Dear Friends and Colleagues and Graduates!

Greetings and Best Wishes from Ann Arbor. I thought it would be worthwhile this year before highlighting some of the recent departmental happenings, to provide an overview of the current composition and state of the department as of Spring 2009.

We currently have 47 faculty members with appointments in Biological Chemistry, including 21 faculty for whom the department is wholly responsible for space and salary support and 26 faculty with appointments in centers and institutes or other departments.
for whom we have lesser financial responsibilities. In addition, there are five active emeritus and seven “occasional” emeritus faculty. We expect to increase the number of wholly owned faculty to about 25 within the next 4–6 years with a smaller increase (2–5) in joint appointees. We believe that doing so is critical to maintain the Department’s scientific leadership nationally and is a necessary step for improving our national ranking in terms of NIH funding to within the top 10. The most recent rankings put us somewhere around number 15 nationally.

The Department has 31 Ph.D. students. In addition to these graduate students in the Biological Chemistry Ph.D. program, there are two students in Cellular and Molecular Biology, seventeen students in Chemical Biology, and six students in Biophysics who are training under the direction of Biological Chemistry faculty.

We have seven excellent, dedicated staff members who deal with our finances, graduate student support, personnel, ordering, and grants management. Craig Reynolds joined the department in January 2009 as our new Chief Departmental Administrator. Craig has over 18 years of laboratory, federal, and university-wide administrative experience. We are very pleased to have him on board.

As many of you will recall, a number of our faculty relocated to space in the western-most part of the medical school in the Medical Science Research Building III. We currently occupy the 3rd and 4th floors and one-half of the 5th floor and expect to complete occupancy of the 5th floor with further growth of the faculty in the next few years.

I am sure it will be no surprise to anyone, that we live in a world driven more and more by finances or lack thereof. For example, faculty are expected to cover 50% of their salaries from grant funds and to generate on average $110 of facilities and administrative cost reimbursement per square foot of research lab space. Although we have been through some difficult times over the last several years, we have moved from a low of about $180 in research expenditures per square foot on average in FY2006 to almost $300 in FY2009, a 63% increase within three years. This is a tribute to the aggressiveness of faculty in applying for grant funding and having junior faculty obtain funding.

Some of you may be aware that the University is finalizing the purchase of the “Pfizer space,” which was left unoccupied when Pfizer closed its Ann Arbor research facility. This is a combination of office space and laboratory space. The office space will be used to accommodate many of the medical school administrative offices that are scattered in rented space in various parts of Ann Arbor. The research space, roughly 500,000 sq. ft., will gradually be occupied over the next ten years. It is anticipated that the medical school will be the major tenants. I think that the availability of this facility will reduce considerably some of the current pressures we feel about space.

We have had two additions to the faculty this past year. Assistant Professor Aaron Goldstrohm arrived in
September 2008 as a University of Michigan Biological Sciences Scholar after completing postdoctoral studies with Dr. Marvin Wickens at the University of Wisconsin-Madison. His work, supported by a Rackham Faculty Research grant, involves the study of a family of protein regulators that bind and control specific mRNAs. Dr. Georgios Skiniotis from Harvard University joined the Life Sciences Institute and the Department of Biological Chemistry in November 2008. His lab is employing molecular electron microscopy techniques to study the architecture and conformational dynamics of complex protein assemblies. Fortunately, we have not had any faculty departures or retirements this year.

As shown in the following pages, many of our faculty, including those with joint appointments in other departments and units of the University, as well as many former graduate students and postdoctoral associates, have continued to gain recognition and receive important awards for their achievements.

Last year’s Student Awardees are also listed in this Newsletter. The Committee that makes the choices finds this is a very difficult task, and we should emphasize that the awards give us an opportunity to recognize the progress and achievements of all of our graduate students. You will also find below information regarding the presentations given by our 2008 Distinguished Graduate, Dr. Robert Landick, and by speakers selected for three endowed lectureships: Dr. Roger D. Kornberg (Martha Ludwig lecture), Dr. Christopher J. Frederickson (Lands lecture), and Dr. Stephen G. Withers (Goldstein lecture). I am very pleased to announce that Susan Greenberg has made a major contribution to create an endowed lectureship in the name of Professor Robert G. Greenberg, Emeritus Professor of Biological Chemistry, who passed away in 2005. Dr. Margaret Lomax and I will soon be soliciting additional support for this lectureship.

As I mention each year, I hope that you will take the time to keep us apprised of your activities—if you send me a note (smithww@umich.edu), I will make sure the relevant information makes it into the newsletter next year. Finally, please check our new, more user friendly Biological Chemistry website: http://www.biochem.med.umich.edu/.

Best wishes for the coming year.

Regards,
Mary Sue Coleman, President of the University of Michigan, Professor of Biological Chemistry in the Medical School, and Professor of Chemistry in the LS&A College since 2001, has played a key role in the development of the Life Sciences Institute (LSI), an interdisciplinary research center. The directorship of the Institute has been named for Dr. Coleman, and Dr. Alan R. Saltiel now holds the title of the Mary Sue Coleman Director of LSI. The directorship was endowed by a gift from Paul and Susan Meister. An accomplished biochemist and member of the Institute of Medicine, Coleman has been an “influential ambassador” for LSI’s collaborative, interdisciplinary approach to research, Saltiel said.

Dave Ballou teamed up with Alex Ninfa and Marilee Benore (U of Michigan, Dearborn) to totally rewrite and produce the second edition of *Fundamental Laboratory Approaches for Biochemistry and Biotechnology*. This text is used in more than 130 colleges and universities in the United States and worldwide. Dave attended a Gordon Conference on Thiol-based Redox Regulation and Signaling that was held in II Ciocco Hotel near Pisa, Italy, and then proceeded to Jaca, Spain for the 16th International Symposium on Flavins and Flavoproteins. Also at that conference were Bruce Palfey and Charles Williams. He also was a speaker at the Second International Interdisciplinary Conference on Vitamins, Coenzymes, and Biofactors that was held in Athens, Georgia in October. Dave continues to collaborate with Pimchai Chaiyen, a former student, who is now a professor at Mahidol University in Bangkok, and he is also collaborating with Cathy Drennan (MIT), a former student with Martha Ludwig, Barrie Entsch, who has been a close collaborator with Dave Ballou for 37 years, and who has visited Ann Arbor many times from his home in Australia, again spent the month of October 2008 in Dave’s lab. Their work has resulted in much of the defining work on flavoprotein hydroxylases.

Ruma Banerjee was invited to join the ASBMB Task Force on International Members, chaired by Judith Bond and created by the current President of the Society. Ruma’s research group discovered the human vitamin B12 decyanase, an enzyme that has been presumed to exist since the discovery of the cyano-form of the cofactor sixty years ago. This work was published in PNAS.

Jud Coon was recently elected Honorary Life Member of the International Society for the Study of Xenobiotics in recognition of his pioneering research on cytochrome P450, which he describes as Nature’s most versatile biological catalyst. Jud and his associates showed that P450 isozymes purified from liver microsomal membranes catalyze the oxygenation of physiologically important steroids, fatty acids, eicosanoids, and retinoids. However, of particular interest, they also catalyze transformations of chemically unreactive “foreign” substances such as drugs, anesthetics, terpenoids, pesticides, and environmental carcinogens to products that may be more or less toxic than their precursors.

Francesco De Matteis (visiting professor collaborating with Dave Ballou, Jud Coon, and Paul Hollenberg) recently came to the University of Michigan to carry out research on the mechanism of bilirubin metabolism by...
cytochrome P450. He holds a Medical Degree from the University of Bari, Italy, and a Ph.D. in Chemical Pathology from the University of London and was formerly Professor of Toxicology at the University of Turin Medical School and then Visiting Professor of Toxicology with the MRC Bioanalytical Science Group, Birkbeck College, University of London. Professor De Matteis is very widely known for his research on the effects of drugs on the biosynthesis and degradation of heme and hemoproteins, on porphyrias and drug-induced alleviation of jaundice, and the role of genetic predisposition and other risk factors in adverse drug reactions.

Dave Engelke has been awarded the National Institutes of Health’s new training grant to establish the first Postbaccalaureate Research and Education Program (PREP) at the University of Michigan. These programs are designed to provide intense research experiences to recent college graduates from underrepresented minority groups to prepare them for entry into strong PhD programs in the biomedical sciences. The program will be cooperative between the Rackham Graduate School and the Program in Biomedical Sciences.

Gary Glick has been elected a Fellow of the American Association for the Advancement of Science. Dr. Glick was honored for his distinguished scholarship in the field of organic chemistry, particularly the discovery of molecular targets, mechanisms and development of potential therapeutic compounds for the treatment of autoimmune diseases.

Aaron Goldstrohm joined the Department last September as an Assistant Professor, after completing postdoctoral studies with Dr. Marvin Wickens at the University of Wisconsin-Madison. His work involves the study of the family of PUF protein regulators that bind and control specific mRNAs, with the goal of identifying the mRNAs that PUF proteins regulate, determining how they accomplish regulation, and developing a mechanistic understanding of the biological processes they control. He has been awarded a Rackham Faculty Research Grant for “Discovering mRNA regulatory mechanisms using genome-wide RNA interference screens.”

Katrin Karbstein has received a prestigious CAREER Award from the National Science Foundation in connection with her research project, “Dissecting the Regulation of Ribosome Assembly by the Essential GTPase Bms1.”

Tom Kerppola is heading a new collaborative research program directed toward the development of high resolution probes for cellular imaging. The program is jointly directed by Harinder Singh in the Department of Molecular Genetics and Cell Biology at the University of Chicago and Tzvi Tzfira in the Department of Molecular, Cellular, and Developmental Biology at the University of Michigan. The focus of the program is to develop new applications for the bimolecular fluorescence complementation technology developed in the Kerppola laboratory. The program will include studies in cultured mammalian cells, plants and animals. The collaborative nature of the program enables the laboratories to pursue interdisciplinary studies in a wider range of fields than would be possible for each individual laboratory. The complementary areas of expertise of the participating laboratories facilitate the rapid transfer of information and speed up adoption of new technologies.

Dan Klionsky uses baker’s yeast to study how proteins are moved about and “targeted” within cells. He has
been elected a Fellow of AAAS, which recognized him for innovations in teaching cell biology and for research defining the mechanisms and cellular role of autophagy, the process of self-digestion by a cell through the action of enzymes.

**Neil Marsh** has been awarded the Doctor of Science degree (Sc.D.) from Cambridge University. This degree is conferred on alumni of the University who have made important and extensive scholarly contributions to an area of research.

**Steve Ragsdale** is a Michigan Memorial Phoenix Institute Faculty Fellow. He recently gave lectures at the Gordon Research Conference on Environmental Bioinorganic Chemistry and Metals in Biology and at Genomatica, Inc. in San Diego and at the University of Toronto. He served as Chair of the 2008 Gordon Research Conference at Bates College on the Molecular Basis of Microbial One-Carbon Metabolism and is on the editorial boards of the Journal of Biological Chemistry, Current Opinions in Chemical Biology, Biofactors, and BBA Proteins and Proteomics.

**Jochen Schacht** has been named Guest Professor at Liaoning University, Jinzhou, China, and has been elected Fellow of the American Association for the Advancement of Science. He was recognized by AAAS for explaining how aminoglycoside antibiotics cause hearing loss and for developing therapies to protect against it. His team determined that aspirin helps ward off hearing loss caused by the widely used antibiotic gentamicin.

**Georgios Skiniotis** from Harvard University joined the Life Sciences Institute and the Department in October of 2008. Skiniotis’ lab employs molecular electron microscopy techniques to study the architecture and conformational dynamics of complex protein assemblies. Complemented by a variety of biochemical and biophysical methods, the group aims to address structural and mechanistic issues in important biological processes, including chromatin remodeling.

**Bill Smith**’s landmark science was recognized by an article highlighting his career, along with two of his original publications, which appeared in a special “Classics” section of the Journal of Biological Chemistry’s May 16, 2008 issue. Authored by Nicole Kresge, Robert Simoni, and Robert Hill, the JBC picked Bill Smith’s studies to help celebrate scientists whose ground-breaking studies appeared in its pages in the years from 1905–2005.

In 1971, people had been taking aspirin for more than 70 years, but no one knew exactly why it worked. That year, a JBC paper co-authored by Bill Smith, then a graduate student in our Department, and his faculty advisor, Bill Lands, reported that aspirin interferes with the normal activity of an enzyme called cyclooxygenase. Bill Smith, later as a faculty member at Michigan State University, purified and cloned this enzyme, which became known as COX-1. His 1990 article in the JBC showed precisely where aspirin and other COX-1 inhibitors act and led others to identify COX-2 and its inhibitors. In the JBC classic article, Bill Smith is quoted as pointing out that biochemical studies on a newly discovered group of hormones called prostaglandins provided a nice example of how basic research can have a far-reaching impact on the practice of medicine.
In a dual celebration held last October, two members of our faculty, Ruma Banerjee and Randy Kaufman, were awarded endowed professorships. Dr. James Wooliscroft, Dean of the Medical School, welcomed the guests, including members of the recipients’ families and of the Vincent Massey family, and Dr. William L. Smith summarized the achievements of those being honored.

Ina dual celebration

Inauguration of the Vincent Massey Collegiate Professorship in Biological Chemistry for Dr. Ruma Banerjee

Ruma Banerjee, Ph.D. is a widely recognized authority on mechanistic enzyme biochemistry.

She earned a Master of Science degree in 1982 from the Centre for Advanced Studies in Plant Sciences at Delhi University in India. In 1987, she earned her doctorate from Rensselaer Polytechnic Institute in New York with Dr. James Coward, and followed that with postdoctoral studies with Dr. Rowena Matthews at the University of Michigan; she served as Lecturer in the Dept. of Biological Chemistry from 1988–1991, after which she joined the faculty of the University of Nebraska-Lincoln as Assistant Professor of Biochemistry. She was promoted to Associate Professor, with tenure, in 1997 and achieved the rank of full Professor in 2000.

In 2002, Dr. Banerjee was named the Willa Cather Professor of Biochemistry, and in 2003 the George Holmes Distinguished University Professor of Biochemistry at Nebraska. While there, she also founded and served as Director of the Nebraska Redox Biology Center, funded by the National Center for Research Resources. She joined the U-M faculty in 2007 as Professor of Biological Chemistry.

Dr. Banerjee’s research focuses on the molecular mechanisms of redox active enzymes, particularly on...
homocysteine-clearing enzymes and the two known co-
balamin (vitamin B12)-dependent enzymes in mam-
mals. She has edited books on Chemistry and Bio-
chemistry of B12 and on Redox Biochemistry and has
published more than 130 journal articles.

Recipient of the Pfizer Award from the Ameri-
can Chemical Society and an Established Investigator
Award from the American Heart Association, Dr. Ba-
erjee has chaired three Gordon Research conferences
and the 2008 Federation of American Societies for Ex-
perimental Biology Conference on Folic Acid, B12 and
One-Carbon Metabolism.

Her expertise in the field is recognized through mem-
berships on editorial boards, scientific advisory commit-
tees, and National Institutes of Health grant review pan-
els, as well as in national and international leadership
positions.

The Vincent Massey Collegiate Professorship in Bi-
ological Chemistry was established in memory of our
distinguished colleague, who joined the U-M faculty
in 1963 and died in 2002. His many honors included
election as a Fellow of the Royal Society of London and
membership in the National Academy of Sciences.

Other colleagues who spoke about Dr. Banerjee’s ac-
complishments included Dr. James K. Coward, Profes-
sor Emeritus of Medicinal Chemistry, College of Phar-
macy, and Professor Emeritus of Chemistry, College
of Literature, Science, and the Arts at the University of
Michigan.

Re-Seating of the Warner-Lambert/Parke-Davis
Professorship in Medicine for Dr. Randal J. Kaufman

Randal J. Kaufman, Ph.D., Professor of Internal Med-
icine and of Biological Chemistry in the University of
Michigan Medical School and a Research Investigator
in the Howard Hughes Medical Institute, is an interna-
tional authority on protein biochemistry, cell biology,
and coagulation.

He received his Bachelor of Arts degree in molecular,
cellular and developmental biology from the Univer-
sity of Colorado and his doctorate in pharmacology from
Stanford University, where he studied gene amplifica-
tion as a mechanism by which cells become resistant to
anticancer agents. He was a Helen Hay Whitney fellow
with Phillip Sharp at the Center for Cancer Research at
the Massachusetts Institute of Technology, where he de-
veloped gene transfer technologies based on gene am-
plification and expression in mammalian cells.

After postdoctoral studies, Dr. Kaufman was a found-
ing scientist at the Genetics Institute Inc., and during
his time there from 1982-93, he engineered mamma-
lian cells for high-level expression of therapeutic pro-
teins, such as clotting factors that are now used to treat
individuals with hemophilia.

Since joining the U-M faculty in 1993 as Profes-
sor of Biological Chemistry, Dr. Kaufman has focused
on mechanisms by which mammalian cells regulate
protein folding and secretion and a cellular response
known as the unfolded protein response (UPR). He cur-
rently uses mouse models to elucidate the significance
of the UPR in health and disease.

A prolific scholar with a bibliography reflecting more
than 250 original scientific publications and over 100
reviews and book chapters, Dr. Kaufman has served as
a member of numerous editorial and advisory boards,
as well as grant committees of the National Institutes of
Health.

A fellow of the American Association for the Ad-
vancement of Science, he has received numerous
awards, including the Van Wezel Prize of the Europe-
an Society of Animal Cell Technology, the Investigator
Recognition Award of the International Society for
Thrombosis and Haemostasis, and the Internation-
al Association Francaise Des Hemophiles Award, “Prix
Henri Chaigneau.”

Four Medical School professorships have been creat-
ed from a 1993 gift from the Warner-Lambert/Parke-Da-
vis Company, now Pfizer, Inc., to support the research
activities of senior-level faculty members whose exem-
plary contributions to the fields of basic chemistry, mo-
lecular biology, biotechnology, genetics and/or human
gene therapy are widely recognized.

Other colleagues who spoke about Dr. Kaufman’s ac-
complishments included Dr. David Ginsburg, the James
V. Neel Distinguished University Professor of Inter-
nal Medicine & Human Genetics and Warner-Lambert/
Parke-Davis Professor of Medicine at the University of
Michigan.
Anita Payne, reproductive endocrinologist and university professor, died at age 82 on February 15 in Palo Alto, CA. Anita was born in Karlsruhe, Germany and came to San Francisco with her parents and sister Dorothy in 1938. She received her B.A. and Ph.D. in Physiology from the University of California, Berkeley. She was a faculty member in the Departments of Obstetrics and Gynecology and Biological Chemistry at the University of Michigan from 1971–1995 and a Senior Research Scientist at Stanford University from 1995–2007. Over her long and distinguished scientific career, she took pride in serving as a role model and mentor, especially for women scientists. Dr. Payne’s research focused on androgen metabolism in the testis. She made several important contributions in this area, most notably the characterization of major isoforms of 3α-hydroxysteroid dehydrogenase and isomerase, an important enzyme involved in steroid hormone biosynthesis. Dr. Payne trained many graduate students and a large number of post-doctoral fellows. She was elected the President of the Society for the Study of Reproduction in 1990, was the Distinguished Service Award of the Society for the Study of Reproduction in 1994, and won the prestigious Carl G. Hartman award from the same society in 1998. The Endocrine Society honored her with the 1999 Women in Endocrinology Mentor Award. In recognition of her many contributions, her colleagues and the Department of Obstetrics and Gynecology established the Anita Payne Lecture in 1993, which is held in conjunction with the annual research day of the Department of Ob/Gyn and the Reproductive Sciences Program.

Helen Lun Ghen Wu (Ph.D. with Howard Lewis) died last October in Las Vegas. She immigrated in 1947 to Canada as the first Chinese woman to receive a Research Fellowship from that country’s National Research Council. With an M.S. degree from the University of Saskatchewan, Helen then won a Barbour Scholarship at the University of Michigan. Her postdoctoral work in Professor Merle Mason’s lab as a research biochemist was at the U-M, where she met her future husband, Dr. Chung Wu (Ph.D. with Jim Hogg). Chung had a faculty position in Internal Medicine as well as in Biological Chemistry, where he was on our teaching staff.

Student News | Recognition of Achievements

Becky Fagan received the Vincent Massey Award for her presentation at the 16th International Symposium on Flavins and Flavoproteins, in Jaca, Spain. The Vincent Massey Awards were established to honor outstanding graduate students or postdocs attending the triennial symposium for their excellence in research. Awardees are selected by an international committee of experts, receive a medal and cash award, and give a lecture on their research to the symposium. Becky was also awarded a Rackham Graduate Student Research Grant.

Stacie Bulfer in Ray Trievel’s lab and Feng Wang in Ming Lei’s lab were each awarded a Rackham Pre-doctoral Fellowship for 2009–2010. This is one of Rackham’s most prestigious fellowships and supports outstanding doctoral students actively working on dissertation research and writing. It includes tuition, stipend, and grad care health insurance for three terms. Stacie and Feng will both be honored at a Rackham reception in April.
Dr. Robert Landick, Professor of Biochemistry and Professor of Bacteriology at the University of Wisconsin-Madison, was honored to present the Distinguished Alumni Lecture at the annual department student award ceremony last spring.

Dr. Landick was born in Massachusetts but has very strong ties with the state of Michigan. He first received his bachelor’s degree in Chemistry at the University of Michigan in 1975 working with Joe Marino on organic synthesis. He joined the Ph.D. program in our department in 1978 and conducted his thesis research with the late Dale Oxender characterizing the genes for branched-chain amino acid transport in E. coli and their regulation. After receiving his Ph.D. degree in 1983, he began working on RNA polymerase and the structure and regulation of transcription complexes during post-doctoral training with Charles Yanofsky at Stanford, and continued these studies as a faculty member first at Washington University in St. Louis and then at the University of Wisconsin-Madison.

Throughout his career, Dr. Landick’s research focus has been on the detailed molecular mechanism of RNA polymerase function. In his own words: “these studies have defined an elemental mechanism of transcriptional pausing for both bacterial and human RNA polymerases, established how paused states can be prolonged or shortened by regulators, and identified roles for transcriptional pausing in fundamental mechanisms of gene regulation and in RNA folding. Dissection of the regulatory interactions of RNA polymerase has required development of many new methods, most notably analysis of transcription by single molecules of RNA polymerase. Application of these methods has led to many additional insights into RNA polymerase structure and function.”

Dr. Landick has been recognized for his excellence in research and education by numerous honors and fellowships. While he was a graduate student at the department, he received the Rackham first year graduate fellowship as well as the Rackham dissertation research grant. He was an NIH postdoctoral fellow, a Mallinckrodt fellow, a Searle scholar, a presidential young investigator, an NIH merit awardee, and is a fellow of American Academy of Microbiology, a fellow of American Association for the Advancement of Science, and a recipient of University of Wisconsin Kellett mid-career award. He also holds the Ira L. Baldwin professorship of Bacteriology at the University of Wisconsin.

The department faculty and students are enormously proud of the distinguished achievement by Dr. Landick and warmly welcomed Bob back to the department for an exciting seminar.

On the Cover

This issue’s cover of the Newsletter features the work of Robert S. Fuller. It shows the 2.2 Å structure of a complex of Saccharomyces cerevisiae Kex2 protease catalytic domain with the peptidyl boronic acid inhibitor Ac-Arg-Glu-Lys-Arg-boro. Subtilisin domain, green; P-domain, magenta; S1 insertion loop, red; carbons of S1 and S2 acidic residues in yellow; carbons of catalytic triad (D175, H213, S385, N314), light blue, Ca2+ ions, cyan; inhibitor AcREKRboro, CPK colors. The figure shows that the features that distinguish Kex2 and related proprotein processing enzymes (e.g., human furin) from degradative subtilisins all focus on recognition of P1 Arg: the S1 Ca2+ ion, the S1 insertion loop, and the interaction of the P-domain with the subtilisin domain through the three loops of the subtilisin domain that form the S1 subsite and Ca2+-binding pocket.
Inauguration of Endowed Martha L. Ludwig Professorship

In a celebration held last September, Janet L. Smith was installed as the first recipient of the Martha L. Ludwig Professorship in Protein Structure and Function, and a symposium was held in honor of Martha. Dr. James Woolliscroft, Dean of the Medical School, welcomed the guests, including colleagues and former students of Dr. Ludwig, and Dr. William L. Smith commented on Martha as a thoughtful and devoted mentor of her students and a superb classroom lecturer who was internationally recognized for her contribution to our understanding of the B vitamins and their mode of action.

The endowed professorship was established through a very generous gift and pledge from Frederic L. Hoch, M.D., Professor Emeritus of Internal Medicine and of Biological Chemistry, and Dr. Ludwig’s husband for 45 years. Dr. Ludwig, the J. Lawrence Oncley Distinguished University Professor of Biological Chemistry in the University of Michigan Medical School and Senior Research Professor in the Biophysics Research Division, passed away November 27, 2006.

Highlights of Martha Ludwig’s Career

Dr. Ludwig joined the UM faculty in 1967 as an Assistant Professor and maintained an active research program until her death. She was recognized nationally and abroad as a gifted x-ray crystallographer whose specialty was the structure and function of enzymes that employ the vitamins riboflavin and B12 as cofactors. As an Assistant Professor, she solved the structure of the first flavin-containing protein to be thus characterized. Subsequently, her laboratory determined the structure of several other flavoproteins, often in collaboration with other faculty members.

Her interest in B12 stemmed from a collaborative project spearheaded by a young graduate student, Catherine Drennan, now Professor of Chemistry and Biology and HHMI Investigator at the Massachusetts Institute of Technology. The structure of B12 bound to a fragment of the enzyme methionine synthase was the first of that vitamin bound to a protein. Exciting outcomes of her work were movies of molecules in motion, dancing through their catalytic roles.

Martha’s scientific contributions were recognized by the Garvan Medal of the American Chemical Society in 1984, by the Distinguished Faculty Achievement Award from the University of Michigan in 1986, by election as a Fellow of the American Association for the Advancement of Sciences in 2001, and by election to the National Academy of Sciences in 2003 and to the Institute of Medicine in 2006.

She received her undergraduate degree in chemistry from Cornell University in 1952, her Master’s degree in chemistry from the University of California at Berkeley, in 1955, and her Doctorate in Biochemistry from Cornell Medical College in 1956, and then held postdoctoral positions at Harvard and MIT.

She did further postdoctoral training with future Nobel laureate William Lipscomb, with whom she solved the structure of carboxypeptidase A. This was the first structure of a protein to be determined in the United States, and it signaled her as a rising star in the field of x-ray crystallography.

Dr. Ludwig served as Chair of the Biophysics Research Division from 1986–1989 and initiated the Molecular Biophysics Training Program at the University
of Michigan, securing funding from the National Institutes of Health for this graduate training resource and providing leadership of the program for nearly 20 years. She also played a leading role in the development of the Michigan Life Science Corridor-funded beamlines at the Argonne synchrotron.

Protein Structure Symposium Held in Honor of Martha L. Ludwig

Symposium speakers were as follows: Dr. Rowena G. Matthews (U-M), *Methionine Synthase: Guiding an Enzyme Through Complex Conformational Changes*; Dr. Thomas A. Steitz (Yale University), *From Carboxypeptidase A to Crick’s Central Dogma*; Dr. Catherine L. Drennan (MIT), *Crystallographic Snapshots of Metalloenzymes*; and Dr. Carl C. Correll (Rosalind Franklin University of Medicine and Science), *RNA Chaperones Facilitate Ribosome Biogenesis*.

Inauguration of the Martha L. Ludwig Professorship in Protein Structure and Function for Dr. Janet L. Smith

Janet Smith has research interests and accomplishments that made her an obvious choice to be the first to hold the endowed chair. She is a Professor of Biological Chemistry in the Medical School and a Research Professor in the Life Sciences Institute at the University of Michigan. She was recruited to the University of Michigan by Martha Ludwig, a close colleague and friend.

A native of Pennsylvania, Dr. Smith was a National Merit Scholar at Indiana University of Pennsylvania (Bachelor of Science, 1973), where she studied chemistry after an initial journey into political science. The seed for a life-long interest in protein structure and function was planted by a 1972 guest lecture she attended on the relationship of sequence conservation to protein 3-D structure. Her undergraduate thesis research in organic chemistry taught Dr. Smith that she would not become a synthetic chemist. The day sodium caught fire in the lab was a bellwether, she says.

Dr. Smith found biochemistry to be the most stimulating area of chemistry and continued study in that field at the University of Wisconsin-Madison (Ph.D., 1978), where she was convinced of the importance of molecular structure by her Advisor, M. Sundaralingam.

After her thesis research on crystal structures of protein synthesis inhibitors, Dr. Smith pursued a growing interest in protein structure by joining Wayne Hendrickson at the Naval Research Laboratory as a National Research Council Research Fellow. Following postdoctoral work, she was an Associate Research Scientist in the Hendrickson Lab at the Howard Hughes Medical Institute at Columbia University. These stops in Washington, D.C., and New York City allowed her to learn protein crystallography from one of the leading prac-
tioners in the field; the experience also taught her to love urban life.

During her postdoctoral work, Dr. Smith helped develop the “MAD” (multi-wavelength anomalous diffraction) method for solving crystal structures. It also initiated an interest in using synchrotron radiation, a requirement of MAD.

Dr. Smith established a research program in Structural Biology at Purdue University, where she served as a Professor of Biological Sciences from 1987–2004. There, she enjoyed an excellent environment for research and training in Structural Biology with a highly interactive group of colleagues. The importance of the then-new MAD method in her research led to a sabbatical year at the European Molecular Biology Laboratory and the European Synchrotron Radiation Facility in Grenoble, France. This reinforced her enjoyment of visiting places with good food and excellent outdoor opportunities.

Dr. Smith’s research focuses on understanding biological processes through knowledge of the structures of key protein molecules. She is co-author or author of more than 100 publications and has served on the editorial boards of four journals: *Current Opinion in Structural Biology, Macromolecular Structures, Protein Science,* and *Structure*. She is a recipient of a National Institutes of Health (NIH) MERIT Award for her work on understanding the function and structure of complex enzymes.

Janet holds membership in several scientific societies and has served on numerous grant review and advisory panels. From 1996–1998, she chaired the Biophysical Chemistry Study Section A at the NIH. Since 1989, she has advocated for the structural biology community to have access to intense X-rays from synchrotron sources, serving as a member of the Department of Energy Biological and Environmental Research Advisory Committee and as a frequent advisor to synchrotron radiation facilities and synchrotron structural biology labs.

In conclusion, Janet Smith presented a lecture, titled “Aha! Moments in Structural Biology”, in which she expressed her gratitude for selection as the first recipient of the Martha L. Ludwig Endowed Professorship and summarized her current research interests.
Stephen G. Withers is known for his work in the field of enzyme mechanisms, particularly carbohydrate enzymology. These include glucosidases, galactosidases, amylases, cellulases and α-glucan phosphorylases. The approaches adopted to this work involve a combination of classical biochemistry (enzyme purification, enzyme kinetics, labeling and peptide isolation/sequencing, etc.), synthetic organic chemistry (synthesis of substrate analogues and inhibitors) and biophysical chemistry (NMR studies of enzyme-ligand complexes). More recently, these approaches have been coupled with the powerful techniques of protein crystallography, site-directed mutagenesis and electrospray mass spectrometry. His earlier work provided considerable insights into the roles of hydrogen bonding in enzyme substrate recognition and catalysis, which led to the development of methodologies to trap reaction intermediates on glycosidases: enzymes involved in the breakdown of complex sugars. Application of these approaches in conjunction with other mechanistic, structural and molecular biological studies provided substantial insights into the mechanisms of these enzymes, culminating with the demonstration that the textbook mechanism for the enzyme lysozyme, taught to many hundreds of thousands of students each year, is incorrect. These basic mechanistic studies have resulted in a number of spin-offs. These include the development of patented technologies for the synthesis of complex sugars using engineered glycosidases (glycosynthases), the development of new classes of glycosidase inhibitor with therapeutic potential, and the generation of new proteomic tools for profiling and quantitating glycosidase activities. More recently, he has applied the tools of directed evolution to the generation of improved enzymes for the synthesis of glycosides. He has also provided valuable service to the scientific community, particularly in his role as Scientific Director of the Protein Engineering Network of Centres of Excellence of Canada, and more recently in his role as Director of the Centre for High-throughput Biology at UBC.
William E. M. Lands Lectureship on the Biochemical Basis for the Physiology of Essential Nutrients

Dr. Christopher J. Frederickson
NeuroBioTex

“Zinc Secreting Cells: What Cells are Listening to These Zinc Signals?”

Christopher J. Frederickson graduated with a B.S. from Harvard University in 1968 and received his Ph.D. from the University of Chicago in 1973. He then spent three years at Carnegie Mellon University, Pittsburgh, and in 1975 joined the faculty at the University of Texas in Dallas. Dr. Frederickson and the late Mary Frederickson discovered the synaptic release of zinc in the late 1970s and his group discovered the causal role of zinc in excitotoxicity in the mid 1980s, and in synaptic plasticity, in the late 1990s. In 1999, he left the University of Texas to co-found, with Cathy Frederickson, NeuroBioTex, a company devoted to basic and applied research on diagnostic and therapeutic products pertaining to zinc. Dr. Frederickson is committed to advancing the understanding of zinc as a signal ion in all areas of biology with the applied aim of developing research tools, diagnostics and therapeutics relating to the roles of zinc in health and disease. He and his collaborators have established the physiological concentration of ionic or “free” zinc in biological fluids such as the CSF, blood serum, saliva, semen, tears, and the intracellular fluids of cells. Importantly, he has also pursued the biological pathways that are modulated by these free zinc signals. As recently as 20 years ago, the dogma was that all zinc in biological systems was tightly bound to proteins and that free zinc would be impossible to detect or image. Today, imaging of free zinc signaling and between cells is a valuable tool of biology and is used in the study of zinc signaling in brain, heart, pancreas, lung, and many other tissues and organs. Frederickson’s current focus is on the use of free zinc signals from the prostate gland (measured in semen) to detect early prostate cancer.
Martha L. Ludwig Lectureship in Structural Biology

Professor Roger D. Kornberg
Winzer Professor in Medicine
Department of Structural Biology,
Stanford University School of Medicine

“The Molecular Basis of Eukaryotic Transcription”

Roger D. Kornberg was the 2006 Nobel Laureate in Chemistry “for his studies of the molecular basis of eukaryotic transcription.” This citation refers to the x-ray crystallographic studies in his lab of the yeast RNA polymerase II and numerous template, substrate and product complexes of Pol II, that have led to a detailed molecular understanding of the synthesis of messenger RNA in eukaryotic cells. This work, all published since 2000, depended on two decades of work on the purification and reconstitution of the yeast transcriptional apparatus and the development of exacting methods for isolating homogeneous, active forms of Pol II. Structural and biochemical studies of transcription are ongoing in Dr. Kornberg’s laboratory, directed in particular toward understanding the structure and function of protein complexes, such as ‘Mediator,’ that regulate initiation of transcription.

Dr. Kornberg has made other important scientific contributions as well. In a now-classic series of papers he established, using NMR and EPR methods, the extremely rapid rate of phospholipid diffusion in the plane of the lipid bilayer and the exceedingly slow rate of trans-bilayer diffusion (flip-flop). In his postdoctoral work, which focused on the chemical nature of eu-
karyotic chromatin, he discovered the histone octamer and demonstrated that the octamer, in complex with ~200 bp of double-stranded DNA, constituted the basic, repeating unit in chromatin (the nucleosome) that could be visualized by electron microscopy. Dr. Kornberg has also pioneered new methods of structural analysis, notably the development of two-dimensional crystallization of proteins through adsorption to planar lipid bilayers and the analysis of these crystalline arrays by electron diffraction. Two-dimensional crystallization provided a key assay for the homogeneity of preparations of RNA polymerase II, essential for the eventual preparation of three-dimensional crystals.

Dr. Kornberg was raised in a storied scientific family. His parents, Sylvy and Arthur, were both enzymologists. Arthur Kornberg (1918–2008) discovered DNA polymerase, defined the enzymatic synthesis and replication of DNA, and was awarded the Nobel Prize in Physiology or Medicine in 1959. Roger’s brother, Tom, is a Drosophila developmental biologist who has studied the role of the engrailed gene as a master regulator of the anterior-posterior axis in epidermal segments. His brother Ken is an architect whose firm specializes in laboratory design.

Dr. Roger Kornberg received a B.S. in Chemistry in 1967 from Harvard University and his Ph.D. in Physical Chemistry in 1972 from Stanford University, where he worked with Harden McConnell. He pursued postdoctoral work with Aaron Klug at the MRC Laboratory of Molecular Biology from 1972–1973 and remained at the MRC for two more years, first as a member of the Harvard Society of Fellows and subsequently as a staff member of the laboratory. In 1975, Dr. Kornberg returned to the United States as Assistant Professor of Chemistry at Harvard but was recruited in 1976 as Professor in the newly founded Department of Structural Biology at Stanford, where he has remained. He also holds an honorary doctorate from Umeå University in Sweden.
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.

2008 Awardee: Ashley Reinke
Mentor: Jason Gestwicki

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.

2008 Awardee: Ryan Evans
Mentor: Audrey Seasholtz

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.

2008 Awardee: Bin Zhao (Standing in for Bin Zhao is Qian Yang)
Mentor: Kun-Liang Guan (Presenting the award is Bill Smith)

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 Coon, former Chair of the department, and the late Mary Lou Coon who have provided the gift that supports this award.

2008 Awardee: Rebecca Fagan
Mentor: Bruce Palfey
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.

2008 Awardee: Junyu Xiao
Mentor: Zhaohui Xu

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.

2008 Awardee: June Pais
Mentor: Carol Fierke

Biological Chemistry | Ph.D. Degrees Granted

Lance Rider
November 5, 2008
Flavoenzymes involved in pyrimidine oxidation and reduction
Mentor: Bruce Palfey

Pamela Wong
December 11, 2008
Characterization of Amyloid-β interactions at the membrane interface: implications for pathogenesis
Mentor: Ari Gafni

Junyu Xiao
December 12, 2008
Structural basis of Vps4 function and regulation in the multivesicular body pathway
Mentor: Zhaohui Xu

Bin Zhao
February 12, 2009
Inactivation of YAP-TEAD by the Hippo Pathway Is Involved in Growth Control and Cancer
Mentor: Kun-Liang Guan

Rebecca Fagan
February 20, 2009
The Differences are in the Details: The Mechanism of Flavin Reduction in Class 1A and Class 2 Dihydroorotate Dehydrogenases
Mentor: Bruce Palfey
Jennifer Gehret received her Bachelor of Science from the University of Maryland College Park in 2007. Jennifer’s research in Janet Smith’s laboratory involves the study of the polyketide synthesis pathway that produces Curacin A, found to have anti-mitotic activity. Of particular interest is the final cleavage and terminal double bond formation of the pathway, which contains a previously uncharacterized combination of sulfotransferase and thioesterase domains used to complete the reaction. Knowledge of the three dimensional structure of these domains is integral to understanding how this step functions. Jenn is currently working on obtaining the structures of these domains by x-ray crystallography.

Michael Lofgren received his Bachelor of Science from the University of Minnesota in 2006. In Bruce Palfey’s lab, Mike is studying the thermodynamics and the chemical and kinetic mechanisms of flavin-dependent enzymes that are involved in pyrimidine metabolism. Specifically, Mike is interested in the membranous members of the dihydroorotate dehydrogenase (DHOD) family of redox enzymes. These enzymes are participants in the de novo deoxyuridine monophosphate (dUMP) biosynthetic pathway. They are essential for DNA synthesis, and are critical to life, and therefore are common pharmacological targets for the treatment of auto-immunity disorders, cancer, malaria, and African sleeping sickness.

2009 HHMI Award | Ming Lei

Assistant Professor Ming Lei has received an Early Career Scientist award from the Howard Hughes Medical Institute. The award supports scientists who are just beginning their independent research careers, by providing full salary, benefits, and a research budget of $1.5 million over a six-year appointment. The Institute will also cover other expenses, including research space and the purchase of critical equipment.

The selected scientists, who are at 33 institutions across the United States, have led their own laboratories for two to six years. During that time, many have made considerable contributions to biomedical research. Energetic and passionate about a broad range of scientific questions, this group of scientists is at a career stage that many consider to be a scientist’s most productive—and most vulnerable.

In March 2008, HHMI unveiled its new Early Career Scientist program and announced a nationwide competition seeking applications from the nation’s best early career scientists. Those working in all areas of basic biological and biomedical research and areas of chemistry, physics, computer science, and engineering that are directly related to biology or medicine were invited to apply. The competition drew more than 2,000 applicants. To maximize the impact of HHMI’s support, individuals who were selected in the competition cannot hold more than one early career award from another agency or foundation.

The goal of Ming’s work is to understand the organization and dynamics of macromolecular assemblies important for genome regulation and stability. A combination of structural analyses, such as X-ray crystallography and electron microscopy, coupled with biophysical and biochemical experimentation, forms the core of his methodological approach. Some active areas of his investigations include: telomere protection and regulation; searching small molecular inhibitors of the interaction between the single-stranded telomeric DNA and its binding protein POT1 using high-throughput chemical genomics approach; and the molecular mechanism of histone dymethylase.
Alice del Campillo Campbell (Ph.D. with Jud Coon) continues to work at Stanford as a Senior Research Associate in Biology. Together with Allan Campbell, Professor of Biology in the Department of Biological Sciences, she is studying the evolution of phage integration/excision enzymes and their regulation. Richard Beleson, who graduated from Stanford as a bio major in 1976 and did undergraduate research in their lab, recently endowed an undergraduate scholarship in biology in honor of Alice and Allan; this is designed to provide approximately half tuition for selected undergraduates in perpetuity.

Louis DeFilippi (Ph.D. with Don Hultquist) is still an independent consultant. He has completed a project to produce commercial quantities of immobilized regio- and stereospecific pig liver esterase, which is essential in the production of a once-a-day nucleoside reverse transcriptase inhibitor HIV/AIDS drug. More recently, he has focused on applied microbiology projects that have taken him to Taiwan and China, where he started up his patented invention, a Biological Air Treater that will be used to mineralize vaporous pollutants. Currently an expert witness in a case involving contaminated groundwater, Lou is also Vice President of ISoy Technologies, a small start-up firm that is in the early production of a topical sunscreen/antioxidant derived from soybean oil.

Fred Guengerich (postdoc with Jud Coon), Professor of Biochemistry and Director of the Center in Molecular Toxicology at Vanderbilt University, was named an Honorary Professor of the Chinese Academy of Sciences (Chengdu Institute of Biology) and is the recipient of the 2009 AACR Award for Outstanding Achievement in Chemistry in Cancer Research.

Ron White (postdoc with Jud Coon) joined the faculty of the Department of Pharmacology at the University of Connecticut School of Medicine, became a tenured Associate Professor, and in 1987 was recruited as Research Group Leader in the Department of Drug Metabolism at the Bristol-Myers Squibb Pharmaceutical Research Institute in Princeton. His work there centered on providing drug metabolism and pharmacokinetic support for drug discovery. In 1998, Ron moved to the Schering-Plough Research Institute in Kenilworth, New Jersey as Director of Exploratory Drug Metabolism, a group of sixty Ph.D-level and other scientists devoted to optimization of drug discovery in all therapeutic areas. In subsequent years, he was promoted to Senior Director and then Vice-President in charge of drug metabolism, pharmacokinetics, and bioanalytical activities globally. Ron retired from Schering-Plough in mid-2008 but took a position with Bristol-Myers Squibb, as Distinguished Research Fellow with duties that included mentoring mid-career scientists. He has retained academic links as Adjunct Professor of Chemical Biology at Rutgers University and as a member of the Corporate Advisory Board of the University of Washington School of Pharmacy. In addition, he has served as a member of the NIH Pharmacology Study Section and of the Drug Metabolism Technical Group of the Pharmaceutical Research Manufacturers of America and is a member of the Editorial Board of Drug Metabolism and Disposition and of the Scientific Advisory Board of the International Conference on Cytochrome P450.

Quing-Yu Zhang (Ph.D. with Jerry Menon) is an Associate Professor in the Department of Environmental Health Sciences, State University of New York at Albany. She also holds the title of Research Scientist 5 at the Wadsworth Center, State of New York Department of Public Health in Albany. Her research interests center on the environmental and genetic bases of the differences in susceptibility to adverse drug reactions, and development of new strategies for improvement of therapeutic efficacy and prevention of environmental diseases involving the small intestine. Her current projects include the regulation of drug metabolism under pathologic conditions, the role of tissue-selective P450 enzymes in intestinal xenobiotic metabolism, genetic polymorphisms of the human enzymes involved in drug clearance, and the application of novel transgenic mouse models for studying the in vivo function of these enzymes in drug metabolism, chemical carcinogenesis, and intestinal dysfunction.
The G. Robert Greenberg Lectureship

Susan Greenberg, wife of the late G. Robert Greenberg, endowed a lectureship this year to honor Bob's many contributions to the field of molecular biology and his long association with the Department of Biological Chemistry. Bob joined the faculty in 1957 and served the department with distinction for over thirty years, until his retirement in 1988. After retiring, Bob continued his research on the T4 ribonucleotide reductase as an active emeritus professor for another seventeen years.

As was noted upon his passing in 2005, Bob Greenberg transmitted his great enthusiasm for bench research to several generations of graduate students and postdoctoral fellows. Through his contacts with the early pioneers of molecular biology, he launched many students on their academic and scientific careers.

By creating an endowment that will fund an annual lectureship in Bob's name, Susan's generous support has ensured that future generations of biochemists, faculty and students alike, will continue to benefit from Bob's passion for science and mentoring. Each year, students within the department will select a speaker engaged in leading edge research to come to campus, share their knowledge and meet with members of the department, thus helping to promote the environment of inquiry and discovery that Bob held so dear.

For guidance on how to contribute to the G. Robert Greenberg Lectureship Endowment or any other donor fund of the Biological Chemistry Department, please see the following page.

Supporting the Department of Biological Chemistry

As a friend of the department, you are probably aware that the Department of Biological Chemistry is a national leader in biochemistry research. We consistently rank in the top 15 of our 105 peer departments for research support from the National Institutes of Health and are widely known throughout academia for our strengths in structural enzymology, biochemical signaling, regulation of gene expression, and protein processing and folding.

What may surprise you, though, is the extent to which the department relies upon the philanthropic generosity of donors to fund many critical aspects of its operations. Gift funds are essential to supporting activities beyond our basic operations. Indeed, 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. For example, last fall we brought Nobel Laureate Dr. Roger D. Kornberg to campus for a talk on the molecular basis of eukaryotic transcription; it is the Martha L. Ludwig Lectureship endowment that allows us to do this.

As a benefactor of the Department of Biological Chemistry, you can direct your gift in one of several different ways:

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

Professorships
- Vincent Massey Collegiate Professorship
- Minor J. Coon Collegiate Professorship
- Anthony and Lillian Lu Professorship
- Martha L. Ludwig Professorship

Graduate Student Awards
- Halvor N. and Mary M. Christensen Award
- Adam A. and Mary J. Christman Award
- Minor J. and Mary Lou Coon Award
- Dominic D. Dziewiatkowski Dissertation Award
- Lee Murphy Memorial Prize

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
Please be assured that in these difficult economic times, we are constantly on the lookout for new ways to cut costs and make our precious resources go farther. Your gift support is no different. We make this promise to be good stewards of your donation and deserving recipients of your good will.

For additional information on how you can make a positive difference in the University of Michigan Department of Biological Chemistry, please contact:

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