There are five dopamine receptor subtypes (D1, D2, D3, D4 and D5) expressed in the brain. They are members of the seven helical transmembrane spanning G protein coupled receptor (GPCR) superfamily of membrane proteins. Theses receptors play an important role in fine motor skills (movement), behavioral motivation (drug seeking behaviors) and cognitive skills (memory and learning). In collaboration with medicinal chemists we are working on the development D2 and D3 dopamine receptor selective ligands as pharmacotherapeutic and imaging agents to monitor the expression of D2-like (D2 and D3) dopamine.

Graduate Students and Post-Doctoral Fellow working in this laboratory have the opportunity to learn state-of-the-art molecular pharmacology techniques, including radioligand binding and second messenger cell signaling techniques. There is also the opportunity to learn to use behavioral techniques to monitor the behavioral effect of drugs in animals.

We are a molecular pharmacology laboratory using radioligand binding assays and second messenger signaling assays to monitor the effects of ligands binding to receptor proteins. We are currently collaborating with medicinal chemistry laboratories (at the University of Pennsylvania and Temple University School of Pharmacy) and a behavioral pharmacology group (at Arizona State University) on the development and characterization of dopamine and sigma-1 receptor selective ligands. Theses receptors play a pivotal role in fine motor skills, behavioral motivation associated with drug seeking behaviors and cognitive skills. We are working on the development of receptor selective ligands as pharmacotherapeutic and imaging agents to monitor the changes in receptor expression as a function of neurodegenerative disorders, including Alzheimer’s Disease, Stroke, Traumatic Brain Injury, Cancer Chemotherapy and Substance Abuse Disorders.

The dopamine receptors in the brain play a pivotal role in movement, motivation, memory and learning. In collaboration with medicinal chemists throughout the U.S., we have focused on the development of compounds that bind to dopamine receptors for the treatment of sigma-1 receptor selective compounds that are neuroprotective and that represent candidate therapeutic agents for the treatment of Alzheimer's Disease, Stroke and Traumatic Brain Injury.
Alvin Mathe’, DO, University of North Texas Health Science Center
Assistant Professor, Division of Geriatrics
Vicki A. Nejtek, M.S., Ph.D., University of Texas at Dallas
Associate Professor, Department of Pharmacology and Neuroscience
Director of Co-Occurring Disorders Research
The O’Bryant Laboratory is dedicated towards precision medicine in Alzheimer’s disease and other neurodegenerative diseases, including Down syndrome, Lewy Body disease, Parkinson’s disease and traumatic brain injury and others. The fully translational lab has a Biomarker Core (Dr. Hall, Director), Clinical Core (Dr. Johnson, Director), Administrative Core (Dr. O’Bryant, Director) and Data Core (Dr. Johnson, Director). The lab also has a Neuroimaging Core (USC, Dr. Toga, Director). Our multiple NIH grants focus on novel strategies for disease detection, screening into trials (therapeutic and prevention), patient stratification for optimal treatment response. As part of this work, our lab has a strong focus on the impact of ethnicity/diversity on cognitive loss during the aging process and runs the one-of-a-kind Health & Aging Brain among Latino Elders (HABLE) study, which is the most comprehensive study of Mexican American brain aging to date. Our lab is also now running the first-ever prospective study of the accuracy of a blood test for detecting Alzheimer’s disease and pre-clinical Alzheimer’s disease in primary care settings.
Nicole Phillips, Ph.D., University of North Texas Health Science Center
Assistant Professor, Department of Microbiology, Immunology and Genetics

Our group studies the genomic complexities that underlie multifactorial diseases, particularly age-related disease like Alzheimer’s. We utilize a variety of molecular genetic approaches including Illumina platforms for next generation sequencing, whole genome genotyping, epigenetic profiling, and RNAseq analysis—particularly in the context of investigating the roots of mitochondrial dysfunction that is associated with essentially every age-related disease. Naturally, analysis of genomic, epigenomic, and transcriptomic-scale data require robust bioinformatic capabilities for establishing analysis pipelines and data management; many of my students’ projects focus on implementation of novel computational and bioinformatic approaches to answer our specific questions. We currently are studying genetics of several complex disease phenotypes: Alzheimer’s disease & type 2 diabetes (through collaboration with Dr. O’Bryant’s research study, HABLE), and low back pain (through collaboration with PRECISION Texas Registry). Our goal is to deepen our understanding of genetic based risk for complex disease by implementing a more integrative genomic approach which assesses the multi-faced nature of genetic-based control of gene expression. Further, we are using novel cohort designs to understand the root of common multi-morbidities (e.g., Alzheimer’s and type 2 diabetes), specifically in heavily affected populations such as Mexican Americans.

Students in Dr. Phillips’ laboratory are exposed to molecular genetic techniques, both from the wet-lab side and the dry-lab side. While the wet-lab certainly presents its own challenges (e.g., lengthy optimizations of protocols for extraction or amplification), the dry-lab work with very large datasets often presents the steepest learning curve. Students work very closely together to share “tribal knowledge” of -omics scale data analysis. We spend a lot of time as a team discussing results within the biological context of the phenotypes. I encourage and support supplemental training in bioinformatics at various workshops with the top experts in the field. Students bring back materials and a skillset to share with the group.

Active research collaborations within UNTHSC: Dr. John Licciardone, Dr. Robert Barber, Dr. Sid O’Bryant, Dr. Stella Gouloupolou, Dr. Ragu Krishnamoorthy, Dr. John Planz
Outside UNTHSC: Dr. Ryan Huebinger, Dr. Kirk Wilhelmsen, Dr. William Cody, Dr. Deanna Soper

Non-technical summary: We are interested in how genetics and lifestyle intersect in diseases that are increasingly prevalent with advancing age. We study the underlying genetics of the co-occurrence of type 2 diabetes and Alzheimer’s disease in Mexican American populations where there is an increased burden of both conditions. By studying individuals who have co-occurrence of multiple conditions, we hope to learn what genetic factors may render some people more vulnerable than others to age-related changes in metabolic function and cognition. In doing so, more tailored therapies for individual risk factors may be developed to better treatment and prevention strategies in at-risk populations.
Katalin Prokai, Ph.D., University of Veszprem, Hungary
Professor, Department of Pharmacology and Neuroscience
Our research interests are biological phenomena that can be explained with, elucidated through and made beneficial by using the principles of chemistry, especially in the field of neuroscience. Specific projects focus, among others, on the chemical biology of estrogens emphasizing the translation of basic science findings to therapeutic interventions, neuropeptide-based drug discovery, and investigations on how oxidative stress impacts brain proteins causing and/or indicating neurodegenerative diseases. Our studies utilize emerging powerful techniques of biomedical research such as advanced mass spectrometry, proteomics, metabolomics and bioinformatics to understand mechanisms of drug action, to improve diagnosis of devastating diseases and to advance therapy developments that address unmet medical needs.

Students who join Prokai lab can expect to receive training in experimental methods in neurobiochemistry and preclinical drug discovery/development of central nervous system agents, in addition to becoming experts in advanced, mass spectrometry-based bioanalytical methods.

Active collaborations within the UNTHSC: The laboratories of Drs. Katalin Prokai-Tatrai, Michael Forster, Andras Lacko, Robert Barber, Hongli Wu, and the College of Pharmacy’s Preclinical Services.

Non-technical summary: Many maladies of the central nervous system are not completely understood, poorly diagnosed and/or inadequately medicated by currently available pharmaceuticals. Using methods that integrate chemistry, biology and biomedical sciences, we expect to identify safe and effective interventions to treat or prevent neurological/psychiatric disorders, and eye diseases—with the goal of discovering novel therapeutics that can be developed from bench to bedside. In addition, our research will yield insight into how we could use the measurement of proteins and other endogenous biomolecules to understand and diagnose diseases.
Dr. Quiceno is a clinician, clinical researcher and educator. Her clinical practice is focused on older adults with cognitive impairment, such as Alzheimer's disease and Dementia with Lewy Bodies, and movement disorders, for example Parkinson’s disease. She is experienced in designing, recruiting, and conducting clinical research studies for people with all stages of Alzheimer’s disease, from preclinical to late stages of dementia. Dr. Quiceno is interested in the education of the public, people with dementia and health professional students as it relates to brain health and dementia.
The general research interests of our laboratory encompass understanding the integrated cardiovascular, autonomic, and cerebrovascular responses to environmental and behavioral stressors in humans that challenge vital organ perfusion, with an emphasis on hemorrhage, orthostasis, and exercise. A major area of research focus has been on the early detection of hemorrhagic injury in trauma patients, characterizing physiological differences between individuals with high versus low tolerance to this stress. In addition to investigating these physiological mechanisms, we also collaborate with academic, industry, and government partners to develop and test sensor technologies in the laboratory that may improve the early detection of tissue hypoperfusion in the clinical setting. Furthermore, we explore potential therapies that may improve cardiovascular and cerebrovascular responsiveness to tissue hypoperfusion, including resistance breathing, oscillatory perfusion therapy, and occlusive exercise. It is anticipated that these studies will have potential clinical applications to stroke, traumatic brain injury, hemorrhage, migraine, myocardial infarction, and orthostatic intolerance.

Training opportunities for graduate students (M.S. and Ph.D.) and postdoctoral fellows are available.

Active Research Collaborations include Steven A. Romero, Ph.D., University of North Texas Health Science Center.

Non-technical summary: The brain is very sensitive to reductions in blood and oxygen supply. Major clinical events such as stroke, heart attack, and traumatic hemorrhage can challenge this supply, often leading to damage to the brain tissue, and subsequent neurological and physical impairment. My laboratory strives to understand how the heart and brain respond to environmental and behavioral stressors in humans, with an emphasis on hemorrhage, movement to the standing posture (orthostasis), and exercise. We also assess potential therapies that may improve how the heart and brain respond to reductions in blood and oxygen supply, including resistance breathing, oscillatory perfusion therapy, and occlusive exercise.
The Human Vascular Physiology Laboratory utilizes invasive (e.g. microdialysis) and non-invasive (e.g. Doppler ultrasound) experimental techniques to examine human vascular function and control in vivo. The laboratory also utilizes pharmacological approaches and standard “bench” analytical techniques. Together, these experimental techniques allow the laboratory to address mechanistic, yet clinically relevant research questions. Current projects in the laboratory include investigations related to the acute and chronic effects of lower limb heating on blood pressure control and vascular function in the elderly, the protective effect of passive heating on vascular ischemia-reperfusion injury, and skeletal muscle blood flow control during isolated limb heating.

Students in Dr. Romero’s lab receive training in the invasive and non-invasive assessment of human vascular function. In addition, students are exposed to various wet lab and bench techniques.

The laboratory collaborates closely with other UNTHSC faculty members (e.g. Dr. Caroline Rickards) as well as other regional academic institutions such as the University of Texas Southwestern Medical Center.

Non-technical summary: The Human Vascular Physiology Laboratory has two broad research themes. The first research theme centers on investigating how the human vascular system adjusts and adapts to exercise and environmental stress in healthy and diseased populations. The second research theme centers on investigating the vascular and functional maladaptations that accompany various diseases (e.g. hypertension, aging, and peripheral arterial disease,) in addition to identifying novel therapies that may mitigate such detrimental changes.

Follow the laboratories exciting work on Facebook: Romero Lab at UNTHSC
Our research focuses on the molecular and cellular deficiencies of locomotor impairments associated with aging and Parkinson’s disease. The overall goal is to target these deficiencies to improve locomotor function in the elderly and in Parkinson’s disease patients. To this end, we use established rodent models to characterize the neurobiological basis of locomotor deficiencies that are similar to those in human aging and Parkinson’s disease. Accordingly, we have established collaboration with those with expertise in human subjects and clinical research to establish firm lines of inquiry to translate our work into the human condition. We are heavily vested in evaluating relationships of brain neurochemistry with locomotor function. Furthermore, we investigate the mechanisms of non-invasive lifestyle strategies, such as exercise and diet modification. We also have an established research track of repurposing FDA-approved drugs for treating motor symptoms of Parkinson’s disease. Finally, we are investing our research efforts to look at how and why previous clinical trials in Parkinson’s patients failed or did not fail, to unravel additional mechanistic insights for more accurate targeting of motor impairment.

Students in the lab will be well-versed in experimental design of longitudinal evaluation of motor function, rodent surgery, protein expression, and neurotransmitter assessment. The PI has trained 3 doctoral students to completion of their dissertation, each with at least five published peer-reviewed manuscripts. They have conducted postdoctoral work at Brown University, New York University, or in industry.

Active Collaborations within UNTHSC: Vicki A. Nejtek, Ph.D., Evaluation of exercise efficacy in Parkinson’s patients and reverse translation into CNS mechanisms in rodent Parkinson’s models. Nicoleta Bugnariu, Ph.D., Evaluation of exercise efficacy in sedentary adults. Tom Cunningham, Ph.D., Cardiovascular function evaluation to determine exercise efficacy on motor impairment.

My laboratory is interested in understanding how steroid hormones like estrogen, testosterone, and natural estrogens from plants regulate brain function in injury and aging. In vitro, we make use of both cell lines and organotypic brain cultures to study mechanisms of ischemic neuroprotection. In vivo, we use multiple models of brain injury in mice and rats including focal cerebral ischemic (stroke) and repetitive mild traumatic brain injury. Outcomes in young and aged animals include several behavioral assessments including motor function, affective function, and cognition. In addition, the mechanisms underlying neurological injury and repair are examined with techniques such as immunohistochemistry, gene expression, protein phosphorylation, and immunoblotting. Several active research collaborations focus on prevention and treatment of neurodegenerative disorders.

Training Opportunities
Opportunities for students at all levels

Active Research Collaborations:
Rebecca L. Cunningham – testosterone, neurodegeneration, androgen receptors
Robert Luedtke – repetitive mild traumatic brain injury
John Schetz – repurposing drugs for stroke
Ann Schreihofer – metabolic syndrome in Alzheimer’s disease
Nathalie Sumien - repetitive mild traumatic brain injury

Non-technical summary: My laboratory is interested in understanding how steroid hormones like estrogen, testosterone, and natural estrogens from plants regulate brain function in injury and aging. We use both cell and animal models to examine the underlying mechanisms of steroid action under conditions in which they are beneficial and those in which they are not in order to understand what key factors result in beneficial effects on the brain. 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. Additional collaborative projects are using novel compounds to protect and regenerate brain tissue after stroke and traumatic brain injury.
Our research projects focus on developing and enhancing interprofessional approaches to geriatric education for health professional students and practicing primary care providers while examining patient, trainee and system-level outcomes. Using innovative curriculum design and implementation, practice placements, and course work, our goal is to advance education, geriatric care and organizational processes aimed at improving the safety and health of older adults and caregivers. Projects engage a variety of primary care and community providers across increasingly integrated systems of care addressing a wide range of health determinants.

Students can expect to be involved with research projects in various settings and involving community coalitions and partnerships with health systems, long term care facilities and nonprofit organizations. Students working with Dr. Severance will be mentored in collaborative and structured health services research, in addition to becoming familiar with issues relevant to older people and emerging health care systems.

Active research collaborations within UNTHSC: Janice Knebl, DO, MBA; Sarah Ross, MS, DO; Mary Quiceno, MD; Kristen Reuter, MSW, LCSW; Kathlene Camp, PT, DPT; Jessica Hartos, PhD; Alvin Mathe, DO. External research partners include: United Way’s Area Agency on Aging of Tarrant County, Alzheimer's Association of North Central Texas, Texas Christian University, JPS Health Network, Sixty and Better, Inc., Meals on Wheels of Tarrant County. James L. West Alzheimer's Center.

Non-technical summary: Current research projects relate to improving team-based education for health professional students and practicing primary care providers, with a goal to impact care and health outcomes of older adults. Projects also evaluate innovative education programs to advance geriatric education and geriatric practice. We engage various partners to conduct health services research in primary care, long term care, and community settings.
Xiangrong Shi, Ph.D., Yale University  
Associate Professor, Department of Pharmacology and Neuroscience

Research interests include regulation of cerebral blood flow and autonomic nervous function under physical, mental, and environmental stresses; cardiorespiratory and neurovascular response and adaptation to physical activity or exercise training in elderly adults; association of cerebrovascular and cardiorespiratory health with postural balance, orthostatic tolerance, and cognitive performance in elderly adults; and examining and applying novel interventions for prevention, treatment, and rehabilitation of neurovascular and neurocognitive conditions.

Non-Technical Summary: The focus of our research lab is to apply and assess a safe intermittent-hypoxia (IH) procedure as a physical-conditioning regimen to preserve and improve the heart and brain functions in humans. Repeated intermittent-hypoxia induces cyclic, brief, and moderate decreases in blood oxygen concentration, and increases heart rate and breathing rate. We have found that IH conditioning is a safe, novel, and effective way to improve heart function and to optimize oxygen delivery to the brain. We believe this IH intervention is beneficial for older adults, especially those who cannot participate in regular physical activities because of the limitations associated with age-related declining physical or mental functions. Moreover, repeated low-dose intermittent-hypoxia can promote and mobilize the growth factors for healthy nerve system and blood vessel. These physiological and neurobiological reactions and adaptations to IH conditioning may have multi-faceted influences on prevention and treatment for early Alzheimer’s disease related dementia and cognitive impairment associated with aging and neurovascular diseases.
Meharvan ‘Sonny’ Singh, Ph.D., University of Florida
Professor, Department of Pharmacology and Neuroscience
Interim Executive Director, Institute for Healthy Aging
My scientific interest are focused on identifying interventions improving more and cognitive function during aging and disease states. Our focus has been on the interactive effects of antioxidant supplementation and moderate exercise, and whether combining the two anti-aging interventions can further beneficial outcomes on brain impairments associated with aging and Alzheimer’s disease. My laboratory also works on other interventions for other conditions: sigma 1 compounds for traumatic brain injury or chemobrain (brain dysfunction associated with chemotherapy), hyperbaric oxygen therapy to alleviate pathologies associated with Alzheimer’s disease, and a new therapy manipulating internal acidity. Identifying successful interventions and their interaction with factors such as genes and gender will lead to specialized recommendations to patients. Furthermore, it will allow to determine specific mechanisms involved in positive outcomes for the development of therapeutics to improve healthspan of individuals. We have also been working on how exposure to recreational drugs leaves the brain more or less susceptible to ischemic events.

Students in Sumien laboratory receive training in the areas of the neurobiology of aging and disease and will learn a series of behavioral and biochemical techniques. We use rodent models as a tool to study our various interventions.

We have a very collaborative program that includes Drs. Dory, Huang, Forster, Gatch, Ghorpade, Huang, Luedtke, Schreihofer, Singh, Yang and Yan.

Non-technical summary: As we age or under certain conditions, our brains work more slowly, rendering life more difficult. Our laboratory looks at ways we could slow down or prevent this from happening. Eating healthy and exercising are ways we can improve our brain function, and how this happens is important. We also study other interventions such as novel drugs and oxygen therapy. If we understand how successful interventions work, we can design ways to combat aging and other deleterious conditions.
My research interests focus on developing clinically relevant approaches that would help decrease brain injury and restore brain functions in cerebral ischemia, Alzheimer’s disease and traumatic brain injury. These approaches include discovering novel compounds that can be administered at delayed time points and be combined with long-term bioengineering approaches utilizing stem cells as well as rehabilitation programs. I also study the relationships between metabolic syndrome and central nervous system diseases.

Active research collaborations within UNTHSC: Ann Schreihofer, Derek Schreihofer.

Non-Technical Summary: My research interests focus on developing clinically relevant approaches that would help decrease brain injury and restore brain functions in stroke, Alzheimer’s disease and traumatic brain injury. These approaches include discovering novel compounds that can be administered at delayed time points and be combined with long-term bioengineering approaches utilizing stem cells as well as rehabilitation programs. I also study the relationships between metabolic syndrome and brain disorders.
Rosalie Uht, MD, Ph.D., State University of New York at Stony Brook
Associate Professor, Department of Pharmacology and Neuroscience
Director, Institute for Healthy Aging Brain Bank
Long Wong, MD, Ph.D., Norman Bethune College of Medicine, China and University of Minnesota
Assistant Professor, Department of Family Medicine
In particular, we are studying how mitochondrial redox sensitive proteins respond to redox imbalance stress and explore such responses as potential therapeutic targets for fighting aging-related metabolic diseases. Our current projects are focused on two NADH/NAD-dependent mitochondrial proteins: dihydrolipoamide dehydrogenase (DLDH) and complex I (NADH-ubiquinone oxidoreductase), both of which can be simultaneously analyzed by blue native gel electrophoresis and also show adaptive responses to NADH/NAD redox imbalance stress under pathophysiological conditions. The project on DLDH is to study its adaptive response as a viable druggable target for induction of stroke- or hypoxia tolerance and the mechanisms of this protein's oxidative modifications in redox signaling and neuroprotection. The project on complex I is to study the mechanisms of complex I adaptive hyperactivity observed in diabetic pancreas and other tissues with goal of exploring strategies that down-regulating complex I hyperactivity by restoring NADH/NAD redox balance may serve as a therapeutic approach for treating diabetes mellitus.

**Training opportunities:** The lab has trained mainly Pharm D. students but is accepting students who either pursue a master’s degree or a Ph.D.

Our laboratory is currently collaborating with other PIs including Drs. Michael Forster, Nathalie Sumien, Shaohua Yang, and Renqi Huang on stroke neuroprotection by a small chemical called 5-methoxyindole-2-carboxylic acid (MICA). Our lab is also collaborating with Dr. Marianna June on protein oxidation induced by alcohol withdrawal and with Dr. Jack Wang on stem cell neuroprotection after stroke.

Non-technical summary: The long term goal of our research is to investigate the biochemical mechanisms of oxidative stress and its role in adult-onset metabolic syndrome.
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. Our laboratory is interested in understanding the mechanism of neurological disorders and the discovery of novel therapy for ischemic stroke, neurodegenerative diseases, and glioma. Our research has been focusing on the brain metabolism and using cell culture and rodent models of ischemic stroke, neurodegenerative diseases, and glioma to address these issues.

Students join Dr. Yang’s laboratory are expected to receive extensive training in cellular and molecular neuroscience, cognitive and behavioral neuroscience, and rodent models of ischemic stroke and neurodegenerative diseases.

Active research collaborations within UNTHSC:
The laboratories of Drs. Michael Forster, Meharvan Singh, Nathalie Sumien, Kunlin Jin, Ran Liu, Liang-Jun Yan, Anuja Ghorpade, Rong Ma, Robert Mallet.

Active research collaborations outside UNTHSC:
Dr. James W. Simpkins, West Virginia University Health Science Center
Dr. Hai Yan, Duke University
Dr. Zixu Mao, Emory University
Drs. Hanli Liu, Liping Tang, Jianzong Su, University of Texas Arlington
Dr. Chunli Zhang, University of Texas Southwestern Medical Center
Dr. Woo-Ping Ge, University of Texas Southwestern Medical Center

Non-technical summary: Our laboratory is interested in understanding the mechanism of brain disorders and the discovery of novel therapy for ischemic stroke, neurodegenerative diseases, and brain tumor. Our research has been focusing on the brain metabolism and using animal and cell culture models of ischemic stroke, neurodegenerative diseases, and brain tumor to address these issues.