

2024 SUPERR MENTORS:

The mentors listed below were selected on the basis of interest in mentoring undergraduate summer students, including members of groups under-represented in science careers, and research productivity. All mentors are NIH funded and have excellent lab space, facilities, and equipment. We have included basic, translational, and clinical science mentors conducting science that is relevant to the NIDDK/KUHD mission, regardless of whether their research funding is from NIDDK or another NIH institute or the VA.

Archer, David, PhD. Dr. Archer's research program is focused on the pathogenesis of sickle cell disease in respect to the generation, prevention and treatment of organ dysfunction. This is married to his long-standing interest in stem cell therapy and regenerative medicine. In particular, Dr. Archer's lab employs hematopoietic stem cell transplantation to study the effects of long-term correction of the hematological defect in murine models of sickle cell disease. He has considerable experience in the maintenance of multiple sickle mouse colonies, transplantation, hematological and functional analysis of the outcomes. Over the past few years he has focused on the kidney and has generated expertise in renal function testing and renal pathophysiology leading to an ability to investigate the ontogeny of end organ damage in sickle cell disease, especially the development of sickle cell nephropathy. As an active member of the Aflac Cancer Center, Immunology and Molecular Pathogenesis program in the graduate school, Faculty Mentor on Training grants, and core director, he has trained numerous graduate students and 19 undergraduate students, along with post-docs and fellows in the Hematology/Oncology Fellowship training program. Student projects will be focused on determining the pathogenesis of sickle nephropathy and the mechanisms by which therapeutic interventions prevent or repair the damage due to the disease process. Hematopoietic stem cell transplant is the only curative therapy for sickle cell disease and the correction of sickle pathology by this technique is also of interest to Dr. Archer's lab.

Cai, Hui, MD. The main interests of Dr. Cai's laboratory is to investigate the role of WNK kinases in the regulation of sodium chloride cotransporter (NCC) and Maxi K channel. WNK kinase plays an important role in maintaining electrolytes homeostasis. Mutations of WNK kinase result in pseudohypoaldosteronism type II (PHA II), one type of the monogenic hypertension. Dr. Cai's lab has a demonstrated record of successful and productive investigation into the role of WNK signaling pathway in the regulation of NCC and Maxi K channel, both in animals and in cell models. Dr. Cai has mentored over 10 post-doctoral fellows and 8 undergraduate students since 2007. Dr. Cai's expertise and experience have prepared him to mentor summer undergraduate students performing their research projects. The object of summer undergraduate students is to participate in Dr. Cai's ongoing research projects related to WNK's signaling in the regulation of NCC and Maxi K channel. Through 12 weeks of summer research time, students will learn molecular and cell biology techniques as well as metabolic cage studies for small animals. Students will be expected to complete a small research project that yields an abstract to present at a scientific conference and eventually a co-authored paper.

Caspary, Tamara PhD. Dr. Caspary is a mouse geneticist in the Department of Human Genetics. Her lab's research centers on the role of the primary cilium, the slender protrusion found on virtually all eukaryotic cells, including renal epithelial cells. Mutations in ciliary genes lead to diseases known as ciliopathies, which often present with cystic kidneys. Two specific ciliary genes, *PKD1* and *PKD2*, account for over 95% of the cases of Autosomal Dominant Polycystic Kidney Disease (ADPKD). ADPKD has an estimated incidence of 1:500 to 1:1000 live births, making it the most common ciliopathy. Despite its high prevalence, the underlying molecular

mechanism that drives ADPKD pathogenesis remains unknown. Through mouse genetic screens, we have identified several genes enriched in cilia and linked their dysfunction in cilia to cystic kidneys. Our work aims to dissect the molecular mechanisms within cilia that underlie kidney cysts in order to identify new therapeutic targets for ADPKD. Summer trainees in Dr. Caspary's lab will get hands-on experience with mouse handling, mouse genetics, kidney dissection, tissue sectioning and data analysis.

Chicas, Roxana, PhD. RN, Dr. Chicas research is oriented to occupational and environmental health disparities, investigating the physiological effects of chronic heat exposures among agricultural workers through community-engaged research. She focuses on the impact of heat exposure and dehydration on renal physiology and pathophysiology. As a bilingual bicultural nurse scientist, she is committed to conducting research that informs policy to advance environmental justice and mentoring the next generation of scientists.

Eaton, Douglas C., PhD. The goal of Dr. Eaton's research is to examine the cellular signaling mechanisms which regulate membrane ion transport and cellular homeostasis. To examine these signaling mechanisms, his lab uses contemporary methods of cellular and molecular biology including patch voltage-clamp methods and expression of cloned signaling molecules in heterologous expression systems. There are three main areas of cellular signaling research in his laboratory. First, Dr. Eaton has been particularly interested in the cellular responses which involve steroid hormones and other lipid molecules, particularly how some of these molecules are responsible for the regulation of total body sodium balance. This work has led his lab recently to examine defects in cellular signaling which may be responsible for some types of hypertension and electrolyte disorders. Second, Dr. Eaton has been examining the signaling mechanisms responsible for the responses of renal cells to growth factors and vasoactive substances like Angiotensin II. This work has direct relevance to understanding the renal pathology of diabetes. Finally, Dr. Eaton is interested in the signaling mechanisms that control fluid balance in the lungs. This work may provide an understanding of the pathophysiological mechanisms responsible for lung edema and acute lung injury.

Ford, Mandy L., PhD. Dr. Ford's research focuses on the T cell response to transplanted organs, in particular understanding the mechanisms that govern the activation, differentiation, and effector function of alloreactive CD4+ and CD8+ T cells and developing novel strategies to control them. In recent years her work has focused on using both mouse and human systems to explore three main areas of investigation: 1) Understanding how the blockade of CD28 signals in the presence of preserved CTLA-4 signaling results in the upregulation of the novel coinhibitory molecule 2B4 on donor-reactive CD8+ T cells following transplantation; 2) Interrogating the role of CD8+ T cell-intrinsic CD40 signaling on donor-reactive CD8+ T cell responses and CD4+ Foxp3+ Treg during transplantation, and 3) Investigating the differential impact of mTOR inhibition on graft vs. pathogen-specific CD8+ T cells during transplantation. All of these studies are conducted using TCR transgenic mouse models in which we can specifically track the graft-specific CD4+ and CD8+ T cells, thus allowing Dr. Ford's lab to perform detailed and sophisticated analyses that are currently not possible using fully allogeneic model systems in which the target antigens are unknown. Most of her studies in murine systems are complemented by similar analyses of human samples obtained from renal transplant recipients via her collaboration with the Emory Transplant Center Biorepository. An undergraduate summer student in Dr. Ford's lab would spend the first 1-2 weeks getting acquainted with techniques of cellular immunology and in vivo mouse work including tissue culture, CFSE proliferation assay, ELISA, flow cytometry, immunohistochemistry, post-mortem tissue harvest of blood and secondary lymphoid organs, intravenous injection, intraperitoneal injection, peripheral blood collection, and skin transplantation. These techniques

would be taught by Dr. Ford's very experienced senior technician who has been with the lab for >10 years. Students would then go on to address an experimental question with the help of Dr. Ford's post-doctoral associate or a senior graduate student. In general this would involve interrogating the impact of genetic deletion or pharmacologic inhibition of a particular costimulatory or coinhibitory pathway on the generation and maintenance of donor-reactive T cell responses and ultimately on graft survival. Emphasis is placed on data analysis and interpretation. In terms of knowledge gleaned, students will come to understand the immunologic processes that govern transplant rejection, and how specific T cell costimulatory pathways can be manipulated to control graft-specific T cell responses and prevent graft rejection. Students would meet with Dr. Ford twice a week to plan experiments and review data, and are expected to give a lab meeting at the end of their time in the lab. Students would also be expected to attend weekly lab meetings, a weekly Emory Transplant Center-wide Research Conference, and a weekly Emory Transplant Center-wide journal club. Dr. Ford has had 3 previous summer undergraduate trainees, one who became a second author on a manuscript published in Transplantation (3).

Greenbaum, Laurence, MD, PhD. Dr. Greenbaum's research program focuses on clinical research in pediatric nephrology and he participates in a variety of multicenter studies. In some cases, he is the lead investigator. He also performs a variety of retrospective and prospective studies at Emory. He is able to utilize one of the largest pediatric nephrology patient populations in the country, and a robust clinical research infrastructure, including 3 research coordinators and access to a pediatric research center that is part of the Emory CTSA. A student working with Dr. Greenbaum would initially complete the extensive training needed to conduct clinical research (e.g., human subject investigation training required by the IRB). The student would observe his interaction with study subjects, both in the clinic and in the pediatric research center. The student would ultimately be assigned a research project. This might be retrospective study or an existing prospective study. The student would work with either a fellow or a research coordinator, although Dr. Greenbaum would provide overall mentoring. The goal would be to identify a project that could be completed during the student's 10 week summer rotation, permitting the student to participate in data interpretation, and poster, abstract and manuscript preparation.

Harding, Jessica, PhD. Dr. Harding's epidemiology lab conducts chronic disease research at population and system levels in academic and government settings. She also describes trends in diabetes and kidney disease-related complications in the United States. She examines variations in diabetes incidence and complications according to demographic, socioeconomic, and lifestyle risk factors. Dr. Harding is working on improving data collection and quality related to kidney disease and transplantation as a member of the Transplant Health Services and Outcomes Research Program.

Hertzberg, Vicki Stover Ph.D. Dr. Hertzberg's research program focuses on the creation and/or application of advanced data science tools and techniques to a variety of biomedical research problems. One such area is exploring the health effects of environmental and occupational exposures among vulnerable populations, and one arm of her research is designed to elucidate the health impacts, including kidney damage, of occupational exposure to heat stress on migrant farmworkers. Another area is exploring the interrelationships between environmental exposures, the microbiome, and metabolomics. Thus, a second arm investigates environmental exposures in African American women and infants in metro Atlanta and the sequelae associated with these exposures. A third arm investigates the microbiome and the progression of amyotrophic lateral sclerosis (ALS). A third area is machine learning, and a fourth arm is the development of novel machine learning techniques to the identification and prediction of nursing quality indicator events from electronic medical records data. Trainees working with Dr. Hertzberg would have

opportunities to engage in the analysis of data regarding the physiologic effects of heat exposure, particularly on the kidney, which would also include analysis of large scale metabolomic data, environmental exposure data from an Atlanta-based cohort of African American women and children, and longitudinal microbiome and metabolomic data from patients with ALS and their spouses. Trainees would also have the opportunity to participate in machine learning algorithmic development and application for endpoints available from the electronic medical records.

Johnson, Theodore M, MD, MPH. Dr. Johnson's research focuses on older adults in general, and specifically on exercise and rehabilitation interventions that will improve quality of life and well-being. He is currently participating in an NIDDK-supported randomized controlled trial testing the effectiveness of combining behavioral treatment and drug therapy as a way to improve outcomes in the treatment of overactive bladder symptoms in men. He also participates in studies of the management of lower urinary tract symptoms in Parkinson's disease. Students working with Dr. Johnson could participate in ongoing studies evaluating quality of life data among patients enrolled in clinical trials aimed at improving lower urinary tract symptoms and in developing mobile app and technology solutions to problems of the aging bladder. Dr. Johnson has mentored one undergraduate student who was first author on a publication in *Urology* (4).

McCarty, Nael, PhD. Dr. McCarty's lab focusses on the molecular physiology of ion channels and receptors, with an emphasis on epithelial chloride channels. His specific focus is the pathophysiology of Cystic Fibrosis, including the structure/function of CFTR and its many roles in the airway. He pioneered the use of peptide toxins as probes of chloride channels. He also has projects that study the functional consequences of heterodimerization among GPCRs, the role of CFTR in regulation of sweat composition, and the molecular ecology of predator-prey interactions in the marine environment. His translational research in CF targets: (a) the mechanism by which the expression of mutant CFTR in airway epithelial cells impacts the development of CF-related diabetes; and (b) identification of biomarkers of acute pulmonary exacerbations in CF along with development of a novel device for their detection in the home. An undergraduate joining the lab would most likely contribute to understanding how expression of mutant CFTR channels alters epithelial cell function by induction of endoplasmic reticulum stress.

Meeks, Shannon L., MD. Dr. Meeks' research is focused on understanding the mechanisms underlying the immune response to factor VIII. Deficiency of the coagulation cofactor fVIII leads to hemophilia A. Patients with hemophilia A are treated with intravenous infusions of fVIII protein. Approximately 20-30% of severe hemophilia A patients develop an immune response to fVIII leading to inhibitory antibodies. The immune response is typically polyclonal with the A2 and C2 domains most often targeted. Nonclassical C2 antibodies are high titer, type II inhibitors (i.e., they incompletely inactivate fVIII at saturating concentrations of antibody). They are pathogenic in a murine hemophilia bleeding model. However, the pathogenicity can be overcome with a double dose of fVIII. This is in contrast to high titer, type I (i.e., antibodies that completely inhibit fVIII) classical C2 antibodies whose inhibition and bleeding phenotype cannot be overcome. Pathogenic effects are observed even at titers 20-fold lower than nonclassical antibodies. In preliminary studies 10 anti-fVIII antibodies with non-overlapping epitopes across all domains of fVIII were spiked into fVIII deficient plasma. The majority of these plasmas had higher thrombin generation following addition of fVIII +/- recombinant fVIIa (rfVIIa) than with rfVIIa alone. Using a panel of murine monoclonal antibodies (MAbs) with known epitopes, Dr. Meeks will investigate the role of epitope specificity in the hemostatic response as measured by in vitro coagulation assays. Specifically, she will measure the response to fVIII in one-stage and chromogenic fVIII coagulation assays, and the response to fVIII with or without bypassing agents in the thrombin generation assay and a novel microfluidics based system. The student will have the opportunity

to learn 3 major in vitro coagulation assays and perform these assays to assess the response of different antibodies with different epitopes to fVIII alone, rFVIIa alone, or combinations of fVIII and rFVIIa.

Park, Jeanie, MD. Dr. Park's patient-oriented research program focuses on studying derangements of neurovascular control in patients at high cardiovascular risk, particularly those with hypertension and chronic kidney disease (CKD). Her current studies include: 1) the regulation of sympathetic activity, endothelial function, and oxidative stress during exercise in CKD; 2) sympathetic and hemodynamic responses during mental stress in prehypertensive patients; 3) mechanisms of intradialytic hypertension; and 4) clinical trials evaluating the potential benefits of tetrahydrobiopterin supplementation in chronic kidney disease, and device-guided slow breathing in prehypertension. These studies are conducted at the Emory Clinical Research Network (supported by the Atlanta Clinical and Translational Science Institute, ACTSI), and the human physiology laboratory which specializes in performing direct measures of sympathetic activity via microneurography, arterial baroreflex testing, lower body negative pressure, continuous hemodynamic monitoring, and other advanced techniques to study sympathetic control in humans. This environment will provide a unique opportunity for a summer undergraduate student to engage in a breadth of human research experiences including translational research techniques, data interpretation and management, clinical trials experience, scientific communication, and ethical and regulatory considerations.

Patzer, Rachel, PhD, MPH. The goal of Dr. Patzer's research program is to improve kidney transplant access and clinical outcomes for patients with kidney disease. Her research suggests that racial disparities in kidney transplant access are concentrated in the Southeast, where African American patients represent 67% of the prevalent End Stage Renal Disease (ESRD) population and where living and deceased donor kidney transplant rates are the lowest in the nation. The main goal of her NIH-funded research is to improve kidney transplant referral and reduce disparities among African American ESRD patients in Georgia by conducting community-based participatory research with partners throughout the Southeast through the Southeastern Kidney Transplant Coalition. Through these partnerships, she has collected a novel source of surveillance data on kidney transplant referral at the dialysis facility level. These data are being used as a baseline and outcome measure for a group-randomized study among 120 dialysis facilities in GA, where 60 dialysis facilities will receive facility-specific quality of care feedback reports as well as culturally-sensitive education materials for ESRD patients and facility staff aimed to improve transplant referral. The undergraduate summer student would be involved in several components of this research project, including coordination with the Southeastern Kidney Transplant Coalition to help implement intervention activities among dialysis facilities, conduct of an independent short-term research project related to the overall research project with the assistance of an MPH-level epidemiologist, and assistance with preparation of a research poster, abstract and peer-reviewed manuscript of the short-term research project. She expects that the student will learn important concepts in health disparities and epidemiologic research, including: 1) developing a novel research question and hypothesis; 2) testing a research question; 3) analyzing data; and 4) presenting results for dissemination.

Petros, John, MD. Dr. Petros has investigated mitochondrial DNA mutations in prostate and renal cancer since 1993 and remains funded for this investigation. He has discovered that mutations in this genome predispose men to the development of prostate cancer, an effect that is significantly more common in African American men than Caucasian American men. In addition, he has identified a new tumor suppressor gene on chromosome 8p (beta-defensin-1) and continue to study this in transgenic mouse and other laboratory models. He is also actively engaged in drug

discovery with the Liotta group testing synthetic modulators of sphingolipid signaling. Dr. Petros is also engaged in health disparities research in prostate cancer and in biospecimen banking and biomarker and diagnostic test discovery in both prostate and renal cancer. A student in his lab will learn how molecular observations made in patient-derived material (e.g. mtDNA mutations) are tested in the laboratory in controlled experimental conditions (e.g. hybrid cell line studies) and how these laboratory constructs are used to test potential patient interventions (e.g. identification of high risk groups for cancer screening or target drug therapy). Thus the complete cycle of clinically-oriented basic science research from bedside to laboratory bench back to bedside is demonstrated in his work.

Romero, Cesar, MD, PhD Dr. Romero's research is oriented to discover mechanisms of hypertension, and damage associated with hypertension and diabetes. He also explores the sex differences in these diseases. A student participating in his lab will have the opportunity to learn experimental design, data collection and interpretation using genetically engineering animal models of diseases, as well as surgery skills in small animal and classic molecular biology and microscopy techniques.

Sanda, Martin, MD. Dr. Sanda's translational prostate cancer research is balanced by clinical investigation of prostate cancer patient-reported outcomes. The centerpiece of his research is the PROST-QA consortium, an NIH-funded, prospective, multi-center cohort of 1800 prostate cancer patients and spouses whose outcomes are evaluated by a hybrid approach combining phone survey with medical record-based data extraction linked through a web-based interface, that he reported in original investigation articles in the New England Journal of Medicine, JAMA, and other journals. Dr. Sanda has brought his outcomes expertise to national Phase III trials by cochairing NCI Cooperative group phase III trials to evaluate prostate cancer HRQOL. The most gratifying culmination of his academic endeavors has been the opportunity to serve as a primary mentor for more than 30 students, fellows, residents, and junior faculty in translational research, clinical research, or clinical care, and to fuel their potential to become future leaders in urological cancer surgery and research. Many of these trainees have gone on to succeed in their own academic careers, and several have themselves attained leadership positions such as Associate Chairs, and Directors of Urology Resident Education, and Division Chiefs, at prominent academic centers.

Sanz, Ignacio, MD. Dr. Sanz supports research in Lupus nephritis (LN). It remains the most frequent severe manifestation of Systemic Lupus Erythematosus (SLE), with major implications for patients' treatment and survival. Accordingly, more effective and safer treatments are needed for this disease. His studies utilize an integrated characterization of antibody repertoire by next generation sequencing and single cell monoclonal antibody generation; transcriptomics; and epigenetic analysis. His laboratory uses multidimensional flow cytometry and the approaches described above to understand the systemic B cells and plasma cell abnormalities that characterize patients with acute lupus nephritis. These studies will help unravel the immunological basis and correlates of the disease and identify new molecular targets for more effective, safer and personalized treatments.

Sheehan, Vivien, MD, PhD. Dr. Sheehan's laboratory uses genomics to unravel the mechanisms of globin switching and the pharmacogenomics of hydroxyurea in SCD (sickle cell disease), in order to develop new fetal hemoglobin-inducing agents to treat people with sickle cell disease. Her work has led to a clinical trial of metformin as a fetal hemoglobin inducing agent in patients with hemoglobinopathies. Dr. Sheehan has developed rheology biomarkers for use in assessing cure in gene-based therapy, and in collaboration with ELIAD, is developing them as tools to

assess which therapy is best for each individual living with sickle cell disease, as part of precision medicine.

Vaughan, Elizabeth C.P., MD. Dr. Vaughan's research focuses on new approaches to the management of lower urinary tract symptoms in older adults. She studies lower urinary tract symptoms among older adults and has evaluated both epidemiologic and clinical trial data in order to understand functional and quality of life effects of lower urinary tract symptoms. Currently, Dr. Vaughan is investigating exercise-based behavioral therapy for urinary incontinence in Parkinson disease through a multi-site randomized controlled trial at the Atlanta and Birmingham VA Medical Centers. Dr. Vaughan and her team published the results of a pilot study demonstrating the feasibility and potential therapeutic benefit of using exercise-based behavioral therapy to treat urinary incontinence in adults with Parkinson disease. Students working with Dr. Vaughan can participate in ongoing studies evaluating quality of life data among patients enrolled in clinical trials aimed at improving lower urinary tract symptoms, and analyzing epidemiologic data from NHANES to evaluate correlates of lower urinary tract symptoms in men and women.

Wall, Susan M., MD. Dr. Wall's research focusses on the Cl⁻/HCO₃⁻ exchanger, pendrin (Pds, Slc26a4) and its role in collecting duct Cl⁻ absorption and blood pressure regulation. She has localized this protein to the apical plasma membrane of the distal convoluted tubule (DCT), the connecting tubule (CNT) and the cortical collecting duct (CCD), where it participates in the process of HCO₃⁻ secretion and Cl⁻ absorption. Dr. Wall has demonstrated that pendrin, like the epithelial Na⁺ channel, ENaC, is up-regulated with aldosterone analogues, and works in tandem with ENaC, to increase net NaCl absorption following the application of aldosterone. She has observed that pendrin is critical to the pathogenesis of aldosterone-induced hypertension, presumably by mediating absorption of Cl⁻ and by stimulating the abundance and function of ENaC. Dr. Wall has also observed that ablation of the ubiquitin ligase, NEDD4-2, within intercalated cells, greatly stimulates apical plasma membrane expression of transporters, such as pendrin, that are expressed within intercalated cells and that mediate Cl⁻ absorption. Thus, blood pressure rises. A summer student would do balance studies to determine if intercalated cell NEDD4-2 null mice have a reduced capacity to excrete NaCl following a high NaCl diet, and learn to measure blood pressure in mice.

Wang, Xiaonan, PhD. Dr. Wang's research is focused on microRNA 29 and muscle atrophy in chronic kidney disease (CKD). Her research investigates the regulation of muscle physiology and pathology that results in loss of skeletal muscle mass in chronic kidney disease, diabetes, insulin resistance and aging. The specific research project with which a summer student would be involved is determining how insulin/IGF-1 signaling regulates protein metabolism. Her lab uses muscles from diabetic animal models. The student will learn to harvest muscle from normal control and diabetic mice, to prepare the tissue lysates from the muscle, to perform western blot analysis of the proteins in the tissue lysates and to analyze the western blots. IGF-1 signaling proteins (Akt, FoxO, mTOR and P70S6) in their basal and phosphorylated (activation indicator) form will be measured. The students will also learn how to use the Li-cor Odyssey infrared scanning system to identify and analyze the western blot results.

Wainford, Richard, PhD. Dr. Wainford's lab conducts transitional research in cardiovascular medicine. He directs a basic science and translational research program that examines the integrated central and renal mechanisms that regulate blood pressure in health and disease, focusing on the salt sensitivity of blood pressure and age-dependent hypertension. A new focus of Dr. Wainford's program is the investigation of the mechanisms contributing to hypertension-driven vascular cognitive impairment. Trainees can utilize an integrated translational

physiological, pharmacological, molecular, and gene-targeting approach to investigate blood pressure regulation, renal function, and cognition.

Yun, C. Chris, PhD. Dr. Yun's laboratory is investigating the molecular mechanism of Na⁺/H⁺ exchanger NHE3, which is highly expressed in the brush border membrane of the renal proximal tubule where it is responsible for reabsorption of more than 70% of sodium and bicarbonate. A student will be able to investigate the molecular mechanism of NHE3 regulation by using state-of-art molecular and physiologic techniques. The student will gain expertise in molecular (cloning, expression, mutagenesis, yeast 2- hybrid) and biochemical (immunoprecipitation, in vitro binding assays, protein expression and purification, immunohistochemistry) techniques. The student can investigate regulation of NHE3 by angiotensin II or insulin. NHE3 regulation by ubiquitination and recycling of NHE3 are other potential topics.