BMB Active Site News

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Faculty Changes in BMB

BMB Has a New Department Head

Dr. Michal Zolkiewski assumed the leadership of the department in summer 2018 after serving as a faculty at K-State for 20 years. Dr. Zolkiewski received his B.S. and M.S. in Biophysics from the University of Warsaw and Ph.D. in Chemistry from the Polish Academy of Sciences. Then, for 7 years, he performed research on protein structure and stability at the National Institutes of Health in Bethesda, Maryland.

Dr. Zolkiewski's current research is aimed at discovering new antimicrobial drugs. Historically, the introduction of each class of antibiotics has been followed by the emergence of clinically significant antibiotic resistance. As a result, the global healthcare community has been gradually losing the battle against the resistant strains of pathogenic microorganisms. Thus, there is an urgent need to develop innovative and non-conventional antimicrobials that could circumvent resistance and keep the dangerous pathogenic microbes under control.

Dr. Zolkiewski's laboratory is exploring a microbial protein called ClpB as a potential target for new drugs. ClpB is a so-called "chaperone" protein that helps other proteins in a microbial cell maintain their proper structure and biological activity. (The structure of ClpB is in the BMB logo.) It turns out that infecting a host exposes many pathogenic proteins to stressful conditions, which require ClpB's help. So, ClpB appears to be an essential stress-response factor that supports proliferation of many pathogens in the infected host organisms. If a chemical compound is found that targets ClpB without affecting proteins of a host, such compound may become an effective antibiotic.

Dr. Zolkiewski believes that BMB should not only excel in academics and research, but should aim to become an intellectual hub of molecular life sciences with a prominent role on the KSU campus. The interdepartmental graduate program administered through BMB is already making an impact campus-wide. The biochemistry courses are an essential component in many degree curricula in different KSU colleges. BMB faculty lead and participate in multiple collaborative research projects at KSU, at other universities in Kansas, and across the world. We strive to fulfill our missions to the society, educate our students, innovate, and make new discoveries. We also hope to maintain close and lasting contacts with our Alumni and all Friends of Biochemistry and Molecular Biophysics!

Faculty Promotions and Tenure

Dr. Timothy Durrett received a promotion to associate professor with tenure this year. He joined the Biochemistry and Molecular Biophysics faculty in 2011 as an assistant professor. Durrett earned his A.B. from Harvard University in 1999 and his Ph.D. from University of Missouri-Columbia in 2006. The specialties of his lab include understanding the biochemistry of triacylglycerol biosynthesis in plants, the structure and function of membrane bound acyltransferases, and genetically modifying the physical properties of seed oils for industrial and biofuel applications.

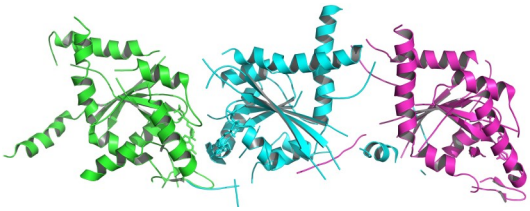
Dr. Erika Geisbrecht was promoted to professor this year. She joined the Biochemistry and Molecular Biophysics faculty in 2013 as an associate professor. Geisbrecht earned her B.S. from University of Wisconsin-Madison in 1996 and her Ph.D. from The Johns Hopkins School of Medicine in 2003. The focus of her lab's research includes studying the formation and maintenance of muscle and heart tissue with a special emphasis on understanding how to prevent muscle disease.

Faculty Profile: Dr. Gregory Finningan

I grew up in the Pacific Northwest, earned a B.S. degree at Gonzaga University (Spokane, WA), and I am a huge fan of college basketball and March Madness.

I was at the Univ. of Oregon (Institute of Molecular Biology) in Tom Stevens' lab from 2005 to 2012. I worked on the assembly, function, and evolution of the highly conserved V-type ATPase proton pump in budding yeast. My graduate work investigated the intracellular trafficking of the V-ATPase complex and the two distinct isoforms in *S. cerevisiae* that reside in specific cellular compartments (the late Golgi/endosome versus the vacuolar membrane). Genetic screens pinpointed the precise positioning of a trafficking signal that was necessary and sufficient for localization of one of the isoforms to the endomembrane system. Additionally, I collaborated with molecular evolutionary biologists at the Univ. of Oregon to predict and synthesize the "ancestral gene" to the duplicated subunit that evolved specific compartmental localization within the fungal lineage. We found that the resurrected ancient subunit could properly assemble with the rest of the modern V-ATPase complex, and illustrated a unique mode of transport through the endomembrane system.

Finally, I reconstructed two additional protein subunits of the proteolipid ring that is different between all animals and fungi (an extra subunit was evolved in the entire fungal kingdom). This billion-year-old ancestral protein allowed us to experimentally determine one mechanism for the evolution of additional molecular components within a protein complex that may involve a simple loss-of-function "ratcheting" through random mutation.



Human Septins

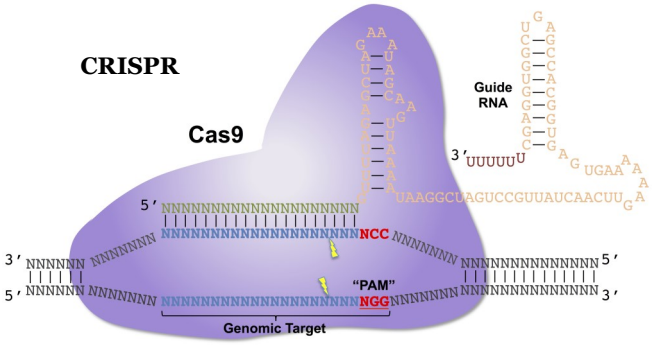
From 2012 to 2016 I was a postdoctoral fellow at the Univ. of California, Berkeley in Jeremy Thorner's laboratory. From 2012 to 2015 I was a recipient of the UC Berkeley Miller Postdoctoral Research Fellowship (other notable awardees include Carl Sagan). My work involved studying the genetics, molecular and cell biology, and biochemistry of the "septin" family of proteins--a cytoskeletal structure found in all fungi and animals on earth. This protein family assembles into a myriad of geometric shapes in the cell, acts as a membrane-tethered corral between distinct compartments, and coordinates information between different signaling pathways. My work involved molecular characterization of various subunits and their individual evolved contribution to the function of the protein network in budding yeast. Additionally, I began work on a novel CRISPR/Cas9 method in budding yeast.

I began as an Assistant Professor at Kansas State University in July 2016. My laboratory includes a large number of undergraduate students and we have several annual lab traditions including a zip lining trip in October. My research interests include molecular characterization of the septin proteins in budding yeast as well as the binding partners that coordinate information with other networks such as the cell cycle, membrane organization, and cytoskeleton. Our lab has received our first grant from the Kansas IDeA Network of Biomedical Research Excellence (K-INBRE) for a Developmental Research Project Program on the molecular analysis of septins during distinct cellular morphological programs in yeast.

Additionally, we have begun a new avenue of work in my laboratory involving yeast as a model system for the study of CRISPR/Cas9 editing and a powerful genetic arrangement known as a "gene drive." This "super-Mendelian" system is of great interest to many fields of biotechnology, academics, and companies for its potential to introduce genetic information rapidly within a population. Our lab has developed an extremely safe model system to study the mode of action of nuclease-based gene drives. We are interested in how this work might be applicable to agriculture, eradication of disease, pests, invasive species, and be used within basic research systems.

A model of the CRISPR/Cas9 gene editing biotechnology. The Cas9 protein (purple) binds to a short strand of RNA (green/orange), and targets the enzyme to a position of DNA in a genome to create a break. Using repair systems, researchers can introduce new genetic information at this DNA site in any organism.

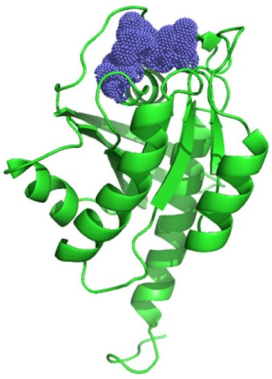
[Image reproduced and adapted from DiCarlo et al. 2013, Nucleic Acids Research 41, 4336-4343. By permission of Oxford University Press.]



Faculty Profile: Dr. Ho Leung Ng

I was a pre-med major interested in the molecular aspects of medicine as an undergraduate at Harvard. I was inspired by my studies with Prof. Martin Karplus to study biophysical chemistry with a computational focus. As an undergraduate and graduate student, I studied broadly in chemistry, physics, mathematics, and computer science. After Harvard, I was in the MD/PhD program at UCLA. I completed two years of medical school but decided to focus on a career in research. Nevertheless, much of my research is driven by finding ways to help patients. I completed my PhD with Profs. David Eisenberg and Richard Dickerson, two leading figures in American crystallography. In their labs, I worked on crystallography of DNA and protein complexes as well as structural bioinformatics. After UCLA, I joined Tom Alber's lab at UC Berkeley as a postdoctoral fellow. In Tom's lab, I dove deeper into crystallography and biochemistry, focusing on proteins involved with tuberculosis, calmodulin complexes, and yeast septins, and computational crystallography. After leaving Tom's lab, I joined the small startup company, ConfometRx, led by Brian Kobilka of Stanford. We worked on crystallography of G-protein coupled receptors (GPCRs) for structure based drug design in collaboration with biopharmaceutical partners. Brian shortly after received the Nobel prize in 2012 for his groundbreaking work on GPCRs.

Ras plus drug



Current Interests:

Our lab, established at K-State in 2017, employs both computational and experimental approaches to study interesting problems and develop new methodology in biophysical chemistry. Our primary focus is on structure-based drug design. We employ virtual docking, molecular dynamics simulations, biochemistry, artificial intelligence, and crystallography to characterize drug targets and identify new drug candidates for cancer, immune disorders, and malaria. Current drug targets of interest include aromatase, estrogen receptor, RORgamma, STAT3, Ras, EZH2, and MHC receptors. Other research areas in the lab are developing new fluorescent proteins as imaging probes with novel chemical properties and improved optical properties. Finally, we also work in developing new computational methods for crystallography and molecular imaging. Our research is highly interdisciplinary and collaborative. I am also interested in mentoring students and trainees and creating a fun, creative lab environment.

Future Directions:

Our creative use of computational chemistry methods rooted in experimental biochemistry has helped us identify many active compounds for many important drug targets. We are collaborating with biologists to explore their action, safety, and mechanism. We will use crystallography to further improve the pharmacological properties of our drug candidates. We have also begun collaborating with Prof. Alan Aspuru-Guzik of Harvard on applying artificial intelligence and quantum computing to drug discovery chemistry and molecular imaging. I see these as transformative technologies that will reshape all areas of science. We will grow our collaborations with biopharma partners to dig deeper into unsolved problems of drug discovery and advance our mission of moving discoveries from the lab to the clinic.

Goldwater Scholar from Biochemistry and Molecular Biophysics

Erianna Basgall, junior in biochemistry, was selected as a 2019 Barry Goldwater Scholar. Basgall is working with CRISPR gene editing and developing applications in the lab of Gregory Finnigan, assistant professor in BMB. The Goldwater scholarship is the premier national undergraduate scholarship for students interested in research careers in engineering, mathematics or the natural sciences. *Photo courtesy of K-State News.*

- KSU Biochemistry & Molecular Biophysics On the Web: www.k-state.edu/bmb
- Connect with K-State Alumni Association: www.k-state.com
- Support BMB through K-State Foundation: https://give.evertrue.com/ksu/arts&sciences
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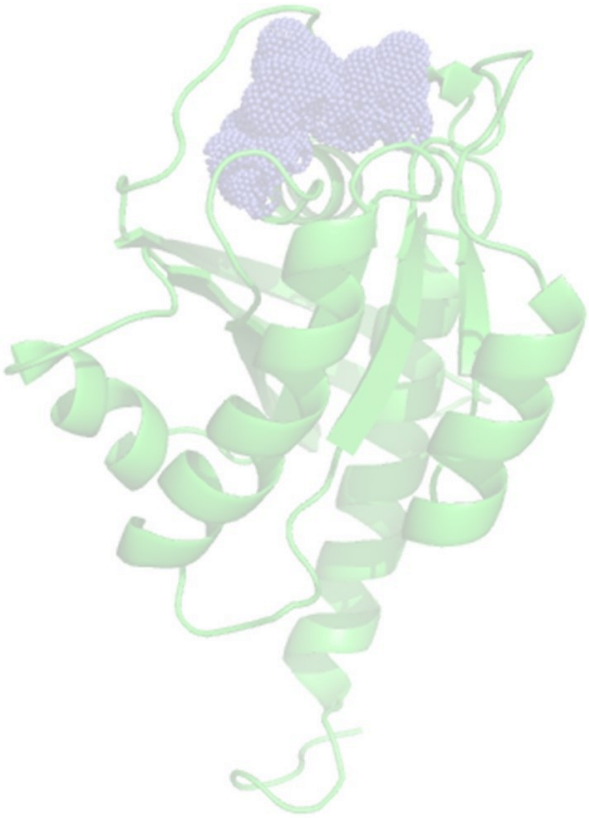

Spotlight on Research Funding: National Institutes of Health

National Institutes of Health (NIH) is the federal agency responsible for funding the basic and clinical biomedical research in the U.S. To obtain funding from the NIH, scientists must submit applications, which are reviewed and ranked by selected panels of experts in the pertinent fields. Currently, only about 10-15% of all submitted applications are funded, so only the best projects have a chance to win the competition. This is why securing an NIH award is considered prestigious among researchers and our department is very proud of all our faculty's projects currently funded by the NIH. Here, we want to recognize the BMB faculty members who are currently directing NIH-supported projects as Principal Investigators:

- **Dr. Brian Geisbrecht**: "Novel Staphylococcal Inhibitors of Neutrophil Granule Enzymes" and "Discovery of Small Molecule Inhibitors of the Classical Complement Pathway Using Cheminformatics".
- **Dr. Erika Geisbrecht**: "Mechanisms Underlying Muscle Development in Drosophila" and "Metabolic Defects Promote Pathogenesis in a Drosophila Muscular Dystrophy Model".
- **Dr. Michael Kanost**: "Proteinase Systems in Insect Hemolymph".
- **Dr. Anna Zolkiewska**: "Role of ADAM12 in Regulatory T-Cell Accumulation within T11 Claudin-Low Breast Tumors"
- **Dr. Michal Zolkiewski**: "High-Throughput Assays for Inhibitors of the Hsp100 Molecular Chaperones" and "Discovery of Hsp100-Selective Inhibitors for Targeting Multiple Microbial Pathogens".

In addition to providing funds for research projects, NIH also supports large instrument purchases, provided that the department matches the federal investment with our own funds. Last year, Dr. Brian Geisbrecht and Dr. Michael Kanost, with matching funds provided by Dr. Ho Leung Ng, won NIH support for purchasing an advanced automated system for preparing samples for protein structure analysis.