In this Issue

2 Letter from the Chair
3 Congratulations to Jack Dixon
3 Best Wishes to Michael Marletta
4 Faculty News - What’s Happening
5 Alumni/ae News Updates
6 Transitions
8 New Students Join Current Ph.D. Candidates
9 Degrees Granted
9 Distinguished Alumni/ae Lectureship
10 Student Awards
12 Faculty Profiles
16 Donations and Gifts

Biological Chemistry
Administrative Staff

Jack E. Dixon, Ph.D.
Chair

Robert Fuller, Ph.D.
Associate Chair

Scott Benjamin
Computer Systems Specialist

Jackie Benson
Timekeeper

Heather Cavin
Administrative Assistant

Bob Elliott
Equipment & Supplies Manager

Beth Goodwin
Student Services Associate

Mary Grapp
Accountant

Pat Haines
Secretary

Sharon Hoffman
Administrative Assistant

Katrina Ward Hope
Basic Science Administrator

DeLynne Lahstinen
Business Manager

Karen Meeks
Office Assistant

Sandra Ridella
Secretary

Pat Urban
Staff Assistant
Letter from the Chair

It is with mixed feelings that I write this last newsletter to you as Chair of Biological Chemistry. When I step down as Chair on July 1, 2001, I will have been here for 10 years. Over that time, we have recruited outstanding faculty and further enhanced our national reputation (as was done so effectively during Jud Coon’s chairmanship). We have renovated some space, yet approximately 50% of the remaining space needs updating. We are a very strong basic science department in the Medical School, and many of our faculty hold key leadership positions that profoundly influence the direction of the School. A search committee has been formed to help recruit the next Chair of Biological Chemistry, and I am extremely pleased that Paul Hollenberg is chair of that committee. The dean has promised that resources will not be a limiting factor in our being able to recruit the best possible candidate. Even though I will step down as Chair, I will continue to be an active faculty member of the Department of Biological Chemistry. I have thoroughly enjoyed my experiences here, and I am grateful for the help, support and guidance that many of you have provided to me over the last 10 years. Personally and professionally, this has been a wonderful time for my family and me.

When I vacate the Chair of Biological Chemistry, I will assume the position of Co-director of the Life Sciences Institute (LSI). For those of you who don’t already know, I’ll give you a brief history of its formation. In 1998, President Bollinger formed a group of faculty called the President’s Commission on the Life Sciences. Chaired by Huda Akil and Bill Roush, this campus-wide group of 20 was charged with assessing the current strengths and weaknesses in research and education as they pertained to the life sciences; the group was further charged to make recommendations to the President, which would enable the University of Michigan to become a more outstanding national leader in the life sciences arena. The committee made several recommendations for moving forth, and a search for the Director of the Life Sciences Institute was launched. After an extensive national search, Scott Emr, Professor in the Department of Molecular Medicine and Investigator in the Howard Hughes Medical Institute at the University of California School of Medicine in San Diego, was offered the position. Scott did not want to spend his entire effort in administrative work and he suggested to President Bollinger the possibility that I serve as Co-director of the Institute. President Bollinger asked me if I would be willing to be a Co-director with Scott. I regard the LSI as such an important part in the enhancement of the overall quality of science at the entire University that I agreed to do so. As Co-director with Scott, I believe the LSI can have a major impact on future faculty recruiting, and, indeed, in recruiting top chairs of science departments throughout the University. Scott and I are committed to help science flourish and expand at the University of Michigan. The LSI will have excellent facilities in buildings that are currently under construction to help recruit the very best scientists to the University of Michigan.

Although I give up my duties as Chair of Biological Chemistry in July, I believe that we are a vibrant and vigorous Department that will continue as a leading voice in shaping science at the University and at the national level. I look forward to working with you in my new capacity, and I hope you will share in my excitement for all the wonderful things that are happening here!

Jack E. Dixon
Marvin J. Coon Professor and Chair,
Department of Biological Chemistry
Congratulations to Jack Dixon

Jack was elected to membership in the National Academy of Sciences last May in recognition of his distinguished and continuing achievements in original scientific research. He was cited for his striking discoveries in the protein tyrosine phosphatase field. These discoveries include the finding that the pathogenic bacteria responsible for "the plague" harbor a virulent gene encoding a PTPase and, more recently, that the tumor suppressor gene, PTEN, functions by encoding a PTPase that dephosphorylates a lipid second messenger.

His other honors include election to the Institute of Medicine and the American Academy of Arts and Sciences, the Henry Russel Lectureship at the University of Michigan, the State of Michigan Scientist of the Year Award, the presidency of the American Society for Biochemistry and Molecular Biology, and, most recently, election as Fellow of the American Association for the Advancement of Science and of the American Academy of Microbiology.

As indicated in Jack’s Letter from the Chair in this Newsletter, he will continue to be a Professor in our Department while assuming his new responsibility as Co-director of the University’s Life Sciences Institute. At a reception held in Jack’s honor at the Rackham Graduate School last fall, the President of the University, Lee Bollinger, complimented him on his election to the National Academy and also for his University citizenship. We congratulate Jack on his achievements during his ten years as Chair, including his research contributions, the strengthening of all aspects of the Department’s activities, and his demonstrated concern for the excellence of science throughout the Medical School and the University.

We wish him much continued success in the years ahead.

Best Wishes to Michael Marletta

Michael came to the University of Michigan in 1987, and is presently Professor of Biological Chemistry in the Medical School, John Gideon Searle Professor of Medicinal Chemistry in the College of Pharmacy, and Investigator in the Howard Hughes Medical Institute. We much regret that he has decided to leave the University on July 1 to join the faculty of the University of California at Berkeley, where he will have his primary appointment in the Department of Chemistry with joint appointments in the Division of Biochemistry and Molecular Biology in the Department of Molecular and Cell Biology at Berkeley and the Department of Cellular and Molecular Pharmacology at UCSF.

He was elected to the Institute of Medicine in recognition of his fundamental discoveries related to the biochemistry and enzymology of nitric oxide, has held a MacArthur Foundation Fellowship, and was named State of Michigan Scientist of the Year. This past year he was given the University’s Distinguished Faculty Achievement Award.

We are very grateful to Michael for his vigorous contributions to all of our activities and wish him much ongoing success in his new position at Berkeley.
Bernard Agranoff was a recipient of the Medical Center Alumni Society (MCAS) Distinguished Achievement Award. The award was created to give special recognition and honor to an individual with exceptional distinction in a particular field.

Jud Coon was recognized as part of the University of Michigan Medical School’s Sesquicentennial Celebration as one of seven scientists who were selected from the basic science departments to have Lecture Halls named in their honor. The occasion was commemorated by multimedia works of art, which hang in the lobby of Medical Science Building II. The Twelfth International Conference on Cytochrome P450 to be held in La Grande Motte, France, next September has been dedicated to him in recognition of his contributions to this field.

David Engelke accepted the position of Assistant Dean for Research and Graduate Studies in the Medical School. In addition to continuing responsibility for graduate admissions through the Program in Biomedical Sciences, the position entails responsibility for graduate and postdoctoral program initiatives and career development.

Renny Franceschi was elected President of the Mineralized Tissues Group of the International Association for Dental Research for 2002.

Robert Fuller received a University of Michigan Faculty Recognition Award for his research accomplishments in studying protein processing and sorting, and for his service to the Department and to the University. He served as Chair of the Gordon Conference on Neural and Hormonal Peptide Biosynthesis last year and has been appointed Associate Chair of our Department.

Daniel Goldman was promoted to Professor of Biological Chemistry, with tenure in the Medical School.

Kun-Liang Guan was promoted to Professor of Biological Chemistry, with tenure in the Medical School.

Tom Kerppola was promoted to Associate Professor of Biological Chemistry, with tenure in the Medical School.

Benjamin Margolis was promoted to Professor of Internal Medicine with tenure, and Professor of Biological Chemistry in the Medical School.

Vincent Massey was honored by the Department by the establishment of a Collegiate Professorship in his name. The Professorship celebrates his career and his work in training more than a hundred biochemists, as well as his continuing vigorous research program.

Rowena Matthews received the William Rose Award from the American Society of Biochemistry and Molecular Biology. She will receive the Repligen Award for studies elucidating the chemistry of biological processes from the Division of Biological Chemistry of the American Chemical Society. She has also been named the Frederick Gowland Hopkins Lecturer for the Twelfth International Symposium on the Chemistry and Biology of Pteridines.

Jairam Menon recently gave a keynote lecture at a symposium at the Institute for the Study of Reproduction in Bombay.

Audrey Seasholtz received the University of Michigan Research Scientist Recognition Award in honor of her achievements and exceptional scholarly promise.

Jeanne Stuckey, Assistant Research Scientist, was named Distinguished Alumnus for Year 2000 by the University of Findlay Board of Governors.

Robert Zand was honored at the Annual Symposium of the University’s Macromolecular Science and Engineering Center in recognition of his 70th birthday. His name is synonymous with that of Sigma Xi at the University of Michigan, where he has been active in the Chapter for more than thirty years. As one of three former Chapter presidents, he attended the 2000 Annual Meeting and Forum in Albuquerque last November.
Ruma Banerjee (Postdoc with Matthews) is the 2001 recipient of the Pfizer Award in Enzyme Chemistry from the Division of Biological Chemistry of the American Chemical Society. She is currently Professor of Biochemistry at the University of Nebraska.

Rodney Boyer (Ph.D. with Coon), formerly the Edward and Elizabeth Hofsmann Professor of Chemistry at Hope College in Holland, Michigan, has moved to Bozeman, Montana to devote more time to writing and biochemical education consulting. He serves on the Biochemical Education Taskforce for the ASBMB and has recently published the third edition of his lab manual "Modern Experimental Biochemistry." The second edition of his book for one-semester biochemistry courses, "Concepts in Biochemistry," will be completed in June.

M. Douglas Benson (Ph.D. with Franceschi) is now a postdoctoral fellow in the laboratory of Dr. Luis Parada at the Center for Development Biology, University of Texas Southwestern Medical Center.

Jason Brickner (Ph.D. with Fuller) has received a Helen Hay Whitney Postdoctoral Fellowship to support his postdoctoral studies with Peter Walter at the University of California, San Francisco.

Jim Clemens (Ph.D. with Dixon) received a Helen Hay Whitney Award to support his Ph.D. studies with Larry Zipursky at the University of California, Los Angeles.

Xin Xin Ding (Ph.D. with Coon) gave a lecture at the 13th International Symposium on Microsomes and Drug Oxidations held in Stresa, Italy.

Fred Guengerich (Postdoc with Coon), Professor of Biochemistry at Vanderbilt University, was the recipient of the School of Medicine Medal of Merit, the first given for mentoring Postdoctoral Fellows and/or Residents in the Research setting at Vanderbilt. He is a member of the Public Affairs Committee of the American Society for Biochemistry and Molecular Biology.

Paul Hollenberg (Ph.D. with Coon), the Maurice H. Seegers Collegiate Professor and Chair of the University of Michigan's Department of Pharmacology, is President-Elect of the American Society for Pharmacology and Experimental Therapeutics.

Don Huddler (Postdoc with Dixon) is now an Assistant Research Scientist with Martha Ludwig.

Lilian Hsu (Ph.D. with Jourdain) has been named the first occupant of the newly endowed Elizabeth Page Greenawalt Chair in Physical Sciences at Mount Holyoke College. In recent years Lilian has chaired the biochemistry and chemistry departments, and served as the college's sponsored research officer. She continues to study transcriptional regulation. At present Lilian is on a two-year sabbatical leave at Berkeley.

Brett Lennon (Ph.D. with Williams; postdoc with Ludwig) has taken a position as Scientist, Product Support at Instrumentation Laboratory in Orangeburg, New York.

Anthony Lu (Postdoc with Coon) was appointed to serve as a member of the Scientific Advisory Committee of the Division of Biotechnology and Pharmaceutical Research, National Health Institutes in Taiwan. The government plans to initiate new drug development, particularly drugs to treat local diseases.

Kevin Morano (Postdoc with Thiele) is currently an Assistant Professor in the Department of Microbiology and Molecular Genetics at the University of Texas-Houston Medical School.

Marco Muda (Postdoc with Dixon) is now a Scientist at Aris Advanced Technology in Randolph, Massachusetts. His research in the Dixon laboratory focused on a new protein tyrosine phosphatase.

Heidi Schubert (Postdoc with Dixon) is now an Assistant Research Professor at the University of Utah, and is studying crystallography.

Henry Strobel (Postdoc with Coon, and then Instructor in the Department), Professor of Biochemistry and Molecular Biology and Associate Dean for Faculty Affairs, The University of Texas Medical School at Houston, makes annual visits as Visiting Professor to the Capitol Institute of Medicine in Beijing, People's Republic of China.

Ted Ueda (Ph.D. with Coon), Professor of Pharmacology in our Medical
Alumni/ae continued

School, gave lectures at Nagoya City University (sponsored by the Japanese Society of Pharmaceutical Sciences, Tokai Branch) at Tokyo University of Pharmaceutical Sciences and Life Sciences, at Tokyo Medical and Dental University, and also at the International Chemical Congress of Pacific Basin Societies (Pacifichem 2000) in Hawaii.

Matt Wishart (Ph.D. with Dixon and John Williams) is now doing a postdoc with Jack Dixon. He received his Ph.D. on the “dead” phosphatase called Styx.

Pengbo Zhou (Ph.D. with Thiele) is currently an Assistant Professor of Pathology in the Weill Medical College of Cornell University. Pengbo was recently awarded the 2001 Kimmel Scholar Award from the Sidney Kimmel Foundation for Cancer Research for his project: “A novel protein knockout technology and its implications in cancer gene therapy.” This prestigious award provides $100,000 per year for two years to Pengbo’s laboratory.

Sunny Zhou (Postdoc with Matthews) has taken a position as Assistant Professor of Chemistry at Washington State University in Pullman.

On the Web

To find out what’s new in the Biological Chemistry Department, visit our web site at http://www.med.umich.edu/biochem/

Transitions

Richard C. Adelman, Professor of Biological Chemistry in the School of Medicine, and Senior Research Scientist and Past Director in the Institute of Gerontology, retired from active faculty status last December, after a productive career as a researcher, teacher, and academic administrator.

A native of Newark, New Jersey, he received his undergraduate education at Kenyon College, earning his B.A. in chemistry in 1962. He received his graduate education under the guidance of Sidney Weinhouse at Temple University, earning his M.A. degree in chemistry in 1965 and his doctoral degree in chemistry in 1967. He received his postdoctoral training under the guidance of Bernard Horecker in molecular biology at the Albert Einstein College of Medicine. He then joined the faculty of Temple University as Assistant Professor, Associate Professor, and Professor of Biological Chemistry at the Fels Research Institute of the School of Medicine, and founding executive Director of the Institute on Aging. In 1982 he came to The University of Michigan, where he was appointed Professor of Biological Chemistry and Director and Senior Research Scientist at the Institute of Gerontology.

Dick’s interdisciplinary research interests in gerontology span the biological and social sciences and the humanities, reflecting the scholarly diversity of the Institute during his Directorship. His major contribution to research on the biology of aging is the discovery that alterations in the hormonal regulation of hepatic enzyme activity in rats provide a molecular basis for the impaired adaptive capabilities that accompany increasing age. His more recently developed social research interest emphasizes how aging shapes the social impact and meaning of diseases in newspaper coverage. His foray into the gerontological humanities relates literary images of aging in the novels, short stories, and essays of John Updike with the historical development of science in gerontology.

Dick’s honors, awards, and professional responsibilities include Presidency of The Gerontological Society of America; Chairmanship of the Gordon Research Conference on the Biology of Aging; Fellowships from the American Cancer Society and the American Heart Association; appointment as member and Chairman of many funding agency peer review groups, editorial boards, and corporate and community advisory boards; and 30 continuous years as Principal Investigator of individual research project grants, program project grants, research training grants, and center grants by a broad spectrum of public and private funding agencies. However, he and many of his peers regard his greatest achievement as the recruitment of the outstanding multidisciplinary collection of scholars that constituted the Institute of Gerontology at the University of Michigan during the tenure of his Directorship.

The Regents have recognized his accomplishments by naming him Professor Emeritus of Biological Chemistry.
Irwin J. Goldstein, Professor of Biological Chemistry retired from active faculty status as of December 31, 1999, after a very productive career as a teacher, research investigator and administrator.

A native of Newark, New Jersey, Irwin received his B.A. degree from Syracuse University and his Ph.D. in Biochemistry from the University of Minnesota. His postdoctoral training was at The Lister Institute of Preventative Medicine in London (as a John Simon Guggenheim Memorial Fellow), and at the University of Stockholm in Sweden.

He began his academic career at the Medical School of the State University of New York at Buffalo in 1961 as Assistant Professor of Biochemistry. In 1965 he became an Associate Professor of Biological Chemistry at The University of Michigan, and was promoted to Full Professor in 1972. During his career at Michigan he taught medical students, dental students, graduate students, and undergraduate students. He was chosen by the Medical Class of 1980 to receive the Kaiser-Permenente Preclinical Teaching Award.

For 13 years, Irwin served as Associate Dean for Research and Graduate Studies. This was a period of enormous growth in research funding, interest in the development in the Medical School of technology transfer, and the strengthening of graduate programs. He helped establish the Biomedical Core Facilities, the underpinning of the University’s research enterprise. During this time he was awarded the University of Michigan Distinguished Faculty Achievement Award, and an Outstanding Alumnus Achievement Award from the University of Minnesota.

As a research investigator, Irwin is widely known for his work on the isolation, characterization, and biomedical application of a class of carbohydrate binding proteins know as lectins. He enjoys an international reputation for his contributions to this field encompassed in 300 scientific papers, books and book chapters. Allied studies include research on carbohydrate cleaving and synthesizing enzymes, and the involvement of complex carbohydrates in cellular adhesion. The American Chemical Society recognized these contributions by presenting him, in 1993, with the C.S. Hudson Award, an international award in carbohydrate chemistry. He was previously recognized by the University of Michigan’s Distinguished Faculty Achievement Award, the Medical School’s Distinguished Faculty Lectureship Award in Biomedical Research, and the Stillmark Medal commemorating the 100th Anniversary of the discover of Lectins.

He was recently informed by the National Institutes of Health that his research project, “Protein-Carbohydrate Interaction,” has been renewed for an additional four years, a grant he has held continuously for 35 years.

The Regents cited Irwin’s service to The University by naming him Professor Emeritus of Biological Chemistry.

Glycobiology: The Final Frontier
May 4, 2001
8:00 a.m. - 5:00 p.m.
University of Michigan Rackham School of Graduate Studies Amphitheatre

This symposium is being held in honor of Dr. Irwin J. Goldstein, Professor Emeritus of Biological Chemistry, who has had a most productive academic career as a gifted research investigator, teacher, and administrator.

For more information—contact—
Heather Cavin
734-764-8154
Email
hmoores@umich.edu
Website
http://www.med.umich.edu/biochem/glycobiology.pdf

Fedor Medzihradsky, Professor of Biological Chemistry and of Pharmacology in the Medical School, passed away on March 12, 2001 after a highly distinguished and productive career as a scientist and educator.

Fedor received both his undergraduate degree and Ph.D. degree from the Technische Universität in Munich, Germany. He then came to the United States, where he was an National Institute of Health (NIH) Postdoctoral Fellow at the University of Wisconsin as well as a Trainee of the National Institute of Neurological Diseases and Blindness at Washington University in St. Louis. Fedor joined our faculty in 1969 as Assistant Professor of Biological Chemistry and as Director of the Biochemistry Laboratory in the Upjohn Center for Clinical Pharmacology in the Medical School. He was promoted to Associate Professor of Biological Chemistry in 1973, to Associate Professor of Pharmacology in 1975, and to Professor in both departments in 1981.

Throughout his career, Fedor was interested in drugs that act in the central nervous system. Most notable was his characterization of drug transport in neuronal and blood cells, as well as his contribution to the understanding of the biochemical mechanisms of opioid action. Recently the National Institute of Drug Abuse renewed the research grant "Opioid Receptor Mechanisms" for an additional four years. This project, now in its twelfth year, was directed by Fedor, who continued to provide consultation. During the course of his tenure, Fedor served as thesis chair for 10 doctoral students.

Professor Medzihradsky served on the editorial board of the journal Drug Metabolism and Disposition and as Director and Co-Director of the Biochemistry Core Facility in the Diabetes Research and Training Center in the Medical Center. Fedor was an exceptionally dedicated and popular teacher of medical students and served on numerous committees to evaluate and improve the medical school curriculum. He was recipient of the Kaiser Permanente Award for Excellence in Teaching. Fedor was named Professor Emeritus of Pharmacology after retiring from active faculty status in April of 1998. Professor Medzihradsky will be remembered with fondness and greatly missed by his colleagues and students.

New Students Join Current Ph.D. Candidates

Scott Berger is from Bayside, New York. He received his B.S. in Biochemistry at the University of Buffalo, New York. He was a Howard Hughes Medical Scholar at SUNY Buffalo and a Sigma Xi Fellow at Mount Sinai.

Austin Capper is from Saint Joseph, Michigan. He received his B.S. in Biochemistry at the University of Michigan.

Stephen Cary is from San Diego, California. He received his B.S. in Biochemistry and Biophysics from Yale University. He was the recipient of an Outstanding Student Scholarship from Mission Regional Medical Center in Mission Viejo, California.

Huira Chong is from Chicago, Illinois. She received her B.A. in Biology from Northwestern University in Evanston, Illinois. She received an Undergraduate Research Grant while at Northwestern and was recognized by a Young Biologist Award, Illinois Scholar, and George Pullman Scholar.

Peter Clapp is from Ann Arbor, Michigan. He received his B.A. in Biology from Haverford College, Pennsylvania. He belongs to the National Honor Society.

David Pagliarini is from Wyoming, Pennsylvania. He received his B.S. in Biochemistry from the University of Notre Dame, Indiana. He received a NSF Summer Research Fellowship from Michigan State University and a Howard Hughes Research Fellowship as an undergraduate.

Mark Ribick is from Palatine, Illinois. He received his B.S. in Biology from MIT in Cambridge, Massachusetts.

Michael Roh, a Medical Scientist Training Program student, is from Beltsville, Maryland. He received his B.A. in Biology from John Hopkins University in Baltimore, Maryland. He was given a Provost Undergraduate Research Award and the Marsho Outstanding Presentation Award and was a recipient of a Howard Hughes Research Fellowship.

Feng Shao is from P.R. China. He received his B.S. in Applied Chemistry from Peking University in Beijing, China and his M.A. in Molecular Biology from the Chinese Academy of Sciences.

Xiaohua Shen is P.R. of China. She received her B.S. in Biochemistry from Nankai University in Tianjin, China and her M.S. in Biochemistry from the University of Nevada in Reno, Nevada. She received a TOP Students Scholarship and a Graduate Fellowship.

Yannan Shen is from P.R. of China. She received her B.S. in Biochemistry from Xiamen University, Xiamen, China and her Ph.D. in Biology from Syracuse University in New York. At Xiamen she received a Scholarship of Excellent Undergraduate.
Degrees Granted

The Department extends its congratulations to the following students who have completed their Ph.D. degrees since May of 2000.

Faye Bradbury (Menon)
“Post-Translational Processing and Internalization of the Luteinizing Hormone/Human Chorionic Gonadotropin Receptor.” Faye has joined Biomedical Diagnostics, a company located in Ann Arbor, Michigan, that is developing a new drug against breast cancer, where she is a senior research scientist.

Clara Choi (Marletta)
“Investigating the Heme Detoxification Pathway of the Malaria Parasite Plasmodium falciparum - A Key Pathway in the Struggle Between Parasite Survival and Antiplasmodial Therapy Development.” Clara is a Medical Scientist Training Program (MSTP) student at the University of Michigan.

Mark Hilgers (Ludwig)
“The Structure of LuxS, A Mediator of Interspecies Communication in Bacteria.” Mark is now a Research Scientist at Syrrx, Inc. in San Diego, California, a biotechnology start-up company involved in structural genomics.

Nick Santoro (Thiele)
“Distinct Binding Sites and Signaling Pathways Regulate the Saccharomyces cerevisiae Heat Shock Transcription Factor.” Nick is currently a Senior Scientist at Pfizer Global Research and Development in Ann Arbor.

Craig Smith (Saper)
“The Crystal Structure of the Amino-Terminal Domain of YopH from Yersinia pseudotuberculosis.” Craig will be a postdoctoral associate in Dr. Scott Hultgren’s laboratory at Washington University studying pilus biogenesis and assembly.

Bart Lee Staker (Saper)

Lauren Stegman (Ross)
“Magnetic Resonance-Based Markers of Treatment Response and Transgene Expression for Use in Brain Tumor Gene Therapy.” Lauren is currently completing his residency at the University of Michigan Hospital, which takes two years, after which he will be awarded the M.D./Ph.D. degrees.

Distinguished Alumni/ae Lectureship

Daniel Oprian and his wife, Sue Cook

As a means to emphasize the importance of the Department’s annual Student Award Ceremony, we have instituted the Distinguished Alumni/ae Lectureship. The second Distinguished Alumni Lecture entitled “Constitutive Activation of Rhodopsin as a Molecular Mechanism of Retinal Disease,” was given last May by Dr. Daniel Oprian (Ph.D. with Coon), Professor and Chair of the Department of Biochemistry at Brandeis.

His field of research is the structure and function of visual pigments. His interests include using the insight gained from mechanistic studies on rhodopsin to design active site-directed inactivators as potential therapeutic agents for the treatment of the diseases retinitis pigmentos, and congenital night blindness. Sue Cook, Dan’s wife, is also a Michigan graduate, having received her Ph.D. under the mentorship of G. Robert Greenberg.

The Distinguished Alumni Lecturer for May 10, 2001 will be Dr. Sidney Strickland (Ph.D. with Massey), Professor of Neurobiology and Genetics and Dean and Vice President for Educational Affairs at The Rockefeller University. Dr. Strickland studies the mechanisms of cell death and regeneration in the nervous system.
— Christensen Award —

The Halvor N. and Mary M. Christensen Fellowship for Ph.D. Graduate Study in the Department of Biological Chemistry is presented annually to a second-year student on the basis of academic record and performance on the Department’s preliminary examination. This award is given in honor of Professor Halvor N. Christensen, who was Chair of the Department from 1955-1970, and his wife Mary. The 2000 recipient of the award was Elise Manning, whose mentor is Rowena Matthews.

— Christman Award —

The Adam A. and Mary J. Christman Fellowship is presented to a third-year Department student who is judged to be the most outstanding in that class. The award is dedicated to the memory of Professor and Mrs. Christman. The 2000 recipient of the award was Vladimir Ramirez-Carrozzi, whose mentor is Tom Kerppola.

— Coon Award —

The Minor J. and Mary Lou Coon Award is given to the student who best exemplifies overall excellence in research, teaching and service. This award is given in honor of Professor Minor J. (Jud) Coon, who was Chair of the Department from 1970-1990, and his wife Mary Lou. The 2000 recipients of the award were Faye Bradbury, whose mentor is Jerry Menon, and Xiaoli Zhan (photo not available), whose mentor is Kun-Liang Guan.
The Dziewiatkowski Award, which is offered to the student who submits the most outstanding Ph.D. Dissertation during the previous academic year, is given in memory of the late faculty member, Professor Dominic D. (Jay) Dziewiatkowski. The 2000 recipients of the award were Mariliz Ortiz, whose mentors are David Ballou and Vincent Massey, and Bill Ziehler, whose mentor is David Engelke.

The Lu Award is presented annually to a student on the basis of academic background, achievement in the graduate program, and potential as a scientist, with preference to a student who is a non-U.S. citizen. The 2000 recipient of the award was Hao Zhou, whose mentor is Dennis Thiele.

The Lee Murphy Memorial Award is presented 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. The 2000 recipient of the award was Scott Stewart (photo not available), whose mentor is KunLiang Guan.
protein provides the environment to efficiently carry out these hydroxylations. One example is p-hydroxybenzoate hydroxylase. We have constructed numerous site directed mutants, determined X-ray structures of the wild type and the mutants, and carried out detailed kinetic and spectral analyses of their function. We are beginning to gain insight into how the enzyme controls access to protons during the reaction while excluding free access to water, a process uniquely important to many forms of enzymatic catalysis. We have also substituted modified flavins for the FAD, thereby using Hammett-type relationships to investigate how the redox potential and other properties of the flavin affect each of the steps of the reaction.

Nonheme iron-containing dioxygenases and monoxygenases found in soil bacteria are the starting points for activating and utilizing persistent and toxic aromatic and aliphatic compounds in the environment. We are investigating the two-component phthalate dioxygenase system, which is the prototype for the Rieske nonheme iron oxygenases that catalyze dioxygenations of unreactive aromatic compounds. The stability and availability of this enzyme system has allowed us to carry out detailed spectroscopic, crystallographic, kinetic, and biochemical studies of this system. We are characterizing how the reductase, which contains FMN and a [2Fe-2S] iron sulfur center, transfers electrons between its centers and also to the oxygenase component. The latter contains both a Rieske [2Fe-2S] center and a mononuclear ferrous center, the site at which oxygenation occurs. We are also studying the mechanism of the oxygenation reaction.

We are collaborating with several laboratories on studies of a variety of reductase enzymes. Jud Coon's, Paul Hollenberg's, and John Dawson's (South Carolina) labs on P450 enzymes, Rowena Matthews' lab on methionine synthase (cobalamin containing) and methylenetetrahydrofolate reductase, a flavoprotein, Neil Marsh's lab (Chemistry) on glutamate synthase (cobalamin containing), Jim Bardwell's lab (Biology) on disulfite oxidoreductases involved in protein folding, and others.

Our investigations use a variety of techniques and approaches. Spectral and rapid reaction techniques are being used to characterize the active sites and intermediates involved in the reactions. Site-directed mutagenesis allows us to specifically test roles of particular amino acid residues in each of the steps of the reaction. X-ray crystallography, in collaboration with Drs. Martha Ludwig, Domenico Gatti (Wayne State), and Jeffrey Bolin (Purdue) is used to define precisely the relationship of structure and function in these enzymes and their mutants.


When I am not involved in biochemistry, I'm never without things to do. I like to mountain bike, ski (downhill and cross-country), sail, dance, listen to and play music, play tennis, softball, and volleyball. I am married to Jean Ballou and have two children, two stepchildren, and one grandchild.
transcription factors that play important but poorly understood roles in normal metabolism and in the development of diabetes. PPARγ is a member of the ligand activated nuclear receptor family of transcription factors. Activation of this receptor leads to a dramatic improvement in diabetes in animal models and in patients. Several aspects of PPARγ biology are being examined including the identification of the genes regulated by PPARγ, the modulation of its activity by hormone and growth factor induced protein phosphorylation, and the molecular mechanism by which ligand binding induces the transcriptional activity of the receptor. The second transcription factor being studied is HNF4, also a member of the nuclear receptor family. The key role of HNF4 in metabolism was illuminated by the identification of a mutation in the HNF4 gene that causes a rare form of type II diabetes. These patients are unable to release the correct amount of insulin from pancreatic β-cells, indicating an important role for HNF4 in the maintenance of normal pancreatic function, and suggesting that modification of HNF4 activity might contribute to the development of more common forms of type II diabetes. The role of HNF4 in pancreatic β-cell physiology is being explored by examining the activity of the receptor in islets isolated from normal and diabetic animals in various stages of pancreatic failure. Like PPARγ, the activity of HNF4 is modulated by protein phosphorylation, and we are characterizing this phosphorylation and determining its potential role in pancreatic physiology and pathophysiology. In addition, the genes regulated by HNF4 in pancreatic β-cells are being identified using gene-profiling technologies.

The regulation of gene expression by insulin in the liver plays an important role in modulating hepatic glucose output and in regulating whole body glucose homeostasis. In spite of the importance of this process in normal physiology and in disease, it is not understood at the molecular level. Using cell based transcription systems, we are examining this process in cultured hepatocytes. The goals of this project are to identify the transcription factors that mediate hormone responsiveness and to determine how their activities are modified by the insulin-signaling pathway.

---

**Todd Jeff, Ph.D.**
Adjunct Assistant Professor of Biological Chemistry

Many metabolic diseases, such as diabetes and obesity, are accompanied by dramatic alterations in patterns of gene expression in various tissues. The degree to which changes in the expression of specific genes contribute to the development of these diseases is unclear. The primary goals of my research are to understand the role of gene regulation in the maintenance of metabolic homeostasis, and to investigate how the inappropriate expression of specific genes contributes to the generation of metabolic pathologies. More specific experimental goals are to identify and characterize components of the transcriptional regulatory apparatus that modulate the expression of key genes in response to metabolic signals (e.g., insulin) in normal and pathological states. I believe that results obtained from this work will reveal novel approaches for the development of effective medicines for the treatment of these diseases.

Two of the research projects in my laboratory are focussed on specific metabolic diseases, such as diabetes and obesity, are accompanied by dramatic alterations in patterns of gene expression in various tissues. The degree to which changes in the expression of specific genes contribute to the development of these diseases is unclear. The primary goals of my research are to understand the role of gene regulation in the maintenance of metabolic homeostasis, and to investigate how the inappropriate expression of specific genes contributes to the generation of metabolic pathologies. More specific experimental goals are to identify and characterize components of the transcriptional regulatory apparatus that modulate the expression of key genes in response to metabolic signals (e.g., insulin) in normal and pathological states. I believe that results obtained from this work will reveal novel approaches for the development of effective medicines for the treatment of these diseases.

---

**Brian D. Ross, Ph.D.**
Associate Professor of Biological Chemistry

The revolution in molecular biology has expanded our understanding of the genetics and biochemistry of transformed cells. These advances have been made largely through studies of cultured cells or ex vivo studies on tumor specimens. However, it is clear that extrapolations between in vitro and in vivo situations do not always hold true.
Faculty profiles

The next revolution is underway to bridge the great divide between in vitro and in vivo studies in cancer research. This effort involves the development and application of novel imaging tools to noninvasively detect molecular and cellular events in intact organisms for improving our fundamental knowledge of cancer etiology, biology, pathology, and therapy.

We have been actively involved in identifying a surrogate marker that would provide an earlier response to cancer therapeutic efficacy than traditional anatomical assessment of scans from magnetic resonance imaging (MRI). Using diffusion-weighted MRI techniques and rodent tumor models, we have found that changes in the diffusion of water within the tumor mass occurred very early following initiation of treatment. The magnitude of the diffusion change also was found to correlate with the effectiveness of the treatment. We also successfully translated this study into the clinical setting and found that diffusion MRI indeed provided early information related to the effectiveness of the therapeutic intervention. We are currently in the process of accruing more patients into this trial in order to obtain statistical validation of this approach for the clinical management of patients.

A second area of interest is in the use of gene therapy for the treatment of neoplastic disease and in the ability to noninvasively quantitate the dynamics of transgene expression. We have used in vivo MR spectroscopy to quantitate conversion of a nontoxic “prodrug” (fluorocytosine) into the cytotoxic drug (fluorouracil) following insertion of the gene expressing the yeast enzyme, cytosine deaminase. Further work is underway to develop sensitive imaging techniques to monitor for expression levels and location of any transgene of interest in mammals.

Finally, a new field of research termed “molecular imaging” has recently gained momentum following the announcement by the NIH that significant funding would be made available to establish national Centers for Molecular Imaging. We have used this opportunity to develop several novel imaging strategies to noninvasively image specific biological processes in vivo. For example, initiation of tumor formation typically involves a carcinogenic event that results in activation of an oncogene or inactivation of a tumor suppressor gene. Expression of an oncogene such as myc and ras as well as growth factor receptors such as erb-2 (EGF receptor family member) and the HGF receptor (Met) can result in the initiation of a tumor. In contrast, loss of expression and/or function of certain genes are required to initiate the tumorigenic process. Examples of these include p53 which is mutated in almost half of all cancers. These above biological events are not sufficient to lead to cancer but require additional genetic alterations that allow tumor cells to proliferate such as inhibition of the apoptotic pathway. This not only provides for growth advantage i.e. fewer cells dying per generation but also makes the tumor cells more resistant to therapy. In addition, in order for a tumor to establish itself beyond a minimal size, angiogenesis is required to occur such that nutrients and oxygen can provide for an adequate growth environment. This increase in vascularization also plays a role in the tumors ability to spread by metastasis to other organs. Metastasis of cancer cells from one organ to another requires activation of specific genes for example, matrix metalloproteases (MMP’s) and integrins which are needed for cell migration. My laboratory, along with members of the UM Molecular Imaging Center, is involved in the development of novel imaging approaches for studying these biological processes in vivo using a variety of imaging technologies and transgenic animals. The future of molecular imaging in this post-genomic era is very exciting and holds much promise for both basic and translational research endeavors.

Representative Publications
subunit, the protein kinase inhibitor (PKI) proteins also bind to and inhibit the C subunit. Within living cells, the R subunits are largely restricted to the cytoplasm because their large size prevents passive entry through nuclear pores, while the smaller PKI proteins are found in both the cytoplasm and the nucleus. The PKI proteins contain a nuclear export signal that functions to shuttle C subunit out of the nucleus and facilitates holoenzyme reformation after cAMP levels return to basal levels.

We are interested in both cytoplasmic and nuclear substrates of the cAMP-dependent protein kinase. It is generally believed that cytoplasmic phosphorylation events mediate short-term memory while nuclear phosphorylation that leads to changes in gene transcription mediate long-term memory formation. We have characterized the phosphorylation of ion channels as substrates for cAMP-dependent protein kinase in the past and more recently have identified the LKB1 protein kinase as a cytoplasmic substrate for cAMP-dependent protein kinase. The LKB1 protein is thought to function as a tumor suppressor and its deficiency is responsible for the pre-cancerous Peutz-Jeghers syndrome, in which patients show a twenty fold increase in the incidence of multiple forms of cancer. We are currently pursuing the function of the LKB1 protein and its regulation of the cell cycle in multiple cell types, including neurons. We also have a long standing interest in the phosphorylation of transcription factors by cAMP-dependent protein kinase and the role that the PKI proteins play in transcriptional responses of neurons.

The dimeric cGMP-dependent protein kinases are activated by the cGMP in response to nitric oxide and the natriuretic peptides. Unlike cAMP-dependent protein kinase, the regulatory domains and catalytic domains of the cGMP-dependent protein kinases are fused into a single polypeptide gene. Some of our recent studies have focused on the mechanism of activation of cGMP-dependent protein kinase by cGMP, and we have demonstrated that the two major kinase isoforms differ in their mechanism of activation. Since the cGMP-dependent protein kinases are too large to passively enter the nucleus, they phosphorylate primarily cytoplasmic substrates. However, we demonstrated recently that cGMP-dependent protein kinase can however alter gene transcription by phosphorylating a novel protein phosphatase inhibitor found only in neurons, which then leads to increases in the phosphorylation of nuclear transcription factors by inhibition of protein phosphatases. We are currently studying the function of the C. elegans cGMP-dependent protein kinases and plan to use the elegant genetic approaches available in this model system to identify novel neuronal substrates of the cGMP-dependent protein kinase.

Representative Publications
Collins, S.P., Reoma, J.L., Gamm, D.M. and Uhler, M.D. (2000) LKB1, a novel serine/threonine protein kinase and...continued page 16, Faculty profiles
faculty profiles continued

potential tumor suppressor, is phosphorylated by camp-dependent protein kinase (PKA) and prenylated in vivo. Biochem. J. 345(3): 673-80.


Donations and Gifts

We are extremely grateful to all of the individuals and companies whose gifts and donations have provided valuable discretionary funds to support a wide range of Departmental activities.

The following funds, programs, awards, and fellowships are available if you would like to have your contribution to the Department of Biological Chemistry designated more specifically.

- Biological Chemistry Endowment Fund
- Dominic D. Dziewiatkowski Dissertation Award
- Minor J. and Mary Lou Coon Graduate Student Fellowship in Biological Chemistry
- Anthony and Lillian Lu Fund
- Vincent Massey Collegiate Professorship in Biological Chemistry

To find out more about gift opportunities to the Department, please contact:

Katrina Ward Hope
Department of Biological Chemistry
1301 Catherine Street, 5419 Medical Science Building I
Ann Arbor, MI 48109-0606
Phone: 734-764-8155
Fax: 734-763-4581
Email: wardhope@umich.edu

The Biological Chemistry Newsletter is published annually by the Department of Biological Chemistry.

Please send correspondence and address changes to the editor:

Sandra Ridella
Biological Chemistry Department
1301 Catherine Street
5413 Medical Science Building I
Box 0606
Ann Arbor, MI 48100
Phone: 734-763-6489
Fax: 734-763-4581
Email: sandigra@umich.edu

The Regents of the University of Michigan are: David A. Brandon, Laurence B. Deitch, Daniel D. Horning, Olivia P. Maynard, Rebecca McGowan, Andrea Fischer Newman, S. Martin Taylor, Katherine E. White, Lee C. Bollinger, ex officio.

The University of Michigan is an equal opportunity/affirmative action employer, complies with all applicable federal and state laws regarding nondiscrimination and affirmation action, including Title IX of the Education Amendments of 1972 and Section 504 of the Rehabilitation Act of 1973.
Biological Chemistry
Department of Biological Chemistry Newsletter

University of Michigan Medical School
Room 5413 Medical Science I, Box 0606
1301 Catherine Street
Ann Arbor, Michigan 48109