The Department of Pharmacology & Toxicology at the University of Texas Medical Branch (UTMB) provides many exciting opportunities for research and advanced education and training. Pharmacology & Toxicology are unique among the basic biomedical sciences because of the focus on the beneficial and harmful effects of drugs and other chemicals. While pursuing our interests in the mechanisms by which small molecules alter basic biochemistry and cellular function, we also utilize our knowledge of these mechanisms to advance our understanding of disease mechanisms. Most of our faculty, postdocs and students are focused on basic questions related to the mechanisms underlying cancer, drug addiction, mental health disorders, environmental toxicology using a variety of experimental approaches, ranging from whole animal behavioral responses to cellular biochemistry to DNA structure. Our faculty utilizes state of the art methodologies including mass-spectrometry analysis of native nucleic acids and proteins, high resolution imaging, single cell electrophysiology, viral technology, behavioral assays, to answer fundamental questions in cancer research and neuropharmacology that could rapidly translate into new cures for human diseases.

An overview of our program is provided in this booklet. More detailed information about the research interests of individual faculty members and graduate courses about the Pharmacology & Toxicology Graduate Program can be found on our website at http://www.utmb.edu/phtox.

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# GRADUATE STUDENT HANDBOOK
PHARMACOLOGY & TOXICOLOGY GRADUATE PROGRAM

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OBJECTIVE AND SCOPE OF THE GRADUATE PROGRAM

The objective of the Pharmacology & Toxicology Graduate Program is to provide an internationally competitive training program in the disciplines of pharmacology and toxicology leading to the Ph.D. degree. This program consists of course work and research designed to enhance a trainee's ability to become a scholarly and productive research scientist in these and related disciplines, including biochemistry, cell and molecular biology, neuropharmacology, and toxicology. It is anticipated that our graduates will become faculty and/or researcher scientists in academic institutions, industry, biotechnology or government. The program is designed to be rigorous, but flexible, and explicitly multidisciplinary. Research training is currently available in neuropharmacology, cancer cell biology and pharmacology, molecular design/synthesis, and molecular toxicology. Our faculty utilizes state of the art methodologies including mass-spectrometry analysis of native nucleic acids and proteins, high resolution imaging, single cell electrophysiology, viral technology and behavioral analyses to answer fundamental questions that could be rapidly translated into leads for curing human diseases.

Students are exposed to broad, integrated foundation courses in biochemistry, cell biology and genetics, as well as specialized courses involving fundamental concepts in pharmacology and toxicology. Research opportunities for addressing various research questions are available that use a wide variety of experimental approaches, ranging from whole animal behavioral responses to specific drugs or toxins, to the structural and molecular basis of gene expression of specific receptors. Major areas of research strength in the program include drug abuse, addiction, psychiatric disease models, lever function, molecular design, modeling and drug synthesis, nucleic acid biochemistry and cancer biology. Our goal is to train research scientists and teachers who have a broad base of knowledge and experience with modern experimental techniques to apply to problems with special relevance to the disciplines of pharmacology and toxicology.

Program Website: https://www.utmb.edu/phtox/PHTOX-Graduate-Program/
FACULTY

There are currently 18 full time faculty members in the Graduate Program of Pharmacology & Toxicology. In addition, there are 16 associate or special members of the graduate program faculty members that are active in both teaching and mentoring Pharmacology & Toxicology students. Below, please find a list of current graduate program faculty and a brief description of their research interests.

Further information on faculty and the Pharmacology & Toxicology Graduate Program can be found on our website: https://www.utmb.edu/phtox/faculty-staff-students/faculty-and-staff

Discipline

Cancer and Aging Biochemistry & Pharmacology

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Dr. Emmett's current research specializes in identification of novel therapeutic targets and biomarkers in oncology (esp. neuro-oncology). Dr. Emmett utilizes high-resolution mass spectrometry (FT-ICR MS) and develops novel chromatographic and MS based methodology for high sensitivity endogenous biomolecule analysis. Dr. Emmett has established a multi-disciplinary research group enabling a systems biological approach integrating genomics, transcriptomics, proteomics, glycomics, lipidomics, metabolomics, phenotypic responses with computational mathematical data analysis to the study of cancer focusing on the identification of novel biomarkers and therapeutic targets.

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1. Pancreatitis is a necro-inflammatory disease with acute and chronic manifestations. Published and pilot data from our laboratory have established that parathyroid hormone-related protein (PTHrP) plays a key role in the pro-inflammatory and pro-fibrotic responses associated with pancreatitis. We have shown that PTHrP levels are elevated in a mouse model of cerulein-induced acute pancreatitis, and that inhibition of PTHrP expression/signaling attenuates the injurious effects of cerulein in isolated acinar and stellate cells. To further study the role of PTHrP in pancreatic inflammation and fibrosis, our laboratory has developed a mouse model with deletion of the PthrP gene in acinar cells, the initial sites of injury in acute and chronic pancreatitis. PthrP gene deletion in these cells suppressed histological damage (edema and necrosis), inflammation and fibrosis in two well-established models of chronic pancreatitis. Based on these findings, we propose that pancreatic injury results in activation of injurious pathways within the pancreas, with the PTHrP signaling pathway being one such pathway. We are now defining the molecular mechanisms by which PTHrP exerts its pro-inflammatory and pro-fibrotic effects following pancreatic injury, and directly investigating whether small molecule inhibitors of PTHrP signaling exert a protective effect after pancreatic injury.
2. Epidemiological studies strongly support evidence that dietary components can exert protective effects. An inverse correlation exists between colorectal carcinoma (CRC) incidence and serum levels of 25-hydroxyvitamin D (25D). 1,25D decreases cell proliferation and induces cell differentiation and apoptosis. Vitamin D receptor (VDR) levels are decreased in the inflamed colon and in CRC; these effects are mediated via the transcription factors Snail1 and Snail2, and lead to failure of therapy with 1,25D analogs. We have shown that the flavonolignan silibinin reverses upregulation of Snail1 and Snail2 in the 1,25D-resistant human colon carcinoma cells HT-29. These silibinin effects are accompanied by increased VDR levels. While 1,25D had no significant effect on HT-29 cell proliferation and migration, co-treatment with silibinin restored 1,25D responsiveness. In addition, co-treatment with silibinin plus 1,25D decreased proliferation and migration at doses where silibinin alone had no effect. These findings demonstrate that this combination may present a novel approach for chemotherapeutic interventions to target CRC in conditions of chronic colonic inflammation. We will be pursuing these studies in an in vivo model.

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The Macrophage Inflammatory Protein (MIP-1a) is a chemokine produced by viral infected lungs. MIP-1a has potent activities on natural killer (NK) cells and cytotoxic T lymphocytes (CTL) that may function as a bridge between innate and adaptive immune responses to RSV infection. In this project, we will be addressing four aims:

1. To identify the contribution of MIP-1a in the control of viral replication and development of RSV-induced lung inflammation, airway hyperresponsiveness and disease manifestations. In this aim, the role of MIP-1a will be investigated in MIP1-a deficient mice.
2. To investigate the requirement of MIP-1a for the migration and activation of NK cell and NK cell-driven CTL responses in RSV infection.
3. To analyze the spectrum of RSV-inducible proteins in the lung of mice, either control or MIP-1a deficient, using high throughput 2D SDS-PAGE and matrix-assisted laser desorption and ionization time-of-flight (MALDI-TOF) mass spectroscopy. Here we will generate a database of proteins secreted in the bronchoalveolar lavage or lung tissue of RSV-infected mice. This powerful study will identify candidate proteins associated with virus-induced airway pathology controlled by MIP-1a.
4. To determine whether distinct protein patterns at the mucosal site can discriminate infants with different forms of illness or degree of chemokine responses following naturally-acquired RSV infections. The profile of proteins present in nasopharyngeal secretions collected from children with RSV infection will be analyzed by high resolution proteomics.

These studies will identify for the first time protein profiles associated with wheezing and severity of clinical illness in RSV infection.

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Molecular mechanisms of peptide hormone-regulated growth of gastrointestinal cancers
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(Professor and Chairman, Department of Pharmacology and Toxicology) studies DNA damage and repair. The laboratory is interested in damage to DNA resulting from carcinogen exposure, inflammation-mediated reactive intermediates and cancer chemotherapy agents. Many of the methods used in the laboratory are based in chemistry, including chemical synthesis of nucleoside analogs and oligonucleotides, and the analysis of structural and dynamic properties of these molecules using high field NMR and multiple mass spectrometry methods. Current projects include 1) examining the stability and repair of human telomeric DNA sequences, 2) the relationship between DNA damage and epigenetics, and 3) the interaction of modified nucleosides with DNA polymerases and ligases.

The ends of human chromosomes are comprised of a repeating DNA sequence motif that can form unusual structures. These unusual structures interact with telomere-binding proteins to protect the chromosome ends from processing by DNA repair proteins. If the telomere “caps” do not form, telomeres can be degraded, leading to cell death, or inappropriately join with other chromosome ends, resulting in DNA translocations. We have found that several forms of DNA damage can interfere with telomere “cap” formation, including some commonly used chemotherapy agents. We have found also that the repair of telomere ends is complex and different from the repair of DNA within normal duplex B-form regions.

The chromosomal DNA in all cells of an organism is largely identical, yet different regions of the genetic code are expressed and translated in each cell type. The selective control of gene expression is modulated by specific covalent modifications to the DNA and the associated histone proteins which comprise the epigenetic code. The primary modification in human DNA is the enzymatic methylation of specific cytosine residues, forming 5-methylcytosine (5mC). We have found that specific forms of DNA damage can mimic or interfere with epigenetic signals, resulting in inappropriate expression of transforming genes or the silencing of tumor suppressor genes providing a novel mechanism for the development of human tumors. Many modified nucleosides serve as either antitumor or antiviral compounds, including gemcitabine, cytosine arabinoside and AZT. Most of these analogs have no9rmal base components, but have modified sugars that alter the way the analogs interact with specific CAN polymerases and ligases. We are investigating relationships between structure and function for a series of known as well as newly developed analogs. These analogs are synthesized in the laboratory, tested in in vitro studies with DNA polymerases and ligases, and examined in tissue culture with human cells. The results of these studies could lead to more potent and selective antitumor and antiviral drugs.

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Structural and functional studies of antiviral drug toxicity

Antiviral drugs based on nucleoside analogs are effective inhibitors for viral reverse transcriptase and RNA polymerase, thus have been successfully used in treating HIV and HCV infections. With prolonged patients’ life span, the success of the drugs now has to be balanced with their drug toxicity. One of the major target of nucleoside analogs is human mitochondrial DNA polymerase, Pol γ. Because drug efficacy is not completely correlated with drug toxicity, we believe there is exploitable difference in designing potent, low toxic antiviral reagents. To reveal the structural differences between viral target protein and human adverse reaction target, we embarked on structural and functional studies of replicating human mitochondrial DNA polymerase or stalled by antiviral drugs. My laboratory determined the first crystal structures of human Pol γ holoenzyme. Recently, we determined structures of ternary complex of Pol γ-DNA with a substrate or an antiHIV reagent, zalcitabine, lamivudine or emtricitabine. These structures provided unprecedented insight in Pol γ mediated antiviral drug toxicity. As Pol γ mutations are associated with multisystem disorders, the structures have been widely used by basic scientists as well as clinicians to understand the detrimental effects of the mutations. I directed all of these studies.

Mitochondrial DNA repair
Mitochondria contain high concentrations of reactive oxygen species (ROS) due to intrinsic radicals generated through metabolic reactions and extrinsic factors such as anticancer radiation therapy. Consequently, mitochondrial DNA suffers higher likelihood for oxidative damages than chromosomal DNA. While the overall scheme follows that of nuclear BER, mitochondrial BER has distinct differences. Pol γ is responsible for DNA synthesis during replication and repair. I lead investigation of Pol γ activity in BER specific gap-filling DNA synthesis. Our findings indicate Pol γ is very inefficient on 1-nt gapped DNA and no strand displacement synthesis activity, suggesting that the polymerase alone is inefficient to carry out mitochondrial BER function, supporting the importance of repair complex. We studied Pol γ replication on damaged DNA. We recent started structural and functional studies of components of mitochondrial DNA repair complex with a long-term goal of structural determination of the entire mitochondrial DNA repairsome. I am the PI of these studies.

Kangling Zhang, PhD  
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Dr. Zhang was trained at UCSF Mass Spectrometry Facility under the direction of Dr. Alma Burlingame, the chief editor of the Journal of Molecular and Cellular Proteomics. His research interest focuses on the development of state-of-the-art methodologies in mass spectrometry and their applications in epigenetics, with the hope of better understanding the cause of diseases and cancer. His current research is the study of one-carbon metabolism and histone methylation in hypoxic cancer cells by mass spectrometry and biochemistry.

Clinical Toxicology

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- Use of cytochrome P-450 isoenzyme patterns to predict individual toxicity risk for drugs and chemicals that undergo metabolic activation.
- Sedation and analgesia.
- Use of anti-oxidant/NMDA antagonist therapies to decrease anoxic brain injury.
- Use of urinary thioether excretion as an index of exposure to environmental chemicals.
- Use of gastrointestinal dialysis to enhance removal of environmental/occupational chemicals from deep compartment body storage sites.
- Application of stochastic control theory Bayesian population pharmacokinetics to improve individual patient therapeutics.

Computational Biology

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Our laboratory specializes in the research areas of Bioinformatics, Applied Statistics, Mathematical Modeling and Information Theory. We are particularly interested in environmental metagenomics and the analysis of human DNA. Our focus includes the development of new methodologies for the analysis and interpretation of next generation DNA sequencing (NGS) data and to create new computational tools for the rapid analysis of NGS data. Such computational tools under development are for the detection of:
1. Unknown and known pathogens in complex backgrounds such as environmental (soil, water or air)and clinical samples. 2. Changes in the host genome caused by environmental changes or by diseased states all of which can alter the copy number or methylation patterns. 3. Changes in the metagenome of environmental samples due to man-made or natural disasters including the loss of microbial diversity or the appearance of specific bacterial populations. 4. Microbial metagenomes involved in industrial applications such as biofilm analysis and bio corrosion.
Molecular Pharmacology

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Work in the Gagnon laboratory is directed at understanding the structural basis of the functions of proteins and nucleic acids involved in gene expression, particularly translation. In all living cells, translation is mediated by a large macromolecular assembly, the ribosome. We are interested to characterize the mechanisms of regulation of protein synthesis mediated by ribosome-binding proteins, RNAs and small molecules, such as antibiotics. Understanding the mechanisms of protein synthesis in atomic details will lead to new antibiotic targets, which is particularly important nowadays with the increasing occurrence of bacterial resistance to antibiotics being one of the biggest threats to global health. More than half of clinically relevant antibiotics cure infections by inhibiting the bacterial ribosome, making the ribosome a validated drug target in the cell. Many pathogenic bacteria have acquired resistance mechanisms that rely on specialized ribosome-binding proteins capable of rescuing antibiotic-inhibited ribosomes. Rescue of protein synthesis allows pathogens to thrive in the presence of drugs. We are seeking to characterize the molecular mechanisms exploited by many human pathogens to rescue drug-inhibited ribosomes, making them resistant to commonly used antibiotics. To achieve these goals, our laboratory uses an integrated approach combining biochemical, biophysical, genomic, molecular genetics and structure determination techniques.

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Our laboratory’s main focus is to understand the regulation of alternative splicing (AS) networks in the heart and how dysregulation of AS impacts heart function and development. Specifically, we are interested in identifying mechanisms that control differential expression of alternatively spliced variants in the heart. We are currently pursuing two different aspects of AS regulation.

1. Regulation of AS networks in the developing heart
   We are systematically investigating the role of RNA binding proteins in regulating AS networks during murine heart development. Our aim is to identify a regulatory circuitry that controls gene expression via AS during heart development.

   Significance: AS can alter expression of genes drastically by removing or including alternative exons that correspond to the sequences responsible for mRNA stability and translatability. It can also modify the function of proteins by eliminating exons that code for essential domains. Even though AS is critical for gene regulation, the mechanisms that coordinate AS events in the developing heart is not well understood. Identifying AS events with direct impact on gene function may provide ways to treat congenital and adult heart diseases, which can be caused by mutations that affect proper splicing.

2. Dysregulation of AS in the diabetic heart
   Our data show that aberrantly spliced isoforms of genes are expressed in diabetic heart tissues. We are further pursuing the consequences of AS defects in diabetes and analyzing the RNA binding proteins involved in this process.

   Significance: Diabetes is a costly health care problem affecting 8.3% of the US population. The majority of the diabetes patients die from cardiovascular complications. Defining AS events that promote abnormal gene expression in diabetic hearts may reveal novel ways such as oligo-based therapy to correct splicing defects and ultimately prevent/treat cardiovascular complications of diabetes.

   In the laboratory, we use several different model systems including cultured cells, transgenic and knockout mouse models, and rat models to understand the fundamental questions about AS regulation in the heart.
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The research in the laboratory involves work in the areas of: (1) Biophysics, (2) Chemical Physics/Physical Chemistry, and (3) Computational Science. We study:

1. Bacteriophages, found in bacteria-rich locations like rivers and soil, are nature's machinery for viral infection of bacteria. Their genetic material, DNA or RNA, single- or double-stranded, are carried in protein-based capsids and released into the bacteria. Understanding the biophysical basis of the biological process which transfers a viral genome to infect a cell is important to the cellular machinery and many disease related fields. Predicting the thermodynamic pressures including the osmotic pressure necessary to confine DNA in a specific volume, like a phage, is a problem with implications in genomics, nanotechnology, infection, phage therapies and therapeutic delivery. DNA, a charged elastic polymer, undergoes over 250-fold compaction when packed into a capsid overcoming an unfavorable thermodynamic barrier by using ATP. How DNA overcomes the unfavorable thermodynamic barrier to enter and pack inside a capsid depends on the interplay of many different intermolecular interactions. Combined with experimental data, coarse-grained models and multi-scale techniques are being employed to model the structure and, consequently, the thermodynamics of DNA confined by surfaces.

2. Phase transitions in protein solutions. How and why proteins fold is a problem that has implications for protein design and therapeutics. Several groups have had some success in describing some aspects of the problem, such as folding a sequence. However, the discovery that proteins do not always necessarily fold into a single stable structure calls for a redefinition of both the folding problem itself and the mechanisms we use to describe it. We consider commonly used concepts of protein folding in relation to solubility and phase transitions in solution. The formation of many non-enveloped cellular structures are governed by the underlying rules of solubility.

3. Thermodynamics and kinetics in liquid solutions especially aqueous systems. Most difficult is the question of how multicomponent systems including crowding, cosolvents and ions affect proteins and nucleic acids in solution. Given correlations and statistical thermodynamics the relations to experimental observables on the effects ions and osmolytes have on biomacromolecules in solution should then be understandable. At the technical level we are working on activity models and diagramatic expansion.

4. Theory and computational methods to investigate solution systems with couplings and correlations at many disparate length and time scales. There are many problems for which atomic correlations do not provide a direct link to macroscopic properties. Connecting meso scale averaging procedures to the atomic and macro levels via multiscale methods is important for biological/materials applications.

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Research Interest:
- Structural biology
- Synapse biology
- Biochemical and biophysical techniques to study protein interaction networks

There are an estimated hundred billion neurons in the human brain and they are connected to each other via physical contact points called synapses. Synapses enable neurons to communicate with each other. The hundreds of trillions of synapses in our brain establish neural circuitries that guide how we think, move and feel. More than a thousand different proteins are found at synapses and

![Figure 1](image.png)

**Figure 1:** The structure of the extracellular domain of neurexin 1α, a synaptic organizer implicated in autism spectrum disorder, schizophrenia, and mental retardation determined to a resolution of 2.65 Å in our laboratory.
they form complex protein networks. Paradoxically, synapses are both insoluble and yet also plastic. On the one hand, synapses are isolated biochemically as the 'triton-insoluble' fraction. Yet on the other hand, in vivo, synapses come and go. Synapses grow 'weaker' and 'stronger', as their adhesive properties and their ability to transmit signals change. Significantly, properties of synapses also appear to change as a function of their activity. External stimuli such as events triggering memory and learning, stress, and exposure to chemicals such as drugs of abuse, anti-depressants and anti-psychotics, all seem to affect synapses and the connections they form. Many different neuropsychiatric disorders and neurodegenerative disorders are increasingly being referred to as 'synaptopathies', emphasizing the role of disrupted synaptic structure and function in the pathogenesis of these disorders. By unraveling how the many different synaptic proteins interact with each other and form complex protein networks, we hope to not only gain fundamental insight into how neurons communicate with each other enabling the brain to function, but also to discover new potential therapeutic targets.

Figure 2: Synaptic interactome centered around neurexin 1α. Alpha-neurexin splice forms (blue ovals) interact directly with a number of different synaptic proteins including neuroligins, LRRTMs, neurexophilins, alpha-dystroglycan, and GABAA-receptors, while CASK and SHANK are recruited (directly and indirectly) in the cytosol as well. Alpha-neurexins and many of their partners are implicated in autism spectrum disorder, schizophrenia and mental retardation, and strikingly, these same genes contribute to multiple disorders.

Our laboratory is particularly fascinated by the complex protein networks in the synaptic cleft found at chemical synapses, i.e. the 250 Å space between the 'pre-synaptic' membrane which hosts the exocytosis machinery for synaptic vesicles and the 'post-synaptic' membrane which hosts machinery responding to the transmitted chemical signals. We are studying a number of synaptic adhesion molecules and synaptic organizers to understand their role in mediating synapse formation, maintenance, and plasticity. One family of synaptic adhesion molecules that we have studied extensively is the family of neurexins. Neurexins play a role in synapse organization and adhesion. Mutations and lesions in neurexins have recently been implicated in autism spectrum disorder, schizophrenia and mental retardation (Fig. 1).

Excitingly, not only neurexins, but also many of their direct protein partners in the synaptic cleft are implicated in these diseases as well (Fig. 2). Neurexins and their partners must touch fundamental biological processes that are involved in the pathogenesis of these disorders, but it is not clear which processes these are and the exact role that neurexins and their partners play in these processes.

Our laboratory is working to understand on a molecular level how neurexins, their partners, as well as a number of other synaptic organizers recognize, bind, and arrange different synaptic partners in the synaptic cleft impacting synaptic function. By understanding the molecular mechanisms of these molecules, we will be able to not only further delineate their role at synapses but also understand why these molecules, when disrupted, contribute to neurological disorders.

We use biochemical and biophysical techniques as well as protein crystallography.

**Molecular Toxicology**

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Pregnancy is associated with physiological changes that include the pharmacokinetics of administered medications. Human placenta plays a crucial role in regulating fetal growth and development as well as its protection from xenobiotics and administered medications. Investigations in our laboratory focus on understanding the mechanisms underlying the disposition of therapeutic agents used for treatment of the opiate addict and hypoglycemic drugs used for treatment of gestational diabetes. In addition, we are
collaborating with other investigators on developing new drugs for treatment of nicotine addiction during pregnancy. Dr. Ahmed's laboratory, over the last two decades, has provided information on the molecular mechanism(s) leading to the development of tolerance to opiates utilizing human placenta as a model system. His laboratory identified the role of opiate receptors in human placenta, a noninnervated tissue, their endogenous ligand (dynorphin 1-8) and mediated responses (regulation of hCG and acetylcholine release) and demonstrated that the in vitro and or in vivo exposure of human placenta to opiates leads to the development of tolerance. His laboratory also identified a cocaine binding protein in human placenta and conducted a clinical investigation of cocaine use during pregnancy and its effects on maternal and neonatal outcome. Recently, his laboratory identified the role of human placenta as a functional barrier protecting the fetus from exposure to therapeutic agents by its disposition of the drugs. Dr. Ahmed's future research interests include translational and clinical investigations of therapeutics used for treatment of the pregnant patient.

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- Airway remodeling in asthma and COPD
- Inhalation toxicology of small molecule and particulate toxicants
- Upper and lower airway anti-inflammatory effects of novel drug compounds
- Airway smooth muscle biology
- Immune/inflammatory cytokine responses of the airway

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Dr. Ansari’s research interests lie principally in the area of molecular toxicology and systems biology. He uses biomarker signatures and metabolomics to study chemical-mediated liver injury and chemical-mediated autoimmunity.

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The major focus of Dr. Elferink’s research is the role of the aryl hydrocarbon receptor (AhR) in liver function and extra-hepatic processes affecting adiposity and glucose homeostasis. The AhR is a ligand-activated soluble transcription factor historically studied in the context of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD, dioxin) toxicity following DNA binding to xenobiotic response elements (XREs). TCDD toxicity however, represents a disruption of normal AhR biology that influences fundamental physiological processes underlying growth and differentiation. Dr. Elferink’s studies have demonstrated that AhR biology regulates transcriptional and epigenetic processes affecting hepatocyte cell cycle control, apoptosis, and the production of hepatocrines (liver-derived hormones) with systemic properties. The long-term objectives are to garner a comprehensive mechanistic understanding of AhR biology in the liver using contemporary molecular, cellular, and genome-wide methodologies in model systems.

A second major research endeavor in the laboratory is focused on actively seeking to identify and develop serum biomarkers for early detection of hepatocellular carcinoma (HCC) in patients at-risk for developing liver cancer. The approach uses proteomic strategies based sophisticated separation strategies coupled with state-of-the-art mass spectrometry including multiplexed Selected Reaction Monitoring for use in validation studies. Successful development of specific and sensitive serum biomarkers for early HCC will enhance surveillance of millions who are at risk of developing HCC.
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We are working to develop improved drug delivery strategies, with special emphasis on drug and nanoparticle transport across the placenta in order to address the needs of pregnant women requiring medical therapy or diagnostics, and to answer questions regarding the safety of medication during pregnancy in relation to fetal development. Maintenance of the mother's health promotes successful pregnancy outcomes, and this may require pharmacologic therapy for pregnant women with asthma, diabetes, epilepsy, HIV, or other illnesses. For a small but significant percentage of women, cancer is discovered during pregnancy, which presents a special challenge to adequately treat the cancer and simultaneously protect the baby's growth within the womb. In some instances, fetal therapy is required to treat conditions such as fetal arrhythmias or congenital adrenal hyperplasia; these cases may require drug delivery to the fetus while trying to reduce unwanted side effects in the mother.

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My graduate and postgraduate education gave me a broad and deep background in clinical medicine, physiology and pharmacology. My subsequent 20 years in Academia and Industry gave me a broad and deep set of skills and knowledge ranging from basic research and therapeutic target identification to preclinical and clinical drug development. On the academic track, as postdoctoral fellow at the William Harvey Research Institute, my work, under the supervision of Nobel Laureate Sir John Vane, focused on basic research on the role of NO and oxidative pathways in the pathogenesis of critical illness. As Research Director of the Division of Critical Care at Children's Hospital Medical Center in Cincinnati, and later as Professor at UMDNJ/Newark (now part of Rutgers), I expanded my scope to study molecular pathways of oxidative and nitrosative stress, and their applications to a diverse set of pathophysiological conditions including circulatory shock, diabetes, acute lung injury, cardiac diseases, aging, neuroinjury, and various acute and chronic inflammation. For the last 10 years, at the University of Texas Medical Branch, my laboratory integrates contemporary methods of cell biology, pharmacology, and molecular biology with cell-based high-throughput screening approaches and with in vivo models of disease. As PI or co-Investigator on multiple grants funded by the NIH and other agencies, I have discovered multiple novel pathophysiological pathways and processes, some of which became targets for subsequent drug development. Over the last decade, I became an internationally recognized authority in the field of hydrogen sulfide biology and I am currently involved in a variety of studies on the role of hydrogen sulfide in the regulation of mitochondrial dysfunction in various pathophysiological conditions including circulatory shock, vascular dysfunction and cancer. In parallel with my academic work, on the industry track, as Chief Scientific Officer of several successive biotech companies, I led multiple project teams focused on target identification, creation and pharmacological characterization of first-in-class drug development candidates, and their progression through preclinical development into proof-of-concept clinical trials. This work involved diverse targets, including key checkpoints in intracellular signaling and cell death pathways (e.g. PARP1, SHIP1), free radical/oxidant processes, cell membrane receptors (e.g. adenosine receptors) and gaseous transmitters (nitric oxide, hydrogen sulfide). The therapeutic applications of these pathways include inflammation, vascular disease, cancer, lung diseases, ophthalmologic indications, and various forms of critical illness. From an administrative standpoint, I have successfully administered R&D groups of various size, including complex, multidisciplinary research projects, often involving multiple geographical locations. I have published extensively; have received numerous awards (including the Novartis Award of the British Pharmacological Society and the Pharmacia Award of ASPET); have received significant grant funding, including continuous funding from the NIH for the last 20 years. My publications are highly cited in the literature (over 50,000 citations). With an Hirsch-Index of 115, I am listed as one of the top 10 most highly cited scientists in the field of Pharmacology.
Casey Wright, PhD
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My research program is focused on studying the contribution of inflammatory signaling to the development and progression of autoimmune diseases, including hematological malignancies. Specifically, we focus on the regulatory mechanisms of two transcription factors that play a role in promoting cancer and autoimmunity, nuclear factor-kappaB (NF-kB) and the aryl hydrocarbon receptor (AHR). We have found a common link between these two pathways and, given that the AHR is a major sensor of xenobiotics, we are committed to understanding how the environment influences the development of autoimmune disorders. Our long-term goal is to better understand how the NF-kB and AHR signaling pathways are regulated on a molecular level in order to identify possible therapeutic targets for the myriad immunological disorders that arise from deregulated signaling. To achieve our goal we mostly employ molecular, biochemical, and immunological techniques in order to test our hypotheses. I encourage enthusiastic postdoctoral candidates and prospective students with similar backgrounds/interests to contact me regarding available positions in the laboratory.

Neuropharmacology

John A. Allen, PhD
Phone: (409) 772-9621 Email: joaallen@utmb.edu

The main emphasis of the research in the laboratory is to understand the signal transduction of G protein-coupled receptors (GPCRs) and to identify and advance GPCR targeted molecules for therapeutic drug discovery. GPCRs are the largest group of signaling proteins in the human genome and an estimated 30-40% of all marketed drugs act directly to modulate this receptor family. Our primary focus is the neuropharmacology of dopamine, serotonin and other GPCRs that control the striatum and basal ganglia neuronal system. GPCRs within the striatum mediate reward behavior and movement coordination underlying not only addictive effects of abused drugs such as cocaine but also dysfunctions observed in movement disorders such as Parkinson's and Huntington's disease. We apply a synergistic approach using cell/molecular, biochemical and systems pharmacology to reveal the mechanisms of GPCR signaling in cells, neurons and in the brain. We also apply large scale screening technologies to identify novel GPCR ligands and test compounds for their therapeutic potential in rodent models of addiction and related neuropsychiatric diseases.

In our research we use a range of multidisciplinary approaches involving identification of GPCR signaling pathways using proteomics, measurement of GPCR signaling in neurons, drug discovery using high throughput screening platforms, microscopy and live cell imaging of neuronal GPCR trafficking and behavioral characterization of genetic mouse models with altered components of GPCR signaling machinery.

Noelle C. Anastasio, PhD
Phone: 409-772-9656 Email: ncanasta@utmb.edu

My research interests lie at the interface of pharmacology, neuroscience, and psychiatry. Prevention and treatment of neuropsychiatric disorders could be greatly advanced by a more comprehensive understanding of the biology of impulsivity. Our group is focused on deciphering the patterns of individual differences in behavioral disinhibition and decision-making seen with respect to the development and maintenance of chronic neuropsychiatric disorders. In particular, we focus on glutamatergic neurotransmission and disinhibition of cortical top-down output in different facets of impulsive-compulsive traits. There is evidence that glutamate neurotransmission through the ionotropic glutamate N-methyl-D-aspartate receptor plays a key role in the cognitive and/or behavioral dimensions of impulsivity and addictive behaviors, perhaps within the corticostriatal circuit, a network integral to decision-making and goal-directed behavior. An additional focus of the laboratory is to determine that neuronal serotonin and glutamate systems mechanically converge to govern impulsivity and that rebalancing these systems may ultimately support behavioral recovery in disorders marked by impulsivity concomitant with an
imbalance in the reward system and reactivity to reward conditioned cues (e.g., psychostimulant addiction, binge-eating disorder, obesity).

We employ a multi-disciplinary approach (e.g., biochemistry, gene-mediated viral delivery, behavioral models, cellular models) to elucidate the neurobiological substrates (e.g., receptor trafficking, protein:protein interactions, epigenetic modifications) within the corticostriatal circuit that drive the vulnerable vs. resistant phenotypes underlying dysregulated drug- and feeding-related behaviors as assessed in the preclinical environment.

Kathryn A. Cunningham, PhD
Phone: (409) 772-9640 Email: kcunning@utmb.edu

Dr. Cunningham and her team have made multiple contributions to our understanding of the neuropsychopharmacology of abused drugs and psychotherapeutics, the underlying neurobiology of behavior, and new target and drug discovery in neuropsychiatric conditions. With established strengths in pharmacology and neuroscience, Dr. Cunningham focuses on advancing the biological understanding of disorders with an addictive dimensionality (e.g., drug addiction, binge eating disorder, obesity) and developing effective and safe therapeutics to maximize human function. A primary focus is our cross-disciplinary, translational research efforts with medicinal and synthetic chemists, cell biologists, neuropharmacologists, and clinical scientists to pinpoint the critical roles of two serotonin proteins (5-HT2A and 5-HT2C receptors) in cocaine use disorder and the discovery of novel serotonergic medications to extend abstinence. Chemists and engineering collaborators Drs. Scott Gilbertson (University of Houston), Jai Rudra and Jia Zhou, work closely with Dr. Cunningham’s laboratory on additional novel targets for therapeutics and neuroprobes. To facilitate this effort, we have established new cellular, behavioral and molecular screening tools to study these systems.

Dr. Cunningham’s research has been funded continuously by NIH for 26 years, has led to three patents for new chemical entities, 118 peer-reviewed publications in high-quality journals and 29 reviews, chapters and commentaries. She has cultivated and sustained a life-long commitment to fostering the career development of new scientists with over 45 mentees who have crafted successful careers in academia, industry and government. Her research and educational contributions have been recognized by the American Society for Pharmacology and Experimental Therapeutics-Astellas Award for Translational Pharmacology as well as the Marian Fischman Memorial Award and the Mentorship Award from the College on Problems of Drug Dependence. Dr. Cunningham is currently Associate Editor of ACS Chemical Neuroscience and Associate Editor of Nature Neuropsychopharmacology. She is an active educator, mentor and board member for community programs, secondary/high schools and colleges in the region.

Kelly T. Dineley, PhD
Phone: 409-747-060 Email: ktdineley@utmb.edu

RESEARCH INTERESTS:

- Cocaine abuse and addiction.
- Animal models utilizing genetic and pharmacological manipulations.
Omics and bioinformatics approaches for the identification and validation of novel mechanisms that underlie memory and cognitive deficits induced by aging, neurodegenerative disease, and drug abuse.

Nicotinic acetylcholine receptors, nuclear receptors (PPAR), ERK MAPK, CREB, CBP, calcineurin, protein-protein interactions.

Thomas A. Green, PhD  
Phone: (409) 747-7056 Email: tom.green@utmb.edu

Our current research is focused on the molecular mechanisms underlying the protective addiction and depression phenotype produced by environmental enrichment. Rats raised in an enriched condition (EC), with toys and social contact with cage mates, display less addiction-and depression-like behavior than rats reared in an isolated condition (IC). We have already identified the transcription factor cAMP response-element binding protein (CREB) as one major mechanism in the EC phenotype, and we can reproduce the EC phenotype in normal pair-housed animals simply by blocking CREB function in the nucleus accumbens shell using novel viral vectors. However, CREB itself is only a transcription factor, meaning that it can only be a distal mechanism. Our current projects utilize novel genomic and proteomic expression profiling techniques in EC and IC rats to identify CREB target genes as proximal mechanisms mediating the EC phenotype. Viral vectors are being constructed to validate the role of these CREB target genes in mediating the protective EC phenotype by knocking down specific CREB targets in the nucleus accumbens. The overall goal of the project is to identify novel mechanisms of resistance to addiction and depression to ultimately target for treatment as well as prevention of addiction and depression in humans.

Kenneth M. Johnson, Jr., PhD  
Phone: (409) 772-1561 Email: kmjohnso@utmb.edu

Dr. Johnson’s research interests are largely in the area of drug mechanisms, particularly drugs of abuse, and animal models of psychiatric disease. He has a long-standing interest in neurotransmitter receptor function and the mechanisms by which drugs of abuse alter neurotransmitter signaling. In an attempt to discover therapeutic agents for cocaine abuse his lab collaborated with organic chemists and discovered several chemical scaffolds capable of inhibiting cocaine binding with only minimal effects on the uptake of neurotransmitters which were inhibited by cocaine. His major research effort was focused on determining the mechanism by which phencyclidine (PCP) caused psychosis, and how this information might eventually be used to understand how to diminish the symptoms of schizophrenia. This work focused on the long-lasting schizophrenia-like effects of phencyclidine treatment in young rat pups and how this might be used to understanding the cellular/biochemical mechanisms underlying the enduring schizophrenia-like behavioral effects observed following perinatal phencyclidine (PCP) administration. Additional experiments showed that PCP-induced blockade of calcium conducting NMDA receptors resulted in alterations in ERK1/2 and PI3K signaling mechanisms related to BDNF and other important pathways in perinatal rats. Most recently the lab demonstrated that activation of AMPA receptors could prevent PCP-induced neuronal death and that this effect was dependent on depolarization-activation of L-type calcium channels and TrkB, a major BDNF signaling partner. These data suggest that activation of TrkB via calcium influx though these channels may have therapeutic potential.

James Kasper, PhD  
Phone: (409) 772-1561 Email: kmjohnso@utmb.edu

The misuse of prescription opioids can evolve into opioid use disorder; a disturbing chronic health problem marked by relapse and repeated attempts at abstinence. My long-term goal is to drive new therapeutic discoveries by defining novel neurocircuitry and neurotransmitter signaling involved in relapse to opioid use disorder during recovery. To accomplish this goal, we create and employ new viral tools to determine the neurocircuitry involved in behavioral models of opioid use disorder. These studies are supported by viral tracing, immunohistochemistry, and PCR to identify drug targets for development of novel pharmaotherapeutics to treat opioid use disorder.
Rakez Kayed, PhD
Phone: 409-772-0138 Email: rakayed@utmb.edu

- Neurodegenerative disease pathology and mechanisms (Alzheimer's (AD), Parkinson's (PD), dementia with Lewy bodies (DLB) and other tauopathies)
- Mechanisms of protein folding and aggregation
- Molecular mechanisms behind tau oligomer toxicity, propagation, and role in neurodegeneration
- Immunotherapeutic approaches targeting amyloid and tau oligomers
- Diagnostics and biomarkers using CSF and other biological samples
- Amyloid oligomers in amyloidosis, cancer, and diabetes
- Tau aggregation in traumatic brain injury (TBI)

Fernanda Laezza, MD, PhD
Phone: 409-772-9672 Email: felaezza@utmb.edu

Our overall goal is to advance the understanding and therapies of complex brain disorders associated with genetic and environmental factors. To this end, we aim to identify key molecular determinants of intrinsic neuronal properties and synaptic integration at the single cell level that be mechanistically linked to the biological cause of neuropsychiatric disorders. Our approach includes a pipeline of molecular, cellular and functional modules targeting macromolecular complexes of neuronal ion channels. Our approach spans from in vitro to animal-based assays and employs imaging and electrophysiological methods on a multiscale level.

The primary focus of our research is on voltage-gated Na+ (Nav) channels, a family of nine (Nav1.1-1.9) transmembrane proteins abundantly expressed in the brain. Through a complex network of protein:protein interactions (PPI), the Nav channel complex at the axonal initial segment (AIS) provides the basis for electrical excitability of neurons, enabling transmission, processing and storing of electrochemical signals at single synaptic connections. The Nav channel complex is a vulnerable target of genetic modifications and environmental agents. Mutations targeting the pore-forming α subunit of the Nav channel or its accessory proteins, such as intracellular FGFs, ankyrin-G, ßIV spectrin and neurofascin, are recognized causes or risk factors for epilepsy, mood disorder, autism, depression, schizophrenia, pain and neurodegeneration, making the Nav channel complex one of the most appealing targets for drug development. Yet, the mechanisms underlying modulation of the Nav channel macromolecular complex in the brain are still poorly understood, limiting the ability to develop molecular interventions against these relevant proteins. Current projects in our laboratory aim at filling knowledge gaps in this area of research with an emphasis on the intracellular fibroblast growth factors (iFGFs; FGF11-14), a group of versatile and potent regulators of Nav channel biophysics, trafficking and function in the brain.

Ophthalmology and Visual Sciences

Massoud Motamedi, PhD
Phone: (409) 772-8363 Email: mmotamed@utmb.edu

Wenbo Zhang, PhD
Phone: (409) 772-2552 Email: we2zhang@utmb.edu

The long-term research goal in my laboratory is to understand mechanisms of retinal injury in ischemic retinopathy such as diabetic retinopathy, retinopathy of prematurity and glaucoma. Our work includes three areas of the pathology of ischemic retinopathy: retinal neuronal injury, retinal vascular leakage and degeneration, and retinal pathological angiogenesis.

Our group is now assessing the involvement of ER stress and inflammatory cytokines in particular
chemokines in the development and progression of above diseases. In addition to inflammation, we are elucidating novel mediators for pathological angiogenesis and using nanoparticle-mediated drug delivery to treat retinal neovascular diseases such as retinopathy of prematurity and proliferative diabetic retinopathy. Since retina is an extension of the brain, we also collaborate with investigators in the fields of neurodegenerative and infectious diseases such as Alzheimer’s diseases and Zika virus infection using eye as a window.

**Pharmaceutical Chemical Biology**

**Jia Zhou, PhD**  
Phone: 409-772-9748  
Email: jizhou@utmb.edu

My research interests are broadly based on the interface of synthetic organic chemistry and medicinal chemistry, and in particular on the drug discovery of bioactive molecules to probe biological systems or act as potential therapeutic agents in neuroscience, cancer/inflammation, infectious diseases, and other human conditions. With this general idea in mind, and in active collaboration with other biologists and pharmacologists, my group is dedicated to establish a strong and creative research program that applies state-of-the-art chemical approaches to biological problems impacting diagnosis, prevention and treatment of human diseases.

One of our current efforts is focused on design and synthesis of small molecules for probing function and development of pharmacological tools for understanding the workings of the brain and that of novel therapies for central nervous system (CNS) disorders such as drug abuse and addiction, depression, schizophrenia, pain, and neurodegenerative diseases. The proposed projects in this area include the identification, characterization and optimization of allosteric modulators and bitopic ligands of 5-HT$_{2C}$ receptor, neuromedin U receptor 2 (NMUR2) ligands, and other GPCR ligands. We are also working on the discovery of DeltaFosB modulators, neurexin modulators, and FGF14/Nav1.6 channel complex protein-protein interaction modulators as CNS probes and potential therapeutics.

Another line of research development centers on the establishment of novel chemical libraries aiming at mechanism-based or lead compound-based drug discovery for cancer/inflammation, particularly by targeting Bcl-2 family proteins and apoptosis pathways, transcription factors as well as epigenetic therapy with the aid of molecular docking and chemical synthesis. Specifically, we are developing Bax activators, BH4 domain antagonists of Bcl2, orally bioavailable STAT3 inhibitors, AP-1 inhibitors, KLF5 inhibitors, KRAS plasma membrane localization inhibitors, cystathionine-β-synthase (CBS) inhibitors, NNMT inhibitors, and BRD4 inhibitors as a new class of preventive/therapeutic agents for various human cancers including brain tumors, breast cancer, lung cancer, head/neck cancer, colorectal cancer, prostate cancer, and pancreatic cancer as well as inflammation.

Our research efforts on developing chemical probes include design and synthesis of small molecules targeting EPAC, which are exchange proteins directly activated by cAMP including cAMP-regulated guanine nucleotide exchange factors. These EPAC inhibitors have also demonstrated as promising therapeutics for a variety of indications including infectious diseases. Last but not least, we are also working on natural product-inspired diversity-oriented synthesis that may lead to exciting potentials for discovery of novel targets and drug candidates.
PROGRAM OVERVIEW

In the first year students take an integrated Basic Biomedical Science Curriculum (BBSC) that incorporates three foundation courses (biochemistry, cell biology, and molecular biology and genetics), as well as a series of more specialized, advanced short courses (modules) covering the major principles governing the organization and function of cells, tissues, organs and systems, along with seminar courses and laboratory rotations. An introduction to the principles of pharmacology is included in BBSC course work, and this baseline is supplemented in the second year with two specialized courses covering topics in autonomic, cardiovascular, central nervous system pharmacology, as well as endocrine pharmacology, chemotherapy, and toxicology. The pharmacology and toxicology program students take BBSC modules in the first year that will inform students specifically about topics related to their interests in pharmacology and toxicology. Students may then take advanced courses in neuropharmacology, cancer biology, or molecular toxicology in year two, depending on their area of specialization.

By the beginning of the second year students will choose a faculty member with whom they plan to do their dissertation research. To be efficient and effective in this important selection, students are encouraged to visit with and talk to potential faculty dissertation mentors. The BBSC orientation course, seminars, classroom sessions, and lab rotations will provide adequate introduction to many of these faculty during the first year. Students should feel free to visit with faculty privately to discuss their research interests. The program director is also available for consultation on this important decision.

In addition to the second-year programmatic coursework, typically students take their written qualifying exam in the spring and their oral qualifying exam in the summer (justified exceptions can be made upon approval of the Graduate Program Director and the Qualifying Exam Chair). Students then have 3 terms from when they pass the oral component to apply for candidacy, which allows them to register for PHTO 6098 Dissertation. The research culminates in a dissertation, which constitutes an original and independently achieved contribution to knowledge. Students gain speaking and teaching experience by poster presentations and at the annual Summer Symposium.

Course Requirements

Students in the Pharmacology & Toxicology Graduate Program will take the integrated first-year Basic Biomedical Sciences Curriculum (BBSC), unless considered an advanced student. Advanced students will follow a specially designed curriculum, developed by the Pharmacology & Toxicology curriculum committee. In addition, a series of required and elective courses specific to Pharmacology & Toxicology are to be taken. The charts on pages 22, 23 and 24 illustrate the complete set of BBSC and Pharmacology & Toxicology courses (required and elective) available to Pharmacology & Toxicology students.

The basic requirements for Pharmacology & Toxicology after BBSC courses are to take PHTO 6124 Grant Writing, PHTO 6312 Autonomic, Cardiovascular, and Central Nervous System Pharmacology (ACC), and PHTO 6213 Endocrine, Chemotherapy, and Toxicology Pharmacology (ECT). In addition, students will be required to take two credit hours from the provided PHTO list and two more elective credit hours from any graduate program. Students are required to take a minimum of nine credit hours per term including PHTO 6195 Seminar in Pharmacology and Toxicology and PHTO 6190 Student Journal Club, except for their last term in the program. Course evaluations by students are required for all didactic courses with six or more students enrolled. Grades will not be released for any course until all evaluations are received.
**Minimal Performance Criteria**

Students in the Pharmacology & Toxicology Graduate Program need to pass all required courses of the program. Rules and requirements regarding probation and dismissal from the graduate school may be found in section 4.57 of the Academic Policies of the Graduate School of Biomedical Sciences.

**Elective Courses**

Students may choose elective courses to strengthen special areas of interest or weakness, or to provide background for research skills. Pharmacology & Toxicology students must take two elective credit hours from the list on page 24. In addition, two more elective credit hours are required and may be taken from any graduate program offering, but cannot be a seminar, journal club or MD/PhD course.

**Laboratory Rotations/Research**

Each student is required to do three BBSC 6043 laboratory rotations in the first year BBSC curriculum. By the end of summer term during the BBSC curriculum, students will chose a lab to join and register for PHTO 6097 Research each term until they pass the written qualifying exam and apply for candidacy.

**Seminars**

Each student is required to register for Seminar, each term for the duration of his/her tenure in the graduate school, except for the last term. Students will enroll in PHTO 6195 Seminar beginning in the first term of graduate school. For PHTO 6195, each student will attend Program-required seminars regularly each term. In addition students will participate in the Annual Summer Symposium, which gives students the experience to present their research through poster sessions and presentations. Seminars for oral qualifying exams and final defenses are to be scheduled through the Graduate Program Coordinator.

**End of Term Reports**

Semester research reports are due, electronically, to the Graduate Program Coordinator at the conclusion of each semester on the specified date. Research reports should be a one-page summary of that term’s work.

**Qualifying (Comprehensive) Exam**

The Qualifying Exam is typically offered annually during the Spring-Summer Term of Year II. Students are eligible for the exam after successfully completing (B or better) PHTO 6312 (ACC Pharmacology) and PHTO 6213 (ECT Pharmacology). The qualifying exam format involves the preparation of a grant proposal. Students will be asked to submit a written research grant proposal on any pharmacologically-related topic that can include the area related to their individual dissertation research. A second component of the qualifying exam is an oral presentation of the research proposal. Certain guidelines are to be met as listed below.
Written Component

The research proposal will follow NIH PHS398 grant guidelines (http://grants.nih.gov/grants/funding/phs398/phs398.html) as they pertain to the general ‘research plan’ limited to 10 pages, and should describe an original hypothesis/idea based on published literature, and a research plan to test the hypothesis. Published research (with due consideration given to citing the work appropriately) can be used as supporting/preliminary data for the purpose of the proposal. Original data generated by the student can also be used for this purpose in proposals related to their dissertation research. The deadline for submission will be determined annually. Proposals are to be submitted electronically as PDF files to the Pharmacology and Toxicology Graduate Program Administrative Associate (Ms. Nicole Bilotta) or the Qualifying Exam Committee (QEC) Chair (Dr. Elferink, coelferi@utmb.edu) by the deadline.

A one page (or less) letter of intent briefly describing the research area being considered for the proposal (e.g. background and significance, hypothesis and specific aims) is to be submitted 2 months before the proposal deadline to the Pharmacology and Toxicology Graduate Program Administrative Associate (Ms. Nicole Bilotta) for review by the QEC in order to evaluate appropriateness.

The expectation is that student will 1) develop the proposal independently without involvement by the student’s mentor, and 2) continue to be research active during this time, unless granted leave by their mentor. For each proposal, three reviewers (selected from the faculty in the PHTO graduate program) will be assigned to provide a written critique of the proposal, and a score will be assigned using the NIH scoring format. Written critiques will be made available to the student two weeks after the submission deadline date. A preliminary average score will be assigned to each proposal.

Scoring:

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<tr>
<th>Impact</th>
<th>Score</th>
<th>Descriptor</th>
<th>Additional Guidance on Strengths/Weaknesses</th>
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<tbody>
<tr>
<td>High</td>
<td>1</td>
<td>Exceptional</td>
<td>Exceptionally strong with essentially no weaknesses</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Outstanding</td>
<td>Extremely strong with negligible weaknesses</td>
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<tr>
<td></td>
<td>3</td>
<td>Excellent</td>
<td>Very strong with only some minor weaknesses</td>
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<tr>
<td>Medium</td>
<td>4</td>
<td>Very Good</td>
<td>Strong but with numerous minor weaknesses</td>
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<td></td>
<td>5</td>
<td>Good</td>
<td>Strong but with at least one moderate weakness</td>
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<td></td>
<td>6</td>
<td>Satisfactory</td>
<td>Some strengths but also some moderate weaknesses</td>
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<td></td>
<td>7</td>
<td>Fair</td>
<td>Some strengths but with at least one major weakness</td>
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<td>Low</td>
<td>8</td>
<td>Marginal</td>
<td>A few strengths and a few major weaknesses</td>
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<tr>
<td></td>
<td>9</td>
<td>Poor</td>
<td>Very few strengths and numerous major weaknesses</td>
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Reviews will focus on the following three specific criteria:

**Significance** Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field?

**Approach** Are the conceptual framework, design (including composition of study population), methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

**Innovation** Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?
Proposals should also provide a brief (≤200 word) abstract and a separate Specific Aims page. These are not part of the 10-page limited research plan. The written proposal need not provide a description of the budget, resources, animal welfare, human subjects, and biographical materials or personnel justifications.

**Oral Component**

An oral presentation on the proposal will be presented to the entire Department of Pharmacology and Toxicology—as part of the departmental seminar series—following submission of the written proposal, predicated on passing the written component. The oral presentation will be 30 minutes in duration followed by questions from the general audience, and a separate question period limited to the Pharmacology and Toxicology Graduate Program Faculty. Scheduling of the oral component will be determined on an annual basis, but will occur no sooner than three weeks after review and successful completion of the written component.

**Student Evaluation**

Written exam evaluation. A committee comprised of the QEC members and other written proposal reviewers will convene to assess the written proposal(s). To pass the qualifying 3 exam, a student must receive an average score of 4 or better on the written portion. A student must receive a passing grade on the written exam component before the oral exam portion can be taken. The Chair of the QEC will chair the panel discussion, unless in conflict, whereupon an alternate will be assigned from the QEC. Student mentors are considered to be in conflict when their student(s) is/are being evaluated, and will be required to recuse themselves. Oral exam evaluation. Evaluation of the oral presentation will be based on clarity of presentation, and the student’s ability to address audience questions. Oral presentations require that the seminar be attended by a quorum of at least eight graduate program faculty including the three reviewers of the written component.

**Remediation**

An average score >4 on the written component will constitute a failing grade. The student will be afforded no more than four weeks to revise the proposal (in response to the written reviewer comments) for re-review by the same reviewers, and must receive an improved average score of ≤4 to pass. Failure to pass the written component precludes the student from taking the oral exam component. Remediation of the oral component will require the student to represent the seminar, at the earliest opportunity based on scheduling constraints, but within 1 month of the initial oral presentation. In the event that both the written and oral components need to be retaken, a total of 6 weeks will be allotted for remediation of both components.

**Requirements for Entering Candidacy**

A student must pass both the written and oral components to pass the qualifying exam and be considered for candidacy in the Pharmacology and Toxicology Graduate Program. Failure to receive a passing grade in either the written or oral component will constitute non-fulfillment of the qualifying exam requirements. Failure to meet administrative requirements—such as not adhering to deadlines—without obtaining prior written approval from the Chair of the QEC will result in the exam being administratively withdrawn from further consideration. Pending QEC approval determined on an individual case basis, a student who does not satisfy the qualifying exam requirements may be extended a one-time opportunity to retake the exam in the following year. Ultimately, unsuccessful completion of the qualifying exam will constitute failure to meet the candidacy requirements and result in termination from the Pharmacology and Toxicology Graduate Program.
Admission to Candidacy

One of the most important stages of your development as a graduate student and investigator is admission to candidacy. Students will be allowed to register for PHTO 6097 Research for a maximum of three terms once they pass the both portions of the qualifying exam. Within that timeframe students will apply for admission to candidacy. This event implies several things. First, that students have completed all required didactic courses, that they have satisfied any academic deficiencies, and they have passed the written qualifying examination, all of which indicate that they have mastered the fundamental knowledge of the field of pharmacology and toxicology. If a student has not been admitted to candidacy by the end of the third term it is grounds for dismissal.

To apply for candidacy students will create a Supervisory Committee who will oversee their dissertation work. For regular (non-MD-PhD) students, the Supervisory Committee consists of five members: Three faculty members from PHTO graduate program, one from different area of research (Could be from any other department or program) and one from another institution. The three pharmacology and toxicology faculty and the member from off campus are generally supposed to be individuals who are familiar with your field and who can make useful contributions to your success, either by verbal input and/or by assisting with special techniques or approaches. The on-campus faculty member from outside Pharmacology & Toxicology may also be familiar with your field of work, but this is not necessary. This person also serves for general advice and to represent the graduate school to be sure that the entire process is conducted well.

The Supervisory Committee for MD-PhD students is the same as that for regular students, except that one additional requirement exists: this committee must include an MD-degreed faculty member with a primary appointment in a clinical department. This member may be one of the five individuals required by the Graduate School or may be a sixth member -- if a sixth member, he/she does not have to be a member of the Graduate Faculty. The membership of this committee should be determined well before the actual proposal is developed because each of the members should be able to offer constructive advice and each must approve the proposal before it is turned in.

An Application for Candidacy packet will need to be filled out and turned into the Graduate School for Biomedical Sciences by the indicated deadline for each term (please refer to the appropriate academic calendar). Part of the application includes a research proposal. Information on the format can be found at https://gsbs.utmb.edu/current-students/ready-for-candidacy/information-about-candidacy under IX. Instruction Sheet for Preparation of Thesis/Dissertation Research Proposal.

Admission to candidacy actually occurs at the beginning of the term that starts after all the approvals are made. Following admission to candidacy, the student is expected to spend full-time doing research in the mentor’s laboratory (registering for Dissertation, PHTO 6099 each term). At the end of each term the student is required to prepare a one-page summary of that term’s work, and the mentor is to provide a brief written evaluation of the students accomplishments and indicate if there are problems as well as provide a grade of Satisfactory or Unsatisfactory (REDCap Survey). Each term except for the last term students are also required to register PHTO 6190 Student Journal Club and for PHTO 6195 Seminar and to attend faculty and student seminars each term. Students are strongly encouraged to write papers as they progress through their respective projects.

After the student is admitted to candidacy, the Supervisory Committee (at least all on-campus members) must meet with the student at least once per academic year for students through fourth year and at least twice an academic year for students year five and above, until the dissertation is completed. The Supervisory Professor must fill out the Pharmacology and Toxicology Graduate Program Supervisory Committee Report following these meetings. Forms are to be sent to the Program Coordinator for tracking student progress. Even though the off-campus member is not usually present at these meetings, his/her input should be obtained at the time of these meetings and taken into account. These committee meetings
are very important in that they assure timely progress reports and opportunities for constructive criticism of the on-going work.

When the mentor and supervisory Committee are satisfied that the student has done adequate work, the student writes the doctoral dissertation (drafts of which are reviewed by the mentor and Committee) and defends the penultimate draft via a final seminar to the program and the Supervisory Committee, which then has a final private session with the student to assess the student’s work and make any final recommendations for completing the written dissertation. Approval of the dissertation by the Committee and deans, in addition to, the completion of the graduation packet completes the degree requirements.

You may also wish to refer to section 4.61 (Doctoral Degree) of the Academic Policies of the GSBS, available on-line at https://gsbs.utmb.edu/home/policies---ada-essential-functions
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<td><strong>Rotation</strong> (BBSC 6043)</td>
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<td><strong>Laboratory</strong></td>
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<td><strong>Biosafety &amp; Biocontainment</strong> (BBSC 6132)</td>
<td>[prerequisite for BSL3/4 training]</td>
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<td><strong>Animal Models of Human Diseases</strong> (BBSC 6220)</td>
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<td><strong>8-Week Laboratory</strong></td>
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<td><strong>Rotation</strong> (BBSC 6043)</td>
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<td><strong>Neuronal Excitability</strong></td>
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<td>(BBSC 6207)</td>
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<td><strong>Neuronal Transmission</strong></td>
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<td><strong>Principles of Drug</strong></td>
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<td><strong>Action, Pharmacokinetics &amp; Biotransformation</strong> (BBSC 6208)</td>
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<td><strong>Genes, Environment</strong></td>
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<td><strong>and Disease</strong> (BBSC 6118)</td>
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<td><strong>Small Sampling of Big Data</strong> (BBSC 6130)</td>
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<td><strong>Vaccine Development Pathway: From Discovery to Licensure</strong> (BBSC 6219)</td>
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<tr>
<td><strong>Fundamentals of Inflammation</strong> (BBSC 6210)</td>
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*Longitudinal required course, taken in all three terms starting in the Fall.

Red = Required
Blue = Electives
Green = 3 rotations are required (required to do one in 2nd block of Fall term) See GSBS Academic Calendar for drop/add dates

Updated 8/19
# Year 2 Pharmacology & Toxicology Curriculum

<table>
<thead>
<tr>
<th>Fall Term</th>
<th>Spring Term</th>
<th>Summer Term</th>
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<tbody>
<tr>
<td><strong>Research</strong> (PHTO 6097)</td>
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<td><strong>Journal Club</strong> (PHTO 6190)</td>
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<td><strong>Advances Mental Health Research</strong> (PHTO 6123)</td>
</tr>
<tr>
<td><strong>ACC Pharmacology</strong> (Autonomic/Cardiovascular/Central Nervous System) (PHTO 6312)</td>
<td><strong>ECT Pharmacology</strong> (Endocrine/Chemotherapy/Toxicology) (PHTO 6213)</td>
<td><strong>Qualifying Oral Exam</strong></td>
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<tr>
<td><strong>Addiction Sciences and Neurotherapeutics</strong> (PHTO 6120)</td>
<td><strong>Synthetic Methods to Biomolecules</strong> (PHTO 6211)</td>
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<tr>
<td><strong>Neuroaddicts Journal Club</strong> (PHTO 6121)</td>
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<tr>
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<tr>
<td><strong>Principles of Environmental Toxicology</strong> (PHTO 6319) (Taught in odd years)</td>
<td><strong>Qualifying Written Exam</strong></td>
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<tr>
<td><strong>Molecular Toxicology</strong> (PHTO 6214) (Taught based on need)</td>
<td><strong>Neuronal Excitability</strong> (BBSC 6207)</td>
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<tr>
<td><strong>Neuropharmacology</strong> (PHTO 6223) (Taught based on need)</td>
<td><strong>Neuronal Transmission</strong> (BBSC 6126)</td>
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<tr>
<td><strong>Neurons, Environment and Disease</strong> (BBSC 6118)</td>
<td><strong>Hormonal Signaling</strong> (BBSC 6215)</td>
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</tbody>
</table>

The above curriculum is typical depending on student research interests

**Red** = Required Courses

**Blue** = Electives

Updated 8/19
PHARMACOLOGY & TOXICOLOGY COURSE REQUIREMENTS/ELECTIVES

Program Director: Fernanda Laezza, M.D. Ph.D. – MRB 7.102B, x29672 felaezza@utmb.edu
Program Coordinator: Nicole Bilotta – MRB 7.102A, x29626 nabilott@utmb.edu

Notation: Students must be registered for minimum 9 credit hours every term

REQUIRED
PHTO 6022 – Lab Rotation 1-8 credit hours (Spring Year 1 and then until mentor chosen)
PHTO 6097 – Research 1-12 credit hours (Each Fall and Spring term until admitted to Candidacy)
PHTO 6098 – Thesis 1-12-credit hours (Masters)
PHTO 6099 – Dissertation 1-9 credit hours (Each term while in Candidacy)
PHTO 6124 – Grant Writing 1 credit hour (Summer Year 1)
PHTO 6190 – Journal Club 1 credit hour (Each Fall and Spring term, except last)
PHTO 6195 – Seminar in Pharmacology & Toxicology 1 credit hour (Each term, except last)
BBSC 6208 – Principles of Drug Action, Pharmacokinetics, & Biotransformation 2 credit hours (Spring Year 1)
PHTO 6213 – ECT (Endocrine, Chemotherapy & Toxicology) 2 credit hours (Spring Year 2)
PHTO 6312 – ACC (Autonomic, Cardiovascular & CNS Pharmacology) 3 credit hours (Fall Year 2)

Two (2) credit hours from the below PHTO classes are required:

PHTO 6120 – Addiction Sciences and Neurotherapeutics 1 credit hour (Offered Fall/Spring)
PHTO 6121 – Neuroaddicts Journal Club 1 credit hour (Offered Fall/Spring)
PHTO 6123 – Advances in Mental Health Research 1 credit hour (Offered Fall/Spring/Summer)
PHTO 6125 – Bioinformatics Tools and Applications 1 credit hour (Offered Summer)
PHTO 6211 – Synthetic Methods to Biomolecules 2 credit hours (Offered Spring)
PHTO 6214 – Molecular Toxicology 2 credit hours (Offered Fall based on need)
PHTO 6219 – New Drug Development 2 credit hours (Offered Fall based on need)
PHTO 6223 – Neuropharmacology 2 credit hours (Offered Fall based on need)
PHTO 6224 – Intro to Tox Risk Assessment 2 credit hours (Offered every other Fall, even years)
PHTO 6318 – Genome-Wide Analytical Technologies for Biomedical Research 3 credit hours (Offered every other Fall)
PHTO 6319 – Principles of Environmental Toxicology 3 credit hours (Offered Every Other Fall, odd years)

ELECTIVE COURSES
Two (2) additional credit hours from any graduate program offering are also required, including PHTO, but cannot be a seminar, journal club or MD/PhD course.

QUALIFYING EXAM
Both written and oral proposal, typically spring/summer of year 2 once PHTO declared
FALL

Lab Rotation PHTO (6022)
The objectives of this course are to acquaint students with the research activities of individual faculty members and to assist students in choosing their areas of specialization. The faculty member and student will design a research project and work out a time schedule committing the student to three to 24 hours per week in the laboratory. The student will prepare an abstract describing the objectives and methodology of the study and then conduct the study under the faculty member's supervision. A final report stating the methods, results, interpretation, problems encountered, and suggestions for future research will be required. In addition to carrying out the research proposal the student will be expected to gain a knowledge of the current literature relevant to the project. Grading will be based on the student's laboratory performance, final written report, and an oral presentation of the project. Grading will be A, B, C, F. Normally, a student entering the program without an advanced degree will be required to complete 12 hours of credit with a grade of B or better prior to gaining admission to candidacy. Individual requirements may vary depending on the research experience of the student. Prerequisites: None Terms offered: I, II, III Year offered: Annually Hours per week: Laboratory 3 24

Research (PHTO 6097)
Research on thesis or dissertation project under the direction of supervising professor. The research is graded as satisfactory (S) or unsatisfactory (U). Prerequisites: None Term offered: I, II, III Year offered: Annually Hours per week: Laboratory 3 27

Thesis (PHTO 6098)
Once admitted to candidacy, it is required for students pursuing a Master of Science or Master of Arts degree to enroll in this course. This course is for the formal research and writing leading to the preparation and completion of the thesis for the Master of Science or Master of Arts degree while under the direction of the student's supervisory committee. The student will pursue the proposed research and present a progress report and/or agreed upon objectives to the mentor and/or supervisory committee for approval and recommendations. Grading will be based upon the student's level of performance as reported by the chairperson of the student's supervisory committee and will be assigned as Satisfactory (S), Needs Improvement (N), or Unsatisfactory (U). Prerequisites: Admission to candidacy Terms offered: I, II, III Year Offered: Annually Hours per week: Variable 3-9

Dissertation (PHTO 6099)
Once admitted to candidacy, it is required for students pursuing the Doctor of Philosophy degree to enroll in this course. This course is for the formal research and writing leading to the preparation and completion of the dissertation for the Doctor of Philosophy degree while under the direction of the student's supervisory committee. The student will pursue the proposed research and present a progress report and/or agreed upon objectives to the mentor and/or supervisory committee for approval and recommendations. Grading will be based upon the student's level of performance as reported by the chairperson of the student's supervisory committee and will be assigned as Satisfactory (S), Needs Improvement (N), or Unsatisfactory (U). Prerequisites: Admission to candidacy Terms offered: I, II, III Year Offered: Annually
Addiction Sciences and Neurotherapeutics (PHTO 6120)
This course will provide an interactive workgroup for trainees to discuss their research in addiction science with graduate students, postdoctoral fellows, and faculty. Emphasis will be placed on therapeutic development, and trainees will learn how to approach existing projects with a therapeutic development prospective. Presentation formats will vary in scope and level of analysis, depending on the needs of the trainee. Examples of trainee presentation formats include: expansion of an existing project for grant proposal development, and detailed discussion of data analysis and interpretation. Intermittently, faculty will present information on their research program to provide students with an overview of cutting-edge neuroscience and drug discovery/development topics. Grades will be based on in-class participation and presentation quality.

Neuroaddicts Journal Club (PHTO 6121)
The Neuroaddicts Journal Club provides a more cohesive venue for trainees and exposes mentees to a wider range of neuroscience and addictions topics. The goals are for mentees to learn critical thinking of the published literature, the requirements and construction of high quality manuscripts, and presentation skills. Within this environment, mentees have a prime opportunity to refine the ability to converse in both scientific and collegial domains, and become comfortable with asking questions and thinking critical/constructively.

Advances in Mental Health Research (PHTO 6123)
This course will provide a solid understanding of current mental health research and promote understanding of factors advancing future groundbreaking mental health research. The course will have flexible format, including sessions where students discuss relevant papers, present their own data, discuss a wide range of career-development issues, learn about pharmacotherapeutic development, learn advanced grant-writing principles, discuss relevant ethical issues, and learn advanced research techniques. Attendance 50%, participation in classroom discussion 50%. A satisfactory grade requires a score of 80%.

Pharmacology & Toxicology Std Journal Cl (PHTO 6190)
This course is designed to provide an opportunity for students to practice formal presentation skills and discuss science. Students will select research articles from pharmacological journals for presentation to students and student groups. Each student will present and discuss at least one paper per semester depending on the number of students enrolled in the course. Grades will be based on attendance and quality of presentation. Pharmacology students are required to be enrolled in this course every term offered, except for the last term.

Seminar in Pharmacology & Toxicology (PHTO 6195)
Presentations by guest lecturers, staff, and students on the progress of their own research, as well as review of recent advances in pharmacology. Students will receive a grade of satisfactory (S) or unsatisfactory (U) based on attendance and participation. Prerequisites: Students are required to be enrolled in this course every term offered, except for the last term.

Molecular Toxicology (PHTO 6214)
The course is presented in three parts: Part 1 - Metabolism and disposition of drugs and toxicants (i.e., absorption, distribution, activation and deactivation of environmental chemicals); Part II - Genotoxic and epigenetic toxicology; Part III - Toxicology in the age of genomics and proteomics.
New Drug Development (PHTO 6219)
This course will provide a comprehensive overview of the drug discovery and development process, focusing on drug development science, regulation, and industry. Students will learn how promising new drugs are discovered, screened, and evaluated from the standpoint of their safety and efficacy. How drug commercialization decisions are made at each major phase in the drug development process. How information technology is used to increase drug development productivity as well as enhance the commercial potential of drug candidates. Topics include: Molecules to medicines; Drug discovery, design, and screening; Early testing and Safety; Clinical research; Global drug review and approval, Trends and issues in pharmaceutical drug development; Case history, etc. The course grade will be based on class participation (50%) and class project and presentation (50%). Year offered: Fall, Term offered: Annually. Hours per week: Lecture, conference and discussion 4. Faculty: Zhou, Staff.

Neuropharmacology (PHTO 6223)
An eight week course meeting three times per week to present the principles of the study of drugs that influence neural systems. The format of the course will be a combination of faculty and student presentations and discussion. Grades will be based upon two exams, a research paper, and a student presentation. Prerequisites: Permission of instructor or BBSC Core Curriculum Term offered: I Year offered: Annually All course offerings are contingent upon adequate student enroll.

Intro Tox Risk Assessment (PHTO 6224)
The objective of this course is to provide a basic foundation on the toxicological risk assessment process. The course format is lecture-based with supplement from online materials and experiences, as well as practical application aligned with book chapter commentary, and case studies. Students will be provided a risk assessment simulation exercise to experience and understand the risk assessment process. Within this course, students learn about: 1) the building blocks of risk assessment, 2) the risk assessment process, 3) how risk assessment is applied and used in decision making scenarios, 4) current and emerging issues in risk assessment, and 5) the skills and professional resources available to those interested in risk assessment. After completing the course, the student will be able to: 1) define and explain toxicological risk assessment, 2) comprehend the application of risk assessment, 3) demonstrate effective use of risk assessment technique, 4) demonstrate competent science and math skills associated with risk assessment, 5) employ ethical principles in the application of risk assessment, 6) demonstrate the ability to work effectively in teams and in discussion-based format. Course performance grading will be standard letter grades, based on exams, individual projects, class participation/discussion, and attendance.

ACC Pharmacology (PHTO 6312)
This fifteen-week course serves as an introduction to the cellular, biochemical, and molecular effects of pharmacological agents acting on the autonomic and central nervous systems as well as the cardiovascular and renal systems. Prior to detailed presentations of the various classes of agents used to treat disorders of the aforementioned systems, the pertinent physiology of each system will be reviewed. The therapeutic use, mechanism of action, adverse effects, and absorption, distribution, and metabolism will be emphasized for each pharmacological agent presented in class. This course will be graded on the basis of four in-class examinations.

Genome-Wide Analytical Technologies for Biomedical Research (PHTO 6318)
New developments in technologies such as proteomics, metabolomics, epigenetics, and molecular imaging are expanding our knowledge of the biological world at a rapid pace. These analytical approaches and expertise are accessible at UTMB. The student is offered education in cutting-edge technologies for application in biomedicine. The course is a blend of lectures, literature seminars, and practical demonstrations of data acquisition and data analysis. At the end of the course, the student will be able to identify and apply experimental strategies that best fit their biomedical experimental hypothesis. Grading: The examination will consist of a 5 page research proposal that describes the
application of genome-wide technologies to a biomedical hypothesis. The exam will effectively integrate the student's working knowledge of materials discussed in seminars, lectures and practical demonstrations.

**Principles of Environmental Toxicology (PHTO 6319)**
This course will be a graduate-level presentation of fundamental principles of environmental toxicology, including basic concepts like ADME (absorption, distribution, metabolism, and excretion), mechanisms of toxicity and injury, inflammation and ROS, overviews of discipline-specific toxicology (e.g., genetic toxicology, immunotoxicology, and toxicant-associated carcinogenesis), as well as organ-system-based toxicology covering major organ systems of the body (e.g., neurotoxicology, hepatotoxicology, renal toxicology, cardiovascular toxicology, and respiratory toxicology), and including developmental toxicology. Grades will be calculated based on upon 2 mid-term and final in-class exams, and class attendance.

**SPRING**

**Lab Rotation PHTO (6022)**
The objectives of this course are to acquaint students with the research activities of individual faculty members and to assist students in choosing their areas of specialization. The faculty member and student will design a research project and work out a time schedule committing the student to three to 24 hours per week in the laboratory. The student will prepare an abstract describing the objectives and methodology of the study and then conduct the study under the faculty member's supervision. A final report stating the methods, results, interpretation, problems encountered, and suggestions for future research will be required. In addition to carrying out the research proposal the student will be expected to gain a knowledge of the current literature relevant to the project. Grading will be based on the student's laboratory performance, final written report, and an oral presentation of the project. Grading will be A, B, C, F. Normally, a student entering the program without an advanced degree will be required to complete 12 hours of credit with a grade of B or better prior to gaining admission to candidacy. Individual requirements may vary depending on the research experience of the student. Prerequisites: None Terms offered: I, II, III Year offered: Annually Hours per week: Laboratory 3 24

**Research (PHTO 6097)**
Research on thesis or dissertation project under the direction of supervising professor. The research is graded as satisfactory (S) or unsatisfactory (U). Prerequisites: None Term offered: I, II, III Year offered: Annually Hours per week: Laboratory 3 27

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**Seminar in Pharmacology & Toxicology (PHTO 6195)**
Presentations by guest lecturers, staff, and students on the progress of their own research, as well as review of recent advances in pharmacology. Students will receive a grade of satisfactory (S) or unsatisfactory (U) based on attendance and participation. Prerequisites: Students are required to be enrolled in this course every term offered, except for the last term.

**Synthetic Methods to Biomolecules (PHTO 6211)**
Modern methods for the synthesis of biomolecules will be covered. Biomolecules include various natural products, unnatural amino acids, peptides, nucleotides, carbohydrates, bioactive small molecular chemical probes and drug candidates. The lecture topics will include modern synthetic methods that are useful to access various biomolecules. These synthetic methods include but not limit to solid phase synthesis, combinatorial synthesis, and fundamental organic synthetic approaches such as reductions, oxidations, functional group protections, carbon-carbon bond formation, asymmetric alkylation, asymmetric allylation, metal-halogen exchange, organolithium reagents, directed ortho metatalation, Stille reaction, Suzuki reaction, Heck reaction, stereoselective aldol reaction, olefination, asymmetric epoxidation and catalytic epoxide-opening reactions, asymmetric Diels-Alder reaction, olefin metathesis, synthetic methods for heterocyclic compounds, etc. Course consists of two exams and the grading system Standard A-F.

ECT Pharmacology (PHTO 6213)
Survey of Pharmacology course covering drugs that affect the endocrine system, drugs used in cancer chemotherapy, anti-parasitic drugs, drugs to treat gastrointestinal (GI) system, anti-dhistomines, anti-inflammatory drugs and an introduction to toxicology and specific toxic agents

SUMMER

Lab Rotation PHTO (6022)
The objectives of this course are to acquaint students with the research activities of individual faculty members and to assist students in choosing their areas of specialization. The faculty member and student will design a research project and work out a time schedule committing the student to three to 24 hours per week in the laboratory. The student will prepare an abstract describing the objectives and methodology of the study and then conduct the study under the faculty member’s supervision. A final report stating the methods, results, interpretation, problems encountered, and suggestions for future research will be required. In addition to carrying out the research proposal the student will be expected to gain a knowledge of the current literature relevant to the project. Grading will be based on the student’s laboratory performance, final written report, and an oral presentation of the project. Grading will be A, B, C, F. Normally, a student entering the program without an advanced degree will be required to complete 12 hours of credit with a grade of B or better prior to gaining admission to candidacy. Individual requirements may vary depending on the research experience of the student. Prerequisites: None Terms offered: I, II, III Year offered: Annually Hours per week: Laboratory 3 24

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Once admitted to candidacy, it is required for students pursuing the Doctor of Philosophy degree to enroll in this course. This course is for the formal research and writing leading to the preparation and completion of the dissertation for the Doctor of Philosophy degree while under the direction of the student's supervisory committee. The student will pursue the proposed research and present a progress report and/or agreed upon objectives to the mentor and/or supervisory committee for approval and recommendations. Grading will be based upon the student's level of performance as reported by the chairperson of the student's supervisory committee and will be assigned as Satisfactory (S), Needs Improvement (N), or Unsatisfactory (U). Prerequisites: Admission to candidacy Terms offered: I, II, III Year Offered: Annually

**Advances in Mental Health Research (PHTO 6123)**
This course will provide a solid understanding of current mental health research and promote understanding of factors advancing future groundbreaking mental health research. The course will have flexible format, including sessions where students discuss relevant papers, present their own data, discuss a wide range of career-development issues, learn about pharmacotherapeutic development, learn advanced grant-writing principles, discuss relevant ethical issues, and learn advanced research techniques. Attendance 50%, participation in classroom discussion 50%. A satisfactory grade requires a score of 80%.

**Grant Writing (PHTO 6124)**
This course is designed to advance the knowledge that graduate students receive in basic grant-writing skills from their mentor. At the same time, it will teach graduate students who have not learned the basic skills what they need to know in order to write a viable research fellowship or grant award application. The course will include topics on grantsmanship, writing specific aims, and research strategy sections, and writing a compelling biosketch/CV. A session on NRSA and other types of fellowships also will be provided. At the end of the course, participants should have achieved core competency in writing a grant as well as qualifying exam proposals that may take on a grant proposal form. Satisfactory/unsatisfactory grades will be based on attendance, drafting the sections of the application, and participation in classroom discussion.

**Bioinformatics Tools and Applications (PHTO 6125)**
The goal of the class is to introduce the students to the various bioinformatics tools available for the analysis DNA and RNA sequencing data. Students will be provided with an overview of the most common bioinformatics tasks they will face in the research. During the class, students will have hands on experience performing analysis of the data generated by the variety of scientific instruments and bioinformatics tools addressing real-life clinical and scientific applications. The class will be divided into three sections: pathogen detection, gene expression, and microbiome analysis. Students will be taught how to use public bioinformatics resources such as GeneBank, SRA, PATRIC, SILVa, and I2B2.

**Seminar in Pharmacology & Toxicology (PHTO 6195)**
Presentations by guest lecturers, staff, and students on the progress of their own research, as well as review of recent advances in pharmacology. Students will receive a grade of satisfactory (S) or unsatisfactory (U) based on attendance and participation. Prerequisites: Students are required to be enrolled in this course every term offered, except for the last term.