



**GRADUATE SCHOOL OF BIOMEDICAL SCIENCES**

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**DEPARTMENT OF MOLECULAR AND MEDICAL GENETICS**

***BIOCHEMISTRY AND CANCER BIOLOGY  
GRADUATE PROGRAM  
STUDENT HANDBOOK  
2014-2015***

**Alakananda Basu, Ph.D.  
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, nanotechnology/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 faculty advisors 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

**Riyaz M. Basha, Ph.D.**  
Associate Professor  
Pediatrics/ Molecular & Medical  
Genetics

### Research Interests

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 are 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  
Molecular & Medical Genetics  
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  
Cell Biology & Immunology

The goal of Dr. Borejdo's research is to identify kinetic defects in heart muscle 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 - the only signal with enough sensitivity to report behavior of single molecules. Dr Borejdo's lab uses two approaches to this problem; the first is to study autocorrelation of the polarized fluorescence rather than signal itself. This has the advantage that autofluorescence is greatly diminished. The second approach is to visualize polarized fluorescence by high-sensitivity video camera. This is more difficult, but is conceptually simple.

**David Cistola, M.D., Ph.D.**

Professor and Vice President for Research  
Integrative Physiology and Anatomy

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  
Molecular & Medical Genetics

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 Science

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 cancer, prostate cancer, glaucoma, leukemia and neuroblastoma.

**Abe Clark, Ph.D.**  
Professor

Dr. Clark's research focuses on understanding the molecular, biochemical, and cellular mechanisms involved

Cell Biology & Immunology

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.

**Hirday Das, Ph.D.**

Professor

Pharmacology & Neuroscience

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 Ca<sup>2+</sup> leak channel and is the catalytic subunit of the PS1/ $\gamma$ -secretase complex. PS1/ $\gamma$ -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/ $\gamma$ -secretase mediated processing of APP. Same pathogenic mutations of the PS1 gene also potentiate IP3R-mediated Ca<sup>2+</sup> liberation from ER to cytoplasm. Transcriptional regulation of the PS1 gene appears to modulate both PS1/ $\gamma$ -secretase activity and ER Ca<sup>2+</sup> 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 Ca<sup>2+</sup> 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 ER Ca<sup>2+</sup> 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.

**Dan Dimitrijevic, Ph.D.**

Adjunct Research Associate

Professor

Integrative Physiology &  
Anatomy

Dr. Dimitrijevic's laboratory is interested in Tissue Engineering with particular emphasis on the control of proliferation and differentiation of normal human epithelial cells. The goal is to extend proliferation without initiating cancerous phenotype. To date his lab has employed ectopic expression of human telomerase reverse transcriptase for this purpose and are also studying 14-3-3 proteins in this context. Both have resulted in generation of several cell lines with extended life span, but intact p53 and pRb expression. Another goal is to delay differentiation of epithelial cells. This is a more difficult task to accomplish as the early events in initiation of differentiation are not well understood. Since most of

the human cancers are of epithelial cell origin, understanding epithelial cell proliferation and early differentiation signals are also important in cancer where the proliferation is uncontrolled and differentiation is inhibited. Because telomere maintenance is a global mechanism, involving vast majority of somatic cells, our interests in 14-3-3 proteins is related to the possibility of studying epithelia cell specific mechanism of cell cycle regulation (or dysregulation in the case of cancer cells). We also have experience and expertise in three-dimensional tissue constructs using human cells which has yet to be translated into *in vitro* models for evaluation of cancer chemotherapeutic agents.

**Anthony Di Pasqua, Ph.D.**  
Assistant Professor  
Pharmaceutical Science

Work in the Di Pasqua laboratory focuses on the development and use of novel delivery systems to enhance the efficacy of therapeutically-active compounds, while minimizing their side-effects in patients. Chemo- and/or radiotherapeutics are incorporated into various nanoparticle systems and their effects against tumors in animal models studied. Separately, inductively coupled plasma-mass spectrometry is used to detect potential cancer biomarkers, with the goal being the development of an assay that can detect lung cancer at an early stage.

**Ladislav Dory, Ph.D.**  
Professor  
Integrative Physiology &  
Anatomy

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.

**Art Eisenberg, Ph.D.**  
Professor & Chair  
Molecular & Medical Genetics  
Director of DNA Identity Lab

Dr. Eisenberg was a pioneer in the development of DNA Identity testing. He is a world-renowned molecular geneticist who helped develop many of the procedures, techniques and quality-control standards currently used in human identification testing. As director of the DNA Identity lab, Dr. Eisenberg has been responsible for developing a state-of-the-art clinical reference laboratory using DNA technology for the determination of paternity,

forensic casework analysis, the identification of missing persons, cancer diagnostics and the analysis of genetic diseases. His research on the analysis of DNA polymorphisms has been in the development of tests for the detection of several types of leukemia and lymphoma. Dr. Eisenberg is considered one of the top DNA advisors for the Federal Bureau of Investigation, Laboratory Division. He was appointed chairman of the United States DNA Advisory Board, which recommended standards to the Director of the FBI for quality assurance and for proficiency testing of forensic laboratories throughout the United States. He served on the Histocompatibility and Human Identification committee for the College of American Pathologists. The committee evaluated the performance of different laboratories that have used the analysis of genetic polymorphisms to monitor residual disease following a bone marrow transplant. Bone marrow transplant has been used for the treatment of certain forms of leukemia.

**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.**

Chair/Professor

Cell Biology & Immunology

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)- $\alpha$ , interleukin (IL)-1 $\alpha$ , IL-1 $\beta$ , IL-6, and tumor growth factor (TGF)- $\beta$ 1], 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- $\kappa$ B, 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  
Pharmacology and Neuroscience

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  
Cell Biology & Immunology

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

Dr. Zygmunt Gryczynski and his colleagues have established a Center for Commercialization of Fluorescence Technologies (CCFT) with support from

## Cell Biology & Immunology

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<sub>2</sub> 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,  
Cell Biology and Immunology  
Associate Dean GSBS

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<sup>flox/flox</sup>). 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.**

Breast cancer and breast cancer treatment can often

Assistant Professor,  
Cell Biology and Immunology  
Basic Science Research Chair  
for the Osteopathic Heritage  
Foundation

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.**  
Assistant Professor  
Molecular & Medical Genetics  
Director Center for Institutional  
Diversity

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 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  
Integrative Physiology &  
Anatomy

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  
Cell Biology & Immunology

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 against 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 for eliminating tumor cells. The functional role of LLT1 and CS1 in regulating immune responses is being investigated. 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 for eliminating tumor cells.

**Stephen Mathew, Ph.D.**  
Assistant Professor  
Cell Biology & Immunology

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.

**Anindita Mukerjee, Ph.D.**  
Research Assistant Professor  
Molecular & Medical Genetics

Dr. Mukerjee is trained as a biomedical engineer in the fields of drug delivery, biomaterials and nanotechnology. Her current research focuses on applying my knowledge of nanotechnology-based drug delivery systems in an attempt to develop safe and targeted therapy and diagnostics for cancer.

**Mark Mummert, Ph.D.**  
Associate Professor  
Psychiatry & Behavioral Health

Dr. Mummert's laboratory is developing new technologies for the treatment and management of malignant melanoma. The two major projects are being pursued. *Project 1: Development of imaging technologies for the detection of cutaneous malignant melanoma margins.* Surgical excisions of the cutaneous malignant melanoma tumor coupled with histology to map the margins provide the best chance for a cure. Unambiguous detection of the tumor margins for complete excision can be technically challenging using histology. The use of specially developed confocal microscopes and other optical imaging devices has been suggested for tumor margin demarcation of skin cancers, including malignant melanoma. Optical imaging of skin cancers have so far relied largely on intrinsic contrast between normal and malignant tissues (e.g., differences in the refractive index of the tumor as compared with skin). However, exogenous contrast reagents (e.g., tumor targeting reagents or activatable molecular probes) are expected to increase the detail of lesions for the demarcation of tumor margins. In collaboration with researchers in the CCFT at UNT Health Science Center as well as in the Department of Radiology at UT Southwestern Medical Center, we have developed a number of tumor targeting fluorescence probes and activatable fluorescence probes that we are testing *in vitro* and *in vivo*. *Project 2: Development of novel chemotherapeutics for the treatment of metastatic malignant melanoma.* Dacarbazine, the most common

chemotherapeutic used for treating metastatic malignant melanoma, has a complete response rate of ~5% [1]. The low response rate of malignant melanoma to dacarbazine and the aggressive nature of this cancer have resulted in significant efforts to develop new drugs for treating metastatic disease. In collaboration with OMM Scientific, Inc. we are testing novel synthetic reagents alone and in combination with chemotherapeutic drugs using in vitro and in vivo models.

**Laszlo Prokai, Ph.D.**  
Professor  
Pharmacology & Neuroscience  
Robert A. Welch Professor 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 (ii) proteomic assessment of (a) the impact of oxidative stress in cancer and during chemotherapy, and (b) signaling events associated with cancer. 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, neuropeptides, proteomics.

**Amalendu Ranjan, Ph.D.**  
Research Assistant Professor  
Molecular & Medical Genetics

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 lipopolymeric 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.

**Meharvan Singh, Ph.D.**

The research interests of my laboratory relates to

Professor  
Pharmacology & Neuroscience  
Dean  
Graduate School of Biomedical  
Sciences

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.**  
Associate Professor  
Cell Biology & Immunology

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  
Molecular & Medical Genetics  
ICR Scientific Director

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 Science

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  
Pharmacology & Neuroscience

Estrogen receptors (ERs) are believed to be ligand-activated transcription factors belonging to the nuclear receptor superfamily, which upon ligand 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 of 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 6301 Principles of Biochemistry
- BMSC 6302 Molecular Cell Biology
- BMSC 6303 Physiology
- BMSC 6304 Pharmacology
- BMSC 6305 Microbiology & Immunology

#### Advanced Courses (6 - 8 SCH):

- MOLB 6200 Advanced Molecular Biology: Transcriptional and Translational Regulation: offered every other fall (even years)
- CBIM 6220 Cellular and Molecular Fluorescence: offered each fall
- MOMG 6250 Molecular and Cell Biochemistry of Cancer: offered each spring
- PHRM 6270 Drug Discovery & Design: offered each fall
- MOMG 6435 Molecular Aspects of Cell Signaling: offered every other fall (odd years)

#### Elective Courses:

- BMSC 5203 Regulation of Human Subject Research
- MOLB 6220 Cellular and Molecular Fluorescence
- MOLB 6270 Drug Discovery and Design
- MOLB 6361 Biomedical Mass Spectrometry
- CBIM 6360 Advanced Biophysics and Biochemical Methods, offered on demand
- CBIM 6440 Methods in Molecular Biology
- PHRM 6200 Mitochondria and Complex Diseases
- FGEN 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.

- MOMG 5103 Seminar in Current Topics
- CBIM 5121 Seminar in Cell Motility: offered each fall and spring
- MOMG 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 tenure/tenure-track faculty members within two to three weeks of orientation to set up at least 2 laboratory rotations before deciding on a major advisor.
- 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 second 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. At least two members of the master's degree committee (a total of 3 or more members) and 3 members of the doctoral dissertation committee (a total of 4 or more members) must be graduate faculty of Biochemistry & Cancer Biology.
- 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. **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.
- 4.5. **Committee Meeting:** The students will meet with their advisory committee at least once every year.
- 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. 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 register for Grant Writing (Advance to Candidacy Qualifying Examination).

##### **Specifics:**

- i. The comprehensive examination will be scheduled at the end of 1<sup>st</sup> 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. The students will have to answer questions from Principles of Biochemistry and Molecular Cell Biology core courses. Additional core courses may be included based on the student's primary affiliation.
- iv. The length of the examination will be approximately 2 h. The student will be given the question set thirty minutes 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, such as Enzymes and Metabolism, Molecular Biology and Cell Biology.
- 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 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.

#### 4.11. Grant Writing Exam (Advancement to Candidacy): BMSC 6310

**Purpose:** Students must pass Grant Writing Exam to attain status as a doctoral degree candidate. This examination is designed to test the student's aptitude for independent research by assessing his/her ability to develop a research hypothesis and design ways to address it. The student is required to prepare an **NIH-style (R21)** research grant proposal and to present, discuss and defend this proposal before an examination committee. This examination must be completed within the semester registered.

**Specifics:**

**i. Prerequisite:** A student must have passed the Oral Qualifying examination to be eligible to enroll in Grant Writing. A student must register for Grant Writing in the first long semester immediately following successful completion of the oral examination and before the completion of 84 SCH.

**ii. Examination Committee:** The examination committee will consist of Biochemistry & Cancer Biology faculty (4 members) appointed by the Graduate Advisor. The chairperson of the committee (appointed by the graduate advisor) will serve as exam coordinator and will meet with the student at the beginning of the semester to review guidelines and answer relevant procedural questions. The University member of the student's dissertation committee will oversee the entire examination process. The student's mentor will be excluded from this committee.

**iii. Topic:** A student may choose an area related to his/her dissertation research but it must be based on an original hypothesis. The major professor will indicate, in writing, that the hypothesis and aims of the proposal were developed without the assistance of the major professor.

**iv. Pre-proposal:** The student will first construct a short pre-proposal comprised of a brief background, a hypothesis, an outline of the specific aims designed to test the hypothesis and experimental approaches. Following approval by the committee members, the student will make a brief oral presentation (15-20 min) to the examination committee, which will assess appropriateness based on originality and scientific soundness. The decision of the examination committee to accept or reject the pre-proposal as suitable for development into a final proposal will be by majority vote of the members. If the pre-proposal is accepted with some reservations, those reservations will be conveyed in writing to the student by the chair of the examination committee.

**v. Submission of Proposal:** Upon approval of a pre-proposal, the student must submit a completed proposal typed on official NIH forms. The committee members will review the proposal and will inform the chair if there are any concerns. The members will submit their comments to the chair and the chair will summarize the comments and ask the student to resubmit a revised proposal taking into account committee's critique. The chair will decide the date when to resubmit the revised proposal. The final proposal must be presented to the examination committee at least one week prior to the date of the examination. The student must also inform the Graduate Secretary of the date and location of the examination.

**vi. Examination procedures:** At the examination, the student will make an oral presentation (30-45 min) before the examination committee and other interested faculty

(including the major professor) and students. Immediately following the presentation, questions will be invited from the general audience. Subsequently, non-committee persons will be excused and the student will proceed to defend his/her proposal before the examination committee. The oral examination will focus on the students understanding of the topic presented and knowledge of the strategies and techniques employed. The entire examination process should be completed within 2 to 3 h.

**vii. Assessment:** The grant proposal and the student's oral presentation and defense will be evaluated on the basis of originality and ability to communicate the proposal content, and follow the Grant Writing Scoring Rubric developed by the GSBS. Three out of four voting faculty members will have to agree with the final decision. Upon successful completion of this course, the student is advanced to doctoral candidacy. Two attempts to successfully pass the BMSC 6310 Grant Writing are allowed. Failure of the student to pass the BMSC 6310 Grant Writing results in dismissal of the student from the doctoral program. In this case, a student may be allowed to complete the requirements for a Master of Science degree.

#### **Tentative deadlines to be met for 6310 Grant Writing Exam:**

- Jan 7:** The student sends the tentative abstract to the graduate advisor
- Jan 15:** The Exam committee is formed
- Jan 21:** The Exam committee approves the abstract
- Feb 15:** Pre-proposal meeting
- Mar 15:** Additional pre-proposal meeting at the discretion of the committee
- Mar 31:** Exam date is finalized
- Apr 15:** Send the copy of the proposal to the committee members
- Apr 30:** Examination completed
- May 5:** Revised proposal submitted (if necessary)
- May 10:** Approved by the committee members and filed at the graduate office

**4.12. Research Proposal:** All students are required to submit a dissertation research proposal that includes a summary of the project, problem/hypothesis, significance of the project, background, research design and methodology. The proposal should be submitted during the long semester after successful completion of Grant Writing Exam. It must be submitted prior to registering for dissertation. The research proposal must be approved by the advisory committee 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.

**4.13. 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 graduation. 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:** Lab rotation

**Year 1, Spring/Summer:**

- Select major professor
- Form an advisory committee
- Assignment of University Member

**Year 1, Summer:** Oral Qualifying Exam

**Year 2, Fall/Spring:**

- Fulfill advanced course requirements
- 6310 Grant Writing Exam

**Year 3, Fall/Spring:** Research Proposal

**Year 5:** Thesis Defense

## 6. Degree Plan

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

#### **Year 1: Fall**

BMSC 6301	Integrative Biomedical Sciences I: Principles of Biochemistry	4 SCH
BMSC 6302	Integrative Biomedical Sciences II: Molecular Cell Biology	4 SCH
BMSC 5135	Introduction to Faculty Research	1 SCH
BMSC 5150	Laboratory Rotation	2 SCH
BMSC 5160	Biomedical Ethics	1 SCH
		<hr/>
		<b>12 SCH</b>

#### **Year 1: Spring**

BMSC 6303	Integrative Biomedical Sciences III: Physiology	3 SCH
BMSC 6304	Integrative Biomedical Sciences IV: Pharmacology	2 SCH
BMSC 6305	Integrative Biomedical Sciences V: Immunology and Microbiology	3 SCH
BMSC 5135	Introduction to Faculty Research	1 SCH
BMSC 5998	Individual Research for MS Students	1-4 SCH
		<hr/>
		<b>12 SCH</b>

#### **Year 1: Summer**

BMSC 5400	Biostatistics for Biomedical Sciences	4 SCH
BMSC 5998	Individual Research for MS Students	2 SCH
		<hr/>
		<b>6 SCH</b>

#### **Year 2: Fall**

BMSC 5998	Individual Research for MS Students	4-5 SCH
	Elective course*	3-4 SCH
	Journal Club/Current Topics**	1-2 SCH
		<hr/>
		<b>9 SCH</b>

#### **Year 2: Spring**

BMSC 5998	Individual Research for MS Students	3 SCH
BMSC 5395	Thesis	3 SCH
		<hr/>
		<b>6 SCH</b>

**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 6301	Integrative Biomedical Sciences I: Principles of Biochemistry	4 SCH
BMSC 6302	Integrative Biomedical Sciences II: Molecular Cell Biology	4 SCH
BMSC 5135	Introduction to Faculty Research	1 SCH
BMSC 5150	Laboratory Rotation	2 SCH
BMSC 5160	Biomedical Ethics	1 SCH
		<u>12 SCH</u>

### **Year 1: Spring**

BMSC 6303	Integrative Biomedical Sciences III: Physiology	3 SCH
BMSC 6304	Integrative Biomedical Sciences IV: Pharmacology	2 SCH
BMSC 6305	Integrative Biomedical Sciences V: Immunology and Microbiology	3 SCH
BMSC 5135	Introduction to Faculty Research	1 SCH
BMSC 6998	Individual Research/laboratory rotation	3 SCH
		<u>12 SCH</u>

### **Year 1: Summer**

BMSC 5400	Biostatistics for Biomedical Sciences	4 SCH
BMSC 6998	Individual Research	2 SCH
	Oral Qualifying Exam	0 SCH
		<u>6 SCH</u>

### **Year 2: Fall**

BMSC 5310	Scientific Communication (optional)	3 SCH
BMSC 6998	Individual Research	4-6 SCH
	Advanced course	2-6 SCH
	Journal Club/Current Topics	1-2 SCH
		<u>12 SCH</u>

### **Year 2: Spring**

BMSC 6310	Grant Writing	3 SCH
BMSC 6998	Individual Research	5-7 SCH
	Advanced course/Electives	2-4 SCH
	Journal Club/Current Topics	1-2 SCH
		<u>12 SCH</u>

### **Year 2: Summer**

BMSC 6998	Individual Research	6 SCH
		<u>6 SCH</u>

### **Year 3: Fall**

BMSC 6998	Individual Research	4-7 SCH
	Electives*	0-3 SCH
	Journal Club/Current Topics	1-2 SCH
		<u>9 SCH</u>

### **Year 3: Spring**

BMSC 6998	Individual Research	4-7 SCH
	Journal Club/Current Topics	1-2 SCH
		<u>9 SCH</u>

### **Year 3: Summer**

BMSC 6998	Individual Research	6 SCH
		<u>6 SCH</u>

**Year 4: Fall**

BMSC 6998	Individual Research	6 SCH
BMSC 6395	Doctoral Dissertation	3 SCH
		<u>9 SCH</u>

**Year 4: Spring**

BMSC 6998	Individual Research	6 SCH
BMSC 6395	Doctoral Dissertation	3 SCH
		<u>9 SCH</u>

**Total** **90 SCH**

## 6. Contacts in Situations of Uncertainty or Emergency

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