Graduate Program in Biochemistry and Molecular Biology

Program Exposure
September 8, 2015
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Biochemistry and Molecular Biology Graduate Program Director:

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Introduction

If you are driven by a curiosity to explore the molecular foundations of biology, including mechanisms of diseases like cancer, metabolic disorders, or infections, then consider pursuing your graduate research in Biochemistry and Molecular Biology. Our department always seeks creative and ambitious graduate students who are motivated to address critical questions in the biomedical sciences. In turn, our faculty is committed to furnishing students with the requisite skills and knowledge, within a challenging and stimulating environment, to prepare students for outstanding careers in science.

The Department of Biochemistry and Molecular Biology offers an interdisciplinary and collaborative research program in diverse areas, such as cardiovascular disease, cancer biology, mitochondrial pathophysiology, cell signaling, apoptosis, and infectious diseases, while employing state-of-the-art methodologies and approaches, including molecular biology, nucleic acid and protein biochemistry, genetics, high throughput screening, microarrays, mass spectrometry, NMR spectroscopy and X-ray crystallography. The Department boasts particular strengths in the investigation of bioactive lipids (lipidomics), in DNA and RNA biology, and in structural biology.

Currently, the Department of Biochemistry and Molecular Biology has 80 members, including 29 faculty, 25 postdoctoral scholars, and 22 graduate students. The Department has an outstanding record of extramural funding. NIH funding in 2014 was $4.5 million (ranked 44 among Biochemistry departments in the US) and is increasing. Following the appointment of Dr. Philip Howe as Chair in 2013, the department has expanded significantly with the recruitment of five faculty members. In addition, we have tripled the number of graduate students training in the department over the past three years.
The success of the Department of Biochemistry and Molecular Biology in biomedical research is also exemplified by the number and quality of publications in major international journals. Additionally, our faculty has been recognized on numerous occasions for success in teaching, service or research. As one example, the MUSC Developing Scholar Award for Basic Sciences has been awarded to Biochemistry faculty in 2002 (Sergey Krupenko, PhD), 2003 (Christopher Davies, PhD), 2004 (Besim Ogretmen, PhD), 2005 (Maurizio Del Poeta, MD) and 2011 (Ashley Cowart, PhD).

Research Facilities
The Department of Biochemistry and Molecular Biology boasts state-of-the-art laboratories fully equipped with modern instrumentation for cutting-edge biomedical research. As a department conducting cutting-edge research, we also house several major instrument cores that serve the entire research community at MUSC, including lipid synthesis and analysis, X-ray crystallography, Nuclear Magnetic Resonance (NMR) and protein production.
PhD Program in Biochemistry & Molecular Biology

First Year
Basic Biomedical Science - Common Curriculum. There are two main elements in the first year of graduate study at MUSC: a common curriculum and laboratory rotations. The common curriculum is offered by the College of Graduate Studies and provides foundations in biomedical sciences. During the first year, students participate in a program of laboratory rotations, which expose students to new areas of research and provide opportunity to learn new experimental techniques. Towards the end of the first year, students select a Major Advisor in whose laboratory they wish to conduct their thesis research and their Graduate Program.

Second Year
In the second year, our students begin to define and refine their research project, while always remaining cognizant of the ultimate goals of publishing peer-reviewed papers and defending a dissertation. Students also select their Dissertation Advisory Committee, comprising their advisor and four additional faculty members (one from outside the department). In tandem, students accumulate course credits in areas that complement their laboratory research.

At the end of the year, students take the Written Qualifying Exam, which is administered by the Graduate Training Committee during the first or second week of June. The objective of the examination is to determine whether a student understands the principles of biochemistry and molecular biology, can read and comprehend relevant literature, can construct convincing hypotheses and an experimental plan. These attributes and skills are essential for a successful career in research.

Third Year
The third year is a continuation of laboratory research, with additional course work as needed. Before the end of the third year and within one year of passing the Written Qualifier Exam, students take the Oral Qualifier Exam, administered by their Dissertation Advisory Committee. For this, students develop a written research proposal in an NIH-grant format on his/her research project. There is then an oral defense of the proposal, comprising a public presentation of the research project to the department, followed by more detailed examination by the Advisory Committee. After passing the Oral Qualifier, the student is then certified as a candidate for the PhD degree.

Fourth/Fifth Year
During the fourth and subsequent years of graduate study in Biochemistry and Molecular Biology, students focus primarily on their research project. The culmination of this endeavor is a dissertation that is based on the research conducted and which shows evidence of mature scholarship and critical judgment. In common with all PhD students at MUSC, the candidate presents his/her dissertation research at a public seminar, followed by a closed session with the Advisory Committee.
Requirements of the Biochemistry and Molecular Biology PhD program

1. Successful completion of the 1st Year Core Curriculum.
2. Successful completion of 12 credit hours of course work in the 2nd year and beyond, including Advanced Biochemistry (BMB-735).
3. Successful completion of the written qualifying examination at the end of 2nd year.
4. Successful completion of the oral qualifying examination within 12 months of passing the written qualifying examination.
5. Attendance at the Research Methods Seminars and a minimum of two thirds of MCBP seminars.
6. At least one original research article published in a peer-reviewed journal as a first author.
7. 15 credit hours of laboratory research in each semester in the 2nd year and beyond.

Graduate Courses
The Department of Biochemistry and Molecular Biology offers a range of graduate courses designed to provide essential knowledge and to complement their laboratory research. A program of study is developed based on the specific needs and scientific interests of the individual student and can include courses offered by other programs. The Biochemistry and Molecular Biology faculty is fully committed to providing the most vigorous and stimulating courses for our graduate students. The program is always being revised and updated, with new courses being developed to reflect the evolving composition of the department and the best interests of our students.

Advanced Biochemistry Spring Selective (BMB/PCOL-735) – Co-Directors: Christopher Davies, PhD, and Lauren Ball, PhD (Pharmacology), Credit hours: 3. This course is designed to equip students with foundational knowledge that is considered essential for a successful career in the field of biochemistry. It includes training in core areas such as enzyme kinetics, thermodynamics, biomolecular interactions, structural biology and biophysics, alongside in-depth examination of publications where such approaches have made a critical impact.

Lipids in Pathobiology (BMB-748/MCBP-748) - Co-Directors: Drs. Samar Hammad and Ashley Cowart, Credit hours: 3
This multidisciplinary course addresses biochemical, applied, and translational approaches to the study of lipids. The course is composed of three main sections: lipid biosynthesis, lipid signaling, and lipids and disease. The first section is a comprehensive treatment of nomenclature and synthesis of major lipid classes, including glycerophospholipids, sphingolipids, and sterols, as well as methodology for lipid study. The second section addresses roles of bioactive members of these lipid classes in the regulation of cell signaling and downstream events. The third section is largely translational, with many lectures on human diseases that involve the lipids and signaling pathways discussed. This course also contains a brief hands-on laboratory segment. Offered every other Spring.

Halley Rycenga, a second-year graduate student in the laboratory of Dr. David Long, investigates the role of p97 in DNA repair and its involvement in cell sensitivity to cancer therapies.
RNA Biology and Disease (BMB-737) - Co-Directors: Tilman Heise, PhD, and Gunhild Sommer, PhD. Credit hours: 3
Alterations in the posttranscriptional control of gene expression can be linked with human diseases such as cancer and viral infection. This new course examines mechanisms of posttranscriptional control, including alternative splicing, changes in mRNA stability or localization, protein synthesis, and expression of micro RNAs, in order to understand how aberrant regulation of gene expression provokes cellular malfunction and potentiates human disease.

Molecular Foundations of Medicine (BMB-605) - Director: Christopher Davies, PhD. Credit hours: 3
Recognizing that to understand the pathogenesis of disease requires a molecular approach, this course focuses on a number of human diseases or pathologies. The subjects rotate every year:

**BMB-605A. Mechanism of Aging and Life Span.** Many pathological processes have become amenable to study using the various tools and approaches of biochemistry, molecular biology, genetics, chemistry, and bioinformatics. This is perhaps best illustrated in the study of aging. After decades of little progress, it is now apparent that fundamental processes regulate lifespan of organisms ranging from yeast to Caenorhabditis elegans, to Drosophila, to mice, and, by extension, to humans. These common mechanisms involve transcription factors, insulin-like signaling, lipid signaling pathways, and telomerase. Disorders in these pathways result in disturbances in lifespan, and in some cases in human diseases. This course will provide the students with the necessary foundation in understanding the various models employed for the study of aging and lifespan. The course will rely primarily on original literature and in-depth discussion of key foundation papers. The discussion will be led by expert faculty who will introduce each topic and provide the students with the necessary foundations.

**BMB-605B. Mechanisms of Cancer Pathogenesis.** The abnormal behavior of neoplastic cells can often be traced to alterations in posttranscriptional control of gene expression. Alternative splicing, changes in mRNA stability, the translational control, and expression of micro RNA having a significant impact on the development of human disease and viral infection. This course will provide the study of basic molecular mechanism and of cellular malfunction provoked by alteration of RNA synthesis and processing.

**BMB-605C. Mechanisms of Inflammation.** One of the emerging areas of research is the understanding of the mechanism involved in the inflammation process. In particular, bioactive molecules produced by immune system cells are involved in inflammatory diseases such as rheumatoid arthritis, sepsis, asthma, inflammatory bowel disease, and atherosclerosis. This course will provide a study of mechanisms leading to and maintaining the inflammation process, such as dyslipidemia, the leading cause of the inflammation process that leads to the atherothrombotic disease, and the oxidative stress, the pathological factor responsible for this damage. In addition, the course will focus on a variety of stimuli, such as mechanical, anoxic, chemical (e.g. oxidized LDL), immunological or infectious ones, that are responsible for activation of the endothelium. Finally, the course will also examine how many infectious agents regulate the inflammation process, leading either to the control of the infection or the development of infectious disease, depending on the cross talk between the host and the pathogen.

**BMB-605D. Pathogenesis of Diabetes.** Obesity and its pathological sequelae remain a primary health concern. While obesity is associated with diseases including
type 2 diabetes, non-alcoholic fatty liver disease, and heart disease, mechanisms by which these occur remain unknown. Recent literature implicates altered lipid metabolism in these conditions, including compromised fatty acid oxidation, changes in lipid ‘packaging’ in lipoproteins, and aberrant production of signaling lipids such as diacylglycerols and sphingosine-1-phosphate. Cellular processes linking these biochemical changes to disease include induction of ER stress, apoptosis, autophagy, and induction of oxidative stress responses. This course will provide an overview of clinical, cellular, and molecular/biochemical features of the most common diseases associated with obesity and discuss recent literature providing mechanistic insights into the etiology of these pathophysiological processes.

An "open book" surface representation of an E1-E2 complex with atoms involved in direct contacts colored (structure solved in the Olsen laboratory).

**Journal Clubs**

**RNA Club: RNA and Disease** – Director: Tilman Heise, PhD
In this forum, faculty, postdocs and students meet once a month to share data, discuss projects, review publications and establish collaborations. Topics cover different aspects of RNA biology and post-transcriptional control of gene expression, with special emphasis on the role these processes play in the development of human disease (every Fall and Spring).

**Biochemistry Journal Club**
The department has an active journal club in which students or post-docs present published papers of significance and broad interest.

**Seminars**

**Research and Methods Seminar Series (BMB 730)** – Director: Vamsi Gangaraju, PhD
Credit hours: 1
In this series, students present seminars based on their own research to the Department. This is a great opportunity for students to present their work in an informal setting and to receive feedback from a large audience with different scientific backgrounds. Students are required to give at least two seminars during their training. Held the second and fourth Tuesdays of every month (Fall & Spring).

**MCBP/Biochemistry Seminars**
The MCBP seminar program provides all students with an opportunity to attend seminars by distinguished scientists from both foreign and domestic institutions. Biochemistry and Molecular Biology hosts many of the speakers within the MCBP seminar program. Held every Thursday (Fall & Spring).
Research Interests

The primary focus of our laboratory is on the investigations of the molecular mechanisms of replication fork arrest, genome stability, checkpoint controls using *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe* as model systems. These are topics of intense current interest, not only from the perspectives of eukaryotic DNA transactions, but also of cancer biology. Our laboratory is also interested in the molecular analysis of the human “timeless” protein and TIPIN (timeless-interacting protein). Our laboratory offers outstanding training in nucleic acids biochemistry, enzymology of DNA replication and on protein-nucleic acid and protein-protein interactions.

**Molecular Mechanisms of Cellular Aging:** Recently, using yeast as a model system, we have elucidated a major pathway of cellular aging. We have shown that two molecular mechanisms act in a sequence to control replicative life span: (i) autoinhibition of a replication terminator protein called Fob1 and chromosome kissing. Further work is underway to study the molecular mechanisms that lead to aging and senescence.

**Recent Publications**


Julie Chao, PhD
Professor
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Research Interests
We have been studying the role and molecular basis of tissue kallikrein, kinin B1 and B2 receptors, prostasin and kallistatin in hypertension, cardiovascular and renal injury, and ischemic stroke for 40 years. Our work has involved a wide range of activities, including protein purification, molecular cloning, regulation of enzyme activity and gene expression, signaling pathways, and therapeutic gene/protein delivery in various animal models with vascular diseases. We have discovered, purified and cloned two new human proteins: designated as “prostasin” and “kallistatin”. Prostasin, a serine proteinase, plays crucial roles in regulating sodium balance, bladder inflammation and tumor invasion. Kallistatin, a specific tissue kallikrein inhibitor, exerts pleiotropic functions in modulating angiogenesis, inflammation, apoptosis, fibrosis, and tumor growth and metastasis. We are currently investigating the role and mechanisms of kallistatin in vascular repair. Our hypothesis is that kallistatin prevents vascular injury by stimulating the mobilization and functional activity of endothelial progenitor cells, and preventing endothelial senescence through increasing nitric oxide production and inhibiting oxidative stress. Our objective is to identify new avenues in rejuvenating endothelial function in cardiovascular and related diseases.

Recent Publications


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**L. Ashley Cowart, PhD**  
**Associate Professor**

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**Research Interests**

Our laboratory studies how plasma lipids affect tissue sphingolipid metabolism. This is important because obesity and diabetes increase plasma lipid concentrations, and this increase has been demonstrated to change sphingolipid profiles in tissues including adipose, liver, skeletal muscle, and heart. In fact, elevation of plasma lipids probably contributes to pathologies observed in these tissues from diabetic patients. We hypothesize that aberrant sphingolipid synthesis promotes tissue pathologies including inflammation, muscle wasting, and cardiac hypertrophy. To address this hypothesis we use a combination of tissue culture and rodent models. Placing rodents on a high-fat diet increases plasma fatty acids and dramatically impacts tissue sphingolipids. These changes precipitate major changes in gene regulation and signaling pathways. We have dissected some of these
changes using microarrays, and with collaborators in the department of Biostatistics, Bioinformatics, and Epidemiology, we also are actively developing novel bioinformatics strategies for co-analysis of gene expression data from microarrays and sphingolipid levels from lipidomics analysis. These strategies have allowed us to find “needles” in the “haystack” of lipid-mediated cell signaling.

Recent Publications


Cowart LA, Gandy JL, Tholanikunnel B, Hannun YA. (2010). Sphingolipids mediate formation of mRNA processing bodies during the heat-stress response of


Christopher Davies, PhD
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**Research Interests**

Understanding the function of a macromolecule involved in a particular biological process often requires knowledge of its precise three-dimensional structure. This is especially relevant in cases where the molecule has a role in disease. Our group uses the technique of X-ray crystallography, as well as other biochemical approaches, to determine high-resolution structures of macromolecules in a variety of systems. The primary focus of the laboratory is to decipher the structure and function of enzymes involved in peptidoglycan synthesis in bacteria. These include penicillin-binding proteins (PBPs), the well-known molecular targets for β-lactam antibiotics. Due to the prevalence of antibiotic resistance in bacteria, which poses an increasing threat to public health, these enzymes are of considerable interest. Using structures of several PBPs solved in our lab, we are developing novel antimicrobials directed against pathogenic bacteria. In tandem, we are elucidating many of the molecular mechanisms that underlie antibiotic resistance in *Neisseria gonorrhoeae* by determining the structures of key proteins involved with the goals of designing new inhibitors against PBPs.

**Recent Publications**


Tomberg J, Unemo M, Ohnishi M, Davies C & Nicholas RA. (2013). Identification of the amino acids conferring high-level resistance to expanded-spectrum cephalosporins in


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**J. Alan Diehl, PhD**  
**Professor**  
Endowed Professor of Lipidomics and Pathobiology  
Associate Director of Basic Sciences, Hollings Cancer Center  
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**Research Interests**  
Our group focuses on defining the biochemical and molecular basis of cancer development and translating this knowledge into better treatments for cancer patients. We work in two fundamental areas of biochemical and molecular interest: 1) cell division and 2) cell survival signaling. With respect to cell division, our work has contributed to a precise molecular understanding of how cyclin dependent kinases (CDKs) regulate normal versus tumor cell growth. These developments have been translated into new cancer therapies that directly target specific cell cycle enzymes and have exhibited significant therapeutic efficacy in cancer patients. With regard to cell survival signaling, we seek to define how cancer cells escape normal microenvironmental cues that trigger normal cells to die. Our use of biochemistry, cell biology and animal models has identified the PERK protein kinase as a new therapeutic target that we hope to translate into new anti-cancer therapies.
Recent Publications
Research Interests
Using Drosophila as the model system, one of the major goals of my lab is to delineate the molecular mechanisms by which the Piwi-piRNA pathway silences transposons and maintains genome integrity. Our recent work has shown that epigenetic regulation by Piwi prevents trans-generational phenotypic variations. This work has revealed an unprecedented link between Hsp90, a highly selective molecular chaperone and an anti-cancer target, and Piwi. My lab will extend these studies and further unravel the mechanisms by which heat shock machinery regulates Piwi-piRNA pathway. Lastly, we are also interested in understanding if and how the relationship between piRNA pathway and heat shock machinery plays a role in generation of trans-generational epialleles in response to extreme environmental stress. We hope that this study will provide novel insights into stress response pathways and provide us tools to counteract adverse effects of extreme environmental stress and prevent human disease.

Recent Publications


Research Interests
The maturation of mRNAs is a complex row of processing steps crucial for gene expression. The co-transcriptional processing, the nuclear export, the translation and the decay of a specific mRNA are strictly regulated events. Malfunction in those processes correlating with the development of human diseases. Our long-term goal is to firmly establish the role and function of RNA-binding proteins in cancer development and viral infection. Our research focuses on the cancer-associated RNA-binding protein La, a known RNA chaperone, which regulates e.g. the translation of cellular and viral key factors. Currently we focus on the regulation of La functions by posttranslational modification such as SUMOylation and phosphorylation. Furthermore, we aim to develop high-throughput assay to identify small molecule inhibitors blocking the binding of La to specific RNA molecules. In addition we are studying the function of other RNA-binding proteins as well as the cellular function of a fusion protein, consisting of an RNA-binding protein and a transcription factor, implicated in the development of childhood leukemia.

Recent Publications
Philip Howe, PhD  
Professor and Chairman  
Hans and Helen Koebig Chair in Clinical Oncology

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Research Interests
Research in the Howe laboratory is focused on understanding the signaling pathways activated by transforming growth factor β1 (TGFβ1), interleukin-like EMT inducer (ILEI) and Wnt in cellular models of differentiation and cancer. One major area of interest is a recently identified signaling pathway whereby TGFβ regulates epithelial-mesenchymal transitions (EMT) and metastasis through a post-transcriptional mechanism involving the regulation of an RNA binding protein, heterogeneous ribonucleoprotein E1 (hnRNP E1). We are focused on how TGFβ regulation of hnRNP E1 phosphorylation not only regulates translational silencing of select mRNAs involved in EMT/metastasis but also of IncRNAs that may also contribute to tumor progression. Candidate mRNA targets and IncRNAs are actively being pursued and one mRNA target in particular, the cytokine ILEI, has become a major focus of the laboratory. Aside from its known role in EMT, relatively little is known regarding ILEI. We have identified ILEI as a potent stem factor in breast epithelium and are actively investigating the molecular mechanisms through which it mediates its progenitor effects.

In another focus area we are investigating the role of the adaptor molecule, disabled-2 (Dab2), as a mediator of the cross-talk between the TGFβ and Wnt signaling pathways. We have shown that the tumor suppressor functions of Dab2 are mediated thru its attenuation of canonical Wnt/β-catenin signaling by selectively recruiting the Wnt co-receptor LRP6 to the clathrin-dependent endocytic route, thereby sequestering it from caveolin-mediated endocytosis and signaling. TGFβ levels in cells and tissues regulates Dab2 expression and thereby regulates, thru Dab2, Wnt signaling. We are currently investigating this cross-talk in the developing zebrafish and in animal tumor models. We have also made the recent observation that Dab2 regulates TGFβ-induced apoptosis and autophagy. We have shown that mechanistically Dab2 serves as a molecular switch to control whether cells undergo apoptosis or autophagy in response to TGFβ, and significantly this switch may be underlie chemosensitivity and acquired-resistance during tumorigenesis.

Recent Publications


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**John Lemasters, MD, PhD**

**Professor**

Director, Center for Cell Death, Injury and Regeneration

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Dual Appointment in the Departments of Biochemistry & Molecular Biology and Pharmaceutical Sciences

**Research Interests**

My research interests relate to mitochondrial and cellular bioenergetics, including studies of oxidative phosphorylation in isolated mitochondria, mitochondrial dysfunction in toxic, hypoxic and reperfusion injury to hepatocytes, cardiac myocytes and organs stored for transplantation surgery, and control of metabolism. Our in vitro and in vivo studies of living cells and tissues have shown that mitochondrial calcium uptake, iron translocation from lysosomes to mitochondria, and oxidative stress promote the mitochondrial permeability transition (MPT). The MPT initially induces lysosomal degradation of mitochondria by autophagy, a selective process called mitophagy. However, excess MPT induction induces both necrotic cell death from ATP depletion and apoptosis due to cytochrome c release after mitochondrial swelling. Despite a detailed understanding of their metabolism, mitochondria often behave anomalously. In particular, global suppression of mitochondrial metabolism and metabolite exchange occurs in apoptosis, ischemia/hypoxia, alcoholic liver disease and aerobic glycolysis in cancer cells (Warburg effect). My lab is examining and supporting the novel hypothesis that closure of voltage-dependent anion channels (VDAC) in the mitochondrial outer membrane accounts for global mitochondrial suppression consistent with a role for VDAC as a dynamic regulator, or governor, of global mitochondrial function both in health and disease. For these projects, my laboratory extensively applies new techniques of quantitative laser scanning confocal and intravital multiphoton microscopy for physiological analysis of single cells and living tissues.
**Recent Publications**


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**David T. Long, PhD**  
**Assistant Professor**

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Lab (BSB-517): 843-792-8906

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**Research Interests**

To counter the accumulation of DNA damage, eukaryotic cells employ an intricate network of pathways that promote damage recognition, checkpoint signaling, and ultimately DNA repair. This damage response network has been linked to various genetic disorders, typified by hypersensitivity to DNA damaging agents and a high predisposition to developing cancer.
A major component of this network is the breast cancer tumor suppressor BRCA1. BRCA1 has been described as a master regulator of genome stability due to its involvement in regulating multiple aspects of the DNA damage response. Using Xenopus egg extracts, my lab seeks to understand how BRCA1’s different repair functions cooperate to promote efficient and accurate repair of DNA lesions. Our recent work has shown that BRCA1 helps to dismantle the replicative helicase from chromatin after collision with a DNA crosslink. Although helicase unloading is required to resolve the stalled fork and repair the underlying lesion, the mechanism whereby BRCA1 evicts the helicase is unknown. Going forward, we hope to connect this and other BRCA1 functions with clinical phenotypes to support individualized cancer therapies.

Recent Publications


Shaun Olsen, PhD
Assistant Professor

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Research Interests
Post-translational modification of proteins by ubiquitin and ubiquitin-like modifiers (collectively termed Ubls) is a means of regulating fundamental cellular processes such as cell cycle control, signal transduction, and differentiation. Ubiquitin conjugation proceeds through the sequential activities of three enzymes (E1, E2, and E3) and alters target protein properties such as activity/conformation, subcellular localization, stability, and capacity for
intermolecular interactions, ultimately accounting for the cellular response. The lab aims to understand the molecular mechanisms by which ubiquitin proceeds through its enzymatic cascade and is ultimately conjugated to target proteins in a specific and regulated manner. In addition to its role in maintaining homeostasis, the ubiquitin pathway is implicated in a number of human pathologies including cancer and neurodegenerative disorders and we frame our studies around proteins that when dysregulated are implicated in these disorders. To achieve these goals, we employ a multidisciplinary approach that includes X-ray crystallography complemented with biochemical/biophysical techniques and yeast genetics.

**Recent Publications**


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**Besim Ogretmen, PhD**  
**Professor and Eminent Scholar**

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**Research Interests**

Molecular mechanisms of the regulation of telomerase and telomeres by ceramide signaling.  
Mechanisms of ceramide-mediated regulation of PP2A by lipid-protein interactions.  
Regulation of ER stress and apoptosis by sphingolipid metabolism.  
Mechanisms of lipid-regulated cancer metastasis and drug resistance.  
Mechanisms of autophagy and necroptosis-mediated cancer cell death pathways by lipid signaling.

**Recent Publications**

of the sphingolipid S1P to hTERT stabilizes telomerase at the nuclear periphery by allosterically mimicking protein phosphorylation. *Science Signaling* 8(381):ra58.


**Research Interests**

My research interest is concentrated on identifying the role of RNA-binding proteins in cancer. Functional RNA-binding proteins are crucial players during all steps of mRNA metabolism, including co-transcriptional processing, nuclear export, translation and decay. Malfunction in those processes can correlate with aberrant gene expression during tumorigenesis. By understanding the molecular mechanism of RNA-binding proteins contributing to cancer pathobiology, we aim to identify new avenues for anti-cancer drug development. To study the malfunction of RNA-binding proteins in cancer, we are applying a broad spectrum of methods in biochemistry, molecular and cell biology, like RNA interference, quantitative RT-PCR, protein-RNA binding assays, immunoprecipitation assays (coIP, ChIP), mammalian cell culture of normal and cancerous cells, immunofluorescence to study the cellular localization and co-localization of proteins, proliferation, migration and invasion assays.

**Recent Publications**


Research Faculty

Alacja Bielawska, PhD
Research Professor

Director, Lipidomics Shared Resource

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Research Interests
Research focuses on lipid synthesis, analysis and therapeutic application of novel bioactive molecules targeting sphingolipid metabolism. Current research interest relates to organelle-targeting sphingolipids and organelle-targeting inhibitors of sphingolipid metabolizing enzymes concentrating on mitochondria and lysosomes. Lipidomics Shared Resource at MUSC, directed by me, provides conceptual and practical training in various aspects of lipidology, qualitative and quantitative analysis of lipid components from different biological materials, synthetic molecular tools to study lipid metabolism and assists investigators in experimental design, selection of lipid of interest and interpretation of the analytical results. Analytical approach is based on High Performance Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) technology.

Recent Publications


squamous cell carcinoma by the inhibition of angiogenesis through an increase in ceramide. *Int. J. Clin. Oncol.* 20:438-446.


Bidyut Mohanty, PhD
Research Assistant Professor

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Research Interests
Genome stability in yeast. (I) Genome Integrity: Cells are constantly exposed to various genotoxins that can cause DNA replication stress and affect genome integrity. However, cells employ various means to respond to insults by the genotoxins. Checkpoints, DNA replication machinery and DNA repair systems maintain genome integrity. Data from budding yeast show that various other pathways also respond to genotoxin exposure. We are studying cross-talks between the DNA integrity pathway proteins and proteins of other pathways such as sphingolipid pathway, actin and actin regulators in the maintenance of genome integrity and cell survival.

(II) Recombination and aging: Programmed replication arrest in yeast ribosomal DNA has been shown to induce recombination that plays a key role yeast lifespan. Our interest is to dissect the recombination pathways that controls yeast lifespan.

Recent Publications


## Graduate Students in Biochemistry and Molecular Biology, 2014-2015

<table>
<thead>
<tr>
<th>Student's Name</th>
<th>Matriculation Date</th>
<th>Mentor</th>
<th>Degree Sought</th>
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<td>2013</td>
<td>Ashley Cowart, PhD</td>
<td>PhD</td>
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<td>Atkinson, James</td>
<td>2011</td>
<td>Shaun Olsen, PhD</td>
<td>PhD</td>
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<td>Brown, Andrew</td>
<td>2010</td>
<td>Philip Howe, PhD</td>
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<td>Chavis, Georgia</td>
<td>2013</td>
<td>Ashley Cowart, PhD</td>
<td>MS</td>
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<td>De Palma, Ryan</td>
<td>2011</td>
<td>Besim Ogretmen, PhD</td>
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<td>El-Sabban, Maya</td>
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<td>Guo, Youming</td>
<td>2014</td>
<td>Julie Chao, PhD</td>
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<td>Harland, Michael</td>
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<td>2012</td>
<td>Philip Howe, PhD</td>
<td>MD/PhD</td>
</tr>
<tr>
<td>Patel, Mehul*</td>
<td>2012</td>
<td>Visu Palanisamy, PhD</td>
<td>MS</td>
</tr>
<tr>
<td>Radomski, Justin</td>
<td>2014</td>
<td>Paula Traktman, PhD</td>
<td>PhD</td>
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<td>Rycenga, Halley</td>
<td>2014</td>
<td>David Long, PhD</td>
<td>PhD</td>
</tr>
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<td>Thomas, Raquela</td>
<td>2010</td>
<td>Besim Ogretmen, PhD</td>
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<tr>
<td>Turner, Jonathan</td>
<td>2013</td>
<td>Christopher Davies, PhD</td>
<td>MS/PhD</td>
</tr>
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<td>Washispack, Abigail</td>
<td>2012</td>
<td>Ashley Cowart, PhD</td>
<td>MD/PhD</td>
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<td>Williams, Katelyn</td>
<td>2012</td>
<td>Shaun Olsen, PhD</td>
<td>MS/PhD</td>
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<td>Woosley, Alec</td>
<td>2013</td>
<td>Philip Howe, PhD</td>
<td>PhD</td>
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<tr>
<td>Young, Brandon</td>
<td>2013</td>
<td>Christopher Davies, PhD</td>
<td>MD/PhD</td>
</tr>
</tbody>
</table>

* degree awarded this year
^ Enrolled at Kent State University
Student Publications 2014-2015

Over the past few years, our students have published their work in high profile journals such as Nature, Genes & Development, Journal of Clinical Investigation, PNAS, EMBO Journal, J. Biol. Chem., MBC, MCB, and Biochemistry. Publications authored by students training in the Department of Biochemistry and Molecular Biology students in the past year:


Student Presentations 2014-2015

Andrea Anderson
Sphingosine kinase 1-mediated effects on adipose tissue adiponectin. Poster presentation at the International Ceramide Conference/ Sphingolipid Club Joint Meeting, May 2015, Izmir, Turkey.
**Jordon Gruber**
Role of 2,4-Dihydroxyquinoline (DHQ) in Pseudomonas aeruginosa pathogenicity. Poster presentation at the North American Cystic Fibrosis Conference 2014, Atlanta, GA.

**Michael Harland**
Role of sphingosine kinase 1 and ceramide synthase 6 in NAFLD induced ER stress. Oral presentation at the Southeastern Regional Lipid Conference (SERLC), November 2014.

Roles for sphingolipids in nonalcoholic fatty liver disease. Poster presentation at the International Ceramide Conference/ Sphingolipid Club Joint Meeting, May 2015, Izmir, Turkey.

**Rose Ndeto**

Molecular mechanism of FTY720-induced necroptosis in lung cancer cells: Role of ceramide. Poster presentation at the Annual Hollings Cancer Center Research Retreat, November 2014.


**Raquela Thomas**


Human papillomavirus and regulation of ceramide-mediated mitophagy in head and neck cancer. Oral presentation at the MUSC Lipid Signaling in Cancer/Center of Biological Research Excellence February 17, 2015.

Role of the HPVE7/p130/E2F5 axis in sensitization to ceramide-induced lethal mitophagy in head and neck cancer. Biology Departmental Seminar, Northern Arizona University, November 20 2014.


Role of the HPVE7/p130/E2F5 axis in sensitization to ceramide-induced lethal mitophagy in head and neck cancer. Poster presentation at Hollings Cancer Center Annual Research Retreat, November 2014.

Regulation of ceramide-mediated mitophagy by human papillomavirus oncoproteins in head and neck cancer. Poster presentation at the Southeastern Regional Meeting of the American Chemical Society, October 17, 2014.

**Abigail Washispack**
The roles of Atg7 and p53 in sphingolipid-dependent autophagy. Oral presentation at the 49th Annual Southeastern Regional Lipid Conference, November 5-7, 2014, Cashiers, NC.


**Alec Woosley**
The role of disabled-2 in autophagy inhibition. Poster presentation at the Annual Hollings Cancer Center Research Retreat, November 2014.

Brandon Young, an MD/PhD student in the Davies lab, is researching how mutations in penicillin-binding proteins cause resistance to β-lactam antibiotics.

**Student Honors and Awards 2014-2015**

**Jordon Gruber**

Outstanding Supplemental Instruction Award from the MUSC Center for Academic Excellence.
Binding of an inhibitor to its enzyme target. Many investigators in the Department of Biochemistry engage in drug discovery using various approaches, including X-ray crystallography, as shown here.

Andrea Anderson
Raymond S. Greenberg Presidential Scholars 2015-2016.
Travel Award, International Ceramide Conference/ Sphingolipid Club Joint Meeting 2015.

Michael Harland
Travel Award, International Ceramide Conference/ Sphingolipid Club Joint Meeting 2015.

Ken Noguchi
MUSC Hollings Cancer Center Abney Foundation Scholarship, July 2014-June 2015.

Raquela Thomas
Best Presentation Award at International Ceramide Conference/ Sphingolipid Club Joint Meeting 2015.
Travel Award for International Ceramide Conference/ Sphingolipid Club Joint Meeting 2015.


Abigail Washispack