

Pharmacology and Neuroscience Discipline Handbook 2022-2023

Regardless of the discipline, each SBS student (MS or PhD) will receive the degree of Biomedical Sciences. The discipline is listed on the transcript as the Major.

The information provided in this document serves to supplement the requirements of the School of Biomedical Sciences detailed in the UNTHSC Catalog with requirements specific to the discipline of Pharmacology and Neuroscience.

Table of Contents

| Page |) |
|--|---|
| Description of the Pharmacology & Neuroscience Discipline3 | |
| Graduate Faculty and Their Research4 | |
| Course Requirements | |
| Required Courses | |
| Required Elective Courses | |
| Required Activities | |
| Sample Degree Plans14 | |
| Advancement to Candidacy | |

Pharmacology & Neuroscience Discipline

Nathalie Sumien, Ph.D., Graduate Advisor Center for BioHealth Building, Room 549 817-735-2389 Nathalie.Sumien@unthsc.edu

Graduate Faculty: Barber, Clark, Colon-Perez, Cunningham R, Dong, Forster, Gatch, Jin, Johnson, Kerr, Liu, Luedtke, Mallet, Nejtek, Ortega, Park, Phillips, Prokai L, Prokai-Tatrai K, Salvatore, Schreihofer D, Shetty, Shi, Siderovski, Stankowska, Su, Sumien, Yang

Pharmacology is a discipline that bridges the basic and clinical sciences. Classically, pharmacologists sought to understand the pharmacological responses, mechanisms and clinical uses of drugs. In recent decades, the scope of pharmacology has expanded dramatically to include cutting edge research in signal transduction and cellular & molecular biology.

Neuroscience combines the fields of anatomy, physiology, molecular biology and cytology to study the function of the brain and nervous system. The goal of these studies is to gain a fundamental understanding of the biological basis of learning and memory, as well as the processes involved in neural development and neurodegeneration. The scope of neuroscience includes molecular and cellular studies of individual neurons to imaging the circuitry of sensory and motor tasks within the brain.

The Pharmacology & Neuroscience faculty maintain active research programs in the following areas: aging and Alzheimer's disease; drug discovery; glaucoma and ocular pharmacology; stroke; Parkinson's disease; learning and memory; neurobiology of drug and alcohol abuse; neuronal degeneration and protection; neuropsychopharmacology; pharmacogenetics; and receptors and ion channels.

Students in the Pharmacology & Neuroscience Discipline may choose from a number of advanced elective courses that are related to their individual research interests. Students are also required to participate in seminars, works in progress presentations and group discussions of current research topics, and will be trained in a number of techniques required to address existing research problems in the field. Both MS and PhD students will conduct original, publishable research and will be expected to present their results at national scientific conferences. Completion of the master's degree typically requires two years while the PhD degree is generally completed in four to five years.

Students who successfully complete a graduate degree in the Pharmacology & Neuroscience discipline will be well prepared for careers in academic or government research laboratories, as well as in the pharmaceutical/biotechnology industry.

Graduate Faculty and Their Research

To find out more specific information about faculty, please refer to: https://experts.unthsc.edu/en/

Graduate Faculty Membership Categories:

<u>Associate members</u> of the Graduate Faculty are able to serve as members of thesis or dissertation advisory committees, as major professors or co-major professors on thesis advisory committees, and as co-major professor on dissertation advisory committees with a full member as the other co-major professor.

<u>Full members</u> of the Graduate Faculty are able to serve as members of thesis or dissertation advisory committees, and as major professors or co-major professor on thesis or dissertation advisory committees.

Suchismita Acharya, Ph.D. Assistant Professor, Full Member

The Acharya laboratory's research is focused on expanding the chemical toolbox for neural signaling and anti-inflammation/anti-oxidant pathways to understand the mechanism of action of the disease pathology associated with glaucomatous optic neuropathy, Alzheimer Diseases, Ischemic stroke, substance abuse disorder as well as angiogenesis. The lab integrates medicinal chemistry, chemical biology, bioengineering, and drug delivery via nanotechnology. We employ synthetic organic and organometallic chemistry to generate small molecule library for low throughput as well as high throughput screening (target based as well as phenotypic). The projects involve traditional medicinal chemistry SAR for property optimization to find hit to lead and structure, fragments or ligand-based drug design using structural biology, and computational chemistry tools. Fluorescent and ESR active probe design for signaling study as well chemoluminoscense assays are used. Pro-drug design to achieve chemical and metabolic stability, use of nanomeric materials and polymeric particles for drug delivery study is another core interest of Acharya lab.

Robert Barber, Ph.D. Professor, Full Member

Research in my group is focused on identifying genetic and epigenetic risk factors for neurodegeneration. Work in our group is collaborative and translational in nature. Ongoing projects include efforts to use patterns of DNA variation and differential methylation to predict the risk and progression rate of Alzheimer's disease. I am also interested in the biology of Alzheimer's among Mexican Americans and how disease etiology may differ between this underrepresented ethnic group and Caucasians. A second area of research interest is how individual gut bacteria profiles may impact risk for neurodegeneration and the age at onset of cognitive decline.

Collaborations are established with researchers at UNTHSC and other Texas institutions, as well as West Virginia University. Active projects are ongoing with Drs. O'Bryant, Allen, Planz, Cross, Hall, and Cunningham at UNTHSC; Chumley and Boehm at Texas Christian University; Royall and Palmer at UT Health Science Center at San Antonio and Wilhelmsen at West Virginia University School of Medicine.

Abe Clark, Ph.D. Regents Professor, Full Member

Dr. Clark's major research focus is to discover the molecular mechanisms involved in ocular diseases, particularly glaucoma, in order to develop disease modifying therapies for better management of ocular diseases. Glaucoma is the leading cause of irreversible vision loss and blindness in the world and is also the leading neurodegenerative disease, affecting both the eye and brain. Dr. Clark's research includes molecular genetics, molecular biology, cell biology, physiology, pathology, and mouse models of glaucoma. A main goal in this lab is to perform translational research that eventually will help patients with glaucoma. In addition to research, he trains and mentors graduate students, postdoctoral fellows, and medical students. He also is very active in community-based vision screening events.

Luis Colon-Perez, PhD. Assistant Professor, Full Member

I maintain an interdisciplinary research program to study neurobiological and behavioral relationships of Substance Use Disorders (SUD). I seek to identify basal level alterations in MR-based biomarkers that could serve as potential targets for experimental translational interventions. This is achieved by leveraging the large toolbox of network science to SUDs research in rodents. In addition to network science, I employ a longitudinal MRI approaches with on-going behavioral studies to identify important insights regarding the brain regions and circuits that may precede the long-lasting behavioral alterations in SUDs. My work uniquely integrates MRI neuroimaging and behavior studies to determine temporal trajectories of brain changes concomitant with behavior. In the lab we are currently working to establish neuroperturbation approaches, such as optogentics, to establish causal links between MRI biomarkers of brain circuits and specific relationships to SUDs behaviors. In my laboratory, I have eight operant chambers, one small-animal surgical suite, and two optogenetics systems to fulfill the goals of the lab. Connectivity and circuitry studies are gaining a high level of interest among neuroscientists, including, and MRI is one approach that provides us with a unique platform for translational biomarkers of brain structure and function between rodents and humans, in addition to allowing us to probe the entire human and rodent brain non-invasively.

Rebecca Cunningham, Ph.D. Professor, Full Member

Through her lab work, Dr. Rebecca Cunningham studies the role of steroid hormones, specifically androgens, during aging. Most of the team's research has been focused on androgen signaling mechanisms and defining the effects of androgens on central nervous system function.

One of Dr. Cunningham's long-term research goals is to determine how development and aging alters steroid hormonal responses in the central nervous system. In pursuing this goal, Dr. Cunningham and team use in vitro, in vivo, and clinical approaches to understand the how androgens affect brain function. It is hoped that this research will expand the understanding of how steroid hormones in the brain participate in aging. At the same time, she is expecting new insights that can lead to a better understanding of the role of gender in central nervous system disorders.

Xiaowei Dong, Ph.D. Assistant Professor, Full Member

Dr. Xiaowei Dong received a BS in Industrial Analysis and a MS in Applied Chemistry from the universities in China, and a PhD in Pharmaceutical Sciences from the University of Kentucky. Dr. Dong was selected as one of six students nationwide to participate in the 2008 AAPS Graduate Student Symposium in Drug Delivery and Pharmaceutical Technology. She has worked as a lead formulator for drug development at Novartis Pharmaceutical Corporation for four years. In 2013, she joined UNT Health Science Center as an assistant professor in the Department of Pharmaceutical Sciences at the College of Pharmacy. Dr. Dong's research has focused on drug delivery and formulation development.

Michael Forster, Ph.D. Regents Professor, Full Member

There are two programs of research in our laboratory, each focused on the analysis of rodent behavior. One program targets the neurobiology of substance use disorders involving stimulants, cannabis, opioids and tobacco, with a focus on using rodent models to identify therapeutic chemicals to promote recovery. These models include drug induced arousal and depression, discrimination, conditioning and self-administration. Another program is focused on understanding the neurobiology of aging and neuro-degenerative disease. This program is focused on the analysis of rodent behaviors reflecting sensory and motor capacity, learning, memory and executive functions. We know that it is possible to combat aging neurobiology because humans may achieve advanced age in truly great condition and in the absence of neurodegenerative disease. Lower organisms grow old more rapidly and, like humans, show great differ-

ences among individuals in terms of how long they remain robust and resist disease and injury. By studying rodents, our laboratory is focused on the promise that we can rapidly discover ways to combat deleterious aging conditions, study how they work, and design trials in humans.

Michael Gatch, Ph.D. Professor, Full Member

The focus of our research is on two broad aims. One aim is to screen compounds that will attenuate the subjective and reinforcing effects of abused drugs as part of a NIDA-funded contract searching for effective treatment drugs for addiction to cocaine, methamphetamine, nicotine and marijuana. Another aim is to evaluate the potential abuse liability of novel designer drugs that are increasingly available as "legal" alternatives to controlled substances. We use drug discrimination procedures which assess the subjective effects of common drugs of abuse such as cocaine, methamphetamine, nicotine and marijuana, with designer drugs like MDMA (Ecstasy), with opioids like morphine, or with hallucinogens such as LSD. We also test the reinforcing/rewarding effects of drugs using the conditioned place preference and self-administration assays.

Kunlin Jin, M.D., Ph.D. Professor, Full Member

Post-stroke cognitive impairment (PSCI), occurring in an estimated 30% of post-stroke patients, is the second most common cause of cognitive decline, yet no effective treatment is available to pre-vent or attenuate PSCI. Although aging correlates with poorer ischemic outcomes and cognitive de-cline, the mechanisms underlying the link between aging and PSCI remain elusive. One of my lab projects is to explore the link between aging and stroke outcomes, we are particularly interested in the role of exosomes in synaptic plasticity via microglial activation signaling. In addition, my lab is also studying on the role of Alzheimer's disease (AD)-derived exosomes in the spread of AD pa-thology using cutting-edge cell imaging techniques to visualize cellular trafficking and release of fluorescently labeled AD exosomes in living animal and use a 7T MR Solutions system to monitor

the pathologic features. We will define the mechanisms through which mTORC1 regulates the exosomes-mediated propagation of $A\beta$ and tau aggregation. Our goal is to identify novel targets for clinical interventions with the aim of disrupting or delaying spread and the further progression of disease.

Leigh Johnson, Ph.D. Associate Professor, Associate Member

My area of expertise is in translational aging research. I am the Co-I of Health & Aging Brain among Latino Elders (HABLE) study (R01AG054073), and the Director of the Clinical and Outreach cores for this study. I have spent a great deal of time studying factors related to cognitive loss among Mexican Americans with specific emphasis on the link between depression and cognition. I have developed and cross-validated a depressive endophenotype (DepE) of cognitive aging across multiple national and international cohorts. This work has been translated into a proof of concept clinical trial (The DEMO trial).

Marcel Satsky Kerr, Ph.D. Professor, Full Member

Dr. Kerr is an experimental psychologist with specializations in human development and statistical research methods. She teaches biomedical statistics, epidemiology research methods, analysis of scientific literature, and foundations of psychology. Dr. Kerr's research and publications focus on survey development and psychometrics. Her most notable measure is the Test of Online Learning Success (ToOLS), which resides in the public domain and is used internationally by over 250 institutions of higher education to assess students' readiness for internet delivered coursework. ToOLS has also been used for research purposes in numerous theses and dissertations, was adopted for collaborative use into the Merlot II learning community, and was published in the Internet and Higher Education journal in 2006. Other research areas include the scholarship of teaching and learning, emotional intelligence, resilience, and

lifelong learning. Her current research focuses on the effects of mindset (fixed vs. growth) on physical health and healing as they relate to the medical placebo effect.

Ran Liu, M.D. Research Assistant Professor, Associate Member

The principal goals of my research are focused on translational stroke research. Although rtPA is the sole FDA approved treatment for ischemic stroke, very few patients have been benefited from rtPA treatment because of its limited therapeutic window and the increased risk of hemorrhage transformation due to blood-brain barrier breakdown. We are among the first to explore the combined therapy to extend rtPA's therapeutic window in ischemic stroke models. We have demonstrated that estrogens could extend the therapeutic window of rtPA for the treatment of ischemic stroke. In addition, our research has provided insight to target ischemic penumbra and beyond for the treatment of ischemic stroke. Currently we repurpose a century-old drug, methylene blue, for the treatment of ischemic stroke. Our study demonstrates that large MCA territory infarct may induce long-lasting elevated GABAergic tonic inhibition in the hippocampus and, thus, contributes to cognitive impairment after ischemic stroke. All these results have led us to explore the role of GABAA receptor mediated neurotransmission in the cognitive impairment after large MCA territory infarct and to determine the effect of methylene blue on cognitive impairment after ischemic stroke.

Robert Luedtke, Ph.D. Professor, Full Member

Our laboratory is interested in development and pharmacological characterization of dopamine receptor subtype selective drugs for the treatment of individuals afflicted with Parkinson's Disease or Alzheimer's Disease. We have also worked to develop D3 vs. D2 dopamine receptor subtype selective drugs that can be used to assist in the rehabilitation of individuals who abuse psychostimulants, such as cocaine. We are also working on the development of sigma-1 receptor selective compounds as therapeutics for the prevention of neurodegenerative disorders including traumatic brain injury and dementia. These studies have provided insights into the function of D2-like dopamine and sigma-1 receptors in the brain.

Robert Mallet, Ph.D. Regents Professor, Full Member

Dr. Robert Mallet's research focuses on developing treatments to protect the heart and brain from heart attack, stroke, and cardiac arrest. These three diseases, which result from interruptions in the blood flow to the heart and/or brain, are among the leading causes of death and disability in the United States. Dr. Mallet's team has discovered that breathing air containing reduced amounts of oxygen, for a few daily exposures lasting a few minutes each, causes adaptations in the heart and brain that make these organs much more resistant to interruptions in their blood flow. As a result, the damage to the heart and brain inflicted by temporary loss of blood flow is greatly decreased, enabling these vital organs to recover and resume their normal function.

Current work in the Mallet laboratory is studying the favorable changes in the brain's and heart's biochemical makeup which underlie the adaptations to low oxygen, so that these adaptations can be safely harnessed to help human patients survive and recover from strokes, heart attacks, and cardiac arrest.

Vicki Nejtek, Ph.D. Associate Professor, Full Member

The Nejtek lab currently examines biomarkers and cognitive functioning outcomes to predict risks for Parkinson's disease (PD) in veterans with and without mild traumatic brain injury (mTBI). We have successfully used BDNF, cortisol, and interleukin to identify treatment response, and have used cognitive functioning tests to predict mood state, and drug relapse. We have also used MRI with and without diffusion tensor imaging (DTI) to identify brain anomalies in patients with bipolar disorder with cocaine dependence in comparison to healthy controls. In a recent collaboration with Dr. Michael Salvatore, the

Nejtek lab has received funding to conduct cross-species translational studies in parallel with our veterans with and without mTBI using a Parkinson's genetic PINK1 rat model compared to wild type.

Sterling Ortega, Ph.D. Assistant Professor, Full Member

The overarching theme of my research program is to discover novel therapeutics that can reverse immune-mediated neurological dysfunction. In line with this focus, my lab studies two debilitating neurological diseases.

Stroke, which is caused by the loss of blood flow to the brain, results in neurological injury and inflammation. Our previous studies have revealed a dynamic interaction between the adaptive immune system and the injured ischemic brain. This project will characterize the adaptive immune response (specifically CD8 T-cells) and determine if they can indeed modulate neuropathology and neurorecovery. Our preliminary data shows autoreactive CD8 T-cell responses to a subunit of the NMDA receptor as early as four days after stroke induction in two different murine strains. These neuronal GluN2A-reactive CD8 T-cells produce both interferon-gamma and tumor necrosis factor-beta, both highly inflammatory cytokines. The immuno-biology of CD8 T-cells makes them perfect harbingers of neuropathology. In my lab, we will use advanced immunological and neuroscientific assays to test our hypotheses. Our translational studies will determine if these cells are present and functional in post-stroke patients. In addition, my lab also studies the role of neuroprotective myelin-specific CD8 T-cells in a mouse model of Multiple Sclerosis (MS). Multiple sclerosis is a disease whereby the myelin sheath around nerve axons is lost, disrupting communication between the brain and the body. Our preliminary data show that myelin-reactive CD8 T-cells expeditiously (2–6 days) and robustly reverse disease, access the brain during disease amelioration, and produce interferon-gamma. This cytokine has been shown to exhibit neuro-reparative properties. Taken together, we believe that myelin-reactive CD8 T-cells employ "neuro-reparative" mechanisms that we will evaluate. In summary, using in vitro and in vivo approaches, we will delineate mechanisms involved in the cerebral functional recovery that myelin-reactive CD8 T-cells possess. Investigating the immune mechanisms that potentiate direct activation of brain reparative processes is a novel approach that directly addresses the goal of understanding how we can restore function in MS patients. Our translational studies will determine the role of these cells in MS patients.

InWoo Park, Ph.D. Associate Professor, Full Member

The first is HIV-1-mediated aggravation of liver disease in HCV virus co-infectees. Due to the shared routes of infection, HIV-1/HCV co-infection is common, with 15~30% of all HIV-1-infected persons estimated to be co-infected with HCV. In the co-infected patients, HIV-1 is known to accelerate every stage of HCV-mediated liver disease progression. However, the molecular details regarding how co-infection of HIV-1 and HCV brings about a more severe deterioration of the liver than a single infection of HCV are unknown at present.

Second, HIV-1 viral proteins are generated in a stage-specific manner; that is, regulatory proteins, such as Tat, Rev, and Nef, are expressed at the early stage, while structural proteins, such as Gag, Pol, and Env, are produced at the late stage of virus infection. Molecular regulation of viral gene expression in protein production has been studied comprehensively, whereas the elimination processes using the ubiquitin proteasome system for the synthesized proteins after completion of their duties in the infected cells are generally unknown, representing a current gap in understanding the smooth stage-specific transitioning through the HIV-1 life cycle, crucial to viral pathogenicity.

Nicole Phillips, Ph.D. Assistant Professor, Full Member

Our laboratory has a several areas of interest: 1) studies of mitochondrial DNA and mitochondrial function, in the context of various disease states such as Alzheimer's disease, type 2 diabetes and preeclampsia (in collaboration with Dr. Stella Goulopoulou); 2) genetic aspects of pain and pain management, as

the Director for Genomic Research for PRECISION Texas; 3) genetic risk for age-related disease and comorbidity patterns, via genome-wide genotyping, methylation profiling, and data mining.

Laszlo Prokai, Ph.D. Professor, Full Member

Dr. Prokai is the first Chair in Biochemistry endowed by the Houston-based Welch Foundation, one of the United States' oldest and largest private funding sources for basic research, at the UNT Health Science Center. He is affiliated with the UNTHSC's Department of Pharmacology and Neuroscience, and is an Associate Member of the Graduate Faculty at the Department of Chemistry and Biochemistry of the Texas Christian University. His interests focus on chemistry-driven multidisciplinary research and include the discovery, chemical biology, bioorganic and medicinal chemistry of central nervous system agents, as well as neuropeptides, proteomics and mass spectrometry. Dr. Prokai has maintained an actively funded research program from grant support by the National Institutes of Health (NIH) as well as through collaborations with pharmaceutical and chemical companies, and was the recipient of the 2017 Wilfred T. Doherty Award of the Dallas/Fort Worth Section of the American Chemical Society (ACS) and the 2017 Southwest ACS Regional Award.

Katalin Prokai-Tatrai Ph.D. Professor, Full Member

The research in our laboratory is directed at medicinal chemistry-based drug design and delivery into the central nervous system with translational medicine in mind. We focus on agents (neuropeptides and estrogens) that are beneficial for brain and retinal health. Our projects involve pharmacokinetics, metabolism and drug distribution studies in early-phase drug discovery and

the aging/diseased brain and retina. The current federally funded main project in our lab is entitled "A Novel Neuroprotective Approach for Glaucoma."

Michael Salvatore, Ph.D. Professor, Full Member

Our lab goal is to understand the molecular basis for locomotor impairment in aging and Parkinson's disease. Once we have identified differences in specific dopamine or glutamate-regulating proteins that are associated with locomotor impairment, we can use approaches that target these proteins and determine if experimental changes in protein expression or function can improve locomotor function. Therefore, our immediate and long-term goals are to delineate optimal molecular, pharmacological, and non-invasive (exercise, calorie restriction) approaches that can target proteins associated with motor impairment. Once we have gained such results in rat models, we aim to translate these findings into the human condition. Ultimately, we use our results toward the goal of reducing or eliminating locomotor impairment associated with aging and Parkinson's disease. Dr. Salvatore has obtained funding from the National Institute on Aging and Department of Defense to maintain this research program and has served as a reviewer for multiple funding mechanisms for the Parkinson's Foundation.

Ann Schreihofer, Ph.D. Professor, Full Member

My goal is to better understand how the brain controls blood pressure, both under normal conditions and in the presence of disorders that raise blood pressure. Currently, my laboratory focuses on two conditions that lead to high blood pressure: obesity and sleep apnea. Both of these conditions change how the brain controls blood pressure, but the mechanisms are not well understood. Although, ideally, obesity and sleep apnea can be managed, many find it difficult to control body weight in the long term and not may tolerate current treatments for sleep apnea. As these conditions continue to become more prevalent, the cardiovascular disease that accompanies them also becomes a major health issue nationwide. The current treatments for high blood pressure are numerous, and many medications act within the brain to control blood pressure.

Our work examines which treatments are ideal for management of cardiovascular disease with these conditions by determining how the brain changes with obesity and sleep apnea and whether current medications can reverse these changes. Because high blood pressure has many causes, treatments should

be individually optimized to best manage control of blood pressure in the context of the conditions that accompany it.

Derek Schreihofer, Ph.D. Associate Professor, Full Member

My laboratory is interested in the prevention and treatment neurodegeneration. Using cell and animal models of stroke, traumatic brain injury, and metabolic syndrome, we examine the factors that reduce injury and prevent or delay the onset of motor and cognitive disfunction. Ongoing projects 1) examine how steroid hormones like estrogen, testosterone, and natural estrogens from plants regulate brain function in injury and aging and the underlying mechanisms of steroid action; 2) determine the role of sport-related head injury in aging-induced neurodegeneration and Alzheimer's disease; 3) determine precursors of cognitive decline associated with metabolic syndrome; and 4) identify new drugs for treating stroke injury. Our goal is to determine the conditions in which these compounds can be safely and effectively used to provide ongoing brain health and treat brain injury and disease. My lab uses rodent injury models to study behavior, gene expression, cell signaling, and pharmacological interventions. In vitro, we make use of cell lines, primary cell cultures, and organotypic brain slice cultures with fluorescent markers and live cell imaging.

Ritu Shetty, PhD., R. Ph. Research Assistant Professor, Associate Member

Long-lasting drug related memories can play an important role in addiction cycle and relapse. I am interested in understanding the mechanisms behind formation and consolidation of memories; predominantly drug-related memories. The main focus of my research is to understand the acquisition and development of drug-seeking behavior using various rodent models, and also identify molecular targets in different brain regions involved in expression of such behaviors.

Xiangrong Shi, PhD Associate Professor, Full Member

Main goal of Dr. Shi research aims to develop low-dose intermittent hypoxia (IH) exposures as a non-pharmacological therapeutic intervention to improve cognitive function and physical health in elderly humans with mild cognitive impairment (MCI), early Alzheimer disease (AD) or AD-related dementia (ADRD), and ischemic stroke. Low-dose IH exposures have proved to be readily tolerated by elderly adults without adverse incident (PMID: 31557538, PMID: 31902230). IH exposures induce hypoxemia, not ischemia, which in fact, stimulate cerebral vasodilation and mobilize oxygen delivery (PMID: 20660087, PMID: 29074711). IH training (IHT) shows the potential to improve short-term memory and attention in MCI patients (PMID: 31902230). The rationale of IHT that can be applied as novel therapy for MCI, AD/ADRD, and stroke is based on the mechanisms that include the IHT improved cerebrovascular reserve and cardiorespiratory function (PMID: 25056104, PMID: 25504012, PMID: 31902230), and promoted neuroprotective growth and trophic factors (PMID: 34276338). Dr. Shi lab is currently planning a NIA-sponsored clinical trial to test the safety and efficacy of IHT with optimal IH dose to improve cognitive function in adults with MCI.

David Siderovski, Ph.D. Professor & Chair, Full Member

G protein-coupled receptors (GPCRs) remain the single largest group of "druggable" proteins that continue to find tremendous utility in drug discovery programs. In 1994, Siderovski was the first to report the sequencing of a "Regulator of G protein Signaling" (RGS protein): 'G0/G1-switch gene-8' or G0S8 (subsequently renamed RGS2). What Siderovski originally identified as the G0S8-homology ("GH") domain in proteins from several eukaryotic genomes (human, *Drosophila melanogaster*, *Caenorhabditis elegans*, *Saccharomyces cerevisiae*) is now known as the "RGS domain", a 130 amino-acid domain that contacts G-alpha switch regions to stabilize the transition state, thus accelerating GTP hydrolysis. Discovery of this superfamily of proteins that negatively regulate G-alpha-dependent signaling resolved a prior paradox that GPCR-stimulated signals are seen to terminate much faster in vivo than predicted

from the slow GTP hydrolysis rates exhibited by purified G-alpha subunits in vitro. RGS proteins are now considered key desensitizers of heterotrimeric G protein signaling and, as such, as new drug discovery targets. The lab is currently pursuing RGS protein inhibitors as potential agents against cocaine and opioid abuse.

Dorota Stankowska, Ph.D. Assistant Professor, Full Member

Glaucoma is an eye disease commonly associated with an increase in intraocular pressure, afflicting nearly 3 million Americans and 70 million people world-wide. Current therapies are aimed at lowering intraocular pressure, however, damage to the optic nerve continues to occur despite these treatments. There is a pressing need for adjunct therapies aimed at protecting the optic nerve from further damage. My laboratory research focuses on the development of strategies for neuroprotection in glaucoma. Specifically, we are testing various small molecules and adeno-associated viral gene therapies for their ability to attenuate neurodegeneration in animal models of glaucoma. We also aim to unravel cellular and molecular mechanisms underlying the pathophysiology of glaucoma.

Concepts/techniques: We carry out these studies using in vitro rat primary retinal ganglion cell cultures, ex vivo adult rat retinal explants, and various in vivo rodent models of glaucoma. We use visual function tests including pattern ERG and optomotor test to determine the efficacy of clinically relevant experimental pharmacotherapies. Our ongoing studies have the potential to develop novel therapeutic agents for neuroprotection in glaucoma.

Dong-Ming Su, Ph.D. Professor, Full Member

The strength of our research projects is using and generating genetically-engineered animal models in understanding genetic and epigenetic regulation of the T-cell immune system and its microenvironment during aging. Our aim is to determine mechanistic insights into poor (immunosenescence) and harmful (autoimmune) T-cell immunity in the elderly for developing rejuvenation strategies to combat age-related chronic inflammatory diseases and cancer recurrence. Our current NIH- & AAI-funded and potentially NIH-funded projects include: "Balance of thymic negative selection vs. Treg cell generation in the elderly (NIH-funded R01)"; "Biased Treg TCR specificity and its impact on immunity in the elderly (Potential NIH R01)"; and "Role of the central immune organ in cancer chemoimmunotherapy (AAI-funded fellowship).

Nathalie Sumien, Ph.D. Associate Professor, Full Member

My scientific interests lies with the study of interventions to alleviate the effects of aging and age-related diseases on motor, cognitive and affective function and the role oxidative stress and inflammation may play in the success of these interventions. Currently, we have three on-going studies: (1) hyperbaric oxygen therapy as a novel intervention for Alzheimer's Disease, (2) developing a model of childhood leukemia "chemobrain" to study interventions, and (3) long-term consequences of psychostimulants on brain function. All our studies are done in rodents and include male and females to determine the impact of sex differences on interventions.

Shaohua Yang, M.D., Ph.D. Regents Professor, Full Member

In biology, energy is an attribute of all living organism from bacterial to human being. The conversion between mass and energy are fundamental to our understanding of the biological processes defined as metabolism by which living organisms cycle energy through different mechanisms to produce the necessary molecules and perform the necessary functions of life. As the metabolism goes on, the life goes on. Dr. Yang's laboratory is interested in understanding the mechanism and discovery of interventions for brain aging and aging-related neurological disorders, including ischemic stroke, vascular dementia, and Alzheimer's dementia. His research has been focusing on the brain metabolism and using cell culture and rodent models of ischemic stroke and neurodegenerative diseases to address these issues.

Requirements

The requirements below are in addition to the SBS requirements listed in the <u>SBS Degree Programs</u> chapter of the <u>UNTHSC Catalog</u>.

Grades

For either the MS or PhD program, it is required that a student maintain a GPA of 3.0. In addition, each student must make a grade of at least B in all Pharmacology & Neuroscience courses.

PhD students who fail to make a B in required courses (PHRM 6400 and PHRM 6410) will be required to retake these courses or other courses with contents covering OQE topics and will have to delay their oral qualifying exams.

Core Required Courses

For MS and PhD Program

- Biomedical Ethics (BMSC 5160) 1 SCH (Spring)
- Responsible Conduct of Research (BMSC 6101) 1 SCH (Summer)
- Grant Writing (BMSC 6102) 1 SCH (Fall)- Master's degree students are encouraged but not required to take BMSC 6102
- Diversity, Equity and Inclusion (BMSC 5109) 1 SCH (Spring)
- Transferable Skills (BMSC 5108) 1 SCH (Summer)

Discipline Required Courses

- o Pharmacology & Neuroscience Seminar (PHRM 5140)-1 SCH (required registration for at least one semester, but attendance mandatory throughout degree)
- o Pharmacology & Neuroscience Journal Club (PHRM 6140) 1 SCH (attendance required for Spring Year 1, required registration for Fall/Spring Year 2)
- o Pharmacology & Neuroscience Work in Progress (PHRM 5150)- 1 SCH (required registration for every long semester throughout degree * potential exception for last semester)

For PhD Program*

- o Functional Neuroscience (PHRM 6400) 4 SCH
- o Basic and Clinical Pharmacology (PHRM 6410) 4 SCH

<u>Discipline-Specific Required Elective Courses</u>

Must include at least 2 SCH in PHRM courses, excluding Special Problems courses

Elective courses offered by other departments can also be taken, provided that the required electives in Pharmacology and Neuroscience are completed. The student is referred to the Catalog for course offerings in other departments.

Offered every semester:

Techniques in Biomedical Sciences: Multifactor Experiments (BMSC 5170.400) - 1 SCH Drug Discovery and Design (PHRM 6270) - 2 SCH

^{*}Master's Degree students are encouraged, but not required to take these 2 courses

Offered every year:

Mitochondria and Complex Diseases (PHRM 6200) - 2 SCH (Spring) Methods in Molecular Biology (PHRM 6440) – 4 SCH (Summer)

Offered in "even" fall semesters:

Receptors and Drug Action (PHRM 6480) - 4 SCH

Offered in "even" spring semesters:

Neurobiology of Aging (PHRM 5300) - 3 SCH

Offered in "odd" fall semesters:

Neuropharmacology (PHRM 5470) - 4 SCH

Receptors and Second Messenger Signaling (MIMG 6435) - 2 SCH

Kinases and Phosphatases (MIMG 6436) – 2 SCH

Offered in "odd" spring semesters:

Biomedical Mass Spectrometry (PHRM 6361) - 1-2 SCH

Required Activities

Journal Club: Students are required to register for Journal Club for Year 2, and will be required to attend and participate during Spring Year 1

Seminars: Student are required to register for Seminar course, and will be required to attend and participate throughout their degree. Course can be taken more than once for credit.

Work in Progress: Starting in Year 2, the students will be required to register and participate in this course every long semester. The semester they defend they may choose to not register after discussion with graduate advisor and mentor.

Others activities: It is required of all students to attend as many research proposal defense, thesis and dissertation defense as possible, to support fellow students and to remain engaged within the program.

Sample Degree Plan

Master of Science Degree Plan – The sample below does not imply that all requirements for graduation will be met with 30 SCH of course work. While it is possible to complete the requirements in this time frame, most research projects require additional semesters to complete. The typical time-to-degree for MS students is two years.

| Dept | Number | Title | SCH | Semester | |
|---|--------------|--|-----------|---------------------------|--|
| BMSC | 5150 | Lab Rotations | 2 | Fall Year 1 | |
| BMSC | 6200 | Intro to Experimental Design & Biostatistical | 2 | Fall Year 1 | |
| | | Methods | | | |
| BMSC | 6201 | Fundamentals of Biomedical Science I | 2 | Fall Year 1 | |
| BMSC | 6202 | Fundamentals of Biomedical Science II | 2 | Fall Year 1 | |
| BMSC | 6203 | Fundamentals of Biomedical Science III | 2 | Fall Year 1 | |
| BMSC | 6204 | Fundamentals of Biomedical Science IV | 2 | Fall Year 1 | |
| | | Subtotal | 12 | | |
| Milestones | to be comple | eted: Selection of Major Professor, Change of Discipline | 1 | | |
| | -1.50 | | | | |
| BMSC | 5160 | Biomedical Ethics | 1 | Spring Year 1 | |
| BMSC | 5315 | Principles of Scientific Communication | 2 | Spring Year 1 | |
| BMSC | 5109 | Diversity, Equity and Inclusion in Biomedical Sci- | 1 | Spring Year 1 | |
| DMCC | 5000 | ences: Fundamental Concepts | 0.6 | Contra Vara 1 | |
| BMSC | 5998 | Individual Research Pharm & Neuro Seminar | 0-6 | Spring Year 1 | |
| PHRM | 5140 | | 1 | Spring Year 1 | |
| PHRM | 6140 | Pharm and Neuro Journal Club | 1 | Spring Year 1 | |
| | | Advanced Courses | 0-6 | Spring Year 1 | |
| Milastonas | to be comple | Subtotal telegration of Advisory Committee, Degree Plan. Th | 12 | ah Duanasal must ha filad | |
| | | nea. Designation of Advisory Commutee, Degree 1 am. 116 Thesis (BMSC 5395). | e Keseurt | n i roposai musi ve jueu | |
| BMSC | 5108 | Transferable Skills | 1 | Summer Year 1 | |
| BMSC | 5998 | Individual Research | 0-5 | Summer Year 1 | |
| BMSC | 6101 | Responsible Conduct of Research | 1 | Summer Year 1 | |
| BMSC | 5395 | Thesis | 0-5 | Summer Year 1 | |
| | | Advanced Courses | 0-5 | Summer Year 1 | |
| | | Subtotal | 6 | | |
| Milestones to be completed: Annual Committee Meeting. Research Proposal must be filed prior to enrollment in Thesis | | | | | |
| | | are accumulated at this point. If degree requirements are no dent completes the research proposal, SCH can be reduced | | | |
| BMSC | 5998 | Individual Research | 1-10 | Fall Year 2 | |
| BMSC | 5395 | Thesis | 1-10 | Fall Year 2 | |
| PHRM | 5150 | Pharm & Neuro Work in Progress | 1 | Fall Year 2 | |
| PHRM | 6140 | Pharm and Neuro Journal Club | 1 | Fall Year 2 | |
| | 02.10 | Subtotal | 12 | 1 441 1 441 1 | |
| BMSC | 5998 | Individual Research | 1-10 | Spring Year 2 | |
| BMSC | 5395 | Thesis | 1-10 | Spring Year 2 | |
| PHRM | 5150 | Pharm & Neuro Work in Progress | 1 | Spring Year 2 | |
| PHRM | 6140 | Pharm and Neuro Journal Club | 1 | Spring Year 2 | |
| | | Subtotal | 12 | 1 5 | |
| | | Minimum Total for Degree | 30 | | |

Doctor of Philosophy Degree Plan - The sample below does not imply that all requirements for graduation will be met with 90 SCH of course work. While it is possible to complete the requirements in this time frame, most research projects require additional semesters to complete. The typical time-to-degree for PhD students is four-to-five years.

| Dept | Number | Title | SCH | Semester | |
|--|--------------|--|-------------|---------------|--|
| BMSC | 6150 | Lab Rotations | 2 | Fall Year 1 | |
| BMSC | 6200 | Intro to Experimental Design & Biostatistical Methods | 2 | Fall Year 1 | |
| BMSC | 6201 | Fundamentals of Biomedical Science I | 2 | Fall Year 1 | |
| BMSC | 6202 | Fundamentals of Biomedical Science II | 2 | Fall Year 1 | |
| BMSC | 6203 | Fundamentals of Biomedical Science III | 2 | Fall Year 1 | |
| BMSC | 6204 | Fundamentals of Biomedical Science IV | 2 | Fall Year 1 | |
| | | Subtotal | 12 | | |
| Milestones to be completed: Selection of Major Professor, Change of Discipline | | | | | |
| BMSC | 5160 | Biomedical Ethics | 1 | Spring Year 1 | |
| BMSC | 5315 | Principles of Scientific Communication | 2 | Spring Year 1 | |
| BMSC | 5109 | Diversity, Equity and Inclusion in Biomedical Sciences: Fundamental Concepts | 1 | Spring Year 1 | |
| PHRM | 6400 | Functional Neuroscience | 4 | Spring Year 1 | |
| PHRM | 6410 | Basic and Clinical Pharmacology | 4 | Spring Year 1 | |
| | | Subtotal | 12 | | |
| Mileston | es to be cor | mpleted: Designation of Advisory Committee, De | egree Plan | | |
| BMSC | 5108 | Transferable Skills | 1 | Summer Year 1 | |
| BMSC | 6998 | Individual Research | 0-5 | Summer Year 1 | |
| | | Advanced Courses | 0-5 | Summer Year 1 | |
| | | Subtotal | 6 | | |
| Mileston | e to be com | pleted: Oral Qualifying Examination, Annual C | Committee N | Meeting | |
| PHRM | 5140 | Pharm & Neuro Seminar | 1 | Fall Year 2 | |
| PHRM | 6140 | Pharm & Neuro Journal Club | 1 | Fall Year 2 | |
| PHRM | 5150 | Pharm & Neuro Work in Progress | 1 | Fall Year 2 | |
| BMSC | 6102 | Grant Writing | 1 | Fall Year 2 | |
| BMSC | 6998 | Individual Research | 0-8 | Fall Year 2 | |
| | | Advanced Courses | 0-8 | | |
| | | Subtotal | 12 | | |
| PHRM | 6140 | Pharm & Neuro Journal Club | 1 | Spring Year 2 | |

| Dept | Number | Title | SCH | Semester |
|------|--------|---------------------------------|------|---------------|
| PHRM | 5150 | Pharm & Neuro Work in Progress | 1 | Spring Year 2 |
| BMSC | 6998 | Individual Research | 0-10 | Spring Year 2 |
| | | Advanced Courses | 0-10 | Spring Year 2 |
| | | Subtotal | 12 | |
| BMSC | 6998 | Individual Research | 0-5 | Summer Year 2 |
| BMSC | 6101 | Responsible Conduct of Research | 1 | Summer Year 2 |
| | | Advanced Courses | 0-5 | Summer Year 2 |
| | | Subtotal | 6 | |

Milestone to be completed: Research Proposal and Annual Committee meeting (which can be combined. An approved Research Proposal (and advancement to candidacy) must be on file prior to enrollment in Doctoral Dissertation. Once a PhD student has advanced to candidacy (completed the oral qualifying exam and research proposal milestones), they are able to enroll in a total of 6 SCH per semester.

| PHRM | 5150 | Pharm & Neuro Work in Progress | 1 | Fall Year 3 |
|------|------|--------------------------------|-----|----------------|
| BMSC | 6998 | Individual Research | 0-8 | Fall Year 3 |
| | | Advanced Courses | 0-8 | Fall Year 3 |
| | | Subtotal | 6-9 | |
| PHRM | 5150 | Pharm & Neuro Work in Progress | 1 | Spring Year 3 |
| BMSC | 6998 | Individual Research | 0-8 | Spring Year 3 |
| BMSC | 6395 | Doctoral Dissertation | 0-8 | Spring Year 3 |
| | | Advanced Courses | 0-8 | Spring Year 3 |
| | | Subtotal | 6-9 | |
| BMSC | 6998 | Individual Research | 0-6 | Summer Year 3 |
| BMSC | 6395 | Doctoral Dissertation | 0-6 | Summer Year 3 |
| | | Advanced Courses | 0-6 | Summer Year 3 |
| | | Subtotal | 6-9 | |
| BMSC | 6998 | Individual Research | 0-9 | Fall Year 4 |
| BMSC | 6395 | Doctoral Dissertation | 0-9 | Fall Year 4 |
| | | Advanced Courses | 0-9 | Fall Year 4 |
| | | Subtotal | 6-9 | |
| BMSC | 6395 | Doctoral Dissertation | 3 | Final Semester |
| | | Total for Degree | 90 | |

^{*} Once a PhD candidate submits the "Declaration of Intent to Graduate" Form, they can enroll in a total of 3 SCH of Doctoral Dissertation (BMSC 6395) in the semester in which they will defend their dissertation (the final semester of enrollment).

For additional information regarding Academic Procedures, please refer to the School of Biomedical Sciences Catalog at: Academic Procedures (SBS)

^{* 130} SCH is the maximum hours for in-state tuition, resulting in 40 SCH Flex hours. 3-40 SCH Research hours can be applied to the 90 SCH degree total, and excess of 40 SCH research hours will be applied to the 40 SCH Flex hours. 1-12 SCH Dissertation hours can be applied to the 90 SCH degree total, and excess of 12 SCH Dissertation hours will be applied to the 40 SCH Flex hours. In some cases, a different degree plan may be applicable. In all cases, the degree plan must be approved by the student's advisory committee and the Dean of the GSBS.

Advancement to Candidacy

Master of Science

Advancement to master's Candidacy is achieved after successful completion of a research proposal.

Each student will be required to submit a research proposal to their advisory committee. The student and their mentor will decide upon the format of the research proposal: 1) traditional proposal with no page limits, or 2) NIH style grant including all its limitations (F31, R21)). Traditional proposal format is as follows: Abstract (1pg), Specific Aims (1pg), Background and Pilot Studies (3-5pgs), Experimental Design and Methods including an anticipated results section (4-5pgs), References (unlimited). For NIH-style grant format, refer to the National Institutes of Health website for current information.

Once a date and time have been determined, the student must prepare a Notice of Research Proposal Seminar and Defense, including securing a room reservation and committee signatures. The form must be submitted to SBS no less than 30 days prior to the event date.

The research proposal should be provided to all committee members at least 14 days prior to the presentation to the advisory committee. The student will then conduct a public seminar of the research proposal, followed by a private discussion with the committee.

The advisory committee will determine if the proposal is satisfactory. The proposal must be approved by the advisory committee and submitted to the SBS during the semester prior to the student's final semester, at the latest. Submission of an approved research proposal is prerequisite for registration in Thesis (BMSC 5395)

Research Proposal Guidelines and the Research Proposal approval forms are available on the <u>SBS</u> Forms and Guidelines website.

Once a master's student has successfully advanced to candidacy, they may use "MS Candidate" as a title on any general business correspondence such as business cards, e-mail messages, etc.

Doctor of Philosophy

Advancement to Doctoral Candidacy is a <u>two-step process</u>. The first step of this process is successful completion of the Oral Qualifying Examination, a common milestone in most doctoral programs regardless of the field of study. The second step of this process is the preparation and defense of a research proposal. Below are details of the Pharmacology and Neuroscience specifications for advancing to candidacy.

Oral Qualifying Examination

The doctoral student will successfully defend their general knowledge of pharmacology and neuroscience in an Oral Qualifying Examination (OQE) before an examination committee comprised of 3-5 members of the Pharmacology & Neuroscience graduate faculty and the student's university member. The graduate advisor will chair these examinations (another faculty will be asked to chair if the student taking their OQE is mentored by the graduate advisor). The committee will be appointed by the department chair and graduate advisor early Spring semester. This examination will be held during the Summer semester of Year 1 (typically June/July).

The student will be given a list of questions covering topics from core and required advanced courses early Spring semester. The student will be given one hour of preparation time to review the questions and select a specified number of questions upon which they will be examined. The student will address the selected topics as well as any questions from the committee that may arise from the question and answer session.

Successful completion of this requirement will be determined by the OQE committee. If unsuccessful on the first attempt, a student may be allowed to retake the examination. The second examination should be completed within twelve weeks of the original examination, unless otherwise specified by the examination committee. If unsuccessful on the second attempt, the students may be allowed to transfer to the MS degree program to complete the requirements for the MS degree.

The chair of the committee will obtain the signatures from the examination committee members, university member, graduate advisor, and department chair upon completion of the exam. The appropriate form may be obtained from the SBS Forms and Guidelines website.

Research Proposal

Each student will be required to submit a research proposal to their advisory committee. The student and their mentor will decide upon the format of the research proposal: 1) traditional proposal with no page limits, or 2) NIH style grant including all its limitations (F31, R21)). Traditional proposal format is as follows: Abstract (1pg), Specific Aims (1pg), Background and Pilot Studies (3-5pgs), Experimental Design and Methods including an anticipated results section (4-5pgs), References (unlimited). For NIH-style grant format, refer to the National Institutes of Health website for current information. The committee must approve of the format and topic, a decision that can be made via email or meeting. Once a date and time have been determined, the student must prepare a Notice of Research Proposal Seminar and Defense, including securing a room reservation and committee signatures. The form must be submitted to SBS no less than 30 days prior to the event date.

The research proposal should be provided to all committee members at least 14 days prior to the presentation to the advisory committee. The student will then conduct a public seminar of the research proposal, followed by a private discussion with the committee.

For PhD students, the proposal should be completed within a year of having passed the OQE. The proposal must be approved by the advisory committee and submitted to the SBS during the semester prior to the student's final semester, at the latest. Submission of an approved research proposal is prerequisite for registration in Doctoral Dissertation (BMSC 6395)

Research Proposal Guidelines and the Research Proposal approval forms are available on the <u>SBS</u> Forms and Guidelines website.

Once a PhD student has advanced to candidacy (completed the oral qualifying exam and research proposal milestones) they are able to enroll in a total of 6 SCH per semester. Once a PhD candidate submits the "Declaration of Intent to Graduate" Form, they can enroll in a total of 3 SCH of Doctoral Dissertation in the semester in which they will defend their dissertation (the final semester of enrollment)." Additionally, they may use "PhD Candidate" or "Doctoral Candidate" as a title on any general business correspondence such as business cards, e-mail messages, etc.

Additional Information

The following topics can be found in the SBS catalog at **UNTHSC Catalog.**

Leave of Absence Enrollment Requirements Annual Progress Reports Graduate Teaching Assistant