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 and 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, 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, graduate courses, and laboratory rotation is available and can be found about the Pharmacology & Toxicology Graduate Program on our website at http://www.utmb.edu/phtox.
Objective and Scope of the Training 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, cytochrome P450, molecular design and modeling, 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: [http://www.utmb.edu/phtox/](http://www.utmb.edu/phtox/)
FACULTY

There are currently 17 full time faculty members in the department of Pharmacology and Toxicology. In addition, there are 11 affiliated 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: http://www.utmb.edu/phtox/

DISCIPLINE

Cancer and Aging Biochemistry & Pharmacology

Mark. R. Emmett, Ph.D.
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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.

Miriam A. Falzon, Ph.D.
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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.

Mark R. Hellmich, Ph.D.
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Molecular mechanisms of peptide hormone-regulated growth of gastrointestinal cancers
A key issue in vaccine development is balancing immunogenicity with safety and vaccine safety gets more public attention than vaccine efficacy. Many of the successful vaccines we have today are based on live-attenuated or inactivated pathogens or live vectors such as non-replicating bacteria or viruses that induce robust antibody and cellular immunity. However, antivector immunity and safety concerns associated with live vectors complicate their use in infants and aged populations and in people with immunocompromised systems. Our lab is interested in the development of nano-scale biomaterials such as nanofibers, nanoparticles, virus-like particles, and hydrogels for engaging the immune system to induce protective antibody and cell-mediated immune responses against diseases such as tuberculosis, melanoma, and flavivirus infections (West Nile and Zika). We are also investigating the development of vaccines against drugs of addiction such as cocaine.

Biomaterials immunoengineering is a multidisciplinary field that lies at the intersection of materials science, chemistry, immunology, and vaccinology. We collaborate with virologists, immunologists, and clinicians not only to develop synthetic vaccination platforms but also to understand how biomaterials interact with the immune system and continue to develop novel materials and creative tools to tackle multidisciplinary problems in vaccine development and immunotherapy.

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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.
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 $\gamma$. 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 $\gamma$ holoenzyme. Recently, we determined structures of ternary complex of Pol $\gamma$-DNA with a substrate or an antiHIV reagent, zalcitabine, lamivudine or emtricitabine. These structures provided unprecedented insight in Pol $\gamma$ mediated antiviral drug toxicity. As Pol $\gamma$ 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 $\gamma$ is responsible for DNA synthesis during replication and repair. I lead investigation of Pol $\gamma$ activity in BER specific gap-filling DNA synthesis. Our findings indicate Pol $\gamma$ 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 $\gamma$ 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, Ph.D.
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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

Wayne R. Snodgrass, M.D., Ph.D.
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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**

Yuriy Fofanov, Ph.D.
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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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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.

Gabrielle Rudenko, Ph.D.
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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 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.

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).

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.
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**

**Mahmoud S. Ahmed, Ph.D.**  
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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.

**G.A. Shakeel Ansari, Ph.D.**  
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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.

**Cornelis Elferink, Ph.D.**  
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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 on 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.

Erik Rytting, Ph.D.
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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.

Csaba Szabo M.D., Ph.D., D. Sc., F.B. Ph.S.
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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.

Neuropharmacology

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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, Ph.D.
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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 mechanistically 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, Ph.D.**  
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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-HT$_{2A}$ and 5-HT$_{2C}$ 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, Ph.D.**  
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**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, Ph.D.  
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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., Ph.D.  
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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.

Fernanda Laezza, M.D., Ph.D.  
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The research in our laboratory is directed at understanding the cellular and molecular mechanisms underlying modulation of ion channels in relationship to intrinsic excitability, synaptic transmission and plasticity. Rapid progress in the complementary fields of molecular genetics and cellular electrophysiology has led to the appreciation of mechanistic links between ion channel dysfunction, long-term alterations in neuronal activity and the phenotypic expression of a variety of neurological disorders. Hence, ion channels have become a promising and attractive target for drug discovery and for the development of new therapeutic treatments against human diseases. Our major effort is currently focused at understanding the physiological activity of the intracellular fibroblast growth factors (iFGFs), a set of four genes (FGF11-14) abundantly expressed in neurons of the central and peripheral nervous systems.
Ophthalmology and Visual Sciences

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

Wenbo Zhang, Ph.D.  
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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, Ph.D.  
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-HT2C 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.

The second-year programmatic coursework culminates in taking the written qualifying examination at the beginning of the summer term (early May). Thereafter, students have 12 months to spend almost full time in their mentor's lab (registering for "Research" and "Seminar") developing the dissertation proposal. This proposal must be successfully defended before the student becomes a full-fledged doctoral "candidate". In many ways this period is the most crucial of the graduate-school career.

To summarize, during the first five terms (about 20 months), students have an opportunity to achieve a strong general knowledge of basic biomedical sciences as well as in-depth knowledge of pharmacology and toxicology and extensive lab experience with a mentor chosen by the end of the first year. After the qualifying examination, they have one year in which to develop a dissertation proposal prepared in the format of an NIH research grant application. Students choose and pursue a research problem for the dissertation under the supervision of a faculty mentor, or advisor, and a supervisory committee. The research culminates in a dissertation, which constitutes an original and independently achieved contribution to knowledge. Students gain speaking and teaching experience by giving seminars on a regular basis under the direct supervision and evaluation of the faculty.

Course of Study for the Pharmacology & Toxicology Graduate Program

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 and toxicology curriculum committee. In addition, a series of required and elective courses specific to pharmacology and toxicology are taken in subsequent years. The charts on pages 22 and 23 illustrate the complete set of BBSC and pharmacology and toxicology courses (required and elective) available to pharmacology and toxicology students. The basic requirements for the pharmacology and toxicology curriculum after BBSC are to take the course Autonomic, Cardiovascular, and Central Nervous System Pharmacology (ACC) (PHTO 6312) and Endocrine, Chemotherapy, and Toxicology Pharmacology (ECT) (PHTO 6214). In addition, students will be required to take 2 credit hours from the provided PHTO list and may take other courses as needed. Students are required to take a minimum of 9 credit-hours per term including Seminar in Pharmacology and Toxicology (PHTO 6195) and Journal Club (PHTO 6190). (The second number in each 4-number course identification code represents the credit hours for the course.) Course evaluations by students are
required for all didactic courses in the program. Grades will not be released for any course until all evaluations are received.

**Minimal Performance Criteria**
Students in the Pharmacology and Toxicology Graduate Program should maintain a grade of B or higher in all required courses of the program. Students who fail to do so will be required to make up the deficiency by any of a variety of means, including but not limited to, retaking examinations, taking a readings or special topics course, or repeating the course the next time it is offered. The remedial action to be utilized will be determined by the Advisory Committee and Program Director. 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**

1. Students may choose elective courses to strengthen special areas of interest or weakness, or to provide background for research skills. A minimum of 2 credit hours of elective courses is required. Students may take additional hours if appropriate.

2. The elective courses available include any of the courses shown on the chart. Courses offered by other graduate programs may be taken in lieu of the electives listed, but approval of the Program Director is required for the substitution.

**Laboratory Rotations/Research**

1. New students will participate in an orientation program (BBSC 6195) in the first term in which they will be introduced to the research activities of eight basic science graduate programs including pharmacology and toxicology.

2. In addition to the orientation program, each student will rotate through at least 2 laboratories of his/her choice during the first (BBSC) year. Registration is for BBSC 6301 Lab Rotations. Students continue to register for lab rotation (Research) in the pharmacology and toxicology program (PHTO 6097) in the lab they chose to join by the end of the BBSC year and continue to register for PHTO 6097 each term until they pass the written qualifying examination. Credit hours depend on the time commitment of the student and faculty member but may not be for less than 3 credit hours (9 contact hours per week) per term.

**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. In the first two terms of the first year students will take the PHTO 6195 seminar course, and thereafter, continue the pharmacology and toxicology seminar course (PHTO 6195). For PHTO 6195, each student will attend Program-recommended seminars regularly each term, and in addition, each student will present one seminar each year of the pharmacology and toxicology program, including the dissertation proposal, the dissertation defense, and other annual presentations. Students must begin presenting seminars in the semester following the successful completion of the Qualifying Exam. Student seminars should be scheduled through the Graduate Program Coordinator.

**Semester Research 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 scheduled for during the 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, which 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](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 Qualifying Exam Committee (QEC) Chair (Dr. Elferink, coelferi@utmb.edu). The expectation is that students 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 from their mentors. For each proposal, three reviewers (selected from the faculty in the PHTO graduate program) will be assigned to provide a written critique the proposal, and a score will be assigned using the NIH scoring format. Written critiques will be made available to the students two weeks after the submission date. A preliminary average score will be assigned to each proposal.

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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>
</tr>
<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>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Good</td>
<td>Strong but with at least one moderate weakness</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Satisfactory</td>
<td>Some strengths but also some moderate weaknesses</td>
</tr>
<tr>
<td>Low</td>
<td>7</td>
<td>Fair</td>
<td>Some strengths but with at least one major weakness</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Marginal</td>
<td>A few strengths and a few major weaknesses</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Poor</td>
<td>Very few strengths and numerous major weaknesses</td>
</tr>
</tbody>
</table>

**Scoring:**

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, but need not provide a description of the budget, resources, animal welfare, human subjects, biographical materials or personnel justifications.

A one page (or less) letter of intent briefly describing the research area being considered for proposal (eg. background and significance, hypothesis and specific aims) is to be submitted 2 months before the proposal deadline to Dr. Elferink for review by the QEC in order to evaluate appropriateness.

**Oral Component:**
A 30-minute oral presentation on the proposal to the entire Department of Pharmacology and Toxicology—integrated into the departmental seminar series—will follow submission of the written proposal. Scheduling of the oral component will be determined on an annual basis, but will occur no sooner than three weeks after submission of the written component. Evaluation of the oral presentation will be based on clarity of presentation, and the student’s ability to address audience questions.

**Student Evaluation**
A committee comprised of the QEC members and the written proposal reviewers will convene (after the oral presentation) to assess the student’s written proposal and evaluate the oral presentation. To pass the qualifying exam, students must receive an average score of 4 or better on the written portion, and receive a pass grade from the committee for the oral presentation. The Chair of the QEC will chair the panel discussion, unless in conflict, whereupon an alternate will be assigned from the committee. Student mentors are considered to be in conflict when their student(s) are being evaluated, and will be required to recuse themselves from discussions.

**Remediation**
An average score >4 on the written component will constitute a failing grade. The student will be afforded 3 weeks to revise the proposal (in response to the written reviewer comments) for re-review, and must receive an improved average score ≤4 to pass. Failure on the oral presentation portion will require the student to once more present the proposal to the three reviewers of the written component, and earn a passing grade. Remediation of the oral presentation will occur within 1 month of the first 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.

**Admission to Candidacy**
One of the most important stages of your development as a graduate student and investigator is admission to candidacy. Admission to candidacy should occur no later than the beginning of Term III (May) of your third year in the program, 12 months after the written qualifying examination. This event implies several things. First, that you have completed all required and elective courses, that you have satisfied any academic deficiencies, and you have passed the written qualifying examination, all of which indicate that you have mastered the fundamental knowledge of the field of pharmacology and toxicology. More importantly, admission into candidacy indicates that you have spent several months since the written qualifying exam working diligently in a laboratory in order to:

1. accumulate additional specialized knowledge about a specific area of pharmacology/toxicology (this means you’ve been reading many papers in the primary literature about your field, and that you are familiar enough with the area to recognize important unanswered questions that you could pursue as the dissertation research, and that you can place your research in the context of the state-of-knowledge and significance of its subdisciplines),

2. acquire skill and facility with specialized scientific techniques and methodologies (this means you have become reasonably proficient in one or more techniques, such as electrophysiological recording, immunocytochemistry, recombinant biochemistry, binding assays, etc., techniques that you can use effectively to answer the questions you pose),
(3) execute experiments to acquire reliable information (this means you obtain “preliminary data” that demonstrates you can do experiments and that your dissertation project is tractable).

From a practical perspective, what the student does from the time the written qualifying exam is completed is to register for the course “Research” (PHTO 6097), usually for two or three consecutive terms, during which you spend full effort working in the laboratory of your chosen mentor/advisor (future Supervisory Professor). The written qualifying examination is taken in May of the second year. After that term, usually only Research, Journal Club, and Seminar are taken. The basic task to be accomplished is to develop a dissertation proposal, a written plan of the research to be conducted to satisfy the doctoral degree. This needs to be written and defended within one year of passing the qualifying exam. Our program requires that this proposal be written in the format of a complete NIH R01-type research grant application (PHS398). Specific information about this grant may be found on the web at http://grants1.nih.gov/grants/forms.htm.

Why is the dissertation proposal so important and why do we want the proposal done in the style of an NIH grant application? The dissertation proposal is basically a research plan – an account of what hypotheses will be tested, the design and sequence of experiments to be done to examine the hypotheses, a convincing demonstration that you have the ability to do the experiments and interpret the results properly, and an explanation of the significance of the studies to be conducted and why they are important. An NIH research grant application is designed to elicit this information in an orderly, rational sequence. Completing the proposal in the NIH format not only assures that all the relevant information is present, it also provides an opportunity to practice developing a grant application, one of the major tasks that most researchers do as part of their routine work. If you complete an NIH grant application, this indicates that you have done all the necessary preparation to make your future work succeed. Since all the research we do should be planned and executed rationally, a properly prepared dissertation proposal is no more (or less) than an explicit description of the research one wishes to pursue. In many ways, laying out the experimental plan is at least as difficult and demanding as doing the actual experiments, but if one does not first have a detailed and thoroughly reasoned course of action, it is likely that the experiments will either fail or be inefficient and wasteful. Thus, a great deal rests on developing an appropriate proposal, and when it is done well, it indicates that you have accomplished most of the critical skills necessary to perform meaningful research.

You may obtain helpful information on how to prepare an NIH grant application by going to the following UTMB web address http://research.utmb.edu/funding/grantwriting.shtml.

The evolution of the proposal occurs gradually. First you must read a great deal about your area and work very closely with your faculty mentor to learn important concepts and to practice experimental skills and strategies. You will have to execute many experiments to hone your abilities and to accumulate enough preliminary data to convince others that you have the capability to do the experiments you are planning. As the time approaches for actually writing the proposal, you should be thinking about other faculty members who will advise and assist you in your work. Your mentor and these other faculty members will eventually become the Supervisory Committee, the group who will oversee the proposal and the dissertation work.

For regular (non-MD-PhD) students, the Supervisory Committee consists of five members: three from the Pharmacology and Toxicology Graduate Program Faculty, including your mentor (who is called the "Supervisory Professor" and may serve as chair of the committee), and two other faculty members from the pharmacology and toxicology graduate program, and another member whose primary area of scientific expertise is different from that of the Supervisory Professor. In general, this person will be from a Graduate Program other than Pharmacology and Toxicology, but in some cases a faculty member who holds an appointment within the student’s program may qualify. The fifth member of the Supervisory Committee must be 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 two additional requirements exist: this committee must include an MD-degreed faculty member with a primary appointment in a clinical department and a member of the MD-PhD combined-degree advisory committee. These members 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. All students are advised to discuss potential membership of the Supervisory Committee not only with their mentor but also with the program director, the MD-PhD advisory committee (when appropriate) and even the dean before finally settling on the membership composition.

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. There is a set sequence of events that must occur as the time for presenting your dissertation proposal comes about. The critical event is an oral presentation (seminar) by the student for the entire program faculty, including the Supervisory Committee that describes the proposed work. This seminar is followed by a formal meeting of the student with the Supervisory Committee, at which time the committee performs an oral examination of the student, a final test to be certain the student is prepared to do the proposed work. If the committee members have been properly informed about the project in the preceding weeks and were given drafts of the proposal and thus were able to provide feedback to the student before the seminar and exam, then this final oral examination by the committee is routine and generally confirmatory of the proposed work, although last-minute suggestions for improvement in the proposal or experimental plan may occur. Under ideal circumstances, it is appropriate that all members of the Supervisory Committee should be present for the seminar and oral examination. Practically, however, it is often the case that scheduling or expenses prohibit the off-campus member from being present. This is permissible (see below, however), but it is not generally appropriate for any other member not to be at the seminar and exam. This means that the student (and mentor) should plan this meeting well in advance to accommodate everyone’s calendars.

After the seminar and Committee meeting, the student should prepare the final draft of the proposal (the NIH grant application). The original and one copy of the complete NIH R01 grant application is turned in to the program director’s office along with the following items, each of which is absolutely required:

1. A letter to the program director from the Supervisory Professor (mentor) stating that he/she is willing to supervise the student’s work and that all members of the Supervisory Committee have approved the proposal, and that the committee (except possibly the off-campus member) examined the student orally after his/her seminar regarding the proposed work and agree that he/she is ready for admission to candidacy.

2. A separate letter to the program director from the Supervisory Professor (advisor) stating how the advisor intends to provide financial support for the student while he/she is doing the dissertation research in the lab. It is the responsibility of the Supervisory Professor to provide (typically from grant funds) the student’s stipend.

3. A completed form for Admission to Candidacy for the Doctoral Degree, with the Proposed Supervisory Committee form. A copy of these forms is included at the end of this Section (after the articles about grant writing).

The web addresses for obtaining these forms and for more information is http://www.gsbs.utmb.edu/candidacy/info.asp

Make sure that the name, degree, rank, title and address of all proposed members of the supervisory committee are entered on the Proposed Supervisory Committee form.

4. A copy of a curriculum vitae for the proposed off-campus member of the Supervisory Committee, as well as for any other member of the committee (if any) who is not a member of the graduate school
faculty at UTMB. If you are not sure about which individuals are formal members of the graduate school faculty, the program office can assist you.

After all these materials are into the program office, the program director then writes a formal letter to the dean requesting that the student be admitted to candidacy. Included with the program director’s letter are the Application for Candidacy, a copy of the proposal, and any curricula vitae. The dean then separately writes each member of the Committee to determine independently that each approves of the proposal (the dean sends a copy of the final version of the proposal with his letter if the student has not done so already) and agrees to serve on the Committee. After all committee members have responded and the dean has approved, then the student is admitted to candidacy.

Admission to candidacy actually occurs at the beginning of the term that starts after all the approvals are made. Upon admission to candidacy, the student then registers only for “Dissertation” (PHTO 6099) and “Seminar” (PHTO 6195) each term. From this point on until completion of the dissertation, the student is working full-time on experiments and the writing of papers and, eventually, the dissertation itself.

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 year until the dissertation is completed. The Supervisory Professor must provide a brief written account of these meetings and assess the student’s progress for the program director. 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. Typically, the candidate will present a seminar as a part of this assessment activity.

You may also wish to refer to section 4.61 (Doctoral Degree) of the Academic Policies of the GSBS, available on-line at http://www.gsbs.utmb.edu/_pdf/BylawsandPolicies.pdf.

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. Students are also required to register each term for Seminar (PHTO 6195) and to attend faculty and student seminars each term. Finally, each candidate is required to present one seminar per year (as an annual progress report) to the program faculty and Supervisory Committee with a follow-up private meeting with the Committee. The Supervisory Professor provides a written account of the students progress to the Program Director as well as a grade of A, B, C or F. Students are strongly encouraged to write papers as they progress through their respective projects. 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 eventually the graduate faculty and dean completes the degree requirements.
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<td>Project Proposal Preparation (BBSC 6221)</td>
<td>Molecular Biology and Genetics (BBSC 6403)</td>
<td>8-Wk Laboratory Pathway: From Discovery to Licensure (BBSC 6219)</td>
</tr>
<tr>
<td>Bioinformatics (BBSC 6223)</td>
<td>Seminar (PHTO 6195)</td>
<td>Principles of Laboratory Safety (BBSC 6217)</td>
</tr>
<tr>
<td>Cell Biology (BBSC 6302)</td>
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<tr>
<td>Biochemistry (BBSC 6401)</td>
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<tr>
<td>Ethics of Scientific Research (MEHU 6101) [2-day course]</td>
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<tr>
<td>8-Week Laboratory Rotation (BBSC 6043)</td>
<td>8-Week Laboratory Rotation (BBSC 6043)</td>
<td>8-Wk Laboratory Rotation (BBSC 6043)</td>
</tr>
<tr>
<td>Animal Models of Human Diseases (BBSC 6220)</td>
<td>Neuronal Excitability (BBSC 6207) [PHTO]</td>
<td>7-Wk Laboratory Rotation (BBSC 6043)</td>
</tr>
<tr>
<td>8-Week Laboratory Rotation (BBSC 6043)</td>
<td>Principles of Drug Action, Pharmacokinetics &amp; Biotransformation (BBSC 6208)</td>
<td>Genes, Environment and Disease (BBSC 6118) [PHTO]</td>
</tr>
<tr>
<td>8/29/16- 10/22/16</td>
<td>1/05/17 - 2/24/17</td>
<td>5/01/17 – 6/23/17</td>
</tr>
</tbody>
</table>

**Red** = Required  
**Black** = Electives  
**Magenta** = PHTO Program Required  
**Green** = 3 rotations are required (required to do one in 2nd block of Fall term)  
**Orange** = CTPRERP students only, must have permission to register  
**Blue** = Program Suggestive Elective

*Updated 10/16*
# Year 2 - Pharmacology/Toxicology Curriculum

<table>
<thead>
<tr>
<th>Fall Term I</th>
<th>Spring Term II</th>
<th>Summer Term III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seminar (PHTO 6195) ★</td>
<td>Seminar (PHTO 6195) ★</td>
<td>Seminar (PHTO 6195) ★</td>
</tr>
<tr>
<td>Journal Club (PHTO 6190) ★</td>
<td>Journal Club (PHTO 6190) ★</td>
<td>Research (PHTO 6097) or Dissertation (PHTO 6099) ★★</td>
</tr>
<tr>
<td>Research (PHTO 6097)</td>
<td>Research (PHTO 6097)</td>
<td></td>
</tr>
<tr>
<td><strong>Electives:</strong> Intro to Tox Risk Assessment (Taught in even years)</td>
<td><strong>Electives:</strong> Synthetic Methods to Biomolecules (PHTO 6211) Dr. Zhou</td>
<td><strong>Electives:</strong></td>
</tr>
<tr>
<td>Principles of Environmental Toxicology (PHTO 6319) (Taught in odd years)</td>
<td></td>
<td><strong>COMPREHENSIVE EXAM</strong></td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>ACC Pharmacology (Autonomic/Cardiovascular/Central Nervous System) (PHTO 6312) Dr. Johnson</th>
<th>Electives:</th>
<th>Electives:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Toxicology (PHTO 6214) (Taught based on need)</td>
<td>ECT Pharmacology (Endocrine/Chemotherapy/Toxicology) (PHTO 6213) Dr. Falzon</td>
<td>Neuronal Transmission (BBSC 6126) Dr. Laezza</td>
</tr>
<tr>
<td>Neuroparmacology (PHTO 6223) (Taught based on need)</td>
<td>Electives: Neuronal Excitability (BBSC 6207) Dr. Hamill</td>
<td>Hormonal Signaling (BBSC 6215) Dr. Watson</td>
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<tr>
<th>Electives:</th>
<th>Electives:</th>
<th>Electives:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genes, Environment and Disease (BBSC 6118) Dr. Sherif Abdel-Rahman</td>
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<td></td>
</tr>
</tbody>
</table>

Note: BBSC calendar begins Fall Semester of entering students’ first year (Year-01) and terminates at the end of Summer Semester of students’ first year. PHTO calendar begins Fall Semester Year-02 and continues through graduation.

The curriculum above is typical. Students with proven background in certain topics may not be required to take all courses.

★ PHTO students must register for Seminar and Student Journal Club every term offered, except last. (Required classes are in red)

★★ To enroll in Dissertation student must pass written and oral Qualifying Exam in Spring/Summer of year 2.

Updated 8/16
Pharmacology & Toxicology Course Offerings 2015-2016

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 memberÆs 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 studentÆs 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)
Formal research and writing leading to the preparation and completion of the thesis for the Master of Science degree under the direction of the studentÆs supervisory committee. Grading will be based upon the studentÆs level of performance as reported by the chairperson of the studentÆs supervisory committee and will be assigned as satisfactory or unsatisfactory. Prerequisites: Admission to candidacy for the masterÆs degree Term offered: I, II, III Year offered: Annually Hours per week: Variable Students registering for Thesis are expected to register for a total of 9 credit hours per term.

Dissertation (PHTO 6099)
Formal research and writing leading to the preparation and completion of the dissertation for the Doctor of Philosophy degree under the direction of the studentÆs supervisory committee. Grading will be based upon the studentÆs level of performance as reported by the chairperson of the studentÆs supervisory committee and will be assigned as satisfactory or unsatisfactory. Prerequisites: Admission to candidacy for the Ph.D. degree Terms offered: I, II, III Year offered: Annually Hours per week: Variable Students registering for Dissertation are expected to register for a total of 9 credit hours per term.

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)
This course will explore in detail the molecular and cellular mechanisms responsive to toxic stimuli using selected examples. In addition, the course will also examine current concepts and research strategies employed in toxicology. 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%). Term offered: Fall, Year offered: Annually. Hours per week: Lecture, conference and discussion 4. Faculty: Zhou, Staff.

Molecular Toxicology (PHTO 6214)
This course will explore in detail the molecular and cellular mechanisms responsive to toxic stimuli using selected examples. In addition, the course will also examine current concepts and research strategies employed in toxicology. 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.

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 Hours per week: Lecture 4; Conference or Discussion 1; Laboratory 6 COURSE DESCRIPTIONS 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

Thesis (PHTO 6098)
Formal research and writing leading to the preparation and completion of the thesis for the Master of Science
degree under the direction of the studentÆs supervisory committee. Grading will be based upon the studentÆs
level of performance as reported by the chairperson of the studentÆs supervisory committee and will be
assigned as satisfactory or unsatisfactory. Prerequisites: Admission to candidacy for the masterÆs degree
Term offered: I, II, III Year offered: Annually Hours per week: Variable Students registering for Thesis are
expected to register for a total of 9 credit hours per term.

Dissertation (PHTO 6099)
Formal research and writing leading to the preparation and completion of the dissertation for the Doctor of
Philosophy degree under the direction of the studentÆs supervisory committee. Grading will be based upon the studentÆs
level of performance as reported by the chairperson of the studentÆs supervisory committee and
will be assigned as satisfactory or unsatisfactory. Prerequisites: Admission to candidacy for the Ph.D. degree
Terms offered: I, II, III Year offered: Annually Hours per week: Variable Students registering for Dissertation are
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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,
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Pharmacology & Toxicology Std Journal Cl (PHTO 6190)
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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.

**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 alkylation, metal-halogen exchange, organolithium reagents, directed ortho metalation, 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 memberÆs 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 studentÆs 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)**
Formal research and writing leading to the preparation and completion of the thesis for the Master of Science degree under the direction of the studentÆs supervisory committee. Grading will be based upon the studentÆs level of performance as reported by the chairperson of the studentÆs supervisory committee and will be assigned as satisfactory or unsatisfactory. Prerequisites: Admission to candidacy for the masterÆs degree Term offered: I, II, III Year offered: Annually Hours per week: Variable Students registering for Thesis are expected to register for a total of 9 credit hours per term.
Dissertation (PHTO 6099)
Formal research and writing leading to the preparation and completion of the dissertation for the Doctor of Philosophy degree under the direction of the student's supervisory committee. 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 or unsatisfactory. Prerequisites: Admission to candidacy for the Ph.D. degree Terms offered: I, II, III Year offered: Annually Hours per week: Variable Students registering for Dissertation are expected to register for a total of 9 credit hours per term.

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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.
Pharmacology and Toxicology Courses

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 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 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.

Qualifying Exam: Defense of both written and oral mock proposal, spring/summer of year 2 once PHTO declared.