Biochemistry & Molecular Biology

College of **Natural Science** | Newsletter for Alumni and Friends

From the Department Chair...

rowth. The MSU Department of Biochemistry and Molecular Biology (BMB), already among the largest in the nation, has continued to grow with three new tenure stream professors starting in 2014 (see page 3) and two more have signed letters of offer. In August 2015, Sophia Lunt (from MIT) and Xiangshu Jin (from Columbia) will begin as BMB assistant professors. Sophia studies metabolites and gene expression to understand cancer cell growth, and Xiangshu studies structure of membrane proteins. As I write this, we have two searches underway which, if successful, will bring the total number of professors hired since 2008 to 20. The net increase will be 11. The areas of the department that have grown the most are genes and regulation (increased by 5); and protein structure and molecular biophysics, including computational (increased by 5). In the areas of metabolism and plant biochemistry, we have had a net increase of one.

AII.

Expansion in these areas was planned; however, many of the new positions resulted from opportunities outside of the department. The gene expression hires were promised to the department when I became the chair in 2008, and we steadily worked to identify outstanding assistant professors. While we progressed to fulfill the goals, we also took advantage of offers from the College of Natural Science and the Office of the Vice President for Research and Graduate Studies to expand our growth by adding three more positions. Protein structure and molecular biophysics growth was the result of a strategic plan developed by a committee headed by BMB Professor John LaPres. A joint search resulting from this strategic plan was carried out with the Department of Chemistry, and outstanding candidates

were found. Because of the strength of the candidates, we were given authority to make three hires (two jointly with chemistry and one entirely in BMB). We will complete the hiring recommended by the LaPres committee if this year's searches are successful. BMB Professor Beronda Montgomery is chairing a new strategic planning committee, and their report will guide future growth.

Our mission is to "discover and transfer new knowledge about the molecular basis of life through basic biomolecular science research and cross-disciplinary research and training."

Growth in the number of faculty members presents challenges; the imminent issue is space. The space available to BMB increased in 2013 when the Molecular Plant Sciences Building opened. BMB Professors Christoph Benning and Dean DellaPenna moved to this building, freeing up two labs in the Biochemistry Building. That still left us with the task of fitting 34 professors into 32 labs. We've begun treating some labs as common areas and are making room for two more people than called for in the building design.

However, it's important to emphasize that growth is not an end in itself. Our mission is to "discover and transfer new knowledge about the molecular basis of life through basic biomolecular science research and cross-disciplinary research and training." The total amount of funded research was at an all-time high in 2013 (the last year for which the data is available), but more important are the discoveries being made all of the time. Some of these are highlighted starting on page 4.

Growth in the pace of discovery and the growth in the size of the department require resources. It is unlikely that state support to the university will recover, and tuition is already high enough that the land-grant mission is in peril. That leaves two avenues for growth in revenue—outside research funding and philanthropy. Professors work remarkably hard in the ever more competitive federal funding arena. This past fall, Michigan State announced a capital campaign to grow the endowment that the university has to support its missions. BMB will participate with college and university teams to make it inviting for people to make a difference in higher education and research through philanthropy.



Thomas D. Sharkey, Ph.D. Chair, Department of Biochemistry and Molecular Biology





Joseph Mayo, M.D., Ph.D., biochemistry, '68, is still practicing general pediatrics in Carthage, Mo. From 2005 to 2009, he changed his career from the office to the classroom and taught chemistry, biochemistry and cellular physiology as a single course and how these disciplines are related, at a community college in New England.

Joseph Prohaska, Ph.D., biochemistry, '74, was inducted as a fellow of the American Society for Nutrition last spring in recognition of his distinguished career in the field of nutrition.

Rob Menson, Ph.D., biochemistry, '76, continues his consulting practice in the application of European and U.S. regulations in the design and development of medical products. He recently joined the faculty of the Association for the Advancement of Medical Instrumentation, where he teaches design controls, risk management and U.S. quality system regulations. Menson also rewrote the chapter on risk management for medical devices in *The Quality System Compendium: GMP Requirements* & *Industry Practice*, 3rd edition.

Scott Cooper, biochemistry, '86, is a professor in the biology department at the University of Wisconsin-La Crosse. In 2014, he received the Carnegie Wisconsin Professor of the Year award.

Diane Husic, Ph.D., biochemistry, '86, attended her sixth U.N. Climate Conference in Lima, Peru, this past December and now serves as a member of the international research and independent NGOs steering committee. Because climate change is being considered as part of the post-2015 sustainable development goals as well, she also attended the U.N. Women's Major Group constituency under that goal.

Carole (Smith) Davis, biochemistry '89; M.A., education, '08, was appointed chair of the Kellogg Community College's Math and Science Department in July 2013.

Andrea (Titlow) McCoy, biochemistry, '95, currently serves as the officer in charge of the U.S. Navy Mobile Laboratory at Island Clinic, Bushrod Island, Monrovia, Liberia. The U.S. Navy mobile laboratories are part of Operation United Assistance, conducting Ebola virus disease clinical testing for the U.S. government response to Liberia's Ebola outbreak.

Henry Ng, M.D., biochemistry, '96; M.D., '01, is the center director for Internal Medicine/ Pediatrics at MetroHealth Medical Center in Cleveland, Ohio, and is currently president of the Gay and Lesbian Medical Association.

Daniel Kemp, biochemistry, '99, was recently promoted to director of discovery, quality and risk management at GlaxoSmithKline, where he has worked since 2006. Kemp is also vice president elect of the drug discovery toxicology specialty section of the Society of Toxicology, and is presenting a continuing education course at this year's Society of Toxicologic Pathology meeting. Andrew Zimolak, M.D., biochemistry and molecular biology, '02, graduated in 2013 with a master's degree in medical informatics from Harvard. In October 2014, he started a new position at the Massachusetts Veterans Epidemiology Research and Information Center, working as a clinical subject matter expert on research that uses the VA hospital's electronic medical records system.

Judith Murphy, biochemistry and molecular biology, '06, attended graduate school at Weill Cornell Graduate School of Medical Sciences, and defended her Ph.D. thesis in July 2014. She also published a paper in the journal *Blood* in April 2014.

Edita Klimyte, biochemistry and molecular biology, and Spanish, '10, has been training in the dual degree M.D./Ph.D. program at the University of Kentucky (UK). She is currently studying the entry mechanism of human metapneumovirus in the Department of Biochemistry at UK in the laboratory of Dr. Rebecca Dutch, who is also an MSU alumna. Klimyte recently received an F30 M.D./Ph.D. Predoctoral Fellowship from the NIH to fund her remaining time in the program.

Sean Law, Ph.D., biochemistry and molecular biology, 'II, had a first-author paper published in *Proceedings of the National Academy of Sciences* last fall titled, "Prepaying the Entropic Cost for Allosteric Regulation in KIX."

Save the date!

All alumni and friends are invited.

R. Gaurth Hansen Lecture

Presented by James "Jake" McKinlay Assistant Professor Dept. of Biology, Indiana University

April 15, 2015 Noon - 1:00 p.m. Location: TBD

John A. Boezi Memorial Alumnus Lecture

Presented by John D. Burczak Chief Scientist Advanced Technology Programs

April 16, 2015 11:00 a.m. - 12:00 p.m. 101 Biochemistry Building, MSU

Annual Department of Biochemistry & Molecular Biology Banquet

April 16, 2015 5:00 - 9:00 p.m. Walnut Hills Country Club, East Lansing, Mich.

New Faculty & Staff





Haudek

The Department of Biochemistry and Molecular Biology welcomed five new faculty members and one new staff member since its last newsletter.

Jin He is an assistant professor whose research focuses on gene expression, particularly in epigenetic mechanism and gene regulation in development and diseases. He was an instructor at Boston Children's Hospital of Harvard Medical School prior to coming to MSU. He received his Ph.D. in immunology and microbiology from the University of Florida.

Kevin Haudek is an instructor who teaches biochemistry and biology courses and is involved in a collaborative research project to assess K-12 science teacher pedagogical content knowledge. Haudek was previously



Kingrea

Lee

a researcher in the MSU Center for Engineering Education Research. He received his Ph.D. in biochemistry and molecular biology from MSU.

Staci Kingrea is a secretary who is responsible for coordinating the department's seminars and overseeing student assistants in the main office. Kingrea has a background in office administration from West Virginia State University and MSU.

Mark E. Lee is an adjunct associate professor who works with the BMB admissions committee on recruitment and with department members on strategies for student persistence in the graduate program. Lee is chair and associate professor of biology at Spelman College in Atlanta, Ga., where he is committed to STEM education for underrepresented groups, especially women.



Mias

Ralston

He received his Ph.D. in biochemistry from Clark Atlanta University.

George I. Mias is an assistant professor whose research explores the existing and developing omics technologies and their application in personalized medicine. Prior to coming to MSU, Mias was a post-doctoral scholar in the Department of Genetics at Stanford University. He received his Ph.D. in physics from Yale University.

Amy Ralston is an assistant professor whose work focuses on intracellular interactions of stem cells during early development with the goal of improving fertility, birth defect prevention and stem cell therapies. She was an assistant professor of molecular, cell and developmental biology at the University of California, Santa Cruz prior to coming to MSU. Ralston received her Ph.D. in zoology from the University of Wisconsin-Madison.

Faculty Honors

Kenneth Keegstra, MSU Distinguished Professor of biochemistry and molecular biology, and plant biology, was elected to the National Academy of Sciences as part of the 2014 class. Keegstra earned this honor for his work in investigating the biogenesis of chloroplasts and the biosynthesis of plant cell walls, both unique parts of plant cells that distinguish them from the cells of other living organisms.

Professors Christoph Benning and Lee Kroos were each named a fellow of the American Association for the Advancement of Science in November 2014. Benning was cited for distinguished contributions to the field of plant biochemistry, particularly the study of plant lipids and the enzymes and genes responsible for lipid biosynthesis. Kroos was recognized by AAAS for distinguished contributions to the understanding of the regulation of development in the bacteria Bacillus subtilis and Myxococcus xanthus.

Pam Fraker, University Distinguished Professor Emeritus of biochemistry and molecular biology, has been selected as a 2015 fellow of the American Society for Nutrition (ASN) in recognition of her distinguished career in the field of nutrition. Fraker will be inducted into ASN on March 30, 2015.

Professor Christoph Benning and MSU Distinguished Professor Dean DellaPenna were named MSU Foundation Professors. Benning is one of the world's foremost experts in plant lipid

metabolism. His work could ultimately lead to plant varieties tailored specifically for biofuel production. DellaPenna is a plant physiologist who studies medicinal plant genomics and plant metabolism and micronutrients. He is one of MSU's most visible ambassadors to the international plant science community and to governmental and non-governmental agencies on the importance of basic plant research.

Professor Tom Sharkey received the 2015 William J. Beal Outstanding Faculty Award at the MSU Awards Convocation, held Feb. 10. Sharkey was recognized for contributing several paradigm shifts in the understanding of photosynthesis and is a leader in understanding the roles of isoprene synthesis by plants to include the protection of plants in bright sunlight.

Professors Dave Arnosti and Tom Sharkey received 2014-15 NatSci Outstanding Faculty Awards for exceptional service to the university. Professor Christoph Benning received the 2014-15 NatSci Outstanding Graduate Advisor Award for demonstrated excellence in providing useful educational and career advice to their students.

Professor John Wang was the 2014 recipient of the College of Osteopathic Medicine's Distinguished Service award. Wang was recognized for a career of outstanding contributions to the college and the university.

Research breakthrough may lead to better anti-anxiety drugs

hen new medicines are invented, the drug may hit the intended target and nullify the symptoms, but nailing a bull's eye—one that produces zero side effects—can be quite elusive.

New research conducted at Michigan State University and published in a recent issue of *Science* has, for the first time, revealed the crystal structure of a key protein, TSPO, which is associated with several forms of anxiety disorders. By identifying the structure at the atomic level, scientists can now pinpoint where drugs may interact with the protein.

"Many other scientists have studied this protein, but what exactly it is doing has been very difficult to determine," said Shelagh Ferguson-Miller, University Distinguished Professor of biochemistry and molecular biology. "Drugs and other compounds bind to TSPO, but without knowing the structure, their effects are hard to interpret. Now that we've obtained the structure, it could provide important clues regarding anxiety disorders and the basis for a new generation of anti-anxiety drugs."

Using X-ray technology rather than PET scans, Ferguson-Miller and her team—which included R. Michael Garavito, BMB professor—were able to solve the crystal structure of the protein—creating an image of TSPO at a molecular level. This gave the researchers an increased understanding of how TSPO interacts with cholesterol and how this relationship affects the creation of steroid hormones. It appears that TSPO plays a key role in shuttling cholesterol into



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mitochondria, the cells' powerhouse where the cholesterol is converted to hormones that are essential for our bodily functions.

The team also identified a TSPO mutant, which provided an important breakthrough. People suffering from conditions such as bipolar disease are found to have a higher probability of having this TSPO mutation, which is fairly prevalent. Cholesterol seemed to bind less strongly, perhaps related to the fact that the mutant structure is more ridged, limiting cholesterol interaction. "When we compared the two forms of TSPO, normal and mutated, we were able to see substantial differences in structure," Ferguson-Miller said. "This could be a clue as to why the human mutant form has an association with anxiety disorders."

The TSPO proteins used in this work came from bacteria rather than human cells, but they are closely related. Getting enough of the pure human protein to carry out these types of investigations is difficult, though it's a future objective of these scientists.

New equipment accelerates X-ray diffraction research

Several MSU research groups will benefit from a \$1 million piece of "gently used" X-ray diffraction equipment recently donated by Acceleron Pharma. It will assist MSU scientists in determining X-ray crystallographic structures.

"X-ray crystallography allows researchers to determine the position of every atom within a molecule. This is essential not only for understanding the function of biological mechanisms, but also for designing new drugs," said Erik Martinez-Hackert, BMB assistant professor.

"Currently, MSU researchers go to the Advanced Photon Source at the Argonne National Laboratory to perform these types of experiments. The new instrument will allow MSU scientists to perform most X-ray diffraction experiments in-house now," Martinez-Hackert said.

Due to the instrument's capabilities, experiments that previously took 24 to 48 hours can now be performed in less than an hour.

"Having this top-of-the-line resource here at MSU will be very helpful in future grant applications," he added.

Student Profile

Andrew Baker: Finding the secret to a successful life

t seems as though Andrew Baker has found the secret to a successful life. He is an outstanding student, a dynamic researcher . . . and a humanitarian.

This well-rounded biochemistry and molecular biology senior has worked in the lab of Robert Root-Bernstein, professor of physiology, for three years. He is also a leader in the Multi-Racial Unity Living Experience & Intercultural Aide Program (MRULE/ ICA)—a program that helps freshmen and international students transition into college.

In the lab, he works alongside Root-Bernstein on origins-of-life research specifically, tracing the evolution of the building blocks of life.

Baker said it's the "sense of wonder," and "finding the secret to life," that got him—and keeps him—interested in the work in Root-Bernstein's lab.

Root-Bernstein said, "I 'discovered' Drew by using the clever technique of asking my professorial assistant, Tyler Rhinesmith, to find me a fellow student as clever, independent and hardworking as himself. Tyler suggested Drew. I call the two my 'Dynamic Duo' since they've basically taken over the analytical work related to my origins-of-life research. Drew, in particular, is trying to prove that we've made some of the nucleic acids simultaneously with sugars and amino acids. It's a very tough problem, which he's doing a great job of cracking!"

Baker has also been involved with ReBioGeneSys – Origins of Life, a hybrid installation by MSU artist and associate professor Adam W. Brown, with Root-Bernstein as scientific collaborator. Their influence inspired Baker to enroll in Brown's art class, in which students use digital tools to make art, 3D printed sculptures and similar things.

"The arts' supportive role in science has been a large area of study for Dr. Root-Bernstein and his wife [they have



BMB senior Andrew Baker poses with an apparatus modeled after the closed-system apparatus that was used in the 1953 Miller/Urey Experiment that investigated the origin of life.

written a book on the subject],"Baker said. "This is one reason I enjoy working with him and Adam—and in science. I did a lot of art in high school, then left it to pursue science; now art has found me again!"

As an intercultural aide, Baker mentors students in the Charles Drew Science Scholars program, which provides academic and social support for high-achieving students from diverse backgrounds who are pursuing science and math degrees.

Baker also wants to instill in the students the importance of pursuing humanitarian activities.

"We try to get students to think about their community," Baker said. "We try to get them to think as global citizens."

Last fall, he took a group of students from the residence hall program to work

at a Lansing-area community garden.

"Our work last semester was to expand the garden so they can feed more people," Baker said. "They now have a garden that can support ten more families."

The expanded garden is expected to feed a total of 30 of the community's families this year.

In 2014, Baker received a Pamela J. Fraker Undergraduate Scholarship, which is awarded to students who demonstrate the initiative and capacity to achieve education and professional goals. He also received a College of Natural Science Undergraduate Summer Research Scholarship in 2014, in support of his work in Root-Bernstein's lab.

The Flushing, Mich., native will graduate in May and intends to continue his research in the MSU lab over the summer. Future plans include graduate school.

For more about the Origins of Life art installment, visit http://adamwbrown. net/projects-2/origins-of-lifeexperiment-1/. 🗢

Contact Us

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Michigan State University

Fruit fly eyes provide cancer gene insight

Fruit fly eyes, as miniscule as they are, could be monumental when it comes to revealing the secrets of an important cancer gene in humans.

Mutations in the human retinoblastoma protein gene are a leading cause of eye cancer. Working with fruit flies, Michigan State University (MSU) researchers have provided the first detailed examination of a set of mutations similar to those present in the human cancer gene.

A paper detailing the findings from this research, co-authored by Irina Pushel, a biochemistry and molecular biology senior in MSU's College of Natural Science (NatSci), was featured on the cover of a recent issue of *The Journal of Biological Chemistry*.

"By systematically evaluating mutations of increasing severity, we now have a model to better predict how we think the protein will react with each mutation," said Pushel, who co-authored the paper with Liang Zhang, lead author and MSU graduate student, and Bill Henry and David Arnosti, NatSci molecular biologists. "We're trying to understand the protein, not even in the specific context of cancer, but rather studying how it interacts within the cell, how it interacts with DNA."

The protein, retinoblastoma, would appear to play a key role in everything.



MSU scientists have turned to fruit fly eyes to unlock the secrets of an important cancer gene.

When it's healthy, it helps control cell growth and development. If absent, the organism would die. In its abnormal state, cells can overgrow, as seen in cancer, or undergo premature death, as in other human diseases. Since fruit flies are essentially tiny people with wings, in terms of genetics, these model organisms can play a key role in advancing human medicine.

"If we find one of these mutations in a human, then we can predict what will happen with the protein," Pushel said. "This isn't going to immediately lead to a new drug to treat cancer. However, we have to know how the protein works before we can develop a drug to fix it."

Although a cancer treatment based on this finding may be years away, the insight and understanding into cell development and gene regulation is immediate, Pushel said.

"That's the cool thing about basic research; it may not lead directly to the creation of a new drug, but it helps decipher the genetic code, which for each person controls the unique pattern of how they grow and how they develop; that's amazing," she said. "It will have many impacts, from understanding development to personalized medicine."

Graduate student finalist for prestigious Soros Fellowship

SU biochemistry Ph.D. student Raeuf Roushangar has been selected as one of 77 finalists for the 2015 Paul and Daisy Soros Fellowships for New Americans. The finalists were selected from nearly 1,200 applicants, all of whom are immigrants or the children of immigrants who are pursuing graduate education in the United States.

Roushangar and the other finalists were recently interviewed by Soros representatives during the final stage of the selection process. In April, the organization will announce 30 new fellows, who will each receive grants up to \$90,000 to pursue graduate studies at U.S. universities.

Roushangar is the only finalist who attended MSU as an undergraduate, and the only finalist who attends MSU as a graduate student.

Roushangar works in BMB Assistant Professor George Mias' lab and focuses his research on the applications for omics technologies in personalized medicine.

"This is already a great achievement for Raeuf, given the fierce competition and number of applicants," Mias said.



Raeuf Roushangar

"Cellular snooze button" advances biofuel, cancer research

The discovery of a cellular snooze button has allowed BMB Professor Christoph Benning and his colleagues to potentially improve biofuel production and offer insight into the early stages of cancer.

The discovery that the protein CHT7 is a likely repressor of cellular quiescence, or resting state, is published in an October 2014 issue of the *Proceedings of the National Academy of Sciences*. This cellular switch, which influences algae's growth and oil production, also wields control of cellular growth—and tumor growth—in humans.

The research team unearthed the protein's potential while seeking ways to improve algae's capacity as a biofuel. Its application in cancer research, however, was a surprise finding that is leading Benning's lab in a new direction.

"Algae provide us with model organisms that rival, or possibly exceed, traditional yeast models," Benning said. "It's quite difficult to grow many types of human cells in test tubes. However, we can readily grow, manipulate and study algae, which have the genomic repertoire that make them relevant in their capacity to drive advances in human medicine."

The discovery was made while tackling the conundrum of algae's vexing inverse relationship with growing mass versus producing oil. When algae are awake, they grow; when they're asleep, they produce oil.



The discovery of a cellular snooze button has allowed MSU scientists to potentially improve biofuels and offer insight into the early stages of cancer.

The secret that cues cells to wake up or fall asleep is the protein CHT7. By engineering this protein, Benning's team might one day develop an organism that can't figure out how to doze and is always active. For biofuels, this would remove a major hurdle and gives scientists a way to potentially produce high amounts of oil and biomass. In terms of human medicine, this discovery gives scientists a promising new model to study tumor suppression and growth.

"For cancer research, it's a new paradigm," Benning said. "The switch that tells an organism to grow, or possibly, go rogue and grow uncontrollably—that's exactly what we want to understand. That is the first step of tumor growth."

Identifying the source of stem cells

Research led by BMB Assistant Professor Amy Ralston has identified a possible source of stem cells, which could advance regenerative and fertility research.

Pluripotent stem cells can be produced when scientists reprogram mature adult cells, or they can be created by embryos during the first four or five days of human pregnancy, the stage in which the highest percentage of pregnancies are lost. This crucial four-day window is uniquely mammalian. "Embryos make pluripotent stem cells with 100 percent efficiency," Ralston explained. "The process of reprogramming cells, manipulating our own cells to become stem cells, is merely 1 percent efficient. Embryos have it figured out, and we need to learn how they're doing it."

The research team that included BMB postdoctoral fellow Tristan Frum discovered that in mouse embryos, the gene Sox2 appears to act ahead of other genes traditionally identified as crucial in stem cell formation. Another discovery is that Sox2 appears to help coordinate cells that make the fetus and other cells that establish the pregnancy and nurture the fetus. Future research will focus on studying exactly why Sox2 is playing these roles.

"What we've learned from the embryo is how to improve efficiency, a process that could someday lead to generating stem cells for clinical purposes with a much higher success rate," Ralston said.



DEPARTMENT OF **BIOCHEMISTRY & MOLECULAR BIOLOGY**

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MSU football star has big-league ambitions

ndrew Gleichert has big ambitions—medical school and playing in the NFL.

After earning his bachelor's degree in biochemistry and molecular biology last December, Gleichert decided to pursue his interest in medical school, as a result of shadowing one of the football team's physicians. He is currently enrolled as an MSU physiology major while beginning his training for a professional football career.

The Ann Arbor, Mich., native signed with an NFL agent in January and currently practices 12 hours a week at a training facility in Wixom, Mich. His anatomy class meets three days a week.

Surrounded by a family of engineers and science teachers, Gleichert became interested in the sciences at an early age.

"I grew up really enjoying and excelling in math and the basic sciences [earth science, biology, chemistry]," said Gleichert, who played tight end and fullback positions on MSU's football team. "When I got to college I was originally



Andrew Gleichert excels as a Spartan, both in the lab and on the field.

in chemical engineering, but had to switch majors due to football practice scheduling. I had already taken biochemistry courses and was intrigued with how the body processes glucose and the pathways that take place in the cells. So I chose biochemistry as my major."

Last semester, he completed the second of two lab courses required of all BMB majors. Neil Bowlby, BMB academic specialist and undergraduate lab coordinator, noted that Gleichert had to miss some of his football practices to complete his work for the lab course.

"Managing my time was difficult," Gleichert said. "But at the same time, football allowed me to have a very structured schedule that enabled me to plan my day. The coaches really ingrained mental toughness and self-discipline in us, so I credit them with helping me get done what needed to get done!"

Whatever the future holds for him—playing professional football, earning his medical degree . . . or both—one thing is certain: Gleichert will get done what needs to get done.