PBS Faculty Mentors

The following faculty members have active labs in the Pharmaceutical and Biomedical Sciences Department:

Dr. Michael Bartlett, Associate Dean for Science Education and Georgia Athletic Association Professor in Pharmacy Email: mgbart@uga.edu

The Bartlett lab's research centers around applications of analytical chemistry to study biological problems. Currently, he and his team are studying the absorption, distribution, metabolism and excretion (ADME) of drug substances and environmental toxicants with the goal of developing novel methods to address significant questions in the biomedical sciences. In collaboration with other faculty they aim to provide realistic risk assessments for common environmental contaminants and also study many compounds shown to affect memory and cognition.

Dr. Blake Billmyre, Assistant Professor Email: Blake.Billmyre@uga.edu

Human fungal pathogens cause more than 1.5 million deaths annually. In particular, Cryptococcus species are responsible for life threatening meningitis and kill nearly 200,000 people a year. There are only three classes of effective antifungal drugs available to treat Cryptococcus and developing new drugs is difficult because many potential antifungal drugs are also toxic to humans. Effective use of this small set of drugs and development of new or complementary drugs will be aided by a better understanding of the genetic basis of both virulence and drug resistance. My lab will utilize high-throughput genetic/genomic approaches to identify interesting drug resistance and susceptibility relevant pathways and follow up on those discoveries with targeted molecular biology analyses. We developed a transposon mutagenesis approach for Cryptococcus that uses massively parallel in vivo transposition coupled with targeted high-throughput sequencing (TN-seq) to determine how every gene affects growth in a given condition in a single experiment. This assay allows us to rapidly determine the genes required for resistance and susceptibility to an antifungal agent in Cryptococcus neoformans. More broadly, TN-seq will allow my research group to interrogate evolution of virulence across the Cryptococcus pathogenic species complex, including avirulent sister species.

Dr. Houjian Cai, Assistant Professor Email: caihj@uga.edu

The goal of the Cai lab is to interrogate the molecular mechanisms in facilitation of tumor progression and provide the scientific rationale for using small molecule inhibitors for cancer treatment. Numerous oncogenic proteins require fatty acyl modifications to carry out their functions in cancer cells. Protein acylation, including myristoylation and palmitoylation, is particularly essential for leading these proteins to the correct location at the cytoplasmic membrane, thereby facilitating molecular functions.

Dr. David Crich, DÈSSC, Professor, Georgia Research Alliance and David Chu Eminent Scholar in Drug Design Email: David.Crich@uga.edu

The Crich lab is an organic and medicinal chemistry group with diverse interests in drug design and development, synthetic methodology, and carbohydrate chemistry and biology. Current projects include:

1. The design, synthesis, evaluation, and development of novel anti-infective agents for the treatment of multidrug-resistant infectious diseases. Currently, this project emphasizes the

development of novel aminoglycoside antibiotics with reduced toxicity for the treatment of ESKAPE pathogens.

2. The design, synthesis and evaluation of glycomimetics with potential for use as novel therapeutic agents. The current goal is the exploration of small molecule analogs of the β-(1→3)-glucans for use as immunostimulants.
3. The development of improved chemistry for the stereoselective synthesis of glycosidic bonds of all types. Emphasis is currently placed on the bacterial sialic acids, legionaminic and pseudaminic acid, with the goal of preparing otherwise difficulty accessible bacterial oligosaccharides for applications in glycobiology.
4. The exploration of under-represented functional groups in medicinal chemistry with the aim of expanding chemical space and diversity.

Dr. Eugene Douglass Email: Eugene. Douglass@uga.edu
DOCTORAL RESEARCH: Chemical Biology & Immunology (Yale University)

FLUORESCENT SENSORS:
The metabolite methylglyoxyl (MGO) contributes to diabetes symptoms by non-specifically modifying protein side chains. Until recently, studies on MGO have been hampered by the destructive and time consuming (>24 hours) methods used to quantitate MGO concentration. To address these limitations, I designed and tested a panel of fluorescent sensors for MGO that rapidly and accurately quantitated MGO in high throughput and live cell formats.

SMALL MOLECULE IMMUNOTHERAPIES:
Monoclonal antibody (mAb)-based therapies are one of the fastest growing classes of pharmaceutical today. Unfortunately, the median annual cost of these therapies is over $100,000 due to high production and storage costs. As an alternative, my doctoral laboratory developed small- molecule Antibody-Recruiting Molecules (ARMs) which "reprogram" pre-existing antibodies to target cancer antigens. I designed, synthesized and tested these molecules and worked in teams to show that ARMs can elicit anti-cancer immune responses (antibody-dependent cellular cytotoxicity and phagocytosis) both in vitro and in vivo. In addition, I derived a mathematical model for bivalent drugs that aided design of ARMs and PROTACs(PROeolysis TArgeting Chimeras) at Yale.

Dr. Deborah Elder, Clinical Associate Professor Email: dlstrong@uga.edu
Dr. Elder is PBS's only clinical faculty member. Her current research projects focus on the preparation of extemporaneously prepared sterile and non-sterile pharmaceutical products, beyond-use-dating (expiration) of compounded non-sterile pharmaceuticals, drug formulation for individualized patient care, and the use of technology in teaching and assessing pharmacy skills.

Dr. Phillip Greenspan Email: greenspn@uga.edu
Dr. Greenspan' s research interests center on the health benefits of nutraceuticals and functional foods; these terms can be broadly defined as natural food products that are ingested or incorporated into the diet to help slow the progression of certain disease states. In the past several years, Dr. Greenspan has investigated the effect of muscadine grape extracts (Georgia is

a major producer of this Southern specialty grape) and select sorghum bran extracts on important biological processes such as inflammation, protein glycation and LDL oxidation. These pathways are thought to be the underlying cause of two of the most prevalent diseases in America, coronary heart disease and diabetes. It is interesting to note that while natural products have been shown to inhibit protein glycation and LDL oxidation both in vitro and in vivo, there is currently no FDA approved drug designed to arrest these critical disease pathways. Dr. Greenspan's work in natural product research has led to the commercialization of numerous products both in the United States and on international markets.

Dr. Neil Grimsey, Assistant Professor Email: neilgrimsey@uga.edu
The Grimsey group is driven by two key questions:
1) How do cells regulate the temporal kinetics of signaling cascades?
2) How can we harness or inhibit these processes to alter the progression of disease?
Using multiple cutting edge approaches they are investigating the impact of kinase signaling networks in vascular inflammation, angiogenesis, and the progression of chronic lung disease, retinal disease, wound healing and tumor growth.

Dr. Deigo Huet Email: diego.huet@uga.edu
Dr. Huet's current research focuses on the unusual aspects of apicomplexan biology. This group of protozoan pathogens cause morbidity, mortality and substantial economic loss. Notably, they contribute to more than half a million annual deaths due to malaria. The apicomplexan *Toxoplasma gondii* infects an estimated 25% of the world's population, making it one of the most ubiquitous human parasites, and it is a leading cause of death from foodborne illness in the United States.

Dr. Shelley Hooks, Associate Vice President for Research and Associate Professor
Email: shooks@uga.edu
The Hooks laboratory studies the molecular mechanisms by which cellular signaling regulates cell function, and how these signaling mechanisms go awry in cancer and central nervous system disorders. Specifically, they study G-protein signaling cascades and their dynamic regulation by activating receptors and deactivating RGS proteins (Regulator of G-protein Signaling proteins). They have a long-standing interest in a family of receptors activated by Lysophosphatidic Acid (LPA) and Sphingosine 1-phosphate (S1P), which are important bioactive lipid growth factors that play important roles in normal physiology and in the development of cancer and inflammatory/immune diseases. They are also exploring the ability of RGS proteins to attenuate these effects and impact disease progression. Their current focus is on defining the function and regulation of RGS proteins in cancer and neuroinflammatory disease using a combination of cellular, molecular, and genetic approaches.

Dr. Eileen Kennedy, Dr. Samuel C. Benedict Professor Email: ekennedy@uga.edu
The protein kinase superfamily comprises one of the largest gene families encoded in the human genome. A comprehensive understanding of kinase activity under normal and disease states is critical in order to identify targets for disease intervention. However, studying kinase signaling is inherently challenging since there are more than 500 kinases in the human genome, and as a result, there is significant crosstalk among multiple kinases for phosphorylation

targets. Additionally, multiple isoforms exist for many kinases, thereby making it nearly impossible to address the question using genetic knockdowns/knockouts since other genes will compensate with altered expression levels. To address this question, the Kennedy lab is developing novel chemical biology strategies to synthetically disrupt protein:protein interactions (PPIs) using chemically stabilized peptides. This methodology allows for the development of investigative tools that can be applied to elegantly and selectively manipulate protein-protein interactions that are involved in signaling pathways within a cellular environment. The long-term goal of the lab is to develop synthetic biologics that can be used to probe cell signaling events that are mediated by kinases.

Dr. Dexi Liu, Panoz Professor of Pharmacy Email: dliu@uga.edu
The Liu laboratory is interested in the use of gene/protein as a drug for prevention and treatment of obesity, diabetes, cancer and other diseases. Our emphasis is on identification of genes that code for a therapeutic protein and on illustration of its mechanisms of action. We employ gene cloning, biochemical, cell biological, immunological, and gene delivery/transfer techniques to conduct basic research in cell culture and in animal models.

Cory Momany, Ph.D. Email: cmomany@uga.edu
Application of atomic structures to biological and pharmaceutical problems using molecular biology, biochemistry, structure-based drug discovery and macromolecular X-ray crystallography

Dr. Gurvinder Singh Rekhi, Director, B.S. Program Email: gsrekhi@uga.edu
Nanotechnology – absorption of low solubility / permeability drugs; Immediate and controlled-release dosage forms;Topical and Transdermal Dosage Forms; In vitro in vivo correlation (IVIVC); Chemistry Manufacturing Controls (CMC), Technology transfer; Regulatory Submissions; Patent – Development (US, EP), Interference, Litigation, Expert.

Dr. Brian Seagraves, Academic Professional Associate (Skills Lab Coordinator)
Email: cgraves@uga.edu
Dr. Seagraves coordinates all four Essentials of Pharmacy practice courses for the PharmD program. Under his guidance students will perform clinical assessment of patients using bloodwork and laboratory markers as well as physically assessing a patient; assess the laboratory skills of students by determining clinically acceptable best practices; learn to prepare a S.O.A.P note; and assist in gathering data from patient encounters to be used in research.

Dr. Catherine White, Associate Professor Email: cwhite44@uga.edu
Dr. White's research focuses on the influence of age and gender on the disposition of drugs and toxicants, and their subsequent therapeutic or toxic outcomes, and the physiological-based pharmacokinetic modeling for utilization in predicting toxicity and exposures. She also studies drug:drug interactions occurring at the maternal-placental-fetal interfaces, and pre-clinical evaluation of pharmacokinetics and toxicity of new drug entities. She is also searching for educational strategies that enhance active learning for pharmacy students.

Yaguang Xi Email: xi@uga.edu
Dr. Xi's lab is dedicated to advancing cancer therapeutics and cancer chemoprevention. Comprising a team of senior research faculty and postdocs, our lab offers exclusive hands-on training to students, equipping them with the necessary skills to excel in their future careers in academia or industry. We enthusiastically welcome students who share an interest in cancer research and drug discovery to join our lab for their research training. Our research interests include: (1) Cancer drug development and the investigation of molecular mechanisms involving microRNA in the anti-cancer effects of non-steroidal anti-inflammatory drugs (NSAIDs); (2) Exploring the potential of NSAIDs as novel immune modulators to enhance the response of triple negative breast cancer and colorectal cancer to immune checkpoint inhibitors; (3) Cancer Therapeutics , Cancer Chemoprevention, Tumor Metastasis, Cancer Drug Discovery and Development, Health Disparities, Immunotherapy.

May Xiong, Ph.D. Email: mayxiong@uga.edu
Drug delivery and pharmaceutics, specifically the design of macromolecules to improve iron chelation therapy and strategies to combat multi-drug resistance in bacteria

Dr. Jason Zastre, Associate Professor Email: jzastre@uga.edu
Impact of vitamin B1 supplementation on cancer progression: Vitamin B1 (thiamine) is an essential enzyme cofactor intersecting multiple metabolic pathways within the glycolytic metabolism network. Maintaining thiamine homeostasis requires the activity of two SLC transporters THTR1 and THTR2 to facilitate the intracellular uptake prior to activation into the coenzyme thiamine pyrophosphate (TPP) by thiamine pyrophosphokinase-1 (TPK1). Vitamin B1 is an essential enzyme cofactor for 3 key metabolic enzymes, pyruvate dehydrogenase (PDH) and alpha-ketoglutarate dehydrogenase (a-KGDH) in the tricarboxylic acid cycle (TCA), and transketolase (TKT) within the pentose phosphate pathway (PPP). The overall research objectives are i) characterize the differences in thiamine homeostasis between cancer and normal tissue. ii) determine the impact of vitamin B1 supplementation on cancer cell survival and metabolism. III) Develop strategies to reduce thiamin mediated effects on malignant progression. The results of this research will link dietary influences on cancer progression with alterations in the homeostatic regulation of vitamin B1. In addition the research will contribute new insight into the pro-survival and pro-apoptotic effects of a physiologically and pharmacologically important enzyme cofactor. Overall, the outcomes of this research will require a critical rethinking of the usage and composition of dietary supplements and implementation of nutritional monitoring protocols for cancer patients.

Dr. Y. George Zheng, Professor Email: yzheng@uga.edu
Dr. Zheng's research lab works on the forefront area of chemistry, biology and medicine. They are particularly interested in addressing critical problems and challenges in the rapidly evolving field of epigenetics that describes gene expression profile changes that are irrelevant to genomic sequence. Mounting data show that epigenetic processes play pivotal roles in transforming normal cells into malignant tumors and in various other human pathologic conditions. Abnormality in epigenetic landscape presents characteristic biomarkers for disease diagnosis. Therefore, identifying key chromatin regulatory factors such as histone modifying enzymes and chromatin remodeling complexes, understanding their activity, specificity and functional roles,

and inventing potent and selective drug compounds embody demanding needs in today's biology and pharmaceutical research. The lab is innovating and applying advanced chemical and biological strategies, tools and agents to elucidate functions of epigenetic enzymes in disease mechanism and meanwhile provide new diagnostic and therapeutic regimens. Current active research areas include: (1) development of potent and selective epigenetic therapies, and (2) design of chemical biology strategies and probes to interrogate protein acetylation- and methylation-regulated disease processes.