase in CO_2 that occurs with airway obstruction. Our work has relevance to both SIDS and SUDEP, in both of which death is thought to occur due to loss of protective airway reflexes and hypoventilation. My laboratory also studies GABA transporters and GABAergic mechanisms involved in epilepsy.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Roghair, Robert MD	Associate Professor	Pediatrics	Mentor	For the past 10 years, I have investigated the developmental origins of cardiovascular disease. Mentoring is honestly the best part of my job. I have been driven to make sure others are offered the same opportunities I have been given. In addition to two senior research investigators, I mentor 2 Pediatric Critical Care fellows that have now joined our faculty, 2 current Neonatology fellows, and 6 undergraduate students. I also mentor 3 medical students, Catherine Zhang, a first year student that received an American Heart Association Undergraduate Student Research Fellowship while in my laboratory, Ben Dexter, a second year student that earned 2 summer research grants and a Clinical Research Award from the UI Foundation, and Holly Engelstad, who just joined my lab to obtain research experience prior to Pediatric Residency. I greatly appreciate the K12 support I received and thoroughly enjoy Dr. Sarah Haskell a bright star that just began her tenure as a K12 scholar.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Rosenthal, Gary MD	Professor	Internal Medicine	Internal Advisor	Director of the Institute for Clinical and Translational Science (ICTS). He is nationally recognized for his expertise in T3 and T4 translational science and has played a major role in developing research programs in these areas through his leadership of the ICTS and his prior leadership of the Division of General Internal Medicine (1998–2010), the Center for Comprehensive Access and Delivery Research and Evaluation (CADRE) at the Iowa City VA Medical Center (2001–2011), and the K30 Iowa Scholars in Clinical Investigation Program (2003–2007). Dr. Rosenthal's own research has centered around three related themes: 1) interventions to improve health care quality and the dissemination and implementation of evidence-based practices; 2) measurement of quality of care; and 3) development of novel methods for measuring comorbidity and severity of illness.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Scholz, Thomas MD	Professor	Pediatrics	PI	Dr. Scholz is a pediatric cardiologist and Interim Head of Pediatrics. He has an active research program and has been involved in mentoring trainees at all levels as well as junior faculty. His research focuses on mitochondrial function during development and their production of superoxide species. The reagents and techniques to study mitochondrial function during development have recently been applied to models of fetal programming to define the mechanism of cardiovascular risk following exposure to an adverse intrauterine environment.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Sheffield, Val MD, PhD	Professor	Pediatrics (Medical Genetics)	Mentor	Dr. Sheffield is an investigator of the Howard Hughes Medical Institute. My laboratory is interested in identifying the function of genes that cause a variety of human disorders with the goal of disease prevention and treatment. Our research efforts have focused on the molecular genetics of monogenic disorders, as well as polygenic and multifactorial disorders. We have used a variety of genetic methods to identify genes involved in numerous diseases with a focus on hereditary blindness. Efforts are currently underway to identify additional disease-causing genes. Complex genetic disorders currently under investigation in the laboratory include hypertension, obesity, retinal degeneration and glaucoma. In addition, we have developed mouse and zebrafish models of human diseases to aid in the understanding of disease pathophysiology. We are using these animal models to pursue both gene and drug based therapy. Our work has resulted in the elucidation of biological pathways involved in human obesity and blindness. In addition, our work has provided insight into novel treatments for glaucoma, a common disorder resulting in blindness. We have also had an active role in the human genome project and the rat genome project.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Sigmund, Curt PhD	Professor	Pharmacology (Physiology & Biophysics)	Mentor	Dr. Sigmund's laboratory is primarily interested in investigating the regulation of genes involved in cardiovascular homeostasis and in creating new transgenic and knockout models of cardiovascular disease that will allow us to explore how these genes regulate blood pressure. We use state-of-the-art molecular and physiological approaches to these problems including the extensive use of genetic manipulation including transgenesis, gene targeting and viral gene delivery. For the past 20 years, we have been investigating the mechanisms by the renin-angiotensin system (RAS) regulates blood pressure in normal and pathological states. In recent studies, we have uncovered a high novel link between Ras expression in the brain and the regulation of metabolic rate. We have also identified a novel link between brain and adipose tissue angiotensin signaling which may regulate thermogenesis. We have als9o been exploring the mechanism by which the PPARG transcription factor regulates blood pressure and vascular tone. This project makes extensive use of transgenesis, dominant negative mutants, microassay and computational biology. We have recently uncovered two novel mechanisms and PPARTG target genes which regulate vascular tone in both conduit and resistance vessels. One involves alterations in the regulation of the CRL complex of protein involved in ubiquitination of the major signaling molecule RhoA. The other involves regulation of the PPAR target gene RGS5 which when dysregulated causes increase angiotensin signaling and inhibition of the BK potassium channel.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Smith, Richard MD	Professor	Otolaryngology (Internal Medicine)	Mentor	Dr. Smith directs the Molecular Otolaryngology and Renal Research Laboratories (MORL) since creating them in 1991. He has been involved in hearing research since 1982 and in renal research since 1993. The MORL has Clinical Diagnostics and Basic Research Divisions. The Clinical Diagnostics Division is staffed by five research assistants. It was CLIA certified in 1999 (ID #16D0966193) and accredited by the Joint Commission on Accreditation of Healthcare Organizations in 2001, and is recertified very two years, most recently in November, 2011. Mutation screening is offered for deafness and complement-mediated renal diseases. This type of molecular diagnostic service has changed the evaluation of the deaf person and is essential in the treatment of some complement-mediated renal diseases, in particular Atypical Hemolytic Uremic Syndrome. The Basic Research Division of the MORL has made many significant contributions to our understanding of the biology of hearing/deafness and complement-mediated renal diseases. At the current time, five graduate students, five post-graduate students and one research scientist are doing research here. In the area of hearing/deafness, scientists in the MORL have mapped 19% of all known non-syndromic hearing loss loci and cloned 22% of all genes implicated in deafness; for many of these genes, they have also completed functional studies. In the area of complement-mediated renal diseases, scientists in the MORL are focusing on identifying additional genetic causes of Atypical Hemolytic Uremic Syndrome and clarifying the pathogenesis and genetics of Dense Deposit Disease as a step towards developing a treatment for this disease.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Snyder, Peter, MD	Professor Vice Chair	Internal Medicine (Cardiology)	Mentor	The epithelial sodium channel (ENaC) forms the pathway for sodium absorption in the kidney and other epithelia. ENaC plays a key role in the control of blood volume and blood pressure. This is illustrated by two genetic disorders. Mutations in ENaC that increase channel activity cause Liddle's syndrome, an autosomal dominant form of hypertension. Moreover, nearly all of the identified genetic forms of hypertension are caused by defects in ENaC regulation. Conversely, loss-of-function mutations cause pseudohypoaldosteronism type I, a disorder of salt wasting and hypotension. Defects in ENaC regulation may also contribute to the pathogenesis of lung disease in cystic fibrosis. Research in my lab is focused on the structure and function of the epithelial sodium channel to understand its role in hypertension and other disorders of sodium homeostasis. My laboratory has identified the molecular mechanisms by which mutations in ENaC cause hypertension. Current research in my laboratory focuses on: a) regulation of ENaC trafficking and how defects in trafficking cause disease. b) ENaC has a large extracellular domain that functions as a sensor of a number of molecules in the extracellular environment. Proteolytic cleavage of the extracellular domain also activates channel activity. Additional work in the lab is focused on understanding structure-function relationships involved in this regulation of ENaC gating. c) structure and function of related DEG/ENaC ion channels that play a role in mechanosensation and nociception. A number of approaches are used to accomplish these goals, including techniques of molecular biology, electrophysiology (e.g. voltage clamp, patch clamp), cell biology, and protein biochemistry.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Song, Long-Sheng MD	Assistant Professor	Internal Medicine (Cardiology)	Mentor	Gene regulation of Ca2+-signaling in cardiac excitation-contraction coupling; the cellular and molecular mechanisms of Ca2+-dependent arrhythmias during heart failure, and the roles of Ca2+ signaling dysfunction in other heart diseases.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Stokes, John MD	Professor	Internal Medicine (Nephrology)	Mentor	Dr. Stokes' research addresses the mechanisms whereby ions are translocated across the cell membranes and how these processes are regulated. Recently he has focused on the epithelial sodium channel (ENaC), a highly regulated heteromultimeric ion channel complex responsible for generating and maintaining large gradients across epithelial cells. This channel is highly regulated, as might be expected for its activity in establishing the sodium concentration of urine and other body fluids. Structure-function studies focus on the role of the carboxy termini of the three subunits, including a motif that interacts with proteins responsible for regulating the expression of the channel on the apical membrane of the cell. One of the major factors responsible for increasing ENaC activity is the steroid hormone aldosterone. This hormone acts largely by regulating transcription of genes that in turn regulate channel activity. Recent work is focusing on the role of steroids in regulating expression of each subunit and identifying their individual contribution to channel activity. Other projects in which Dr. Stokes is involved include studies on how ENaC can be inactivated, studies on the mechanisms involved in regulating Mg homeostasis, and a clinical trial of nocturnal dialysis.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Sutterwala, Fayyaz MD, PhD	Assistant Professor	Internal Medicine	Mentor	The focus of studies in the Sutterwala lab are a recently described family of molecules called NLRs (nucleotide-binding domain leucine-rich repeat containing receptors) that are involved in the regulation of innate immune responses and cell death pathways. Some NLR family members promote the activation of pro-inflammatory caspases within multiprotein complexes called inflammasomes. Mutations within NLRP3, a member of the NLR family, have been linked to a group of autoinflammatory disorders in humans collectively known as the Cryopyrin-associated periodic syndromes. The NLRP3 inflammasome can be activated by a number of diverse stimuli including bacterial toxins, endogenous danger signals and environmental pollutants. NLRC4, another NLR family member, has been shown to play a crucial role in response to infection with a number of Gram-negative bacteria. To understand the role of NLRs in coordinating the immune response the Sutterwala lab uses a gene-targeting approach utilizing mice deficient in specific inflammasome components. They are interested in three major areas of study. 1) Characterizing the signaling events involved in activation of the NLRP3- and NLRC4-inflammasomes. This entails determining the specific ligand for NLRP3 and NLRC4 and identifying downstream events mediated by their activation. 2) Determining the role of NLRP3 and NLRC4 in host the response to bacterial infection and identifying mechanisms pathogens use to evade these innate immune defenses. 3) Characterizing the role of NLRs in murine models of autoimmune and autoinflammatory disease and correlating this to disease pathogenesis in humans.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Weeks, Daniel PhD	Professor	Biochemistry (Pediatrics)	Mentor	Dr. Weeks' laboratory selectively alters gene expression to determine the cellular function of a number of genes in heart development. The early embryos of the frog Xenopus are well suited for a variety of developmental studies, including those on cardiovascular and ear development. In part, this is due to the large size of the early embryo, which begins development as a fertilized egg a little over a millimeter in diameter. The size of the fertilized egg makes the introduction of molecules by microinjection straightforward. Secondly, because the Xenopus has long history of use for developmental studies, the normal pattern of tissue differentiation has been well mapped. Thus, by delaying microinjection until several rounds of cell division have been completed molecules can be introduced into the embryonic progenitors of specific tissues. We are currently looking at genes that cause congenital defects in human heart and ear development. These genes include the NKX2-5 gene for heart development, and the EYA1 gene (the genetic cause of Branchio-oto-renal syndrome). Few systems offer the chance to look in detail at the formation of vertebrate hearts and ears in embryos with flexibility of Xenopus laevis. In addition to using methods such as mRNA injection standard to the field, we have designed, synthesized and tested chemically modified oligonucleotides to inhibit gene expression with the specific goal of finding stable non-toxic modifications that work well in vivo.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Weeks, Daniel PhD (cont.)				We are also actively developing and testing methods to simplify transgenesis in Xenopus laevis using an integrase based system. These studies show promise in the efficient generation of transgenic embryos for promoter and mutant expression studies. We have developed ways to generate detailed confocal images of embryonic development and been rewarded with seeing defects not previously noted by others, due to experimental manipulation of genes involved in heart development. In addition we have successfully added physiologic measures of heart condition function to the techniques that can be used to analyze embryonic heart development, successfully reporting for the first time EKG measurements on the 0.3mm hearts of week old tadpoles.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Welsh, Michael MD	Professor	Internal Medicine (Physiology & Biophysics)	Mentor	Dr. Welsh is a Howard Hughes Medical Institute Investigator. The Welsh lab has two main areas of focus. They are working to understand cystic fibrosis and develop new therapeutic approaches. They are also striving to understand how neurons detect the acid that is associated with painful stimuli and cell-to-cell communication. In both areas, the work extends from the study of genes to studies in humans. The long-range goal is to better understand disease and to develop new treatments. Cystic fibrosis (CF) is caused by mutations in the gene that encodes the CFTR chloride channel. The Welsh lab is addressing several key problems in CF. First, how does the CFTR chloride channel work? They are studying how this pore opens and closes. The mechanisms that regulate its gating are key for understanding its function in the trachea, bronchi, and small airways of the lungs. Second, the laboratory is trying to understand how the loss of the CFTR chloride channel leads to the lung infections that plague people with CF. They are using cells cultured from transplanted CF lungs to investigate salt, and water movement across the airway lining and to study how bacteria infect this tissue. Third, they are trying to develop new models for studying CF. The Welsh lab, and other labs, have disrupted the CFTR gene in mice. Because mice do not develop lung disease like humans with CF, they are currently working to develop a pig with CF. It is hoped that developing this novel animal model will yield new insights into the disease and provide a better system for testing novel therapies. Fourth, the laboratory is attempting to develop gene therapy for the disease.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Welsh, Michael MD (cont.)				They are currently in the phase of developing novel vectors, or carriers, of the CFTR gene. Fifth, the lab is trying to develop other new therapeutics for CF that might delay the onset of this devastating disease. The laboratory also focuses on a different family of ion channels that work in the nervous system. They are called ASICs, for acid sensing ion channel. In the skin and muscle, these channels appear to be involved in detecting the sense of touch and in detecting painful stimuli. Through their studies in cultured cells and in mice in which these genes have been disrupted, their work is suggesting that these channels may plan in important role in seizures. They may also contribute to anxiety disorders such as post-traumatic stress disorder and panic attacks. As the work progresses, it is hoped that it will pay dividends in our understanding and treatment of what are relatively intractable neurologic diseases.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Wemmie, John MD, PhD	Associate Professor	Psychiatry (Neurosurgery)	Mentor	As a psychiatrist and a neuroscientist Dr. Wemmie has developed significant expertise in molecular mechanisms of pH and acid-sensing ion channels (ASICs) in neural signaling, synaptic plasticity, learning and memory. Dr. Wemmies lab identified effects of pH and ASICs on fear, anxiety and depression-related behaviors in mice and also their effects on stroke, inflammatory demyelination and seizure termination. To help translate these discoveries to humans, Dr. Wemmie works to develop non-invasive imaging methods to measure pH dynamics in animal models and in the human brain. During this time Dr. Wemmie has mentored a substantial number of trainees and I have served on over a dozen thesis committees. More than twenty graduate students, post-docs, and junior faculty have trained in Dr. Wemmie' s lab, including three MSTP students. Many of these have won awards for work in Dr. Wemmie' s lab and have gone on to successfully continue their academic careers. Most recent was Adam Ziemann who won the Spriestersbach award for best thesis at the University of Iowa and is now a neurology resident at the University of California San Francisco.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Widness, John MD	Professor	Pediatrics (Administration)	Mentor	Since 2006 Dr. Widness has been the PI on a PPG that was recently refunded for 5 years ("Neonatal Anemia and Thrombocytopenia: Pathophysiology and Treatment," P01 HL046925-17). His career-long investigative focus has been fetal and neonatal hematology, with emphasis on erythropoiesis the physiology and pharmacology of EPO, perinatal iron metabolism, and transfusion medicine. The goal of Dr. Widness's current P01 sub-project, "Optimized Epo Treatment of Neonatal Anemia," is to develop a pharmacodynamically-based, individualized mechanistic approach capable of completely eliminating RBC transfusions in an identifiable group of very low birth weight infants by optimally administering erythropoietin. This will be achieved in clinical studies in which RBC survival will be assessed using multi-density biotin labeling of RBCs relying on by flow cytometric detection. He is internationally recognized for his contributions as a scientist and mentor in these areas. In addition to his PPG leadership role, he has led multiple successful collaborations in the United States. Dr. Widness has received continuous NIH research support beginning with his postdoctoral training in 1978.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Wilson, Mary MD	Professor	Internal Medicine (Microbiology)	Mentor	The focus of my research laboratory is the immuno- and molecular biology of infection with the *Leishmania* spp. protozoa. We also conduct collaborative studies with Brazilian and Indian colleagues as a part of Tropical Medicine Research Centers in each of those countries, funded through the NIH. I have had the opportunity to mentor 18 postdoctoral fellows (six of whom obtained independent funding from national agencies), 28 graduate students doing thesis research, 12 medical students doing short-term basic research, 29 undergraduate research projects and 25 students, residents or postdocs on research/clinical rotations at international sites. I have or currently served on executive committees of the Immunology PhD program (past), the Molecular & Cellular Biology PhD program (current), and the Medical Scientist Training Program (past). I also particulated on admissions committees for the Department of Microbiology (past), the College of Medicine (past) and the Genetics PhD program (current). I have taught or currently teach didactic course lectures for graduate students, medical students, postdoctoral clinical Infectious Diseases fellows, clinical Pathology residents/fellows and professional scientific research staff.

Name/Degree(s)	Rank	Primary (& Secondary) Appointment(s)	Role in Program	Research Interest
Zabner, Joseph MD	Professor	Internal Medicine	Mentor	The focus of my research is on the antibacterial innate immunity of the airway epithelia, in particular how does the lack of a chloride channel 'CFTR' results in pulmonary lung infections. I have divided the research in my laboratory into 4 main areas. First, to investigate the antimicrobial properties of the airway surface liquid and how they affect bacterial colonization in cystic fibrosis. My laboratory investigates this question using primary cultures of human airway epithelia at the air liquid interface, animal models including mice and pigs with deletion of the CFTR gene, and humans with cystic fibrosis. We are currently studying the effect of inhaled xylitol to enhance airway innate immunity. Second, I investigate the development of vectors for gene therapy in cystic fibrosis. Currently, I have been using 'directed evolution' to select adeno-associated viruses that efficiently target the airway epithelia of humans and pigs. The porcine model of Cystic Fibrosis will allow us to ask the question if 'gene transfer' can result in 'gene therapy'. Third, my laboratory also investigates how the receptor for adenovirus regulates epithelial functions as well as pathogenesis of adenovirus airway infection. Finally, I have been investigating the effect of an endogenous lactonase 'paraoxonase' that can degrade quorum-sensing molecules used by *Pseudomonas Aeruginosa*. This family of proteins is ubiquitously expressed in the airways and may represent a novel form of innate immunity against quorum-sensing bacteria.