UNT | HEALTH SCIENCE CENTER

GRADUATE SCHOOL OF BIOMEDICAL SCIENCES

BIOCHEMISTRY AND CANCER BIOLOGY GRADUATE PROGRAM STUDENT HANDBOOK 2016-2017

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Professor and Graduate Advisor

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1. Program description

The Biochemistry and Cancer Biology program is an interdisciplinary program that offers both MS and PhD degrees. The goal of this program is to provide students with rigorous education and training in biomedical sciences with a specialty in Biochemistry and Cancer Biology. Students receive training through original research, formal classroom education, problem-based learning, seminars, and journal clubs. The program includes faculty members from several departments engaged in various aspects of biochemical, biophysical and cancer research.

The specific research interests of faculty cover a wide range of topics, including signal transduction, posttranslational protein modification in health and disease, protein structure and function, protein-ligand and protein-protein interactions, metabolism, molecular carcinogenesis, tumor immunology, stem cell biology, tumor invasion and metastasis, tumor microenvironment, cancer therapeutics, drug resistance, drug metabolism, drug delivery, drug discovery, nanotechology/imaging, epigenetic effects on cancer risks, alternative medicine therapies of cancer, disorders of lipid metabolism in atherosclerosis, lipoprotein metabolism and biophysics of muscle contraction. The interdisciplinary research also includes investigation of the link between cancer with other disorders, such as aging & Alzheimer's disease, HIV and ocular diseases. The research projects employ state-of-the-art molecular, cellular and biochemical techniques that include genomics, proteomics, mass spectrometry, protein crystallography, molecular cloning, gene targeting, FACS analysis, advanced fluorescence spectroscopy, optical imaging and advanced molecular technology for the detection of genetic variation between normal and cancer cells.

Students may choose major professors from any department according to their research interests. In addition, students will be able to utilize the resources and expertise of faculty members with diverse backgrounds from several departments. During the first year, students will acquire sufficient background in biological sciences, including biochemistry, molecular biology, cell biology, pharmacology, microbiology and immunology. The students will have the opportunity to rotate in research laboratories in any department prior to selecting their thesis advisors. Students will take two discipline specific courses. They will be able to select additional elective courses from any department based on their needs and interests. PhD students are admitted to candidacy after successful completion of their preliminary oral qualifying examinations and defense of an NIH-style research grant proposal. MS students are expected to graduate in 2 years whereas PhD students usually require 5 years to complete their degree.

2. Graduate Faculty and Research Interests

Faculty and Position	Research Interests
Riyaz M. Basha, Ph.D. Associate Professor Pediatrics/Institute for Molecular Medicine	Dr. Basha's research is in the area of experimental therapeutics. The aberrant expression of certain molecular markers is associated with aggressive disease and poor prognosis in a variety of human malignancies. His lab is working on targeting such candidates, such as c-Met (a receptor for hepatocyte growth factor), Survivin (an inhibitor of apoptosis protein) and Specificity protein 1 (Sp1) transcription factor for enhancing therapeutic efficacy in cancer. Investigational new drugs that have the ability to target these candidates are being screened for developing novel therapeutic strategies. Small molecules such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) have been widely tested in cancer therapy and prevention. NSAIDs' response is typically mediated via cyclooxygenase (COX)-dependent pathways. Recent data identified a NSAID, Tolfenamic Acid (TA), which acts through the COX-independent mechanisms and causes higher efficacy and minimum side-effects (toxicity) in pre-clinical models for some human cancers. TA targets Sp transcription factors that play critical role(s) in the growth and metastasis of cancers. Sp proteins also regulate the expression of Survivin and c-Met which are associated with resistance to chemo- and radiation therapies and impact the disease prognosis. The current research is focused on developing strategies to improve therapeutic efficacy in leukemia, medulloblastoma, neuroblastoma, ovarian, pancreatic and solid tumors using preclinical models and clinical specimens. The combination of investigational agents that targets Sp proteins and other critical markers are being tested to enhance the efficacy of standard treatment options. In addition, the combination therapies using TA and analogs; nifurtimox (reactive oxygen species inducer) and curcumin analogs ae being investigated. Experiments will be conducted for understanding the potential molecular pathways associated with the proposed combinations. These investigational findings are crucial towards developing novel strategies for treating human cancers.
Alakananda Basu, Ph.D. Professor Institute for Molecular Medicine Graduate advisor, Biochemistry & Cancer Biology	Dr. Basu's research is in signal transduction, especially in the context of cancer chemotherapy. Since an ability of cancer cells to evade cell death contributes to cancer and resistance to chemotherapeutic drugs, a major research effort is to investigate how signal transduction pathways regulate cell survival and cell death. She has been studying how various signaling pathways, such as protein kinase C, Akt, mTOR/S6 kinase (S6K) and mitogen-activated protein kinases regulate apoptosis, a genetically programmed cell death and autophagy, a process by which a cell recycles its own components to survive under stressful or nutrient-derived conditions. Three-dimensional cell culture model is being used

to dissect the role of various signaling pathways in breast cancer. Another area of her research is to investigate how signal transduction pathways, such as PKC, AMP kinase, Akt and mTOR/S6K regulate anticancer drug sensitivity and to elucidate the molecular mechanism(s) of drug resistance. The ultimate goal of her research is to identify novel targets for cancer therapy, exploit intracellular signaling systems to develop innovative strategies to treat cancer and identify potential biomarkers to predict patient response to cancer therapy.

Julian Borejdo, Ph.D.
Professor
Institute for Molecular Medicine

The goal of Dr. Borejdo's research is to identify kinetic defects in heart muscle of patients suffering from Familial Cardiac Hypertrophy. He studies kinetics of the interaction at the level of a single molecule. This avoids averaging, which occurs when a large ensemble of molecules are studied by classical methods. He uses polarized fluorescence as a signal - fluorescence is the only signal with enough sensitivity to report behavior of single molecules. Dr Borejdo's lab studies autocorrelation of the polarized fluorescence rather than signal itself. This has the advantage that autofluorescence is greatly diminished.

David Cistola, M.D., Ph.D.
Adjunct faculty
Institute for Cardiovascular & Metabolic Diseases

Dr. Cistola's laboratory is developing new biomarkers based on the properties of biological nanoparticles, particularly the cholesterol-carrying lipoproteins in human blood. His laboratory is translating biophysical methods, such as benchtop time-domain NMR and dynamic light scattering, into the clinical diagnostic setting.

Ranajit Chakraborty, Ph.D.
Professor
Institute for Molecular Medicine

Cancer is basically a cellular disease whose hallmarks include cellular defects initiated by genetic mechanisms. Though family history (and hence likely genetic factors) has been recognized as a significant risk factor for cancer susceptibility and cancer progression, genes involved in cancer are varied, and they are not necessarily the same ones for all site specific cancers. Furthermore, interaction of genetic and life style/environmental risk factors also contribute to initiation of carcinogenesis and cancer progression. Since mid 1980s, Dr. Chakraborty has been involved in various fields of research related to biology and genetic epidemiology of cancer addressing these issues. His publications in this field include: design and conduct of large-scale epidemiologic studies of cancer prevalence and its risk factors, disease-gene association of various site specific cancers, biomarker development for early detection of cancer, modeling inter-individual variation of radiation sensitivity and studying its impact on the risk of development of subsequent cancers after radiation exposure through treatment and/or screening of patients, and understanding the basis of epigenetic changes in relation to traditional exposure to environmental and life style risk factors of cancers. Of his over 550 publications, more than 24 relate to cancer-related research. Currently Dr. Chakraborty's cancer-related research involves characterization of DNA repair genes and

	polymorphisms in different DNA repair pathway genes that contribute to cancer risk with as well as without the presence of environmental or life style risk factors of cancer. In particular, inter-individual variability of radiation sensitivity and effects of therapeutic and/or disease-screening use of radiation in development of cancer has a high priority in his research on cancer biology. Through his continuing involvement in committees of International Commission of Radiological Protection (ICRP) and US National Radiological Protection (NCRP), he brings into this Graduate Program current issues of translational importance of biological and genetic studies of cancer.
YiQiang "Eric" Cheng, Ph.D. Professor Pharmaceutical Sciences	The long-term goal of Dr. Cheng's research is to discover and develop bioactive natural products as drugs or drug leads in the area of oncology and infectious disease. He has been studying the genetics and biochemistry of natural product biosynthesis. In recent years, he redefined his research to focus on discovery of new natural products from underappreciated microbial sources. To this end, his laboratory has discovered a series of potent histone deacetylase inhibitors and pre-mRNA splicing inhibitors. He has forged collaborations with cancer biologists to evaluate some of those small molecules in tumor xenograft models, including neuroendocrine cancer, breast cancer, colon caner, prostate cancer, glaucoma, leukemia and neuroblastoma.
Abbot Clark, Ph.D., FARVO Professor & Executive Director North Texas Eye Research Institute	Dr. Clark's research focuses on understanding the molecular, biochemical, and cellular mechanisms involved in ocular pathology, especially the blinding eye disease glaucoma. His lab utilizes molecular genetics, molecular & biochemical methods, cell culture, *ex vivo* and *in vivo* models to discover and validate pathogenic pathways responsible for ocular diseases.
Hriday Das, Ph.D. Professor Center for Neuroscience Discovery	The long-term goal of Dr. Das' research is to develop cost-effective clinically-useful drug therapies for the treatment of neurodegenerative diseases. Presenilin-1 (PS1) is a transmembrane protein which functions as ER Ca2+ leak channel and is the catalytic subunit of the PS1/γ-secretase complex. PS1/γ-secretase is involved in the proteolytic processing of type 1 membrane proteins including amyloid precursor protein (APP) and Notch-1 receptor. Mutations of the PS1 gene cause early-onset familial Alzheimer's disease by altering PS1/γ-secretase mediated processing of APP. Same pathogenic mutations of the PS1 gene also potentiate IP3R-mediated Ca2+ liberation from ER to cytoplasm. Transcriptional regulation of the PS1 gene appears to modulate both PS1/γ-secretase activity and ER Ca2+ leak channel. His laboratory has shown that PS1 expression can be regulated by the JNK signal transduction pathway involving tumor suppressor protein p53. One goal of this research is to understand how wild type p53 and cancer causing mutations of

p53 differentially regulate the processing of APP and Notch1 as well as PS1-mediated ER Ca2+ leak channel. Another goal is to test the hypothesis that JNK and mTOR inhibitors prevent neuronal cell death by inhibiting PS1 transcription and PS1-mediated ERCa2+ leak channel activity. He is also studying how regulation of PS1 may control cell growth and proliferation via Erb4, a transmembrane receptor tyrosine kinase that regulates cell proliferation and differentiation.

Ladislav Dory, Ph.D.
Professor
Institute for Cardiovascular & Metabolic Diseases

Dr. Dory's research is primarily focused in the area of atherosclerosis, specifically reverse cholesterol transport and apolipoprotein E metabolism. He participated in the pioneering work of characterizing interstitial fluid lipoproteins, peripheral HDL formation and was the first to demonstrate, *in vivo*, the synthesis of apoE by peripheral (non-hepatic) tissues, as part of cholesterol efflux and HDL formation. He also pioneered work on the effects of hyperbaric oxygen on the development and regression of atherosclerosis in animal models and discovered a new allele for murine form of extracellular superoxide dismutase. His present work is aimed at elucidating the role of ecSOD in various diseases, including bacterial infection, asbestosis and irritable bowel disease and colon cancer.

Rafal Fudala, Ph.D.
Instructor
Cell Biology & Immunology

Dr Fudala in his current ongoing studies is using fluorescence-based methods such as: laser confocal microscopy, fluorescence resonance energy transfer (FRET), fluorescence lifetime imaging microscopy (FLIM), and cellular imaging as well as polarization-based techniques. Recently, Dr Fudala's interests have expanded to include fluorescence-based methods in biology and cellular imaging, as well as biological/biophysical applications of new nanophotonics processes and single molecule studies in the biomedical and diagnostic fields, especially for early malignant melanoma detection.

Anuja Ghorpade, Ph.D.
Professor, Interim Vice President of Research
Institute for Molecular Medicine

The research in Dr. Ghorpade's laboratory focuses on the inter- and intra-cellular signaling mechanisms implicated in inflammation, HIV-1 and other neural injury. Cytokines, including [tumor necrosis factor (TNF)-α, interleukin (IL)-1α, IL-1β, IL-6, and tumor growth factor (TGF)-β1], have all been associated with both HIV-1-associated dementia (HAD) and are implicated in a variety of cancers. Thus, inflammation that begins with the injury in the brain, is amplified through interactions with other neural cells, will likely serve as a model for better understanding of a variety of diseases. More specifically, several distinct pathways are currently under investigation. These include, but are not be limited to, role of matrix metalloproteinases and their tissue inhibitors, other chemokines such as CXCL8 and CCL2, molecules upregulated in activated astrocytes such as CD38 and molecules that are involved in microglial infection and activation. We believe that

	the role of signaling molecules such as NF-kB, STAT3, SHP-2, all implicated in both inflammation and cancer biology will improve our understanding of the cellular mechanisms involved in neural injury and also facilitate our understanding of the mechanisms involved in brain tumors.
Eric B. Gonzales, Ph.D. Assistant Professor Center for Neuroscience Discovery	Dr. Gonzales's laboratory is focused on the relationship of structure and function of proteins important in disease, including cancer. To understand the role each plays in disease, we are focused on solving these biologically important protein structures to atomic resolution, using protein crystallography and x-ray diffraction studies. Our work will provide a template for developing novel therapies and understanding disease states when these proteins mutate and elicit their deleterious effects. We have initiated collaboration with Dr. Hriday Das to determine the crystal structure of a MYM gene family member, a ZNF protein. Members of the MYM gene family may contribute to myeloproliferative neoplasm, which is associated with thrombocythemia, primary myelofibrosis, and chronic myeloid leukemia. To our knowledge, the structure of the ZNF protein has not been determined. Solving a crystal structure of any protein is a daunting task. However, we will use fluorescence detection size exclusion chromatography, or FSEC, to identify suitable protein constructs and purification conditions, to solve the structure of a MYM gene family protein.
Ignacy Gryczynski, Ph.D. Professor Institute for Molecular Medicine	Dr. Ignacy Gryczynski's research is focused on fluorescence spectroscopy and its applications in biochemistry and biology. Fluorescence spectroscopy and microscopy progressed recently towards nanotechnology. The technological advances in optics, computers, surface science and engineering made possible single molecule detection and overcame the diffraction limit. His laboratory is working on fluorescence enhancements near metallic surfaces and particles. The enhanced fluorescence is being applied to sensing devices and bioassays. He co-manages the time-resolved fluorescence laboratory, which carries basic spectroscopy research and is open to the needs of researchers from other departments.
Zygmunt "Karol" Gryczynski, Ph.D. Professor Institute for Molecular Medicine	Dr. Zygmunt Gryczynski and his colleagues have established a Center for Commercialization of Fluorescence Technologies (CCFT) with support from Emerging Technology Funds (EFT) of Texas. His early work at the University of Maryland was focused on ultrafast time-resolved fluorescence spectroscopy, intrinsic fluorescence of hemoproteins as well as the thermodynamics of ligand binding and the allosteric mechanism of O_2 binding in hemoproteins. He has pioneered the use of multi-photon excitation and light quenching in time-resolved fluorescence spectroscopy. His focus has been on applications of fluorescence spectroscopy to study biological systems using time-resolved fluorescence, anisotropy, and FRET. He also pioneered novel fluorescence sensing methods for biomedical applications in tissue and blood. His interest includes modern optical imaging methods with focus on

fluorescence microscopy. For the last six years his interests expanded to nanotechnology and applications of novel plasmonic effects induced by light in metallic nanostructures to fluorescence spectroscopy. He pioneered metal enhanced fluorescence and surface plasmons coupled emission phenomena for biomedical and diagnostics application. His current focus is to explore quantum-level interactions to study the dynamics of biophysical and biochemical processes at the molecular level.

Johnny He, Ph.D.
Professor, Associate Dean GSBS
Institute for Molecular Medicine

Dr. He's lab cloned Tip110, which stands for HIV-1 Tat-Interacting Protein of 110 kDa and was also known as squamous cell carcinoma antigen recognized by T cells 3 (SART3). Since then, studies from his group have attributed several functions to this protein, including regulation of gene transcription, pre-mRNA splicing, stem cell biology, and tumor immunology. Since Tip110 expression is low in non-dividing cells and normal tissues and is highly elevated in a variety of human cancers, his lab has stipulated and obtained several lines of evidence to support its involvement in tumorigenesis. Tip110 regulates homeostasis of several cancer-related proteins including p53, c-Myc, and others. To understand the biological functions of Tip110 and their underlying molecular mechanisms, Dr. He's lab has created several lines of genetically modified Tip110 mice including three lines of Tip110 transgenic mice (Tip110-Tg A, B, and C), Tip110 knock-down mice (Tip110-KD), and Tip110 conditional knock-out mice ($Tip110^{flox/flox}$). These studies are expected to advance our understanding of Tip110 protein and likely to provide clues for therapeutic development for human cancers.

Lisa Hodge, Ph.D.
Associate Professor
Institute for Cardiovascular & Metabolic Diseases

Breast cancer and breast cancer treatment can often result in secondary lymphedema. Currently, there are no effective pharmaceutical agents to relieve lymphedema; however, treatments such as manual lymph drainage, decongestive lymph therapy and lymphatic/pneumatic pump treatments have been shown to relieve the symptoms of secondary lymphedema. While these treatments may offer relief to patients suffering from lymph edema, many manual medicine therapists are reluctant to perform these techniques on patients with cancer, for fear of promoting metastasis through the lymphatic system. Dr. Hodge's lab has demonstrated that lymphatic therapies have diverse effects depending on the location of the primary tumor. These studies will significantly enhance our understanding of the role of the lymphatic system during solid tumor growth and metastasis. Most importantly, we will determine if the location and metastatic potential of a solid tumor is a factor that should be considered when advocating the use of lymph enhancing or manual medicine therapies in patients with cancer.

Harlan Jones, Ph.D.
Associate Professor
Institute for Molecular Medicine

There is increasing evidence that psychological stress is an important risk factor in the initiation and progression of chronic disease (e.g. cancer, atherosclerosis, and chronic infectious

Director, Center for Institutional Diversity	disease). Dr. Jones' research interest include the investigation of how stress affects host immune mediation of chronic disease states with the intention of facilitating comprehensive therapeutic approaches against stress-induced disease pathogenesis.
Andras Lacko, Ph.D. Professor Institute for Cardiovascular & Metabolic Diseases	Delivery of anti-cancer drugs to cancer cells and tumors, and currently working on a targeted drug delivery system utilizing reconstituted high-density lipoproteins. Dr. Lacko's lab developed a robust, targeted drug delivery system that has proven particularly effective against cancer cells and tumors. This delivery utilized biocompatible nanoparticles (rHDL) that are built from natural blood components that normally comprise high-density lipoproteins (the good cholesterol carrier). Paclitaxel is 5-20 times more effective than the free drug against cancer cells when delivered via the rHDL nanoparticles. Similarly, the rHDL nanoparticles enhanced the cytotoxicity of valrubicin (AD-32) against cancer cells while the encapsulation of the drug protected the non-malignant (normal) cells against toxic side effects. The selective delivery of anti-cancer agents to tumors was also demonstrated in a mouse model where the drug loaded rHDL nanoparticles were able to induce >80% tumor ablation, a five fold increase in apoptosis and three fold decrease in tumor angiogenesis. This work is now proceeding in three directions towards the translational developments of these findings to allow their utilization at the bedside.
Porunelloor Mathew, Ph.D. Associate Professor Institute for Molecular Medicine	Dr. Mathew's research is in the area of Cancer Immunology. Natural killer (NK) cells are a subpopulation of lymphocytes that play an important role again tumor metastasis and various viral and bacterial infections. NK cells are also involved in the rejection of allogeneic bone marrow transplants. The molecular basis of NK cell recognition and activation by target cells is poorly understood. NK cell functions are controlled by a balance between positive and negative signals through various receptors. We have identified, cloned and characterized several receptors expressed on NK cells. One of the receptors, 2B4 (CD244), is a member of the immunoglobulin superfamily and is involved in killing cancer cells and virus-infected cells by NK cells. We have determined CD48 as the counter-receptor for 2B4 in both mice and humans. Recently, we have generated 2B4 knockout mice and this will allow us to study the biology of this molecule in the immune system. We are investigating the signal transduction pathway via 2B4. We have also identified two other novel receptors called LLT1 and CS1 (CD319). The functional role of LLT1 and CS1 in regulating immune responses is being investigated. CS1 is overexpressed in multiple myeloma and a humanized monoclonal antibody against CS1 (HuLuc63 or Elotuzumab) is in clinical trial against multiple myeloma. The major objective of Dr. Mathew's laboratory is to decipher the molecular basis of tumor cell recognition by NK cells. The information obtained in these studies will be utilized towards developing new strategies

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Stephen Mathew, Ph.D.
Assistant Professor
Institute for Molecular Medicine

Dr. Stephen Mathew's research focuses on developing molecular immunological strategies against diseases like cancer, HIV and lupus. Natural killer (NK) cells are cells of the immune system that form the first line of defense against cancer and infectious diseases. The research in our laboratory is focused towards unraveling the molecular basis of tumor cell recognition by NK cell and its multiple receptor ligand interactions. Specifically, in collaboration with pediatric oncologists and epidemiologists, we are investigating the role of immune receptors and DNA methylation in acute lymphoblastic leukemia (ALL) in children. This will provide important insights into the etiology of childhood leukemia as well as the development of new treatments that may improve the outcome of children with leukemia by modifying the function of immune cells and the methylation profile of these patients. The other projects in the laboratory deal with deciphering the role of immune receptors 2B4, CS1 and LLT1 in prostate cancer, breast cancer, lupus and HIV.

Laszlo Prokai, Ph.D.
Professor
Center for Neuroscience Discovery
Robert A. Welch Chair in Biochemistry

Dr. Prokai is recognized nationally and internationally for his work on discovery, bio-organic and medicinal chemistry of central nervous system agents, as well as on neuropeptides, proteomics and mass spectrometry. His cancer research interests focus on (i) prevention of estrogen-related malignancies associated with hormone therapy by discovering and developing compounds with improved safety and selectivity compared to current estrogen products, and (ii) proteomic assessment of (a) the impact of oxidative stress in cancer and during chemotherapy, and (b) signaling events associated with cancer. Other interests include combinatorial and rational drug discovery, brain- and eye-targeted drug therapy, the role of oxidative stress and posttranslational protein modifications in health and disease, neurosteroids and metabolomics.

Amalendu Ranjan, Ph.D.
Research Assistant Professor
Institute for Molecular Medicine

Dr. Ranjan's research interest is primarily formulation and evaluation of nanotechnology based therapeutics/ theranostics for cancer therapy. He is a biochemical/biomedical engineer trained in the fields of nanotechnology, drug delivery, modeling, optimization and scale up of nanoparticle formulation. He uses biodegradable and biocompatible polymeric or lipo-polymeric nanoparticles with the ability to tailor the release kinetics of drugs from these nanoparticles. We have encapsulated various types of hydrophobic, hydrophilic and small molecule drugs for nanoparticles in cancer. His research also comprises of gene delivery via nanoparticles. This platform may be used for

designing theranostic agents where in a dye can be encapsulated along with a drug and later tracked in vivo for imaging and evaluated for therapy. All such technologies may find use in imaging and therapy of cancer, cardiovascular and neurodegenerative diseases. His research specialization includes optimization and scale-up of these nanotherapeutics/theranostics for making large batches for pre clinical studies.

Sangram Raut

Meharvan Singh, Ph.D.
Professor
Center for Neuroscience Discovery
Dean, GSBS

The research interests of my laboratory relates to understanding and characterizing novel mechanisms by which gonadal steroids, including androgens, elicit their effects. Within this context, we have recently described a novel membrane androgen receptor that is associated with the promotion of cell death. Our data, therefore, suggest that within a given cell type, there may be two competing pathways by which androgens elicit their effects: one that promotes cell survival (through the classical androgen receptor), and the other that promotes cell death (through activation of the membrane androgen receptor). Thus, we argue that androgens may exacerbate the growth of certain androgen-sensitive tissues or cancers depending on the relative abundance of the two receptor mechanisms. As such, we believe that the more complete characterization of the membrane androgen receptor may be valuable in defining a novel cellular target that can be exploited for the development of safer and more effective treatments for androgen-sensitive neoplasms (such as prostate cancer).

Dong Ming Su, Ph.D.
Professor
Institute for Molecular Medicine

Dr. Su's research focuses on T cell immune system aging, which reduces immunosurveillance and promotes cancer development. One of Dr. Su's projects is to determine how the thymus, particularly atrophied aged thymus, plays a role as a reservoir (shelter) for tumor cell resistance of chemoradiotherapy, and mechanisms responsible for tumor dormancy and metastatic relapse associated with immune system microenvironment. Currently, the survival rates of cancer patients have markedly improved with earlier detection and advancements in therapy. However, many cancer patients, particularly breast cancer, lymphoma, prostate cancer, and melanoma patients, still suffer from metastatic relapse upon several years. This recurrence is the major cause of cancer death. Evidence shows that tumor cells move to secondary sites throughout the body and hide in certain organs, where they acquire chemo-resistance and stem cell-like properties to form dormant tumors obtaining the potential for metastatic relapse. Lymphoid system and lymph-nodes are a common route and reservoir for tumor cell transferring throughout the body and becoming dormancy. Whether the largest "lymph node" in the body, the thymus, is a potential pre-metastatic niche for tumor cell shelter and dormancy is largely unknown. Therefore, our project is to determine how different conditions in the thymus (normal or injured, young or old) provides a

	hospitable environment to induce tumor dormancy for subsequent recurrence, and to explore a novel strategy to kill dormant tumor cells in the thymus by waking up the “sleeping” tumor cells and then applying a second round of chemotherapy. The signaling pathway work (How the thymic microenvironment promotes tumor cell signaling changes) in this project is collaborative with Dr. Alakananda Basu.
Jamboor Vishwanatha, Ph.D. Professor Institute for Molecular Medicine Vice-president, Health Disparity	Dr. Vishwanatha’s research is in cancer molecular biology and experimental therapeutics. His laboratory has established the role of Annexin A2 in ECM degradation and angiogenesis. They identified the function of a novel gene C17orf37 in cancer cell migration and invasion that resulted in a new nomenclature of the gene as MIEN1 (Migration and Invasion Enhancer 1). Their current studies have established Annexin A2 as a novel biomarker for triple negative breast cancer. In other projects, his laboratory has developed sustained release polymeric nanoparticles for targeted delivery of biologicals for cancer therapy. 2) Prostate cancer, molecular markers for progression of oral dysplasia, biological response modifiers, nanoparticle mediated gene delivery.
Hongli Wu, Ph.D. Assistant Professor Pharmaceutical Sciences	The central theme of Dr. Wu’s research is to understand the role of oxidative stress defense enzymes in age-related eye diseases. He also investigates natural product-derived antioxidants that may serve as leads for the development of new pharmaceutical products that may eventually cure age-related eye diseases.
Shaohua Yang, Ph.D. Professor Center for Neuroscience Discovery	Estrogen receptors (ERs) are believed to be ligand-activated transcription factors belonging to the nuclear receptor superfamily, which upon ligan binding translocate into nucleus and activate gene transcription. To date, two ERs have been identified: estrogen receptor alpha (ERalpha) and estrogen receptor beta (ERbeta). ERalpha plays a major role in the estrogen-mediated genomic actions in both reproductive and non-reproductive tissue, while the function of ERbeta is still unclear. We and other laboratories recently demonstrated the localization off ERbeta in mitochondria, suggesting the involvement of ERbeta in mitochondria function. Down regulation of ERbeta in various cancer has been well demonstrated, suggesting the anti-cancer property of ERbeta. My current research interests are to determine the mechanism underlying the ERbeta’s anti-cancer effect, with a focus on mitochondrial function.

3. Course Offerings

Core Courses:

BMSC 6201 Fundamentals of Biomedical Sciences 1

BMSC 6202 Fundamentals of Biomedical Sciences 2

BMSC 6203 Fundamentals of Biomedical Sciences 3 Genetics

BMSC 6204 Fundamentals of Biomedical Sciences 4

BMSC 6300 Scientific Writing

Advanced Courses (6 - 8 SCH):

MMED 6202 Advanced Molecular Biology: Techniques and Principles: offered every other fall (even years)

MMED 6220 Cellular and Molecular Fluorescence: offered each fall

MMED 6250 Molecular and Cell Biology of Cancer: offered each spring

PHRM 6270 Drug Discovery & Design: offered each fall

MMED 6435 Receptors and Second Messenger Signaling: offered every other fall (odd years)

MMED 6436 Kinases and Phosphatases: offered every other fall (odd years)

Elective/Methods Courses:

MMED 5150 Introduction to Flow Cytometry

MMED 5201 Bioimaging

MMED 5202 Introduction to Confocal Microscopy

PHRM 6361 Biomedical Mass Spectrometry: offered every other spring (odd years)

MMED 6360 Advanced Biophysics and Biochemical Methods, offered every other Spring

NTER 6440 Methods in Molecular Biology

MMED 6303 Statistical Genetics (Offered every other spring, odd years)

Journal Clubs/Current Topics: Students are required to register for Journal clubs and/or Current topics courses each semester.

MMED 5140 Seminars in Current Topics

MMED 5121 Seminar in Cell Motility: offered each fall and spring

MMED 5210 Signal Transduction: offered each fall and spring

PHRM 6140 Current Topics in Pharmacology

4. Discipline policies

4.1. Laboratory Rotations: The students will interview (informal) with the faculty members within two to three weeks of orientation to set up 2 laboratory rotations before deciding on a major professor.

4.2. Selection of Advisory Committee: Once a student decides on the major professor, s/he should form an advisory committee and file with the graduate office by the end of the first semester. The major professor serves as the chair of the advisory committee and assists the student in selecting faculty members to serve on the committee. A committee should include at least two (Master's) or three (Ph.D.) graduate faculty members besides the major professor.

4.3. University member: Once the advisory committee is formed, the graduate dean will appoint the University member who ensures that the policies and procedures of the Graduate School of Biomedical Sciences and UNT Health Science Center have been upheld. The university member must be present at all formal hearings that require a vote.

4.4. Committee Meeting: The students will meet with their advisory committee at least once every academic year.

4.5. Degree plan: The students should consult with the major professor to prepare a degree plan listing all courses. The degree plan must be approved by the advisory committee and the graduate advisor, and filed with the graduate office before completion of 30 SCH.

4.6. Seminar and Grand Round: Seminars are important part of our graduate program. Students are expected to attend departmental seminars and Grand Round.

4.7. Work-in-Progress Seminar: Students will present their research annually at the Work in Progress (WIP) seminar. Faculty members are expected to provide specific critiques/evaluations of the presentations in order to assist the students with their presentation skills.

4.8. Research Appreciation Day (RAD): All students are required to present their research annually at UNTHSC Research Appreciation Day (RAD).

4.9. Scientific meetings/Conferences: Students are encouraged to present their research at relevant scientific meetings/conferences.

4.10. Advancement to Candidacy: All doctoral students are required to compete a two-step process to be advanced to candidacy.

Step 1: Students will have to successfully complete their oral qualifying examination.
Step 2: Students will have to submit a research proposal.

4.10.1 Oral Qualifying Examination:

Purpose: This qualifying examination is to ensure that a doctoral student has sufficient mastery of fundamental principles of biomedical sciences to be successful as a Ph.D. candidate and independent researcher. Students should take the Oral Qualifying Exam (OQE) before they complete 72 SCH. Students are required to pass this examination before they can submit their research proposal.

Specifics:

i. The comprehensive examination will be scheduled at the end of 1st year following completion of the core courses.

ii. A four-member committee will be formed, and 3 out of 4 will be needed for approval. The exam will be open to any program faculty who is willing to serve in the exam committee. S/he will have to notify the graduate advisor prior to the exam so that the student, university member and the committee members are aware of the presence of additional faculty members. S/he may be required to submit questions for the exam and will have the right to vote. The major professor will not have voting rights.

iii. The topics of the examination will be based on the core courses and discipline-specific advanced courses.

iv. The length of the examination will be approximately 2 h. The student will be given the question set an hour prior to the oral examination. The questions should be answerable in approximately 15 min so that the students can be tested in all of the defined areas. The students will be required to answer 6 out of 12 questions. The students will have to select at least two questions from different categories.

v. Upon completion of the examination, the faculty will vote on a pass/fail grade for the student. At least 75% favorable vote will be required for the student to successfully pass. The entire committee should approve for distinction. If a student does not pass, the faculty will inform the student of specific areas of weakness in writing.

vi. If necessary, a student will be allowed to retake the oral qualifying examination once but this must be completed before the end of the following semester. Failure on the second attempt will result in dismissal from the doctoral program, although the student will be permitted to pursue a Master of Science degree.

vii. It is the responsibility of the student to obtain signatures from the Examination Committee Chair, Graduate Advisor, University Member and Department Chair on completion of the examination. The appropriate form may be obtained from the graduate school website.

viii. An evaluation document has been developed by the graduate school in order to provide students feedback on their oral qualifying exam and to ensure that the students have demonstrated the appropriate knowledge required for advancement to candidacy.

4.10.2. Research Proposal

All students are required to submit a research proposal no later than the end of the third year. The proposal should be based on the dissertation project and include a summary of the project, problem/hypothesis, significance of the project, background, research design and methodology. The student must meet with the advisory committee and see their guidance before preparing the research proposal. The research proposal must be approved by the advisory committee and the dean prior to registration for doctoral dissertation (BMSC 6950). Research proposal guidelines and the research proposal approval form are available on the GSBS Forms and Guidelines website.

4.11. Dissertation: The Advisory committee follows the progress of the students. The students are required to submit a copy of the dissertation to the members of advisory committee at least two weeks prior to the defense. A graduating doctoral student must have at least one first-author research article published (or in press) from their dissertation research in a peer-reviewed journal at the time of defense. Students having more than one article are permitted to file a non-traditional dissertation where the published articles constitute individual chapters. A formal public seminar of the dissertation research followed by an oral defense of the thesis to the advisory committee will constitute the final exam.

5. Tentative time-line at a glance:

Year 1, Fall:

-Core courses
- Lab rotation
- Select a major professor

Year 1, Spring/Summer:

- Form an advisory committee
- Assignment of University Member
- Submit a degree plan

Year 1, Summer: Oral Qualifying Exam

Year 2, Fall/Spring:

- Fulfill advanced course requirements
- Journal club/seminar

Year 3, Fall: Research Proposal

Year 5: Thesis Defense

6. Degree Plan

6.1. M.S. Degree plan for Biochemistry and Cancer Biology

Year 1: Fall

BMSC 6201	Fundamentals of BMSC 1	2 SCH
BMSC 6202	Fundamentals of BMSC 2	2 SCH
BMSC 6203	Fundamentals of BMSC 3	2 SCH
BMSC 6204	Fundamentals of BMSC 4	2 SCH
BMSC 5150	Laboratory Rotation	1 SCH
BMSC 5150	Laboratory Rotation	1 SCH
BMSC 6200	Experimental Design and Biostatistics	2 SCH
		12 SCH

Year 1: Spring

BMSC 5160	Biomedical Ethics	1 SCH
BMSC 5315	Principles of Scientific Communications	2 SCH
	Advanced course	2-4 SCH
	Journal Club/Current Topics	1-2 SCH
BMSC 5998	Individual Research for MS Students	2-6 SCH
		9-12 SCH

Year 1: Summer

BMSC 6100	Scientific Communication Competencies	1 SCH
BMSC 5998	Individual Research for MS Students	1-5 SCH
		6 SCH

Year 2: Fall

BMSC 5998	Individual Research for MS Students	3-6 SCH
	Advanced course/Elective course*	2-4 SCH
	Journal Club/Current Topics**	1-2 SCH
		9 SCH

Year 2: Spring

BMSC 5998	Individual Research for MS Students	3 SCH
BMSC 5395	Thesis	3 SCH
		6 SCH

Total minimum credit hours required for MS degree **30 SCH**

6.2. Ph.D. Degree plan for Biochemistry and Cancer Biology

Year 1: Fall		
BMSC 6201	Fundamentals of BMSC 1	2 SCH
BMSC 6202	Fundamentals of BMSC 2	2 SCH
BMSC 6203	Fundamentals of BMSC 3	2 SCH
BMSC 6204	Fundamentals of BMSC 4	2 SCH
BMSC 5150	Laboratory Rotation	1 SCH
BMSC 5150	Laboratory Rotation	1 SCH
BMSC 6200	Experimental Design and Biostatistics	2 SCH
		12 SCH
Year 1: Spring		
BMSC 5160	Biomedical Ethics	1 SCH
BMSC 5315	Principles of Scientific Communications	2 SCH
	Advanced course	2-4 SCH
	Journal Club/Current Topics	1-2 SCH
BMSC 6998	Individual Research	3-6 SCH
		12 SCH
Year 1: Summer		
BMSC 6100	Scientific Communication Competencies	1 SCH
BMSC 5998	Individual Research for MS Students	1-5 SCH
		6 SCH
Year 2: Fall		
BMSC 6998	Individual Research	4-9 SCH
	Advanced course	2-6 SCH
	Journal Club/Current Topics	1-2 SCH
		12 SCH
Year 2: Spring		
BMSC 6998	Individual Research	1-11 SCH
	Advanced course/Electives	2-4 SCH
	Journal Club/Current Topics	1-2 SCH
		12 SCH
Year 2: Summer		
BMSC 6100	Scientific Communication Competencies	1 SCH
BMSC 6998	Individual Research	1-5 SCH
		6 SCH
Year 3: Fall		
BMSC 6998	Individual Research	1-8 SCH
	Advanced course/Electives	0-4 SCH
	Journal Club/Current Topics	1-2 SCH
		9 SCH
Year 3: Spring		
BMSC 6998	Doctoral dissertation	1-8 SCH
	Journal Club/Current Topics	1-2 SCH
		9 SCH
Year 3: Summer		
BMSC 6100	Scientific Communication Competencies	1 SCH
BMSC 6998	Doctoral dissertation	1-6 SCH
		6 SCH
Year 4: Fall		
BMSC 6998	Doctoral Dissertation	1-8 SCH
	Journal Club/Current Topics	1-2 SCH
		9 SCH
Total		**93 SCH**

7. Contacts in Situations of Uncertainty or Emergency

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