



Department of Biochemistry & Molecular Biology

Newsletter for Alumni and Friends

DECEMBER 2009

From the Department Chair...

This is an important year for self-reflection. The department is undergoing a mandated review within the university. In addition, difficult budgets from the State, that are not likely to turn around, mean that the university is looking closely at all programs. Strong programs will be strengthened while other programs may have to be cancelled. I am working to position BMB to play an even bigger role in the future of MSU than it does today.



Tom Sharkey

In the past 10 years, MSU's research expenditures from federal grants have increased 58%, to \$400 million this year, while state support has dwindled to only 32% of the total MSU budget. Thus grants and philanthropy are rapidly replacing state funding that supports academic and research programs. BMB is one of the top four research programs at MSU and its faculty contributes to two of the other top four funded programs on campus, the Plant Research Laboratory, and the Great Lakes Bioenergy Research Center. Nevertheless, recruiting and retaining our best students and faculty in the face of ever decreasing state funding requires resources that must now be obtained from other sources.

The faculty of BMB have been successful in getting research grants, including seven stimulus funding grants so far. The quality of science in these proposals is first rate. The research covers our three focal areas of gene expression, computational and structural biochemistry, and plant biochemistry. Another focal area is the grass-roots internal seminar series called 3M (Membranes, Metals, and Metabolism).

Another thrust gaining critical mass is metabolic biochemistry. Professor and National Academy member Pam Fraker has been looking at immune function in patients that have undergone bariatric surgery. New faculty member Barbara Atshaves, who studies proteins that bind cholesterol and other lipids, will advance research in this area. Plant biochemistry is a top priority for growth for the university and we continue to hire new faculty in this area. We anticipate two searches for new faculty each of the next two years (see story on new plant science building on page 3).

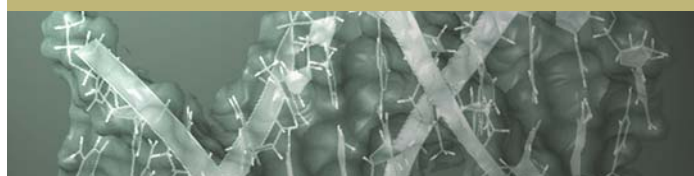
The popularity of biochemistry as an undergraduate major continues to grow as students recognize the importance of biochemistry as a foundation to many areas of biology and medicine. The two-semester, intensive course we offered was overrun with students interested in applying to medical school, while the one semester course dwindled. We will reemphasize the year-long course as a mechanistic treatment for BMB majors and others preparing for research in BMB and related fields. At the same time we are recommitting the one semester course to serving the needs of most biological science majors and premed students. Kathy Foley will start teaching the one semester course in an on-line version in the Fall 2010. Off-campus students have flocked to the summer offering and we anticipate the other sections will do well.

Another teaching technology innovation started this year was with the medical school teaching in southeast Michigan. Fifty students of the College of Osteopathic Medicine started at the Detroit Medical Center site and another 50 students started at the Macomb University Center site. Medical Biochemistry was taught at both sites with all sites linked. We welcomed Pam Osenkowski as a member of the BMB faculty stationed at the Macomb site to help with the expanded medical school teaching.

The next few years will be a period of significant change for MSU as it refocuses on its core missions and invests in those areas most important to the future of the institution. BMB is well-positioned to play a central role in the future of MSU with our outstanding research and commitment to teaching. I hope you will read some of the articles in this newsletter and share my confidence in the future.

Thomas D. Sharkey
Department Chair
B.S. Lyman Briggs '74
Ph.D. Botany and Plant Pathology (Plant Research Laboratory) '80

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Grand Opportunities grant improves drug development



Doctoral student Ziruo (James) Li (left) and postdoctoral researcher Sean Weise (right) examine an Arabidopsis plant in the new biochemistry growth chamber facility. The facility, located in the area formerly occupied by the BMB Research Store, provides researchers immediate, enclosed access and is home to 24 new growth chambers.



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Scientists at Michigan State University are receiving nearly \$3 million from the National Institutes of Health (NIH) as part of a Grand Opportunities grant to uncover how several popular plants make medicinal compounds.

The funding, part of a larger \$6 million award via the American Recovery and Reinvestment Act, will provide scientists the resources to understand exactly which genes are involved in the synthesis of medicinal chemicals in several plants — clearing the way for cheaper and more effective ways to produce drugs. NIH “GO” grants are awarded to fund short term projects with specific goals that have the potential to significantly advance biomedical research in a short period of time.

Scientists on the grant — including researchers at the University of Kentucky and the Massachusetts Institute of Technology — seek to learn which of the roughly 30,000 genes in a plant are actively being transcribed into RNA in a tissue and the exact expression level of each gene. They will assess the types and levels of several hundred chemicals within the tissue and combine these two data sets to figure out which genes are being expressed in concert with specific chemicals.

A short list of those genes most likely to be involved in synthesis of the medicinal compound of interest will be developed. The team then will conduct additional research to demonstrate each of these gene’s individual functions in detail and provide the basis for synthetic biology techniques needed to develop drugs.

The research relies on high-throughput DNA sequencers at MSU. Each experiment can yield as many as 500 million base pairs of DNA sequence, and the entire project will generate approximately 240 billion base pairs of information, the equivalent of roughly 80 human genomes.

“Ongoing advancements in life sciences technology allows us to efficiently interrogate these very large parts lists and efficiently do experiments on a scale that just wasn’t possible three years ago,” Dave Dewitt, associate dean for research in the College of Natural Science, said. “DNA sequencing and metabolite analysis has become immensely more efficient to a point where we can make new discoveries using methods and approaches previously not easily employed in metabolic engineering.”

The 14 plants the scientists will be researching include *Digitalis purpurea* (foxglove), from which the heart drug digitoxin is derived; *Atropa belladonna*, from which the drug Atropine is produced; and *Catharanthus roseus* (periwinkle), from which the anti-cancer drugs vincristine and vinblastine are obtained. More information can be found at <http://medicinalplantgenomics.msu.edu>.

“Many plants make compounds that we use directly as medicines or that we modify slightly to create widely used medicines, but in almost all cases we do not understand how the plants synthesize these compounds,” said MSU biochemistry professor Dean DellaPenna, one of three principle investigators on the grant. “Identifying and understanding the genes involved in synthesis of these plant compounds is a first step that can lead to new drug development and increased production efficiency.”

MSU is receiving \$2.9 million of the \$6 million grant. Other co-investigators on the grant include Joseph Chappell from the University of Kentucky, Sarah O’Connor from the Massachusetts Institute of Technology and Robin Buell of MSU.

Department research receives stimulus funding

Seven biochemistry professors have been awarded nearly \$1.7 million in research funds as a part of the American Recovery and Reinvestment Act. These funds are expected to lead to discoveries ranging from the pure science of how human bodies function to the treatment of disease and drug production.

Christina Chan was awarded \$189,920 to support her ongoing study of disease mechanisms and drug target identification. Her focus is on high levels of fats in the liver and the biological role of saturated fatty acids.

Shelagh Ferguson-Miller was awarded \$85,000 to support continued research into understanding the structure of cytochrome c oxidase, an important protein in humans, and understanding how it regulates how humans use energy from food.

Laurie S. Kaguni was awarded \$259,165 for her research into understanding how animal mitochondrial DNA is replicated. Understanding how mitochondria operate is important for human health as they are the energy-producing units within animals and their activities affect cellular functions.

Charles Hoogstraten was awarded \$70,000 to support his studies of catalytic RNA molecules, or ribozymes. Since these RNA molecules can cleave RNA molecules in a designable, sequence-specific fashion, ribozymes are possible therapeutic agents for certain viral diseases and cancers.

David Arnosti was awarded \$211,028 to study the molecular analysis of transcriptional repression through collaboration with Saurabh Sinha at the University of Illinois Urbana-Champaign. They expect to unravel the “cis regulatory grammar” at the heart of eukaryotic transcription enhancers.

Robert Hausinger was awarded \$105,045 to characterize Fe(II) /alpha-ketoglutarate-dependent hydroxylases, which are important enzymes for mammals and microorganisms.

This funding will provide the U.S.-manufactured instrumentation that will accelerate their research.

Beronda Montgomery was awarded \$765,249 to research how plants sense and respond to changes in light by doing molecular genetic analysis of spatial-specific phytochrome responses in *Arabidopsis thaliana*.

“These grants provided by federal stimulus monies are a solid investment in solution-driven research,” said Tom Sharkey, department chair. “The department faculty and a strong cadre of students really collaborated well in recognizing our strengths and leveraging those as we scrambled to meet the grant deadlines without disrupting ongoing projects.”

“The excitement of exploring the mechanisms that operate inside cells in humans and plants is a driving force among everyone in the department as they know their hard work will lead to many advances in treating diseases and improve the lives of people around the world,” Sharkey added.

Plant science expansion planned for 2010

MSU will be expanding facilities to serve the plant sciences with a new Plant Science Expansion - a 4-story building which will serve plant science research across MSU, including laboratories associated with biochemistry. The facility will be located at the Southwest corner of the Bogue and Wilson intersection, and will connect to the Plant Biology and the Plant and Soil Sciences Buildings. Connecting the buildings will allow scientists to travel between all the South campus greenhouses and facilities without having to travel outside and risk exposing research to extreme temperatures or contamination.

“The physical connection along with the designed interaction space on the main level will enhance collaboration and connectedness among the faculty in many departments,” said Dave Dewitt, associate dean for research in the College of Natural Science. “This affords us the resources for our expanding research while serving as a focal point to bring together scientists across disciplines.”

The 80,000 square foot facility will have 2 levels of open research labs providing scientists with nearly 40,000 square feet of lab space. The basement is designed for the 60 growth chambers needed to accommodate the growing areas of research. The new space will house the increased number of plant science researchers



An artist's rendering of the Plant Science Expansion.

related to funded NIH and NSF initiatives, the Great Lakes Bioenergy Research Center and the Michigan Agriculture Experiment Station. Construction is expected to begin in May.



Sweeley continues to explore new areas



This fall, Chuck Sweeley (left) welcomed Robert Desnick (right) from the Mount Sinai School of Medicine as the speaker for the Sweeley Lectureship. The presentation was on enzyme replacement in Fabry disease – a disease which remained a dermatologic curiosity until Sweeley and Kliensky published their seminal findings in 1963.

Join us on Facebook and LinkedIn

Connect with BMB alumni and faculty on Facebook and LinkedIn by joining the College of Natural Science alumni Facebook group at <http://bit.ly/CNSfacebook> or be a part of the college LinkedIn group at <http://bit.ly/CNSlink>.

Help Support BMB

If you want to join me in supporting the long-term, financial viability of BMB, I suggest contributions to the Biochemistry Enrichment Fund endowment. To honor Biochemistry professor and first Dean of the College of Natural Science, you can donate to the Richard and Claire Byerrum Endowed Fellowship, an endowed fund to support graduate students. Your gifts to these funds will forever support essential components of the BMB program at Michigan State. Use the envelope provided or for a complete list of BMB endowments and other funds, go to: <http://bit.ly/BMBgift>. Thank you.

- Tom Sharkey

While 17 years have passed since his official retirement, Professor Emeritus Chuck Sweeley still has a passion for science and it continues to drive him to explore new areas of research. Sweeley has assembled an interdisciplinary team of scientists at MSU who are hoping to begin a translational research project examining the effects of using a ketogenic diet to treat brain cancer.

“Ketogenic diets have been used for several decades in treating epilepsy and we hope to build off this research to learn how it may influence the treatment of brain cancer,” said Sweeley. “Many researchers across MSU have expressed interest and we now have a team of faculty from physiology, food science, oncology, radiology, and family practice.”

The group recently brought Tom Seyfried from Boston College to MSU to share his findings in managing complex diseases through principles of metabolic control theory. This theory is based on the idea that compensatory or redundant brain metabolic pathways are capable of modifying the pathogenesis of complex diseases despite the continued presence of the genetic or environmental defects responsible for the disease. By shifting the brain metabolic environment, diet therapies can potentially mask or neutralize molecular pathology.

Sweeley hopes to have funding in place in the near future so the team can

begin work in the spring. By reducing carbohydrates with a ketogenic diet, Sweeley says they hope to see evidence manifested through imaging of the tumors before and after treatment.

Sweeley’s career at MSU has spanned five decades. He joined the MSU biochemistry faculty in 1968 and served as chair of the department from 1979-1985. He received his B.S. in chemistry from the University of Pennsylvania and Ph.D. from the University of Illinois. After a postdoctorate at the National Institutes of Health in the 1950s, he began his academic career at the University of Pittsburgh.

His accomplishments have been recognized with the Distinguished Faculty Award, the Michigan Scientist of the Year award, and as a University Distinguished Professor.

When Sweeley joined Biochemistry in 1968, he organized the mass spectrometry facility, which became one of the first NIH-supported national resources in this field.

Tran retires after 16 years

Huong Lee Tran retired in November after working 16 years at MSU. Tran worked in the department’s Instrument Repair Shop and was known to many faculty and students as he serviced scientific research equipment ranging from centrifuges and ultra-centrifuges to balances and incubators.

“The best things about working at this shop is that I made a lot of friends,” Tran said. “Most of the customers are scientists, so besides providing a service I was also able to learn a lot from them.” Tran also repaired equipment in the surrounding community and other universities. He trained students to repair equipment and has enjoyed watching them flourish in their careers. Tran began his retirement by moving to Fort Meyers, Florida.



Accelerating analysis with mass spec

If “Mass Spectrometry Guru” were a title at Michigan State, Dan Jones would have it. Jones, professor of biochemistry and chemistry, has spent four years at MSU involved in research projects across the campus studying metabolomics.

“Metabolomics is the crazy idea that we can study how organisms function by measuring as many different chemicals that they produce as possible,” Jones said. “For example, when you go to your physician, they will take some blood and measure your glucose or cholesterol. Based on a few measurements, they will tell you if you are healthy or not.”

In a similar fashion, Jones uses a combination of mass spectrometry, liquid chromatography, and gas chromatography to characterize hundreds of compounds inside plant and animal tissues.

Jones’ lab has developed tools that enable them to test for more than 100 different chemicals from a single sample in less than one minute. “Only a few years ago, it would take an hour to test for 20 or 30 chemicals,” he said.

His goal is to continue to make the technology more efficient so they can test more compounds on more samples, thereby enabling research that previously couldn’t even be imagined.

Jones is involved in the recent National Institutes of Health grant to uncover how 14 medicinal plants make valuable compounds used to treat human disease. To decode the relationship between the genetic make up of these plants and the compounds they produce, scientists have several distinct tasks. They will understand the expression of genes in these plant tissues using transcriptomics and high-throughput DNA analysis. They will also create detailed chemical profiles of the same tissues.

They are also generating databases of the chemical properties. Each of the 14

plants will require as many as 20 tissue samples, which means hundreds of samples will be analyzed for more than 100 different chemical forms.

When the chemical profiles and genetic profiles are complete, they will be joined using bioinformatics to create a database that connects genetic information to chemical pathways.

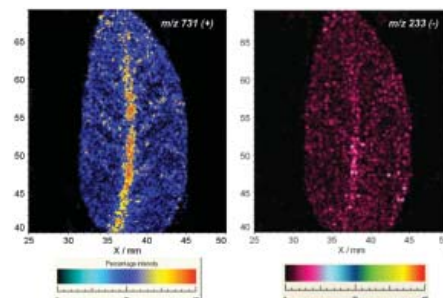
“This knowledge will improve plant production of a chemical or give us the ability to put these genes in yeast or bacteria, which will make it more efficient to harvest them,” Jones said. “Some of the chemicals we are testing now are effective cancer treatments, but they are expensive because they are difficult to produce.”

Jones is also investigating how new chemicals attack cancer cells inside animal tissues. He is working with Babak Borhan, professor of chemistry, to investigate a plant-derived chemical that is a promising new cancer drug.

They have sampled cells treated with traditional cancer treatments over time to see how their chemical composition changed and then compared it to Borhan’s new drug. Comparing the results allows them to determine how the cancer cells were killed.

“We would like to understand how the chemicals Borhan synthesized kill cells,” Jones said. “If they kill cancer cells in a different way than other drugs, which preliminary results show that they do, then these chemicals could provide an additional mechanism for treating drug-resistant cancers.”

Jones has also developed a new tool to continue to improve mass spectrometry: mass spectrometry



These two mass spectrometry images from Dan Jones’ lab are of the leaf of a wild relative of tomato. They show the locations and amounts of two different metabolites present in the glandular trichomes of the leaf (detected at two different masses). Images were generated by chemistry graduate student Chao Li.

imaging. It uses a laser to take samples at any point on an image. For example, they can transfer the glands from a leaf onto a specially tailored carbon surface and then use a laser to take 40 or 50 mass spectrometry readings.

This new technology allows them to ask whether a particular cell in the edge of the leaf is doing similar things to a cell near a vein inside the leaf.

“It turned out that location has a lot to do with chemistry, and when we take a sample of the whole leaf –we are taking the average of all the different cells there,” Jones said.

Jones is involved in projects all across the campus, but he said that none of it could be done without MSU’s investment in core facilities.

“MSU has long been a leading institution in mass spectrometry and we continue to be a leading institution,” Jones said. “We have fantastic experts and resources. A lot of that comes from phenomenal access to core facilities and instrumentation.”

Pierce to receive Boezi Award



John Pierce will receive the 2010 Boezi Award.

John Pierce (Ph.D. '80) has been selected to receive the 2010 John A. Boezi Memorial Alumnus Award for his accomplishments in the field of biochemistry. Pierce is Vice President for DuPont Applied BioSciences – Technology. He received his B.S. in biochemistry from Penn State and his Ph.D. in biochemistry from MSU.

Pierce is responsible for DuPont's biotechnology research and development efforts in the production of fuels, chemicals, and materials. He is a founding board member of the Society of Biological Engineering and currently serves on the Management Board of the BioEnergy Science Center at Oak Ridge and on the Scientific Advisory Board of the Great Lakes Bioenergy Research Center- two DOE sponsored consortia developing biofuels from renewable resources.

At MSU, Pierce's thesis explored sugar phosphates using nuclear magnetic resonance, and catalysis and activation

of ribulose biphosphate carboxylase/oxygenase. He held postdoctoral positions at Cornell University and the University of Wisconsin before beginning his career at DuPont in 1982.

As a recipient of the award, Pierce will present a seminar and be honored at the department's annual awards banquet on April 15, 2010. For information on the seminar or attending the banquet, contact Billy Yang at yangwi@msu.edu.

The Boezi Award is presented to a distinguished alumni in honor of John A. Boezi - a renowned researcher and excellent teacher. Boezi's dedication to teaching and his uncompromising principles of integrity and performance were respected by students and faculty colleagues. His death in 1980 inspired the establishment of an award, given every even numbered year, to an alumnus who has gone on to a distinguished career that reflects the qualities personified by Boezi.

Matthews first Hansen Award winner



Professor Tim Zacharewski (left) presents Jason Matthews (right) with the 2009 R. Gaurth Hansen Award.

The first annual R. Gaurth Hansen Alumnus Award was presented to Jason Matthews (Ph.D. '01) on April 19, 2009. Matthews is an assistant professor in the Department of Pharmacology at the University of Toronto where he recently received the Canadian Institutes of Health New Investigator Award recognizing his training, productivity and promising academic research potential.

At MSU, Matthews worked as a graduate student with Tim Zacharewski in the Center for Integrative Toxicology from 1997-2001. He pursued postdoctoral training with Jan-Ake Gustafsson at the Karolinska Institute in Stockholm from 2001-2006 where he investigated the interaction of ER alpha and beta with other transcription factors and the effect of these interactions on subsequent gene expression.

The Hansen Award recognizes outstanding young scientists who received their training in the department and are now in the early stages of a promising academic career. The award honors the memory of Gaurth Hansen, the founding department chairperson, who provided critical judgment in selecting the early members of the department and helped their continued development as teachers and investigators during his tenure as chairperson from 1957 to 1968. The award is presented in odd numbered years at the annual spring awards banquet.



ALUMNI CLASS NOTES



Gary Steinman, MS '63, is chairman of biochemistry of Touro College of Medicine in New York City. His area of research is spontaneous twinning and he was featured in an episode of National Geographic Explorer which aired in November.

Lori (Hallman) Conlan, BS '66, is a nationally recognized speaker in career development topics and is at the NIH in the Office of Intramural Training & Education assisting the 4,000 NIH postdocs in their personal career choices. She also serves as a Board member for the National Postdoctoral Association.

John Hess, PhD '66, is retired from Virginia Tech and contributes as a tutor with Literacy Volunteers to the learning of persons with minimal basic literacy skills and to adults for whom English is not a primary language. He also studies with a group that explores non-violent communication which contributes to his connection with the Center for Peace Studies and Violence Prevention at Virginia Tech.

Fred Kayne, PhD '66, continues to do lab consulting in clinical chemistry and help with teaching in the pathology residency program at Hahnemann Hospital which is affiliated with Drexel University.

Marlene Kayne, PhD '66, is retired but still teaching online for 3 universities in chemistry, geology, biology, clinical chemistry and molecular biology.

Robin Berglund, BS '67, is in the private practice of child and adolescent psychiatry in the Los Angeles area.

Robert Bumgarner, BS '67, MD '74, is a senior program manager for WMD/CBRNE Effects Assessment and Analysis at Science Applications International Corp.

James Behnke, PhD '73, is retired from Asbury College in Wilmore, KY. He recently went on a medical trip to Moldova with a group organized by the Christian Medical and Dental Association where he lectured on the molecular biology of diseases, ethical issues in science, and the philosophy of science and religion.

Marian Kaehler, PhD '78, is on sabbatical for the year at Luther College in Decorah, Iowa, where she teaches genetics, molecular biology, and radiation biology.

Karen Bratus, BS '79, was recently promoted to Dean of Health Sciences at Baker College in Allen Park, Michigan.

David Lapenson, PhD '83, is working as a computer specialist in Winthrop, Mass.

Marco Villanueva, MS '84, PhD '88, is a professor at the Institute for Marine Science and Limnology of UNAM in Puerto Morelos, Mexico. He is studying signal-transduction and cytoskeletal proteins in photosynthetic algae with a focus on how they participate in the establishment of symbiosis.

Charles Yokoyama, BS '87, was recently promoted to Senior Editor at the scientific journal *Neuron* - part of the Cell Press family of journals. He handles editorial and peer review of manuscripts in all areas of neuroscience and experimental psychology, manages an international network of authors and reviewers as well as the *Neuron.org* website and review articles, and travels to conferences and universities to recruit and advocate for neurobiology.

Marty Zaluski, BS '92, is the State Veterinarian for Montana at the Montana Department of Livestock.

Anne Quillevere, PhD '92, is a technical writer for the acoustics and vibration company 01dB-Metravib.

Amanda (Barrett) Levin, BS '98, is a pediatric ICU fellow at Children's Memorial Hospital, Northwestern University, in Chicago.

Travis Reed, BS '05, is currently pursuing a small animal internship in Canada at the University of Guelph, Ontario Veterinary College.

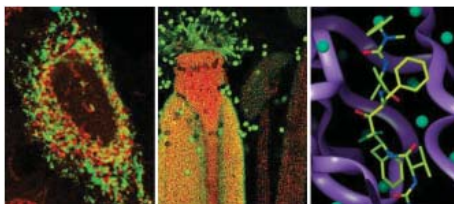
Let us share your career news and accomplishments with students and alumni. E-mail NatSci4u@msu.edu.

HHMI's Tjian awarded honorary doctorate

Robert Tjian, president of Howard Hughes Medical Institute, was the commencement speaker at MSU's advanced degree ceremony this fall. Tjian received an honorary doctor of science degree and also presented a seminar for biochemistry students.

Tjian studies the biochemical steps involved in controlling how genes are turned on and off. An HHMI investigator since 1987 and a professor of biochemistry and molecular biology at the University of California-Berkeley, Tjian discovered proteins that play a critical role in controlling how genetic information is transcribed and translated into the biomolecules that keep cells, tissues and organisms alive. Since becoming HHMI's president in April 2009, he has continued to be actively engaged in research.





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BMB club connects students with alumni

The BMB Undergraduate Club continues to grow and is helping its 300 student members prepare for the future as well as organizing opportunities to volunteer and help the community. The group became an official registered student organization on campus nearly two years ago.

The group conducts regular meetings bring undergraduate students together with alumni to help showcase career paths and better prepare students for their career.

"A lot of our meetings center around preparing students for the future," said Dennis Miner, biochemistry senior and club president. "We host sessions about resume building and applying to grad school. We bring in speakers from all over to tell us what their professions are really like."

Students are very interested in finding out about all of the different career choices alumni undertake with their degrees. "Our speakers have been really open about their lives and sharing what they really enjoy about their career," said Sarah Haskins, biochemistry senior and club vice president.



Biochemistry Undergraduate Club members at a recent meeting in November.

In addition to the speakers, each year the club sponsors a poster session in conjunction with the University Undergraduate Research and Arts Forum and also participates in Relay for Life, Toys for Tots and Operation Good Cheer.

Alumni interested in coming to campus and speaking with the club should contact department chair Tom Sharkey at tsharkey@msu.edu.