

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.

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 regulation of total body sodium balance. This work has lead 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 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.

Hoover, Robert S., Jr., MD. Dr. Hoover's research is focused on the examining the molecular physiology of the thiazide-sensitive sodium chloride cotransporter (NCC), one of the key effectors of blood pressure. This protein plays a key role in the regulation of blood pressure and thus the pathophysiological hypertensive state. A summer student in his lab would learn how blood pressure is regulated by the renin-angiotensin-aldosterone system and the key role of salt handling in that process. From an experimental standpoint a student would learn procedures such as immunoblotting, RT-PCR, real-time PCR, cell culture, and biotinylation. Dr. Hoover is the PI on an ongoing R01 grant and has a history of funding, including the Robert Wood Johnson Minority medical Faculty Development Award. His research and mentoring experience will allow him to make a substantial and meaningful contribution to the training components of this grant and to the undergraduate students whom he mentors.

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).

Ma, Heping, PhD. Dr. Ma's current research focusses on the regulation of ENaC by membrane lipids. Dr. Ma will initially teach the student about the general concepts regarding the role of epithelial sodium channels (ENaC) in drug-induced hypertension, and then teach the students three techniques that are routinely used in his laboratory: 1. Patch-clamp techniques; 2. Confocal microscopy; 3. Scanning ion conductance microscopy. For each student, he will pick a technique that the student feels comfortable learning and have the student work on a small research projects. The goal is for these projects to result in an abstract and poster. Dr. Ma has the expertise and facilities necessary to teach students these techniques and help them accomplish these proposed projects using the techniques described above. During the past ten years, Dr. Ma has trained 4 technicians, 2 PhD students, 8 postdoctoral fellows, and 3 undergraduate summer students. Two of the undergraduate students were work-study students. This SUPERR grant support will help the undergraduate students to become interested in renal research.

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 via this new R25 SUPERR grant 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.

O'Neill, W. Charles, MD. Dr. O'Neill's research has taken a broad-based approach to the study of vascular biology and of vascular calcification in particular, employing *in vitro* studies, animal studies, and clinical studies. The focus has been on novel approaches such as the first model of vascular calcification in cultured intact arteries rather than isolated cells (recently extended to cardiac valves), aortic transplantation between mouse models to address local versus systemic effects of promoters and inhibitors of calcification and reversibility of calcification, and mammography as a window into medial arterial calcification in humans. This has led to the discovery of the critical role of endogenous calcification inhibitors, particularly pyrophosphate. Study of breast arterial calcification has generated a number of important findings, including the potential role of medial arterial calcification rather than atherosclerosis in peripheral arterial disease. As a practicing nephrologist witnessing far too many amputations in dialysis patients, I am frustrated by the limited knowledge of medial arterial calcification and peripheral vascular disease, and the lack of effective therapies. To that end, a number of novel calcification inhibitors have been developed in the laboratory, some of which have been successfully tested in animals. This work is complemented by clinical studies defining the risk factors, natural history, and clinical significance of medial arterial calcification. This dual approach of basic and clinical research uniquely qualifies me to perform the studies proposed in this application, with the goal of developing new therapeutic approaches.

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.

Plantinga, Laura, PhD. Dr. Plantinga is an epidemiologist with appointments in the Divisions of Renal Medicine and General Internal Medicine and Geriatrics, as well as in the Rollins School of Public Health. Dr. Plantinga's research is focused on studies aimed at improving the quality of care among patients with chronic kidney disease and end-stage renal disease. Her current renal projects include: the investigation of factors associated with hospital readmissions among dialysis patients, particularly those related to pulmonary edema or fluid overload; the development and testing of a comprehensive physical functioning report in dialysis clinics, with the aim of improving patient-centered communication between patient and provider; and the examination of the burden and outcomes of serious injury falls among dialysis and transplant patients. She is also running a pilot project examining cognitive and physical functioning in a cohort of lupus patients, among whom renal complications are common. Each of these projects has multiple potential trainee projects. A trainee working with Dr. Plantinga would have opportunities to learn the fundamentals of epidemiologic and health services research, perform hands-on research with epidemiologic datasets, collaborate with multidisciplinary research teams (including nephrologists, geriatricians, rheumatologists, and/or gerontologists), and present and/or publish the results of the research project.

Rahbari, Frederic. Dr. Rahbari is involved in the study of genetic contributions to drug response in essential hypertension, the role of melatonin in circadian blood pressure patterns in non-dipping essential hypertensives, the mechanisms of cyst formation in autosomal dominant polycystic kidney disease (ADPKD), and discovery of urine and serum metabolomic profiles that may provide new diagnostic markers for ADPKD. In addition she is involved in the CPATH/CDISC program to establish a nationwide registry for disease modeling in ADPKD. Dr. Rahbari is also involved in an interventional study aimed at testing the hypothesis that rigorous blood pressure control blocks the renin-angiotensin-aldosterone system is more effective than rigorous blood pressure control alone in slowing progression to renal failure in ADPKD. Additional projects include: assessing blood pressure response using high quality phenotype data and examining linkage between the rate of kidney/cyst enlargement and qualitative and quantitative end-points. A student with interest in clinical and translational research and/or the epidemiology of renal disease would receive training in the following topics: study design; methods of clinical and observational research emphasizing randomized clinical trials and cohort study; sample size estimation; data collection and management; and statistical analyses (including multivariate modeling of observational data).

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.

Sands, Jeff M., MD. Dr. Sands' research is directed at understanding the urine concentrating mechanism in the inner medulla. Current research projects are focused on defining the molecular physiology of urea transporters since urea transport is a key component in the urine concentrating mechanism. A trainee participating in these studies would learn to design and use animal models of abnormal concentrating and diluting ability, such as: rats with diabetes mellitus or acquired nephrogenic diabetes insipidus due to lithium administration; and genetically engineered mice with sickle cell anemia, knock-out of urea transporter proteins, knockout of protein kinase C alpha (PKC α), or knockout of the V2-vasopressin receptor. Dr. Sands uses a combination of isolated perfused tubule studies to measure urea transport, antibodies to measure changes in the amount, location, phosphorylation, or localization of urea transport proteins, and surface biotinylation and confocal microscopy to measure changes in subcellular localization of urea transporters. This variety of approaches has allowed trainees in Dr. Sands' lab to show that facilitated urea permeability, UT-A1 urea transporter protein abundance, UT-A1 phosphorylation, and UT-A1 apical plasma membrane accumulation are regulated by two vasopressin-stimulated pathways, PKA and exchange protein activated by cAMP, and by hypertonicity via PKC α , in the inner medulla. A student would learn to perform careful metabolic and pair-feeding studies, harvest tissue, dissect kidneys, and perform protein and mRNA analyses. Dr. Sands has trained 23 undergraduate students at Emory, including 3 from under-represented minority groups and 17 who received financial aid (work-study). One undergraduate student mentored by Dr. Blount and Dr. Sands had a first author paper in *AJP-Renal* (2).

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. Multiple obstacles however need to be overcome to achieve this goal including a better understanding of the underlying pathogenic immunological mechanisms, the specific immune cells that mediate disease and the specific effector antibodies that induce tissue damage in the kidneys. Yet, while a wealth of information in mice and humans point to B cells and autoantibodies as major pathogenic players in LN, the specific nature of the relevant cells and antibodies remains to be understood and therefore, we remain ignorant of the molecular mechanisms underpinning B cell dysregulation and autoantibody generation in this condition. Obtaining this knowledge remains a critical unmet need in LN as it would be essential for: i) early disease recognition and treatment initiation; ii) intelligent design of new therapeutic targets and strategies; iii) disease segmentation and personalized treatment; and iv) development of biomarkers of disease development, activity and outcome.

The studies utilize an integrated characterization of antibody repertoire by next generation sequencing and single cell monoclonal antibody generation; transcriptomics; and epigenetic analysis. In particular, bulk and single cell PC are isolated from a dedicated research core biopsy performed in patients with acute lupus nephritis and plasma cells isolated for the above studies. Our final purpose is to understand how the PC that reside in the kidney differ in terms of autoreactivity and survival programs in order to determine their participation in disease and to identify new molecular targets for their elimination.

In addition, our laboratory is using 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. As before, we expect that these studies will unravel the immunological

basis and correlates of the disease and identify new molecular targets for more effective, safer and personalized treatments.

Taylor, Andrew T., Jr., MD. Dr. Taylor's NIH supported research program has led to the identification of three of the best first-generation ^{99m}Tc renal tracers (MAG3, DD-EC, syn-DMAEC), two patents, the development of second generation ^{99m}Tc renal tracers containing a tricarbonyl core and the evaluation of these tricarbonyl tracers in animal models and in humans. The best second generation tracer that he has identified to date is $^{99m}\text{Tc}(\text{CO})_3$ nitrilotriacetic acid (NTA), which exists as a single species, is amenable to kit formulation, has a clearance equivalent to ^{131}I -OIH based on studies in volunteers and CKD patients, and he has recently submitted an eIND to compare NTA to MAG3 in targeted populations. Because of the disruption in clinical care and the disruption of research due to the recent worldwide shortage of ^{99m}Tc pertechnetate, his laboratory is using their expertise in innovative chemistry and ligand design to develop renal tracers labeled with ^{18}F as well as ^{99m}Tc . ^{18}F renal tracers could be used if ^{99m}Tc pertechnetate is unavailable and can take advantage of the increasingly widespread availability of PET scanners and inherently better resolution of PET. Key members of Dr. Taylor's research team are: Malgorzata Lipowska, PhD, who is expert in the design of radioligands that target the organic anionic transporters; Jeff Klenc, PhD, and Dinesh Shetty, PhD, who were instrumental in extending the one-step $(\text{Al}^{18}\text{F})_2^+$ method for ^{18}F labeling of peptides in aqueous solution. In the process of renal radiopharmaceutical development, Dr. Taylor's lab is facilitating the understanding of basic technetium and rhenium (Re) chemistry as well as ^{18}F labeling in aqueous solutions. This core work will facilitate the development by others of new integrated and bifunctional ^{99m}Tc , ^{18}F diagnostic and $^{186}\text{Re}/^{188}\text{Re}$ therapeutic radiopharmaceuticals. A summer student would work in Dr. Taylor's lab to learn the process of radiopharmaceutical development: (1) identifying a clinical problem; (2) searching for candidate ligands that target a particular organ or receptor relevant to the clinical problem; (3) safe handling of radioactive material; (4) labeling the ligand with a radioactive tracer; (5) evaluation in animal models; (6) developing an understanding of structure/functional relationships to enhance ligand design; (7) submission of an eIND; and (8) human testing. In addition to this broad understanding of radiopharmaceutical development, the student would also participate in selected components of ligand synthesis.

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 $\text{Cl}^-/\text{HCO}_3^-$ 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 HCO_3^- 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.

Winterberg, Pamela MD. Dr. Winterberg's research is focused on understanding the consequences of disturbed T cell function during chronic kidney disease (CKD). We have found that patients and mice with CKD have T cell populations similar to aged individuals, including a more differentiated, memory phenotype with increased inflammatory potential. The full impact of these T cell disturbances is unclear. We are currently investigating the role of T cells in the development of a type of heart failure that occurs during CKD, called uremic cardiomyopathy, which is characterized by a thickened and stiff heart. A summer student in this lab would learn about T cell function including co-stimulatory and co-inhibitory receptor signaling. Practical lab experience would include working with *in vitro* assays of T cell function including stimulation for cytokine measurement and proliferation assays, real-time PCR, and multi-color flow cytometry.

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.