MICHIGAN STATE UNIVERSITY

Department of
Biochemistry & Molecular Biology

Newsletter for Alumni and Friends

DECEMBER 2008

From the Department Chair...

Tom Sharkey

Greetings from the Department of Biochemistry and Molecular Biology at MSU. In completing my first year as chair of the department, and my first year back after being away from MSU for 28 years, I am pleased to share some of the excitement from the halls and labs of biochemistry.

Nationwide, the number of undergraduate students majoring in science has increased over the past several years, and that is no different at MSU. Our BMB undergraduate majors have increased 25 percent in the last three years and this semester there are 403 students majoring in the biochemistry and biotechnology programs through both the College of Natural Science and Lyman Briggs College. These numbers reflect positively on our department and we are thrilled to have such a large number of undergraduate students.

Yet with the growth comes the challenge of increased teaching loads and increased class sizes – often with intensive hands-on labs. One solution we are trying is discussed on page 5 regarding Neil Bowlby's combination of the two top-level laboratory courses into one ultra-intensive summer lab experience.

Our signature areas of research continue to evolve. We emphasize gene expression, protein structure and computational methods, and plant biochemistry. This summer we held a retreat to examine if we want to retain these as signature areas for the department. We decided that while they do not describe everything we are and they are not parallel in scope, these do remain focal points for the department.

The big news in the department this year was the beginning of the Great Lakes Bioenergy Research Center. Funding from this center supports plant biochemical research of professors Benning, Hegg, Keegstra, and Pauly, as well as my own research on photosynthesis.

Gene expression continues to develop with the growth of the Gene Expression in Development and Disease initiative. A highlight this year was the international symposium held on campus. David Arnosti led a team that organized the conference on transcriptional regulation and systems biology. The event provided excellent exposure to the hundreds of researchers who attended from around the world. Additionally, we recorded 21 of the scientific presentations and have them on the Internet (www. bmb.msu.edu) so the symposium can continue to serve as a valuable instructional and outreach tool for students and everyone in the field.

Also in the area of gene expression, we currently are searching for a scientist to be the Hannah Professor of Gene Expression - an endowed chair position in the department. We hope to have this filled soon and look forward to having this prominent position in the department.

Plant biochemistry continues its large successful projects on plastid gene function and analysis of genes in the trichomes (leaf hairs) of plants in the tomato/potato family. Watch for some exciting news from these faculty in the near future.

Of final note in the department, there is a hint of sadness among us all as the retirement of Jack Preiss looms in the months ahead. Jack has touched thousands of lives over his 50 years in science (the last 23 here at MSU). Jack is retiring at the end of the year and deserving of a big 'thank you'. He will be missed and we all hope he continues to visit and find himself welcome in our classrooms and labs.

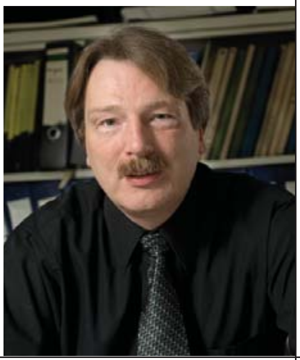
The funding environment for the department is evolving, with a smaller proportion of state funding and more reliance on federal research grants. I believe we are handling these changes well and that we are favorably positioned for the future. I look forward to the excitement we have coming with many of our ongoing initiatives.

There are many promising discoveries ahead in the department. I sincerely hope you join me and other alumni in feeling the pride in knowing our science is transforming lives.

Thomas D. Sharkey
Chair, Department of Biochemistry & Molecular Biology
Michigan State University

New Protein Leads the Way in Biofuels

Fueling a vehicle made with biofuel from a rutabaga may be in the future because of research breakthroughs by a team of scientists led by biochemistry professor Christoph Benning. A newly discovered protein, Trigalactosyldiacylglycerol 4, or TGD4, is directly involved in building chloroplasts, which operate in the conversion of sunlight, carbon dioxide and water into sugars and oxygen during photosynthesis.



Christoph Benning

GREAT LAKES BIOENERGY RESEARCH CENTER

MSU partnered with several other institutions last year to establish the Great Lakes Bioenergy Research Center, one of three new U.S. Department of Energy centers. The center, based in Madison, Wisconsin, is funded with $125 million over five years. MSU will use approximately $50 million for basic science research aimed at solving some of the most complex problems in converting natural materials to energy.

The center focuses on: breeding new varieties of bioenergy plants, developing new processing techniques and agents from microbes for breaking down cellulose, improving the microbial and chemical processes that convert biomass to energy products, providing an environmental and economic framework for sustaining the biomass-to-fuel pipeline and integrating new technologies—including genomics and new computational methods—into bioenergy research.

"Nobody knew how this mechanism worked before we described TGD4," Benning said. "This protein directly affects photosynthesis and how plants create biomass - stems, leaves and stalks - and oils."

The research, published in the August 2008 issue of *The Plant Cell*, shows how TGD4 is essential for the plant to make chloroplasts. Understanding how TGD4 works may allow scientists to create plants that would be used exclusively to produce biofuels, possibly making the process more cost-effective. Corn, soybeans and canola that are used to produce oils – accumulate the oil in their seeds.

"We've found that if the TGD4 protein is malfunctioning, the plant then accumulates oil in its leaves," Benning said. "If the plant is storing oil in its leaves, there could be more oil per plant, which could make production of biofuels such as biodiesel more efficient. More research is needed so we can completely understand the mechanism of operation."

Chloroplasts require extensive lipid movement inside the cell between the endoplasmic reticulum, where lipids are produced, and the plastid, where they are needed. In the TGD4 mutant, diacylglycerol produced in the endoplasmic reticulum is not available for galactoglycerolipid biosynthesis. This mutant accumulates diagnostic oligogalactoglycerolipids and triacylglycerol in its tissues.

Benning's lab has started experimenting with rutabagas modified for biofuel production. They inserted a gene previously discovered by the Benning Lab that regulates the conversion of sugars into lipids called wrinkled1 into the root storage organs. In theory, this gene should cause the plant to produce much more oil throughout the plant, thereby greatly increasing the amount of harvestable oil per acre.

"To maximize efficiency, we need to make oil in not just the seeds," Benning said. "If we could make it in the green tissues, like the leaves, stems or even underground tissues like storage roots, then we think we can make a lot more per land area."

The research was funded by the Department of Energy, National Science Foundation and the Michigan Agricultural Experiment Station.

Benning also is a member of the Great Lakes Bioenergy Research Center, a partnership between MSU and the University of Wisconsin-Madison funded by the U.S. Department of Energy to conduct basic research aimed at solving some of the most complex problems in converting natural materials to energy.

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Unlocking the Secrets of the Chloroplast

MSU scientists are unlocking the secrets of the chloroplast by taking a new approach to genetics in the Chloroplast 2010 Initiative. This new method examines the relationships between thousands of different genes and almost 100 different measurable physical characteristics, called phenotypes, in the chloroplast. The method has already led to new discoveries about gene function and relationships between previously unknown genes and important characteristics like plant oil production.

Claire Moore, a junior from Kalamazoo, and Kayla Kerr, a senior from Chicago, perform a plant morphology assay.

"The hope is to be able to look at the chloroplast as a system rather than a series of not necessarily obviously connected components," said Rob Last, professor of biochemistry. "We want to go beyond the 'one gene, one process at a time' approach and take a more holistic approach to analyzing the data."

Traditionally, genetics was done by choosing a phenotype that could be related to a biological process, exposing plants to a source of mutation and then sorting through the random mutants to find the phenotype of interest. Finding the gene that caused the phenotype leads to explaining how a gene controls a particular physiological process.

More recently, investigators have been reversing the process. They select two or more genes that they are interested in, and they manipulate their function. The plants are grown and the traits of interest are measured. The advantage of this process is that if the phenotype is different, then the scientists already know what gene was the cause of the change. However, the process doesn't always work.

"A lot of the time, you do that and you don't get an expressed phenotype for two reasons," Last said. "The first problem is redundancy. Biological systems are extremely redundant, which is a good thing for plant survival, but to a geneticist is very problematic. If there are two genes that do more or less the same thing, sometimes, or often, the other non-altered gene will take over, preventing any change in phenotype."

The other way Last said the approach can come up short is if the gene does something that scientists didn't anticipate. If the gene isn't involved in the process that is being measured, but it is involved in twenty other processes, then it will be overlooked.

"The collaborating labs at MSU are trying to take a very open ended approach toward genetics," said Last. "We're looking at mutants in several thousand genes instead of just one, two, ten or even thirty. We're screening their phenotypes using 12 different screens, which all together account for about seven dozen different discreet traits that we're measuring."

The project creates huge amounts of data that is entered into a searchable database created at the Research Technology Support Facility. The database is searchable by gene or by phenotype, and it includes data, descriptions and photographs for different mutants. As people in the partner labs complete more analysis, the database continues to grow. As it grows, people are discovering connections between genes and functions that have never been connected before.

This broader search methodology is already showing promise toward understanding earlier MSU discoveries. In the 1980's, Chris Somerville's lab pioneered screening genes that were involved in making fatty acids in plant leaves. A tremendous amount of work has gone into trying to get plants to produce more oil, but so far, it hasn't happened.

"We've run very similar screens to the screens that were previously run in Somerville's lab, and elsewhere, that had been pioneered here at MSU, and we're finding new genes they never discovered," Last said. "New genes that influence oil production are especially valuable to MSU and Michigan because plants are being increasingly relied on to provide biodiesel fuel, fatty acid starting materials for industrial chemicals and as healthy oils for human nutrition."

The MSU faculty involved in the project include Christoph Benning, Dean DellaPenna, Rob Last, Kenneth Nadler, John Ohlrogge, Katherine Osteryoung, Yair Shachar-Hill, Andreas Weber, Bill Wedemeyer and Curtis Wilkerson. Linda Savage is the project manager. Funding for this project is provided by the National Science Foundation.

Explaining Cell Energy

Explaining energy production from food is not as simple as it sounds. At the most basic molecular level, new discoveries are explaining more about how cells create and regulate energy. Professor Shelagh Ferguson-Miller is part of the team of researchers involved with the MSU Center for Mitochondrial Science and Medicine. She is researching energy conversion and regulation with hopes that further discoveries may hold the key to developing a new class of antibiotic drugs and new treatments for obesity.

THE CENTER FOR MITOCHONDRIAL SCIENCE AND MEDICINE

A team of scientists in biochemistry, physiology, toxicology and zoology have established a research center to link mitochondrial function to global cellular processes and pathological changes that lead to aging and disease. The Center for Mitochondrial Science and Medicine (www.mitoscimed.msu.edu) seeks to identify the key cellular players in the mitochondrial life cycle and to leverage this in the design and development of therapeutics for treating diseases that have a mitochondrial component, such as diabetes, Parkinson's disease and cancer.

The research is directed toward understanding how energy balance and other processes of mitochondria are linked to disease progression. Five faculty members comprise the team of investigators:

- Shelagh Ferguson-Miller, biochemistry,
- Kathleen Gallo, physiology
- Laurie Kaguni (program leader), biochemistry
- John LaPres, biochemistry and toxicology
- Kyle Miller, zoology

"We're working at the most fundamental level to ask the question: how do you take electrons, which we get out of our food, and use them to reduce oxygen, which we get from breathing, and in the process create a form of energy that can be used to support most processes in the cell?" said Shelagh Ferguson-Miller, professor of biochemistry.

Ferguson-Miller uses x-ray crystallography to determine the structure and function of the enzyme cytochrome c oxidase which consumes 95 percent of the oxygen we breathe. This technique creates atomic resolution images that show each atom of the enzyme. The process of crystallization is very difficult for membrane proteins, so her lab has benefitted greatly from access to an advanced photon source at Argonne National Laboratory through the Michigan Life Sciences Corridor and from collaboration with a membrane protein crystallography expert at MSU, Mike Garavito.

"Science normally is the process of building data to gradually give you a picture," Ferguson-Miller said. "With x-ray crystallography, you get a wonderfully satisfying answer very rapidly. With the crystal structure, you have something solid to help you understand what is happening."

The enzyme cytochrome c oxidase is an essential player in energy generation in the mitochondria. The protein captures energy that is created from the conversion of oxygen to water. That energy is then used to create another form of energy that can drive processes like making ATP, which is the real currency that all living things use to contract their muscles, send nerve impulses and maintain cell function, said Ferguson-Miller.

Ferguson-Miller has been unlocking the secrets of cytochrome c oxidase for more than 30 years with continuous support from NIH. She believes we are getting close to understanding the mechanism of how the enzyme completes the energy conversion process, but we are still a long way from understanding how the efficiency of the process is regulated.

"Our working hypothesis is that one level of regulation is right at the first stage of energy generation by cytochrome c oxidase itself," Ferguson-Miller said. "There are many layers of physiological regulations of energy production and utilization; hormones, the brain and muscles are all levels of control. At the most fundamental level where the oxygen reduction process is carried out, there also appears to be important regulation."

In mammals, cytochrome c oxidase has 13 subunits, but only three subunits are thought to be directly involved in the catalytic function of the enzyme. The rest are related to regulating the rate and efficiency of the enzyme. The bacterial enzyme is simpler, with only one regulatory subunit, and easier to study.

The mitochondria in human cells have evolved to have features that aren't in lower animals. Human mitochondria have changed the interaction between cytochrome c oxidase and its substrate, suggesting that they have become more sensitive to regulation.

"That is something we're trying to understand and potentially use for designing a new class of antibiotics that will interfere with energy metabolism in lower organisms but not in humans," Ferguson-Miller said.

Lab Classes Combine for Intensive Experience

A new intensive laboratory class is slated to be unveiled for biochemistry students at MSU during the summer of 2009. BMB 473 will integrate the coursework from two capstone laboratories and add longer labs utilizing new technology.

"MSU biochemistry and molecular biology graduates have a great reputation and very high success rates because of our rigorous program," lab manager Neil Bowlby said. "The new lab, like the two current labs, will focus on teaching laboratory techniques and record keeping skills that make them better scientists and researchers. Yet the new lab will be more intensive and provide greater focus as students gain hands-on experience designing their own experiments."

MSU requires 16 hours of laboratory credit for graduation, the highest in the Big Ten. This creates a challenge and strains the class enrollments as more students select biochemistry as a major. Following a national trend, enrollment in science majors at MSU has increased nearly 30 percent over the past six years, and the increase is proportional in biochemistry. Currently, there are more than 400 undergraduate students majoring in biochemistry, Bowlby said.

"The graduating classes increased from around 40 students to around 70 or 80, so the new class will help accommodate the increase while maintaining the quality of the program," Tom Sharkey, chair of biochemistry, said.

The new class will meet three times a week for six hours a day. With these long and intensive timeframes, the students will be immersed in the experience. The class will cover the same topics as BMB 471 and BMB 472 including: spectrophotometery, organelles and lipids, enzymes and other proteins, transformation and PCR. Students learn laboratory techniques, design their own experiments and learn record keeping skills.

"All the graduates I get feedback from say two things," Bowlby said. "First, the courses were extremely difficult. Second, they say that having completed the classes they are much better suited to do whatever they are doing now. It is kind of like 'hell week' in football; it is really hard to make it through, but when you've finished, knowing you're prepared makes all the difference in the world."

The success of biochemistry students reflects on the success of the program. In three of the last five years, a biochemistry student has been awarded a Udall scholarship. For the last two years, biochemistry students have won the grand prize at the University Undergraduate Research and Arts Forum at MSU.

"We have top notch students," Bowlby said. "This year we sent students to Berkeley, Yale Medical School and Harvard. Almost all of our students that want to go to graduate school or medical school do, and all of them that want to go into private industry do because we put out top quality students."

Plant Genomics Attracts Students, Teachers

Professors teach students about science every day in classrooms across the country, but some labs at MSU are taking the next step in providing a summer of hands-on science as part of a program funded by the National Science Foundation.

Undergraduate students from many colleges in Michigan, and across the U.S., and secondary school science teachers from Michigan participate in Plant Genomics at MSU. The 10-week program pairs genomics laboratory staff with college students and high school science teachers where they learn about plant genomics.

"We trained a large number of students from all over the country," program director Linda Savage said. "We brought a very diverse group together in labs from all different backgrounds. It was cool to see kids light up about graduate school. It was something some of them had never thought of before."

The participants were immersed in primary research and mentored by the graduate students, postdoctoral researchers and professors while working in one of the 16 participating biochemistry labs on campus. The group met weekly for faculty research presentations to learn about other research going on and they got together for social events.

Since the program started in 2006, more than 37 undergraduates have spent their summer living and working at MSU. In 2007, the program opened up to high school teachers and a small number of faculty members from primarily undergraduate-serving colleges and universities.

"We give people who don't normally have an opportunity to have these experiences a chance to rekindle or establish excitement in plant genomics," said professor Rob Last. "There is a tremendous amount of plant genomics expertise here at MSU that we can share."

The program is primarily funded by a variety of NSF grants, and provides experience in biochemistry labs as well as the Plant Research Laboratory, Department of Horticulture and Department of Plant Biology. More information can be found at: http://plantgenomics.msu.edu.

Alumnus Nominated to NSB

Douglas Randall

Douglas Randall (Ph.D. Biochemistry 1970) was nominated by President George Bush to serve a second six-year term as a member of the National Science Board. Randall first served as a member of the board from 2002 to 2008 and as his term expired he was re-nominated. He currently serves as a Board consultant pending his confirmation by Congress.

Randall earned his Ph.D. at MSU studying the enzymes involved in plant photorespiration. He worked with the late Ed Tolbert, an authority on plant biochemistry in the area of carbon dioxide fixation and oxygen balance.

"Ed Tolbert had a great passion for science, and he enjoyed the challenge of figuring something out and getting it right," Randall said. "He had a good cadre of graduate students and a good environment. His passion for science spread to all of us."

Randall is a Thomas Jefferson Fellow and former director of the Interdisciplinary Plant Group (which he founded in 1981) at the University of Missouri. His lab is working on improving biodegradable plastic production. A main theme of Randall's research has been the characterization of the plant alpha ketoacid dehydrogenase multi-enzyme complexes, including the identification of the genes, the import and assembly of the component subunits and the regulation of the complexes in various organelles. These multi-enzyme complexes (up to 200 proteins) occupy strategic positions in plant metabolism and are critical to energy production and oil biosynthesis.

Randall's research team established the first plant enzyme to be regulated by reversible phosphorylation (the addition or subtraction of a phosphate group to a protein or small molecule) and that this biochemical switch mechanism regulates which pathway supports mitochondrial energy production during photosynthesis.

Randall is a past officer and chair of the board of the American Society of Plant Biologists, and was named a fellow in 2007. He has received numerous awards including the Alumni Award from the Department.

"A great benefit of MSU is that people are involved in every aspect of the research and are contributors," Randall adds. "I remember the 'can-do' mentality and everyone having a strong desire to want to improve and make things better through science."

2008 Boezi Alumni Award

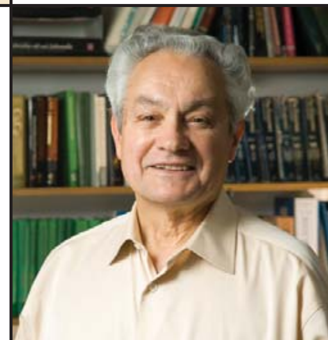
Professor emeritus William Wells presents Michael Washburn with the 2008 John A. Boezi Memorial Alumnus Award.

Michael Washburn (Ph.D. Biochemistry and Environmental Toxicology 1998) was awarded the 2008 John A. Boezi Memorial Alumnus Award. Washburn is known for quantitative analysis of complex protein mixtures and protein complexes, and using mass spectrometry of peptide fragments, particularly to analyze very large protein complexes. The Boezi award is presented annually by the department for outstanding and distinguished achievements by an alumnus.

Washburn studied under William Wells at MSU. While working with Wells, they published seven papers on mammalian glutathione dehydroascorbate reductase and thioltransferase enzymes. Washburn worked at the University of Washington and became a senior staff scientist at the Torrey Mesa Research Institute, contributing to sixteen highly significant publications. He was named director of proteomics at Stowers Institute for Medical Research in 2002.

Jack Preiss to Retire

Jack Preiss will retire at the end of 2008. Preiss has been a leader and mentor for thousands of students in a career which has earned him a global recognition in the biological science community. His passion for science is rivaled only by his passion for opera.



Jack Preiss

Preiss was raised in Brooklyn, N.Y. and received his B.S. in Chemistry from the City College of New York in 1953 and his Ph.D. from Duke University in 1957. He did postdoctoral work at Duke University and with Nobel Laureate Paul Berg at Washington University and the Stanford School of Medicine.

After two years with the National Institutes of Health, he joined the faculty at the University of California, Davis, in 1962. Preiss came to MSU in 1985 when he was named chair of the Department of Biochemistry.

Preiss has taught thousands of undergraduate students with enthusiasm and skill. He is known for teaching photosynthesis to the tune of "Auld Lange Syne" and the TCA cycle to the tune of "Waltzing Matilda" from the Biochemists Songbook by Harold Baum.

While it is his expertise in science on which he has built a successful career, his skills at singing opera are equally remarkable. He has participated in several operas in California and Michigan. His last performance was as Prince Orlofsky in the presentation of "Die Fledermaus" by Johann Strauss held at the MSU's Wharton Center.

Between operas and vocal practice, Preiss has published more than 258 papers in refereed journals, 90 articles and chapters in books and six books or monographs. Beginning with his Ph.D. thesis, he studied regulation of polysaccharide synthesis for more than 45 years supported by grants from NIH, NSF, DOE and USDA. Preiss has studied starch metabolism in leaves, potatoes and corn and continues the study of regulation of starch accumulation via genetic modification of the ADP-glucose pyrophosphorylase with a grant from the Binational Agricultural Research and Development Fund.

Preiss was elected a Fellow of the American Association for the Advancement of Science in 2007 and the American Association of Plant Biology in 2008.

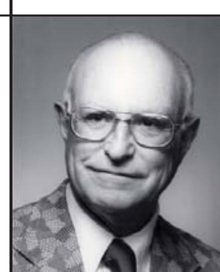
"Jack inspired many scientists, especially the more than 100 graduate students, post-docs, and undergraduate students who worked in his lab," Tom Sharkey, biochemistry chair, said. "For many years Jack was the world leader in understanding starch synthesis in leaves. My research, and that of many other plant biochemists has relied on Jack's seminal contributions. His leadership in the department and nationally, combined with his outstanding dedication to teaching, have had a tremendous impact. Jack always has a smile and respect for everyone; I enjoy his sunny personality and positive outlook."

Preiss has received numerous awards in his career, including the American Chemical Society Charles Pfizer Award in Enzyme Chemistry in 1971. He also received the Alexander Von Humboldt-Stiftung Senior U. S. Scientist Award. In 2001, MSU recognized him as a University Distinguished Professor.

Preiss has touched thousands of lives over the course of his career; including some who may not know the real words to "Auld Lange Syne," yet can recite the process of photosynthesis.

Remembering Richard Byerrum

Richard Byerrum



Richard U. Byerrum, professor emeritus of biochemistry, died September 28, 2008, at the age of 88. Byerrum joined the Michigan State faculty in 1947 and his research dealt with plant metabolism. He was the dean of the College of Natural Science from its creation in 1962 until 1986, and was an instructor at MSU for more than 40 years.

Byerrum authored *Experimental Biochemistry* in 1956 and served as author or co-author of more than 90 abstracts, articles, book chapters and reviews for professional journals. He also held four patents. Byerrum is survived by his wife Claire, three daughters, six grandchildren and two great grandchildren. Memorial contributions can be made to the Dr. Richard U. Byerrum Scholarship, 103 Natural Science Building, East Lansing, MI 48824.

Students participating in the Plant Genomics at MSU *summer program painted The Rock on campus. Jesie Reemmer, a junior at MSU studying biochemistry, biotechnology and plant biology said she learned something new every day. "I got a lot of good experience working in the lab," Reemmer said. "Also the presentations were tremendously valuable to see other people's research and hear their different points of view." Read the story* *on Page 5 for more details on the program.*

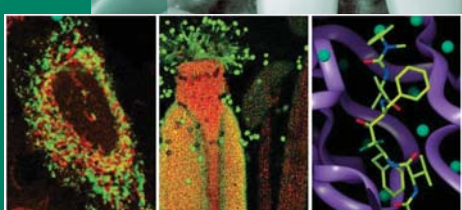
Faculty High-5's

PAMELA FRAKER

Pamela Fraker was inducted into the National Academy of Sciences this April. She is the first woman from MSU to receive this honor and one of eight MSU faculty who are active members of the academy. Fraker is known for her discoveries of the impact of nutritional deficiencies on immune defense. Her work is being used to improve patient health and stabilize immune defense. Fraker's work has been supported by 30 years of National Institutes of Health funding, most recently by a $1.7 million grant.

JACK PREISS

Jack Preiss has been named a fellow of the American Society of Plant Biologists in recognition of his distinguished and long-term contributions to plant biology. Preiss is the fourth MSU faculty member to be named a fellow by ASPB. Ken Keegstra, Tom Sharkey and Jan Zeevaart were among the inaugural class of fellows in 2007. Preiss was recognized for his enormous contributions to understanding starch and glycogen biosynthesis, the determination of the crystal structures of the E. coli branching enzyme and the potato tuber ADP-glucose pyrophosphorylase in the first half of this decade.



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