

Biological Chemistry
2011 NEWSLETTER



A Letter from the Chair : Dr. William L. Smith

GREETINGS FROM ANN ARBOR
TO FRIENDS, COLLEAGUES,
AND GRADUATES

I'll begin like I do most years with an update on the state of the Department.

As a reminder, Biological Chemistry is one of six basic science departments in a medical school with now 26 different departments and two new ones (Cardiovascular Surgery and Bioinformatics) due to be instituted soon. We currently have 47 faculty with appointments in Biological Chemistry all of whom have shared responsibilities for teaching graduate, medical and undergraduate students. The Department averages about 35 graduate students in the Biological Chemistry Ph.D. program as well as having about 20 students from the Cellular and Molecular Biology, Chemical Biology, Bioinformatics and Biophysics Ph.D. programs. There are also about 50 postdoctoral scientists, 10 laboratory staff and an administrative staff of eight.

In addition to our doctoral program and the Medical School "M1" curriculum, Biological Chemistry teaches many classes in the allied health fields. Included is BC212, which primarily serves Nursing students and has an enrollment of over 200. In addition, our faculty teach in the undergraduate Biochemistry concentration (BC452 Lecture) in the Chemistry Department. The Department also teaches a popular one semester general biochemistry course BC415. Demand for BC415 is so strong that last year we increased to three the number of BC415 sections. The total enrollment approaches 700.

There have been several faculty comings and goings this year. Dr. Yang Zhang, who has his primary appointment in the Center for Computational Medicine and Biology, was appointed as an Associate Professor in the Department last spring. Yang and his

laboratory are famously successful in developing algorithms for protein structure predictions. He and his group were ranked No. 1 in both protein structure and function prediction among more than 200 groups in the most recent international competition (<http://zhanglab.ccmb.med.umich.edu/>). Dr. Daniel Southworth has recently been appointed to a tenure track appointment as an Assistant Professor in Biological Chemistry with a research track appointment in the Life Sciences Institute. Most recently, Dan received his Ph.D. from Johns Hopkins and did postdoctoral studies at UCSF. He plans to apply structural biology techniques including cryo-EM to understand the structure and function of p53. Three faculty took other positions this year. Dan Bochar moved to the Cayman Chemical Company in Ann Arbor, Randy Kaufman moved to the Sanford-Burnham Medical Research Institute in La Jolla, and Matt Young is now a Research Assistant Professor in Pharmacology. We are pleased that Dan and Randy retain adjunct appointments in the department.

Our faculty continue to be involved in extramural service activities. For example, Ruma Banerjee is on the ASBMB Council, Janet Smith continues as Director of the NIGMS X-ray Beamline at APS/Argonne National Laboratories, David Engelke is a Deputy Editor of RNA, and Jochen Schacht is a Section Editor for *Audiology & Neurotology*.

Several faculty have also received significant awards this year. Alex Ninfa was elected as a Fellow of the American Academy of Microbiology, Ming Lei received the Dean's Basic Science Research Award, Jerry Menon was named recipient of the EBS/Biological Chemistry Teaching Award and Carol Fierke



will receive the 2012 Repligen Award in Chemistry of Biological Processes from the American Chemical Society.

In the coming year we plan to recruit a new Assistant Professor. To that end we have formulated a faculty-led committee headed by Dave Engelke to look for candidates who would complement our current strengths particularly in the areas of protein processing and folding, regulation of gene expression and biochemical signaling. We have been negotiating with a senior candidate for the endowed Anthony and Lillian Lu Professorship and are hopeful that this will be successful.

Something I have been very pleased about has been the success of our endowed lectureships. We now have four of these lectureships named for current or former faculty, including the William E.M. Lands Lecture in the Biochemical Basis for the Physiology of Essential Nutrients, the Irwin J. Goldstein Lecture in Glycobiology, the Martha L. Ludwig Lecture in Structural Biology and the G. Robert Greenberg Lecture in Biological Chemistry. The lecturers are selected by our Seminar Committee from nominations made by faculty or, in the specific case of the Greenberg Lecture, from student nominations. For example, the Ludwig Lecturer this fall is Venki Ramakrishnan, who shared the Nobel Prize in Biology and Medicine in 2009 for his work on the ribosome structure. Having our students and faculty be able to interact with world class scientists is a very important aspect of Departmental activities. The visibility of these lectures also serves to highlight the importance of the Department of Biological Chemistry to others in the University. These lectureships have come about as a result of selfless contributions from donors and have now become a key part of our Department.

With respect to philanthropy Mr. Greg Witbeck continues to be a very effective and dedicated development officer for Biological Chemistry and other basic science departments. In this role, he has staffed alumni reunions, assisted with our newsletter and generally engaged in developing a culture of giving within the Department. For example, in April of this year, Greg hosted a Biological Chemistry/Pharmacology alumni dinner in Washington D.C. at the Kenne-

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dy Center. More recently, he instigated a program in Chicago for alumni from various basic science departments. I attended this event and was particularly delighted to meet Dr. Evelyn Tyner ('51 Ph.D.) who now lives in Glenview, Illinois. She had been a student with H.B. Lewis, who was head of the department between 1921 and 1954.

One other thing I would like to mention is that Myrna Weissman, the widow of Marshall Nirenberg, recently donated copies of his notebooks and papers relating to his Nobel Prize work in determining the genetic code. These materials are now prominently displayed in a beautiful case located in the atrium of the new A. Alfred Taubman Biomedical Science Research Building (BSRB).

Best wishes for the upcoming year. Please stay in touch (smithww@umich.edu), and I will ensure that all the relevant information is included in next year's newsletter. Alternatively, you can send us an update at the Alumni and Friends page of our BioChem website (www.biochem.med.umich.edu/?q=alumni_reg).



Biological Chemistry
at University of Michigan

Philanthropy at Work : Dr. Ward Smith

“GIVING TO THE DEPARTMENT SEEMED THE BEST WAY TO BENEFIT THE GRADUATE STUDENTS”

Dr. Ward Smith is a man who knows how to make a difference. Every year for more than 20 years, he and his wife, Dr. Cheryl Janson, have given generously to the department in support of a variety of initiatives, including the endowment for the Martha L. Ludwig Professorship in Protein Structure and Function and the endowment for the Biological Chemistry Graduate Student Program, as well as providing unrestricted gifts to the department.

Dr. Smith graduated with a Ph.D. from the Department of Biological Chemistry in 1977, working in the laboratory of Dr. Martha Ludwig. The title of his thesis was *The crystal structure and refinement of clostridium MP flavodoxin in the semiquinone state and some comparisons of the protein in the oxidized, semiquinone and fully reduced states*. Following graduation, Dr. Smith conducted postdoctoral research at the University of California, Los Angeles. He currently works at the National Institutes of Health, where he is chief of the Structural Genomics and Proteomics Technology Branch at NIH's National Institute of General Medical Sciences. His responsibilities include directing the Protein Structure Initiative, a \$270 million program to elucidate the structure and function of protein molecules. Dr. Smith previously worked as a structural scientist at Agouron Pharmaceuticals, served as an associate director in the Department of Structural Biology at GlaxoSmithKline and worked as a protein crystallographer in the Biosciences Division at Argonne National Laboratory.

In this issue of the Biological Chemistry newsletter, we ask Dr. Smith to reflect on his time at the University of Michigan and his and Cheryl's long history of giving to the department.



When did you first decide to make a donation to the Department of Biological Chemistry? What prompted the decision?

Cheryl and I both benefited from graduate educations at Big 10 institutions (Cheryl holds a Ph.D. in Biochemistry from the University of Wisconsin). Once we were working, we felt it was the right thing to do to repay those institutions in a small way for the opportunities we received.

Why have you consistently donated to the Department of Biological Chemistry over the years? Are there particular causes that appeal more to you than others?

I wanted to give to the Department in preference to the University; I feel more of an attachment to the Department than to the University. Giving to the Department seemed the best way to benefit the graduate students in the Department of Biological Chemistry.

What effect do you hope your donations will have?

I hope to help the students in ways that are otherwise difficult to fund, such as speaker programs, science retreats and enhancements to the department library.

How did your studies at UM prepare you for a career in biological chemistry?

At UM, I learned what is now called structural biology in the early days of the science. As I've continued to work in this field, I've also learned that being able to work at something you enjoy is an invaluable gift. I have always felt fortunate to have a career, rather than merely a job.

What is your fondest memory of your time at UM?

As a student, being able to pursue the science that I enjoyed with relatively few other distractions is one of the things I have come to appreciate.

What words of advice do you have for the department's graduate students and newly-minted PhD's?

Pursue your passion. Choose your path based on what truly excites you.

Our Generous Donors : 2010–2011

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Supporting BioChem

The Department of Biological Chemistry relies upon the philanthropic generosity of donors to fund many aspects of its operations. Gift funds are essential to supporting activities beyond our basic operations. From endowed professorships and lectureships, to graduate student fellowships, seminar speakers, and gifts in direct support of research, donations help make the department an intellectually exciting and vibrant community. As a benefactor of the Department of Biological Chemistry, you can direct your gift in several ways:

Lectureships

- G. Robert Greenberg Lectureship
- Irwin J. Goldstein Lectureship
- Martha L. Ludwig Lectureship
- William E.M. Lands Lectureship

Faculty-Specific and General Departmental Support

- Direct Support of a Named Faculty Member's Research
- Biological Chemistry Endowment and Gift Funds
- Graduate Program Endowment Fund

For additional information on how you can make a positive difference in the Department of Biological Chemistry, please visit <http://www.biochem.med.umich.edu> or contact:

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PLEASE NOTE

For 2011 charitable deductions and credits, the IRS has ruled that credit card gifts are deductible only in the year the bank processes the transaction. To be processed for tax year 2011, credit card gifts by mail must reach the University by December 16th; OR you may call 888-518-7888 (toll free) or 734-647-6179 (local), 9 AM – 4 PM EST, between December 15th and 30th, 2011 to donate over the phone. Please have the information requested on the enclosed gift card on hand for your call. Your gift by check must be postmarked by December 31, 2011.

Minor J. Coon : A Celebratory Symposium

FOR HIS 56-YEAR CAREER AT THE UNIVERSITY
A GREATLY RESPECTED PROFESSOR, MENTOR,
AND NOTED RESEARCHER IS HONORED

On Friday, July 15th, the Department hosted a Celebratory Symposium in Palmer Commons that honored the career and 90th birthday of Professor Minor “Jud” Coon. The Symposium marked his 56-year career in our Department, his seminal contributions in characterizing the functions of the cytochrome P450 family of enzymes, and his mentoring of an impressive cadre of highly successful scientists.

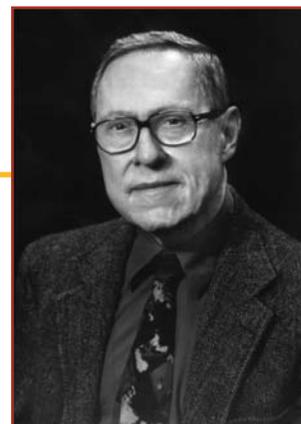


The Symposium’s speakers included students, postdoctoral fellows, and scientists who trained

with Professor Coon and have gone on to distinguished careers in academia and industry. Chairman William Smith and Professor Paul Hollenberg, Chair of the Department of Pharmacology, opened the Symposium with brief remarks about Professor Coon’s research

term as President of the American Society for Biochemistry and Molecular Biology (ASBMB) from 1991-1992.

Following the opening remarks, Dr. Henry Strobel (Professor of Biochemistry at the University of Texas Health Sciences Center) presented the first research talk that described the role of Cytochrome P450 4F in the response to traumatic brain injury. Next, Dr. Alfin Vaz (Associate Research Fellow at Pfizer Inc.) described his work on utilizing isotope effects in enzyme kinetics and pharmacokinetics and the application of this approach to studying drug metabolism in animal model systems. Dr. Xinxin Ding (Professor of Molecular Genetics, Neuroscience, and Toxicology in the Departments of Biomedical Sciences and Environmental Health Sciences at the State University of New York at Albany, and also Chief of the Laboratory of Molecular Toxicology and Assistant Director of the Division of Environmental Health Sciences at the New York State Department of Health’s Wadsworth Center) then discussed his research on mouse ge-



netic studies of NADPH-cytochrome P450 reductase and the involvement of various cytochrome P450 isoforms in lung cancer. After a short break, the talks resumed with Dr. Edward Morgan (Professor of Pharmacology at Emory University), who presented his research on the post-transcriptional regulation of various cytochrome P450 isoforms by nitric oxide and how this signaling pathway controls P450 protein



6 career, history with the Department, and service in various professional organizations, including his

... and a
Note from Jud:

I am very grateful to Bill Smith and his organizing committee, including Dave Ballou, Paul Hollenberg, and Yoichi Osawa, with Amanda Howard, who carried out the plan, for the superb symposium held last July. Many of my former students and postdoctoral associates, some from as far back as 1955, joined us, including six who were fine speakers. As I have often said, despite its size the University of Michigan is exceptional in the ease of collaboration throughout the campus. Whatever success we may have had in our research over many years was greatly aided by such collaborations with our colleagues in other departments. This tradition will continue be a great asset to the U of M in the years ahead.

MINOR J. COON

stability and turnover in cells. Professor Paul Hollenberg then described structural and functional studies of cytochrome P450 mechanism-based inhibitors and their application as active site probes for various P450 isoforms. Dr. Fred Guengerich (Professor of Biochemistry at Vanderbilt University) then provided a historical retrospective of Professor Coon's career and accomplishments in the cytochrome P450 field, dating from his first research article on microsomal P450 that he co-authored with Dr. Anthony Lu in

the *Journal of Biological Chemistry* in 1968. Dr. Guengerich then went on to discuss his own research into functions of the cytochrome P450 family in drug metabolism.



Department of Biological Chemistry

MINOR J. COON

CELEBRATORY SYMPOSIUM

Honoring
Dr. Coon's 90th Birthday

1:00 p.m. Bill Smith & Paul Hollenberg
Opening remarks

1:15 p.m. Henry Strobel
Cytochromes P450 4F and brain

1:45 p.m. Alfin Vaz
Deuterium isotope effects in drug discovery

2:15 p.m. Xinxin Ding
Identification of P450 functions using engineered mouse models

2:45 p.m. snack/coffee break in atrium

3:15 p.m. Edward Morgan
Post-translational regulation of P450 enzymes by nitric oxide

3:45 p.m. Paul Hollenberg
Cytochrome P450: Active site structure and function and genetic polymorphisms

4:15 p.m. Fred Guengerich
Cytochrome P450. 43 years after Lu & Coon: Importance of the basic science and new opportunities with drugs & steroids

4:45 p.m. Ron Estabrook
Travels with Jud Coon – Hats

5:00 p.m. Minor J. Coon
Closing remarks

Finally, Dr. Ronald Estabrook (Emeritus Professor of Biochemistry at the University of Texas Southwestern Medical Center) concluded the talks with a humorous and heartfelt recollection of his travels and adventures with Professor Coon and the many hats that he wore throughout his life.

In the evening after the Symposium, a reception and dinner was held in Professor Coon's honor at the Michigan Union. Among the guests were members of Jud's family, the Symposium's participants, Department faculty, and University of Michigan President

Mary Sue Coleman, who presented a brief address highlighting Professor Coon's scientific accomplishments and contributions to the University community (see page 9). The dinner concluded the Symposium celebrating Professor Coon's remarkable career as an outstanding scientist and mentor to a generation of biochemists who continue to make important strides in understanding the functions of cytochrome P450, which he likes to call Nature's Most Versatile Biological Catalyst.

Remarks by President Mary Sue Coleman at the Symposium Dinner for Dr. Minor J. Coon

I am so happy that my schedule would make it possible for me to attend this dinner this evening, in honor of a scientist that I have admired for decades. During my graduate work at UNC-Chapel Hill, I was of course familiar with the ground-breaking work of Jud Coon in devising an elegant process to purify a soluble enzymatically active form of p450. The work in this area really took off after his classic JBC paper with



Anthony Lu was published.

Perhaps I was particularly interested in this work because one of my graduate school classmates, Henry Strobel, was going to Ann Arbor for a postdoctoral position with Jud. I

heard a lot during that time about the Coon laboratory in Ann Arbor, especially since I was headed in the opposite direction to the University of Texas (as I re-

call, we probably talked a lot about weather). Never then, could I have imagined that I would at this point in my career be entering my tenth year as president of the University of Michigan, where Jud Coon has made so many stand-alone discoveries and been so important for the University in the field of P450 research — and maybe it's a bit ironic now that Henry is in Texas.



As you all know, Jud was recruited to UM in 1955 where he quickly established a vibrant and exciting research laboratory. As his own work became more important and influential, he took on the sometimes onerous task of being the department Chair, and he stayed in the role for twenty years — that is a remarkable service to the University. He served the biochemistry community also in numerous ways, and has been honored many times over. Jud, you deserve every single one of those awards, and more.

We are deeply honored that you made the University of Michigan your home for so many years, and we are thrilled to honor you in the month of your 90th birthday. May you experience many, many more. Congratulations.

A Brief Biography of Minor J. "Jud" Coon

Jud Coon was born and grew up in the Denver, Colorado area. After finishing public schools there, he enrolled at the University of Colorado, Boulder, where he became interested in chemistry and biochemistry, working with Professor Reuben Gustavson. In 1943 he entered graduate studies in Biochemistry at the University of Illinois, with

Professor William C. Rose as his mentor. His thesis work dealt with the essential amino acids, a topic he would continue to pursue following his graduation (1946) in his first faculty position at the University of Pennsylvania in the Department of Physiological Chemistry (1947–1955). In 1955 Jud Coon moved to the Department of Biological Chemistry at the University of Michigan, where he has spent the remainder of his career and is still involved. He was Chair



of the department from 1970 to 1990 and is now the Victor C. Vaughan Distinguished University Professor, Emeritus. His sabbatical leaves were at New York

University with Professor Severo Ochoa and at the ETH (Swiss Federal Institute of Technology) in Zürich with Professor Vladimir Prelog.

In the course of his research on the catabolism of amino acids and then fatty acids, Professor Coon became interested in the mechanism of chemically difficult oxidations of these molecules. This work developed into consideration of the omega oxygenation of fatty acids and alkanes, ultimately leading to his success with his dedicated associates in separating P450 from liver microsomal membranes and reconstituting catalytic activity. Enzyme purification provided unambiguous proof that multiple forms of P450 exist in animals. Other prominent contributions of his



group in the field of P450 included studies on the isolation of other P450s, mechanisms of P450 gene regulation, and heterologous expression of mammalian

P450s. Some of the most important contributions by Jud Coon were in the area of the catalytic mecha-

nisms of NADPH-P450 reductase and P450, establishing an iron-bound oxygen as the powerful oxidant and the radical nature of the reactions. Another major research accomplishment was establishing the stoichiometry of oxygen reduction. New transformations of chemicals by P450s in humans, animals, and plants, including drug metabolism, continue to abound and will continue to occupy P450 researchers seeking to rationalize these enzymes in the context of the insights advanced by the work of Jud Coon and his students.



In addition to his research contributions, Professor Coon has enhanced science in many other ways.



Many current investigators in the field trained with him. He served as President of the American Society for Biochemistry and Molecular Biology (1991–1992). In addition, he chaired the advisory committees

for two of the leading international meetings in this field, the Cytochrome P450 Meetings, and Microsomes and Drug Oxidations, for over twenty years.

In recognition of his research, Jud Coon received the American Chemical Society Award in Enzyme Chemistry in 1959, the Distinguished Faculty



In Memoriam : Saul Roseman 1921–2011

SOME OF HIS MOST IMPORTANT DISCOVERIES WERE THE RESULT OF INSIGHTFUL THINKING ABOUT CHANCE OBSERVATIONS.

Biological Chemistry
Faculty,
1953-1965



Saul Roseman, a pioneer in the field of glycobiology, died on July 2, 2011, ending a distinguished career that spanned nearly seven decades. At the time of his death at age ninety, he had only recently transitioned to Professor Emeritus status but still maintained an active research group at The Johns Hopkins University. Among his many scientific contributions, Roseman published the first correct structure of sialic acid, discovered its nucleotide sugar donor CMP-sialic acid, elucidated the biosynthetic pathways of glucosamine and the sialic acids, demonstrated glycosyltransferase activities in tissues and fluids and discovered and characterized the important, widely distributed phosphotransferase transport system (PTS) present in procaryotes. Roseman was considered a master of serendipity. Some of his most important discoveries were the result of insightful thinking about chance observations. He relished this characterization as evidence of a sharp intellect, an unyielding eye for data, and an open-minded, enthusiastic approach to science. He once said “The unexpected is just Nature’s way of telling researchers where to look for the really interesting and important stuff.” Certainly, his scientific career was marked by interesting and important discoveries.

Roseman attended City College of New York where he majored in Chemistry and double minored in Physics and Biology, three disciplines that served him well throughout his long, productive scientific career. He completed his Ph.D. in Biochemistry and

IO Organic Chemistry at the University of Wisconsin in 1947 under the mentorship of Karl Paul Link where

he worked primarily on the chemistry and metabolism of coumarins. Although his graduate work included some carbohydrate chemistry, it was during his postdoctoral years at the University of Chicago in the laboratory of Albert Dorfman, where he studied glycosaminoglycan biosynthesis and degradation, that his career in Glycobiology started in earnest. His studies on hyaluronic acid biosynthesis brought him to the attention of the Rackham Arthritis Unit at the University of Michigan Medical School where in 1953 he was appointed Assistant Professor of Biological Chemistry.

At Michigan, Roseman initially studied the intermediary metabolism of hexosamines. These efforts ultimately led to his now classical studies on the metabolism of the sialic acids. He and a postdoctoral fellow Don Comb (who later founded New England Biolabs) were studying “NAN-aldolase,” a bacterial enzyme that cleaves sialic acids into two components. Unexpectedly, they discovered that one of the products was not consistent with the then well-established structure of sialic acid published previously by other research groups. Comb and Roseman rigorously characterized the reaction products, crystallized the hexosamine fragment and unambiguously established that the hexosamine fragment was N-acetyl-D-mannosamine and not N-acetyl-D-glucosamine as previously suggested. This finding led to their publication of the first correct structure of the sialic acid(s). This finding firmly established Roseman as a major contributor to the field of complex carbohydrates, the forerunner of modern glycobiology.

The years following the discovery of the structures of the sialic acids were remarkably productive for the Roseman laboratory. They established the en-

zymes involved in the biosynthesis and degradation of the sialic acids, discovered CMP-sialic acid, the nucleotide sugar donor for sialylation, and determined pathways for hexosamine biosynthesis. During a summer sabbatical in 1961 in Vancouver in the laboratory of Nobel laureate H. G. Khorana, Roseman devised an improved method to synthesize nucleotide sugars. The ready availability of these compounds enabled the Roseman laboratory and other laboratories worldwide to study the biochemistry of glycosyltransferases and pathways of glycoprotein and glycolipid biosynthesis.

In an unexpected foray into a completely new area of research, Roseman's group discovered a multi-protein bacterial transport system. The laboratory was studying the biosynthesis of N-acetyl mannosamine 6-phosphate, an intermediate in sialic acid biosynthesis in *E. coli*. It was anticipated that that the phosphorylation of acetylmannosamine would be ATP-mediated. However, as controls, other potential high energy donors including phosphoenolpyruvate (PEP) were added. Surprisingly, the bacteria failed to transfer phosphate from ATP but efficiently transferred phosphate from PEP. That single observation led to the discovery of the bacterial phosphotransferase system (PTS), a pathway widely distributed in prokaryotes including many pathogens. Subsequently at Hopkins, Roseman and his team vigorously explored the biochemistry, biophysics and biology of this fascinating, versatile multi-protein sugar-nutrient transport system.

In 1965, Roseman accepted a Professorship in the Biology Department at Johns Hopkins University where he continued studies on glycosyl transferases, the PTS system, and initiated new avenues of research concerned with the roles of glycans in cell-cell adhesion and chitin metabolism in *Vibrio* and other bacteria. During this time he also served as Chairman of the Department of Biology (1969-1973, 1988-1990). At the time of his death, his laboratory was continuing to study a potent hepatocyte adhesion molecule and the role of chitin metabolism for biofuel production.

Throughout his career Roseman's approach to science — his own and that of others — was remarkably

focused and enthusiastic. Whether he was discussing the latest data with his research team, hosting a visitor in his office, or attending a seminar or a symposium, he was always fully engaged and seeking the essence of the science being presented. He was famous for his keen criticism, and often would raise key alternative interpretations or controls for consideration. Although the laser beam of his intellect was unblinking, his goal always was to advance knowledge and further discovery, pursuits that he truly loved. This philosophy was firmly instilled into his many students and associates.

Roseman's contributions are well-appreciated by the scientific community. His many honors include induction into the National Academy of Sciences (1972), an honorary Doctor of Medicine from the University of Lund (1984), and the Karl Meyer Award from the Society for Glycobiology (1993). A collection of reviews was published in his honor in the first volume of *Glycobiology* in November, 1991. In addition, the *Journal of Biological Chemistry* honored him with a Centennial biography, "Hexosamine Metabolism, Sialic Acids, and The Phosphotransferase System: Saul Roseman's Contributions to Glycobiology" in 2006.

In the introduction to the glycobiology issue in his honor, Roseman reminisced at length about "the way it was," remarking on the sparse attendance at the complex carbohydrate sessions at national meetings early in his career. He noted that the sessions were typically scheduled on the last afternoon of the week-long meetings, and recalled one session in which "... the chairman introduced me and excused himself because he had a 'train to make'. The audience in that case consisted of the last speaker on the program and the slide projectionist." Saul Roseman's persistence and pioneering efforts have contributed meaningfully to the emergence of glycobiology as a vigorous discipline.

Faculty News

BERNIE AGRANOFF received the University of Michigan Medical School's Lifetime Achievement Award in Medical Education. Dr. Agranoff was formerly Director of



the Mental Health Research Institute and is now Professor Emeritus of Biological Chemistry with the same title in the Department of Psychiatry. Bernie has received wide recognition nationally, as

well as in our Medical School, for his major educational influence in neuroscience and richly deserves this award.

MARY SUE COLEMAN, President of the University and Professor of Biological Chemistry in the Medical School and of Chemistry in the College of LS&A, was elected Chair of the Board of Trustees of Internet2. This consortium is led by universities working in partnership with industry and government to develop and deploy advanced network applications and technologies. She will serve in this capacity with Internet2 until July 2012.



CAROL FIERKE will receive the 2012 Repligen Corporation Award for Chemistry of Biological Processes "in recognition of her contributions to our broad understanding of how protein and nucleic acid catalysts achieve high efficiency with rigorous control of reaction specificity," and "significant contributions to our view of metal ion homeostasis in cells." The Repligen Award is administered by the Division of Biological Chemistry of the American Chemical Society.



MING LEI received the University of Michigan Medical School's Basic Science Research Award for his research in the areas of telomere protection and regulation, small molecular inhibitors of the interaction between single-stranded telomeric DNA and its binding protein POT1, and molecular mechanisms of histone demethylase.



JERRY MENON was the recipient of the University of Michigan Medical School's Endowment for Basic Science Teaching Award for Biological Chemistry. Dr. Menon was recognized for his many years of teaching excellence in Biol Chem 415 and the medical student M1 curriculum.



ALEX NINFA was elected a Fellow of the American Academy of Microbiology in recognition of his studies into the signal transduction mechanisms of bac-



teria and into the functions of genetic networks using a synthetic biology approach. The American Academy of Microbiology is the honorific leadership group with-

in the American Society for Microbiology (ASM). Only about seventy-five fellows are elected to the American Academy of Microbiology each year through a highly selective, peer-review process, based on their records of scientific achievement and original contributions that have advanced microbiology.

GEORGIOS SKINIOTIS was named a 2011 Pew Scholar. Pew Scholars are early to mid-career scientists. They receive a \$240,000 award over four years to support and expand their research, as well as to foster collaboration and connection through the exchange of ideas with other stellar scientists. Skiniotis uses electron cryomicroscopy (Cryo-EM) to obtain the 3D architecture of complex and dynamic protein assemblies. A main theme in his lab is the structural biology of signaling cell membrane receptors, which play essential roles in regulating every aspect of normal physiology.



ROBERT ZAND was elected Director of the Research and Doctoral Constituency of Sigma Xi, the Scientific Research Society, for the period July 1, 2011 through June 31, 2013.

New Faculty

DANIEL SOUTHWORTH, PH.D. The Department is pleased to announce that Dr. Daniel Southworth has joined the faculty as an Assistant Professor of Biological Chemistry and a Research Assistant Professor in the Life Sciences Institute.



Dr. Southworth received his Ph.D. in 2004 from Johns Hopkins University under the guidance of Professor Rachel Green, where he studied essential mechanisms of the protein translation machinery. He developed key single-turnover kinetic and *in vitro* translation assays to determine how the tRNA:mRNA complex ratchets through the ribosome during the translocation step. He discovered that ribosomal proteins S12 and S13 act as critical control elements while the translocation mechanism is inherently driven by the ribosomal RNA.

As a postdoctoral fellow, Dr. Southworth joined Professor David Agard's lab at the University of California, San Francisco to study the structure and function of the heat shock protein 90 (Hsp90) molecular chaperone. He achieved several 3-D structures of Hsp90 from different organisms and in different conformational states. This work revealed a 3-state nucleotide cycle that is universal in *E. coli*, yeast and human Hsp90s and identified unique conformational equilibria that are tailored to the different organisms. He has further determined a 15 Å cryo-EM structure of the human Hsp90:Hop complex that identifies a novel substrate loading conformation of Hsp90.

At the University of Michigan, Dr. Southworth plans to study the mechanisms of molecular chaperone-mediated turnover, activation and signal transduction of the p53 tumor suppressor protein. He will expand his *in vitro* assembly system and use cryo-EM methods principally in determining structures of macromolecular Hsp90:p53 complexes trapped in distinct stages of degradation and activation pathways. These approaches will generate tremendous mechanistic insight about how protein interaction networks drive decisions that are critical to cellular growth and maintenance.

YANG ZHANG, PH.D. The Department of Biological Chemistry is also pleased to announce the joint appointment of Yang Zhang, Ph.D. as an Associate Professor without tenure. Dr. Zhang also holds an appointment as Associate Professor with tenure in the Center for Computational Medicine and Bioinformatics.



In 1996, Dr. Zhang earned his Ph.D. in Physics under the direction of Professor Lianshou Liu at Central China Normal University in Wuhan, China. As an Alexander von Humboldt Postdoctoral Fellow, he performed his postdoctoral training in the Physics Department at Free University Berlin in Germany from 1996 through 1998. Dr. Zhang has also held postdoctoral appointments at the Institute of Theoretical Physics of the Chinese Academy of Sciences in Beijing, China and at the Donald Danforth Plant Science Center in St. Louis. Under the mentorship of Professor Jerry Skolnick, Dr. Zhang was appointed as Research Associate in the Center of Excellence in Bioinformatics at the University of Buffalo in October of 2002. In August of 2005 Dr. Zhang was appointed as Assistant Professor in the Center for Bioinformatics, Department of Molecular Biosciences at the University of Kansas, and was promoted to Associate Professor with tenure just three years later. In September of 2009, Dr. Zhang became an Associate Professor with tenure here at the University of Michigan.

Dr. Zhang's research interests include biophysics, structural and chemical informatics, and proteomics, as well as systemic modeling and systems biology. His laboratory focuses on developing bioinformatics approaches to predict the three-dimensional structures of proteins from amino acid sequences and from there to deduce the biological functions based on the sequence-to-structure-to-function paradigm. His group is especially interested in the structures of G protein-coupled receptors (GPCR) and their interactions with ligands. A long-range goal is to develop new drugs to regulate these interactions.

Alumni Updates

JOHN CHIANG (Postdoctoral Fellow, Jud Coon lab, 1976-1978), Professor of Biochemistry and Molecular Pathology at Northeastern Ohio Universities, received an NIH MERIT Award for his proposal entitled "Regulation of Bile Acid Synthesis by Nuclear Receptors." NIH MERIT Awards are offered to a limited number of PI's who have demonstrated superior competence and outstanding productivity during their previous research endeavors and who are likely to continue to perform in an outstanding manner in the future.

HAIYUAN DING (Postdoctoral Fellow, Tom Kerppola lab, 2005-2007) has accepted a position with Roche R&D Center in Shanghai, China.

XINXIN DING (Ph.D. and research scientist, Jud Coon lab, 1988-1994) is Professor of Molecular Genetics, Neuroscience, and Toxicology, and Director of the Toxicology Track, in the Departments of Biomedical Sciences and Environmental Health Sciences at the State University of New York at Albany, and also Chief of the Laboratory of Molecular Toxicology and Assistant Director of the Division of Environmental Health Sciences at the New York State Department of Health's Wadsworth Center.

REBECCA FAGAN (Ph.D., Bruce Palfey lab, 2009) was awarded an American Cancer Society postdoctoral fellowship for her studies on a DNA methylase in the laboratory of Professor Charles Brenner, Department of Biochemistry, University of Iowa.

ROSS FELDBERG (Ph.D., Prasanta Datta lab, 1970) recently retired from the faculty of Tuft's University after 35 years of service and will be going to Hanoi, Vietnam for a year of teaching English.

F. PETER GUENGERICH (Postdoctoral Fellow, Jud Coon lab, 1973-1975), the Harry Pearson Broquist Professor and Interim Chair of Biochemistry and Director of the Center in Molecular Toxicology at Vanderbilt University, received the 2010 R.T. Williams Distinguished

Achievement Award from the International Society for the Study of Xenobiotics and the 2011 American Chemical Society Division of Chemical Toxicology Founders Award.

PAUL HOLLENBERG (Ph.D., Jud Coon lab, 1969), Maurice H. Seevers Collegiate Professor and Chair of the Pharmacology Department at the University of Michigan Medical School, was elected a Fellow of the American Chemical Society in 2010 and received the 2011 International Society for the Study of Xenobiotics North American Scientific Achievement Award for his research on drug metabolism.

DAVID LEONARD (Postdoctoral Fellow, Tom Kerppola lab, 1996-1998) was promoted to Associate Professor in the Department of Chemistry at Grand Valley State University.

EDDIE MORGAN (Postdoctoral Fellow, Jud Coon lab, 1979-1982), Professor of Pharmacology at Emory University, was named a Georgia Cancer Coalition Distinguished Cancer Scholar to support his research in drug metabolism and molecular pharmacology. He organized the 17th North American regional meeting of the International Society for the Study of Xenobiotics held in Atlanta in October.

AUGIE PIOSZAK (Ph.D., Alex Ninfa lab, 2003) was appointed as an Assistant Professor in the Department of Biochemistry & Molecular Biology at the University of Oklahoma Medical School.

HENRY STROBEL (Postdoctoral Fellow, Jud Coon lab, 1969-1970 and Instructor, 1970-1972), Professor of Biochemistry and Molecular Biology at The University of Texas Health Science Center at Houston, received the 2009 Distinguished Medical Educator Award from the Teachers Insurance and Annuity Association — College Retirement Equities Fund (TIAA-CREF) and was elected into The University of Texas Academy of Health Science Educators in 2010.

ALFIN VAZ (Postdoctoral Fellow, Jud Coon lab, 1984-1998) is an Associate Research Fellow in the Pfizer Biotransformation Group, where he works on discovery programs in cardiovascular and metabolic diseases and antibacterials by identifying metabolic hot spots in new chemical entities and their metabolic pathways, altering the pharmacokinetics of new chemical entities, and providing definitive ADME studies for regulatory filings of new drugs in development. He has been credited for the now generally accepted hypothesis and for providing supporting evidence that P450s can use multiple forms of activated oxygen, which in part explains the diversity of reactions catalyzed.

MURTHY YERRAMILI (Postdoctoral Fellow, Vince Massey lab, 1991-1997) has been appointed Director of Corporate Research & Development at IDEXX Laboratories, in Westbrook, ME.

Visiting Alumni

On August 18, 2011 the Department of Biological Chemistry had the pleasure of hosting a visit by Huber Warner and Allan Price, two biochemists with long-time University of Michigan associations.

HUBER WARNER received his B.A. from Ohio Wesleyan, B.S. in Chemical Engineering from MIT, and Ph.D. from UM in the laboratory of Bill Lands in 1962. In fact, Huber was Bill's first graduate student! He then returned to MIT as a postdoctoral research fellow and subsequently joined the faculty of the Department of Biochemistry at the University of Minnesota in 1964. He joined the National Institute on Aging in Bethesda, MD in 1984 where he managed the Molecular Biology Program while also serving as Chief, Biochemistry and Metabolism Branch until 2000, when he was named Associate Director, Biology of Aging Program. In 2005, Huber accepted the position of Associate Dean of Research in the College of Biological Sciences at the University of Minnesota and retired in 2010.

ALAN PRICE received his B.S. from Florida State University and his Ph.D. (1968) from the University of

Minnesota as Huber Warner's first graduate student. Alan also held a postdoctoral fellowship at Michigan State University. He was an Assistant and Associate Professor here on the faculty of the Biological Chemistry Department from 1970-1987, and also held positions as Assistant Dean for Research Development and Assistant/Associate Vice President for Research. In



1987, Alan moved to the National Institutes of Health, where he served as the genetics of aging program officer, and later as the AIDS research assurance coordinator for protection of human subjects. In 1989 he joined the new NIH Office of Scientific Integrity (OSI), which became the U.S. Public Health Service's Office of Research Integrity (ORI). Alan was later promoted to OSI Branch Chief and then to ORI Associate Director for Investigative Oversight. Alan retired in 2006 and began a consulting business, Price Research Integrity Consultant Experts (P.R.I.C.E.), that advises institutional officials and individuals involved in cases of research misconduct.

Marshall Nirenberg Remembrances Available

As reported in last year's newsletter, Biological Chemistry alumnus and Nobel laureate Marshall Nirenberg died January 15, 2010. In that edition, Dr. Bernie Agranoff fondly recollected their friendship and Marshall's illustrious career. Additional remembrances of Marshall Nirenberg written by colleagues Dr. Raymond Holton and Dr. Conrad Wagner are now available from the Biological Chemistry Department. Contact Craig Reynolds, Chief Administrator at 734.763.0185 or creyno@umich.edu, to receive a copy or download them at <http://www.biochem.med.umich.edu/?q=Nirenberg>.

Endowed Lectures

NOTED SPEAKERS ADD VITALITY AND PRESTIGE TO THE DEPARTMENT OF BIOLOGICAL CHEMISTRY

2010 IRWIN J. GOLDSTEIN LECTURESHIP
IN GLYCOBIOLOGY

Pamela Stanley, Ph.D.

REGULATION OF NOTCH SIGNALING BY GLYCANS DURING
EMBRYOGENESIS AND T CELL DEVELOPMENT

Pamela Stanley obtained her Ph.D. in the laboratory of Prof. David White, Department of Microbiology, University of Melbourne, Australia. She was subsequently a postdoctoral fellow of the MRC of Canada in the lab of Dr. Louis Siminovitch where she began her work on somatic cell glycosylation mutants. She was appointed Assistant Professor in Cell Biology at Albert Einstein College of Medicine in New York in 1977 and became a full Professor in 1986. She currently holds the Horace W. Goldsmith Foundation Chair in Cell Biology and is Associate Director for Laboratory Research of the Albert Einstein Cancer Center.

Dr. Pamela Stanley's lab investigates biological functions of mammalian glycans on glycoproteins, such as growth factor and Notch receptors. Certain glycans are required for mammals to develop, and changes in the glycans of cancer cells facilitate tumor progression. Chinese hamster ovary (CHO) cell mutants in glycan synthesis help to identify novel glycosylation activities, functions of mammalian

glycans in cell-cell and cell-pathogen recognition and signal transduction, and for glycosylation engineering. CHO mutants were used to show that Notch



Bill Lands and
Irwin Goldstein



receptors require O-fucose glycans to function. Embryos that cannot transfer fucose to Notch die before birth with a phenotype typical of embryos defective in global Notch signaling. This includes defective formation of the heart and defective vascularization of the yolk sac and embryo. Most recently, a knock-in Notch1 mutation was made to eliminate the single O-fucose site in the Notch1 ligand binding domain. Mouse mutants with this point mutation are viable and fertile but have a T cell development defect. In addition, a vascularization defect becomes apparent when the Notch1 point mutant gene is present in only a single copy. These and other Notch1 mouse mutants are being used to pinpoint roles for glycans in Notch signaling during embryogenesis and immune cell development.

2010 WILLIAM E.M. LANDS LECTURESHIP
ON THE BIOCHEMICAL BASIS FOR THE PHYSIOLOGY
OF ESSENTIAL NUTRIENTS

Patrick J. Stover, Ph.D.

FOLATE-GENOME INTERACTIONS: MANAGING GENE
EXPRESSION AND GENOME STABILITY

Patrick J. Stover, Ph.D. is Professor and Director of the Division of Nutritional Sciences at Cornell University and Director of the United Nation's University Food and Nutrition Program for Social & Human Development. He graduated from



Saint Joseph's University with a B.S. degree in Chemistry and was awarded the Molloy Chemistry Award at graduation. He received a Ph.D. degree in Biochemistry and Molecular Biophysics from the Medical College of Virginia and performed his postdoctoral studies in Nutritional Sciences at the University of California at Berkeley.

Dr. Patrick J. Stover's laboratory studies the biochemical, genetic and epigenetic mechanisms that underlie the relationships between folic acid and human pathologies including neural tube defects &



other developmental anomalies, cardiovascular disease and cancer. Specific interests include the regulation of folate-mediated one-carbon metabolism

and cellular methylation reactions, molecular basis of the fetal origins hypothesis, development of mouse models to elucidate mechanisms of folate-related pathologies, and translational control of gene expression by ferritin. In 1996 he received the Presidential Early Career Award for Scientists and Engineers from President Clinton, the highest honor bestowed by the U.S. government on outstanding scientists and engineers beginning their independent careers. He received the ERL Stokstad Award in Nutritional Biochemistry from the American Society for Nutritional Sciences in 1999 and has been selected as an Outstanding Educator four times by Cornell Merrill Presidential Scholars. He is a current member of the National Academies of Sciences' Food and Nutrition Board. He serves on the editorial board for the *Annual Reviews of Nutrition*, the *Journal of Biological Chemistry* and the *American Journal of Clinical Nutrition*.

2011 G. ROBERT GREENBERG LECTURESHIP
IN BIOLOGICAL CHEMISTRY

Dorothee Kern, Ph.D.

CHOREOGRAPHING AN ENZYME'S DANCE

Dorothee Kern, Ph.D. is Professor of Biochemistry at Brandeis University and an Investigator of the How-

ard Hughes Medical Institute. She received her Ph.D. at the Martin Luther University in Halle, Germany and then carried out her postdoctoral studies at UC



Berkeley. She joined the faculty at Brandeis University in 1999.

Dr. Kern's research group studies the dynamical nature of proteins with the goal to reveal the interplay between structure, dynamics and function. She has been a major contributor in

the experimental characterization of protein dynamics during enzyme catalysis and signaling.

With the unprecedented wealth of high-resolution protein structures churned out by x-ray crystallographers in the last two decades, it might be easy for a structural biologist to develop a sense of complacency. Not so with Dorothee Kern, who sees a real opportunity to augment these otherwise static structural images with new studies designed to reveal what she calls the "dynamic personality" of enzymes, signaling proteins, and the substrates that they affect. Only through such dynamic studies, Kern argues, will researchers develop a realistic picture of how proteins function.

Dr. Kern is combining nuclear magnetic resonance (NMR) spectroscopy with crystallography, computation and single molecule experiments as tool.



NMR, which relies on magnetic fields and radio waves, is capable of observing the motion of the atoms inside functioning proteins.

Dr. Kern is the recipient of the Pfizer Award in Enzyme Chemistry from the American Chemical Society, the Dayhoff Award from the Biophysical Society, the Young Investigator Award of the International Association for Protein Structure Analysis and Proteomics, the Strage Award for Aspiring Young Science

Faculty and the National Lecturer of the Biophysical Society.

2011 MARTHA L. LUDWIG LECTURESHIP
IN STRUCTURAL BIOLOGY

Joan Steitz, Ph.D.

NONCODING RNAs: WITH A VIRAL TWIST

Joan A. Steitz, Ph.D. is the Sterling Professor of Molecular Biophysics and Biochemistry, and Investigator, Howard Hughes Medical Institute. She is a member of the American Academy of Arts and Sciences, the American Philosophical Society, the National Academy of Sciences, and the Institute of Medicine. Dr. Steitz earned her Ph.D. from Harvard University.

Dr. Joan A. Steitz earned her B.S. in chemistry from Antioch College in 1963. Significant findings from her work emerged as early as 1967, when her Harvard University Ph.D. thesis with Jim Watson examined the test-tube assembly of an RNA bacteriophage known as R17.

Steitz spent the next three years in postdoctoral studies at the Medical Research Council Laboratory of Molecular Biology in Cambridge, England, where she used early methods for determining the biochemical sequence of RNA to study how ribosomes know where



to initiate protein synthesis on bacterial mRNAs. In 1970, she was appointed as an assistant professor of molecular biophysics and biochemistry at Yale, becoming a full profes-

sor in 1978. At Yale, she established a laboratory dedicated to the study of RNA structure and function. In 1979, Steitz and her colleagues described a group of cellular particles called small nuclear ribonucleoproteins (snRNPs), a breakthrough in understanding how RNA is spliced. Subsequently, her laboratory has defined the structures and functions of other noncoding RNPs, such as those that guide the modification of ribosomal RNAs and several produced by transforming herpesviruses. Today, her studies of noncoding RNAs include microRNAs.

Her many honors include the U.S. Steel Foundation Award in Molecular Biology (1982), the National Medal of Science (1986), the Lewis S. Rosenstiel Award (2002), the FASEB Excellence in Science Award (2003), the RNA Society Lifetime Achievement Award (2004), E.B. Wilson Medal (2005), Gairdner Foundation International Award (2006), and Albany Medical Center Prize in Medicine and Biomedical Research (2008) [shared with Elizabeth Blackburn]. Dr. Steitz is the recipient of 13 honorary degrees.



Distinguished Graduate Lecture: Beverly L. Davidson

Beverly L. Davidson holds the Roy J. Carver Biomedical Chair in Internal Medicine, and is Professor in Internal Medicine, Neurology, and Physiology & Biophysics at the University of Iowa. She is also Vice Chair for Research in the Department of Internal Medicine, Director of the Gene Transfer Vector Core and Associate Director for the Center for Gene Therapy. She currently manages a research team that includes research scientists, postdoctoral fellows, graduate students and undergraduates.

Dr. Davidson received her Bachelor of Science degree in Biology from Nebraska Wesleyan University and her Ph.D. in Biological Chemistry from the University of Michigan. After a postdoctoral fellowship she was a Research Investigator and subsequently Assistant Professor at the University of Michigan. In 1994, she was recruited to the University of Iowa. Dr. Davidson is a member of several editorial boards, is a member of the American Association

DEPARTMENT OF
BIOLOGICAL CHEMISTRY

2011
**DISTINGUISHED
GRADUATE
LECTURE**



*Emerging Therapies
for Neurogenetic Disease*

**BEVERLY L.
DAVIDSON, PH.D.**

PROFESSOR OF INTERNAL MEDICINE,
PROFESSOR OF NEUROLOGY,
PHYSIOLOGY, AND BIOPHYSICS
AT THE UNIVERSITY OF IOWA

THURSDAY • 12 MAY • 3 PM
NORTH LECTURE HALL

Dr. Davidson is a member of the American Association for the Advancement of Science, American Federation for Clinical Research (Midwest Section), American Society for Neuroscience, American Society for Gene Therapy, and the American Society for Microbiology. Dr. Davidson serves on the Board of Directors for the American Society for Gene Therapy, and is Associate Director of the Center for Gene Therapy for Cystic Fibrosis and other Genetic Diseases, and is past Co-Director of the Iowa Biosciences Advantage Program. She received her Ph.D. at the Department of Biological Chemistry, University of Michigan in 1987.

for the Advancement of Science, American Federation for Clinical Research (Midwest Section), American Society for Neuroscience, American Society for Gene Therapy, and the American Society for Microbiology. Dr. Davidson serves on the Board of Directors (Treasurer) for the American Society for Gene Therapy and is past Co-Director of the Iowa Biosciences Advantage Program.

Dr. Davidson's research is focused on inherited genetic diseases that cause central nervous system dysfunction, with a focus on (1) recessive, childhood onset neurodegenerative disease, in particular lysosomal storage diseases such as the mucopolysaccharidoses and Batters disease; and (2) dominant genetic diseases such as CAG repeat disorders, Huntington's disease and spinocerebellar ataxia type I. Professor Davidson's research in inherited brain disorders and developing novel therapies is nationally and internationally recognized. In 2007, she was named a Fellow by the American Association for the Advancement of Science, received a University of Iowa Regents Award for Faculty Excellence, and was named a University of Iowa Carver Research Program of Excellence. In 2008 she was an Iowa Women of Innovation Nominee for Research Innovation and Leadership. In 2009, Dr. Davidson received the Mathilde Solowey Award, National Institutes of Health, and was named a Member, Electorate Nominating Committee, Medical Sciences, AAAS (2009-12). In 2011, Dr. Davidson gave the S.J. Armond Lecture for the AANP, the University of Iowa Presidential Lecture, was a nominee for the Chair, Electorate Nominating Committee, Medical Sciences for the AAAS, and a Nominee for the Pioneer Hi-Bred Iowa Women of Innovation award.

Annual Student Awards : 2011



The Minor J. and Mary Lou Coon Award

Awarded annually to the student who exhibits overall excellence in research, teaching, and service to the department. This award honors Professor Jud Coon, former Chair of the department, and the late Mary Lou Coon who have provided the gift that supports this award.

Awardee: *Heather Dickson*

Mentor: *Anne Vojtek*

The Lee Murphy Memorial Prize

Awarded annually to the student who embodies the highest ideals of scientific integrity and who has published a paper or a series of papers judged most significant by the Awards Committee. This award is named in honor of Lee Murphy, an alumnus of this department.

Awardee: *Li Li* **Mentor:** *Kun-Liang Guan*

(Unavailable for photographs)

The Dziewiatkowski Award

Dedicated to the memory of the late faculty member, Dominic D. (Jay) Dziewiatkowski, this award is offered to the student who has submitted the most outstanding Ph.D. dissertation during the last academic year.

Awardee: *Ashley Reinke*

Mentor: *Jason Gestwicki*



The Halvor N. and Mary M. Christensen Award

Presented to a second-year student on the basis of academic record. This award is given in honor of the late Mary M. and Professor Emeritus Halvor N. Christensen who served as Chair of Biological Chemistry from 1955–1970. Mary and Halvor Christensen generously provided the original gift that supports this annual award, and their daughter Karen Christensen-Gray has also generously donated funds to support this award.

Awardee: Jenna Hendershot

Mentor: Patrick O'Brien



The Adam A. and Mary J. Christman Award

Presented to a third-year student judged to be the most outstanding in that class. The Christman Award is named in memory of former long-time faculty member Professor Adam Christman.

Awardee: Claudia McDonald

Mentor: Bruce Palfey

The Anthony and Lillian Lu Award

Presented to a student on the basis of academic background, achievement in the graduate program, and potential as a scientist. This award is made possible by the Lu Family who have generously provided the gift that supports this annual award.

Awardee: Swathi Krishnan

Mentor: Ray Trievel



Ph.D. Degrees Granted



ZHONGHUA YAN, October 21, 2010
Thiol-mediated Redox Modulation of the Adaptive Immune Response
Mentor: Ruma Banerjee, Ph.D.



HEATHER BRIANNA CLAXTON, November 22, 2010
Investigation into the Activity and Specificity of the Thioesterase II, Ketoreductase and Dehydratase Domains of Multiple Polyketide Synthases
Mentor: Janet L. Smith, Ph.D.



MICHAEL C. MARVIN, December 10, 2010
Identification and Characterization of Expanded RNA Binding Abilities and Cellular Roles for Nuclear RNase P
Mentor: David R. Engelke, Ph.D.



ASHLEY A. REINKE, February 7, 2011
Conformation-specific Chemical Probes for Amyloid- β
Mentor: Jason E. Gestwicki, Ph.D.



LI LI, February 14, 2011
Upstream Components of mTORC1
Mentor: Kun-Liang Guan, Ph.D.



CHERRISSE RAE LOUCKS, April 25, 2011
Molecular Architecture of a 40S Ribosomal Subunit Maturation Intermediate
Mentor: Georgios Skiniotis, Ph.D.



RYAN T. EVANS, April 26, 2011
Splicing and Multiple Binding Proteins in the Corticotropin-Releasing Hormone Stress System
Mentor: Audrey F. Seasholtz, Ph.D.



VERONICA E. BURNS, July 19, 2011
Structural Basis and Functional Consequences of Alternative ATF2-Jun Heterodimer Orientations at the Interferon-Beta Enhancer
Mentor: Tom K.W. Kerppola, Ph.D.



NIRUPAMA GUPTA, August 15, 2011
Thiol-Based Redox Modulation of Transcriptional Regulators; CprK and Rev-erb β
Mentor: Stephen Ragsdale, Ph.D.



ELIZABETH PIERCE, August 31, 2011
Identification and Characterization of Oxalate Oxidoreductase, a Novel Thiamine Pyrophosphate-dependent Enzyme That Enables Anaerobic Growth on Oxalate
Mentor: Stephen Ragsdale, Ph.D.

New Ph.D. Students & Postdoctoral Fellows

Our New Students

BRITTANY BOWMAN received her Bachelor of Science degree in 2009 from the University of Rochester, NY. *Mentor:* Brian Ross

MELISSA CORDES received her Bachelor of Science degree in 2010 from Eastern Michigan University, Ypsilanti, MI. *Mentor:* Neil Marsh

QINGYUN DAN received his Bachelor of Science degree in 2011 from Peking University, China. *Mentor:* Janet Smith

BENJAMIN ELLINGTON received his Bachelor of Science degree in 2009 from Rice University, Houston, TX. *Mentor:* Ruma Banerjee

MICHAEL HOWARD obtained his Bachelor of Science degree in 2010 from Michigan State University, East Lansing, MI. *Mentor:* Carol Fierke

ERIN MILLER received her Bachelor of Science degree in 2010 from Otterbein University, Westerville, OH. *Mentor:* Pat O'Brien

NICOLE MOTL received her Bachelor of Science degree in 2010 from Southern Illinois University, Edwardsville, IL. *Mentor:* Ruma Banerjee

JENNIFER RAUCH received her Bachelor of Science degree in 2010 from Central Michigan University, Mount Pleasant, MI. *Mentor:* Jason Gestwicki

NATHAN RAYNARD received his Bachelor of Science degree in 2010 from the University of California at Santa Cruz, CA. *Mentor:* Aaron Goldstrohm

ELIA WRIGHT received her Bachelor of Science degree in 2010 from Muhlenberg College, Allentown, PA. *Mentor:* Carol Fierke

And Ten New Fellows

IREENA BAGAI received her undergraduate degree in 2004 from the University and her Ph.D. from the University of Arizona in 2008. *Mentor:* Stephen Ragsdale

VERONICA E. BURNS received her undergraduate degree in 1993 from Bowling Green State University and her Ph.D. from the University of Michigan in 2011. *Mentor:* Tom Kerppola

YUNHUI CHENG received his undergraduate degree in 1993 from Hebei Medical University, China and his Ph.D. from Hebei Medical University, China in 2004. *Mentor:* Tom Kerppola

HUAI DENG received his undergraduate degree in 1995 from Wuhan University, China and his Ph.D. from Iowa State University in 2008. *Mentor:* Tom Kerppola

WEI DENG received her undergraduate degree in 2003 from Wuhan University, China and her Ph.D. from the Shanghai Institute of Organic Chemistry in 2008. *Mentor:* Ming Lei

NIRUPAMA GUPTA received her undergraduate degree in 2001 from Pandit Prithi Nath College, Kanpur, India and her Ph.D. from the University of Michigan in 2011. *Mentor:* Stephen Ragsdale

KENICHI KITANISHI received his undergraduate degree in 2006 from Tokyo University of Science, Japan and his Ph.D. from Tohoku University, Japan in 2011. *Mentor:* Ruma Banerjee

CHANGRUI LU received his undergraduate degree in 2005 from Colgate University and his Ph.D. from Cornell University in 2011. *Mentor:* Tom Kerppola

DARIUSZ SLIWA received his M.S. degree in 2004 from Silesian University of Technology, Poland and his Ph.D. from Utah State University in 2010. *Mentor:* Stephen Ragsdale

PRAMOD KUMAR YADAV received his undergraduate and Ph.D. degrees from Deen Dayal Upadhyay Gorakhpur University, India in 2005 and 2009 respectively. *Mentor:* Ruma Banerjee

Student News

BENJAMIN ELLINGTON (Ruma Banerjee lab) was named to serve on the editorial board of *ASBMB Today*, a monthly publication of the American Society for Biochemistry and Molecular Biology.

SWATHI KRISHNAN (Ray Trievel lab) received an honorable mention for her poster presented at the Summer Symposium on Chromatin and Epigenetic Regulation of Transcription at Penn State University.

DAVE PAI (David Engelke lab) was awarded a 2011 Endowment for the Development of Graduate Education (EDGE) Award by the University of Michigan Medical School's Endowment for the Basic Sciences (EBS).

CLAUDIA McDONALD (Bruce Palfey lab) was awarded the 2011 Vincent Massey Award, given to young scientists for exceptional contributions, at the 17th International Symposium on Flavins and Flavoproteins for her work on the reactivity of flavoenzymes with oxygen. Claudia also received a 2010 Rackham Warner Linfield Award for study outside of the United States and the University of Michigan's Alliances for Graduate Education and Professoriate Service Award. Claudia has so far been an author on four peer-reviewed research papers since joining Biological Chemistry, including two as first author. She has also co-authored a review and is a co-inventor on an invention disclosure.

DONALD RAYMOND (Janet Smith lab) was awarded a Pauling Poster Prize at the 2010 American Crystallographic Association Meeting held in Chicago, IL. Donald was also awarded a prestigious Rackham Pre-doctoral Fellowship for 2011-2012. This fellowship includes tuition, stipend, and grad care health insurance for three terms.

SHAMEKA SHELBY (Debra Thompson lab) was awarded a 2011 King-Chavez-Parks Future Faculty Fellowship.

FENG WANG (Ming Lei lab) received the 2010 Proquest Distinguished Dissertation Award given in recognition of the most exceptional scholarly work produced

by doctoral students during 2010. Feng was honored at a special ceremony at the Rackham Graduate School on April 28, 2011.



Annual Summer Retreat

Each year in late August BioChem faculty, students and postdocs gather at the Michigan State Kellogg Biological Station Conference Center for two days of talks, poster sessions, and general camaraderie. This year papers were delivered by Jennifer Gehret (Janet Smith lab), Scott Horowitz (Ray Trievel & Hashim Al-Hashimi labs), Dave Pai (David Engleke lab), Gerwin Westfield (Georgios Skiniotis lab), Jamie Van Etten (Aaron Goldstrohm lab), Valentin Cracan (Ruma Banerjee lab), Donald Raymond (Janet Smith lab), Srayanta Mukherjee (Yang Zhang lab), Amber Smith (Janet Smith lab), Huai Deng (Tom Kerpola lab), Mark Taylor (Patrick O'Brien lab), Claudia McDonald (Bruce Palfey lab), Yong Chen (Ming Lei lab), and Rajesh Ramachandran (Dan Goldman lab). New faculty member Dan Southworth discussed his

work, and 23 participants presented posters. The retreat has its lighter moments as well: an afternoon ice cream social is held; and Friday evenings always find time for a Bar-B-Que, swimming in Gull Lake and a bonfire.



On the Cover

GRADUATE STUDENT

CLAUDIA McDONALD'S RESEARCH

Life on earth started under anaerobic conditions,

and it wasn't until about a billion years ago that oxygen produced by photosynthesis consumed ferrous iron in the oceans, allowing O₂ to accumulate in the atmosphere. Organisms were challenged significantly by O₂, which can disrupt the normal flow of electrons in metabolism and produces oxygen species that are highly destructive to biochemicals. Organisms had to adapt to these new selective pressures by controlling oxygen reactivity with cellular components. This was especially true for flavin prosthetic groups. Flavin-dependent enzymes participate in all aspects of cellular physiology. Some flavin-dependent enzymes have evolved to be less reactive with oxygen than free flavins, affording kinetic protection. In contrast, many flavin-dependent enzymes – the oxidases and monooxygenases – evolved to use O₂ as a substrate and, therefore, react more quickly than free flavins. Despite a significant amount of research, how proteins control the reaction of O₂ with reduced flavoenzymes, is not fully understood.

Recent work from alumna Marilyn Schuman-Jorns (Ph.D. Biological Chemistry, Massey, 1970) at Drexel University suggests that a positive charge near N5 of the isoxazine of flavoenzymes makes them more reactive with O₂. Professor Jorns showed that mutating a lysine to a neutral residue caused re-

activity with O₂ to plummet. The hypothetical site of reactivity of oxygen near the flavin is illustrated by the O₂ in the picture,

which shows the flavin from an oxidase, a nearby lysine, and O₂ with the two degenerate singly-occupied orbitals which would receive electrons from the flavin.

Claudia McDonald, a graduate student in Bruce Palfey's lab, tested the generality of the idea that lysine near N5 is the site of oxygen activation. The reactivities of several reduced flavoenzymes were determined by mixing with various concentrations of O₂ in stopped-flow experiments. The bimolecular rate constants for the reactions were determined from the time-dependence of flavin oxidation. The removal of a positive charge near N5 of the flavin caused a large change for one model enzyme, fructosamine oxidase. However the reactivities of other model-enzymes having a lysine near N5 (dihydroorotate dehydrogenases) were unchanged by mutagenesis. McDonald found that the positive charge was only important in some enzymes, deepening the mystery of oxygen reactivity [McDonald et al. (2011) *J. Am. Chem. Soc.* 133, 16809-16811].



Some Notes on Our History



THE EVOLUTION OF THE DEPARTMENT OF BIOLOGICAL CHEMISTRY AT MICHIGAN

One of the first members of the Medical School faculty, **Silas Douglas**, was appointed to teach chemistry. In fact, the first chemistry courses taught at Michigan were taught as part of the Medical School curriculum. Dr. Douglas had a small laboratory in the medical building, and he gave chemical demonstrations before the Medical School classes. He persuaded the Regents in 1855 to build the first building at any American university solely devoted to chemistry. Douglas was in charge of the University's building program and he placed the Chemical Laboratory immediately behind the Medical Department. The two buildings were connected by a wooden walkway spanning the mud.

Dr. Douglas and his staff taught chemistry to the rest of the University, and the Chemical Laboratory was repeatedly enlarged. At first, Preston Rose taught toxicology and the elements of urine analysis to medical students, but the latter subject was soon included in a course in physiological chemistry taught by Victor Vaughan, who later became dean of the Medical School.

In 1883, Victor Vaughan was appointed professor of physiological and pathological chemistry. He was the first man to hold a professorship in physiological chemistry in a medical faculty in this country. Under the able leadership of Dr. Vaughan and his pupil, Frederick Novy, the subject was developed as part of the offerings of the combined Department of Bacteriology, Physiological Chemistry, and Hygiene.

After the retirement of Dr. Vaughan in 1921, it was felt that physiological chemistry, in view of its rising importance, could hardly be kept in the position of an adjunct to other subjects. A separate Department of Physiological Chemistry was established in 1922. In 1935, with the approval of the executive

committee of the Medical School, the department's name was changed to Biological Chemistry. It was felt that the broader term "biological" was more in keeping with the recent developments in this branch of chemistry.

*From Medicine at Michigan,
Volume 1, Number 1, Spring 1999. Reprinted with permission.*

For more information, See:

Horace W. Davenport, *Not Just Any Medical School: The Science, Practice, and Teaching of Medicine at the University of Michigan, 1850-1941* (Ann Arbor: University of Michigan Press, 1999).

Howard B. Lewis, "The Department of Biological Chemistry," in *The University of Michigan, an Encyclopedic Survey*, ed. Wilfred B. Shaw (Ann Arbor: University of Michigan Press, 1951).

Minor J. Coon Symposium continued from p. 9

Achievement Award from the University of Michigan in 1976, the William C. Rose Award in Biochemistry in 1978, and the Bernard B. Brodie Award in Drug Metabolism in 1980. Professor Coon is a member of the National Academy of Sciences, the Institute of Medicine, and the American Academy of Arts and Sciences. His honorary degrees include Doctor of Medicine from the Karolinska Institute in Stockholm in 1991. In addition to his scientific research and service to the scientific community, Jud was editor-in-chief of *Biochemical Preparations* and of *Microsomes, Drug Oxidations* and *Chemical Carcinogenesis*. He also served on the editorial boards of several journals, including *Biochemistry*, *Molecular Pharmacology*, and *The Journal of Biological Chemistry*.

In 1998 the Department of Biological Chemistry established the Minor J. and Mary Lou Coon Award, based on a gift of support from Dr. Coon and his wife. This award is given annually to students who exhibit overall excellence in research, teaching, and service to the department. To date, there have been fourteen recipients of this award.

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