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LETTER FROM THE CHAIR

This year has seen many positive developments in the Department of Biological Chemistry, including the recruitment of three exceptional young faculty members and one senior faculty member jointly with the Life Sciences Institute, the recruitment of a promising group of new graduate students, and the well-deserved recognition of the accomplishments of several of our students and faculty. Sadly, however, the year has also been marked by the deaths of two former professors, Hal Christensen and Dale Oxender, both of whom made pioneering and lasting contributions to the Department.

We are actively recruiting new faculty. We currently have 36 faculty members. We expect the number of faculty to increase to about 50 within the next seven years. Among the new appointees are three assistant professors, Daniel Bochar, Bruce Palfey, and Raymond Trievel, who started in late summer and early fall of 2003. Features highlighting each of these new faculty members are found later in this year's Newsletter. Also hired last year was Janet Smith, who

will be joining Biological Chemistry and the Life Sciences Institute in July, 2004.



This winter the Department interviewed nine junior faculty candidates, and we are extending several offers. Those whom we are successful in recruiting will come in the fall of 2004. Assuming that most of the present recruitments are successful, the Department will have developed a very strong cadre of young investigators looking at the dynamics of pro-

tein-DNA interactions at the atomic level (e.g. chromatin remodeling during transcription, replication, and repair). We also have an ongoing search for a more senior person for the Massey endowed chair; this search is on hold until 2005 pending the outcome of our present recruitment. The Department is also working with Internal Medicine, Biophysics, and Bioinformatics on joint recruitments.

Philip Andrews and David Turner were promoted to Professor with tenure and Associate Professor with tenure, respectively.

Bernie Agranoff retired in September, 2003. Phased retirements are in progress for Amiya Hajra (BiolChem/MHRI) and Rowena Matthews (BiolChem/Biophysics/LSI). The Department continues to have a number of active and very productive Emeritus faculty

BIOLOGICAL CHEMISTRY STAFF

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William L. Smith, PhD
Chair

Robert Fuller, PhD
Associate Chair

Jackie Benson
Staff Support

June Bialecki
Assistant to the Chair

Heather Cavin
Administrative Assistant

Bob Elliot
Equipment & Supplies Supervisor

Beth Goodwin
Graduate Student Program Manager

Mary Grapp
Finance Manager

Patricia Haines
Staff Support

Sharon Hoffman
Human Resources Manager

Jonathan Kufahl
Computer Systems Specialist

Merlis Nolan
Department Administrator

Sandra Ridella
Staff Support

Jessica Viskup
Computer Systems Specialist

including Bernie Agranoff, David Aminoff, Jud Coon, Irwin Goldstein, Bob Greenberg, Bill Jourdian, and Paul Weinhold.

We lost one prominent, senior faculty member, Dennis Thiele, to Duke University last year, and Claudia Kent formally retired last July and has moved to San Diego. Claudia and Jack Dixon report that they are enjoying their new environs.

A major issue facing all faculty in the Medical School is the relatively large ratio (>4) of faculty principal investigators to graduate students. At most institutions this ratio is 2-2.5. Of course, the availability of excellent graduate students is a key component of successful research and makes it possible to recruit excellent faculty. To address this problem it is likely that the Medical School will expand the highly successful Program in Biomedical Sciences (PIBS), the programmatic mechanism used to jointly recruit students into the basic sciences. Additionally, the Department has been directly involved in the development of the Chemical Biology Program which, if approved by the Rackham Graduate School, will begin recruiting PhD students in the fall of 2004. The Department is providing funding and staff assistance to this program for its duration. The Chemical Biology program should help address the problem of the decrease in the numbers of PIBS students interested in more chemical topics and the need to develop science at the Chemistry/Biochemistry Interface with other units in the university.

An Endowment for the Basic Sciences (EBS) was established by Dean Lichter two years ago to provide ongoing support for the development of the basic sciences at the Medical School. The EBS receives about \$5 million in support annually which is used to support and augment research initiatives in the basic sciences. This year the Department developed an initiative in Macromolecular

Structure, Dynamics and Design which was approved by the EBS Steering Committee. A task force composed of Dave Ballou, Chair, Martha Ludwig, Erik Zuiderweg, David States (Bioinformatics), Zhaohui Xu, and Roger Sunahara (Pharmacology) is developing a recommendation for consideration by the EBS for enhancing our long-standing strengths in this general area.

The Department continues to be blessed with an excellent staff. A new departmental administrator, Merlis Nolan, joined the Department last May and has done a wonderful job orchestrating the moves and purchases associated with hiring new faculty. And June Bialecki has a flawless record in managing the visits of faculty candidates. Our visitors frequently comment on the professionalism of our staff.

The Life Sciences Institute Building on Washtenaw Avenue was completed and opened in the fall, and several faculty from Biological Chemistry have moved to space in this building including Rowena Matthews, Jeanne Stuckey, Zhaohui Xu, Dan Klionsky, and Kun-Liang Guan. In late 2005 the massive Biomedical Sciences Research Building (BSRB) at the northeast corner of Huron and Glen will open. We expect that Mental Health Research Institute (MHRI) investigators in Biological Chemistry, Mike Uhler, Dan Goldman, Audrey Seasholtz, and Dave Turner will move into BSRB as will a number of investigators from other programs and departments. We will be developing plans over the next two years for moving Biological Chemistry faculty into high quality, contiguous space in Medical Science Research Building III, the newest of the MSRB buildings.

The state of Michigan has been exceptionally supportive of the universities in the state, especially the University of Michigan. However, the last three years have seen very large budget shortfalls that have led to a

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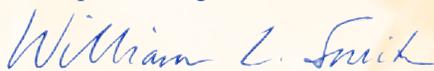
decrease in university funding of 10-15%. As with any organization with financial shortfalls, there has been very considerable belt tightening at U of M along with tuition increases. However, every year a greater proportion of university costs needs to be covered by private donations. Contributions that our alumni and faculty make have become absolutely essential for maintaining the quality of the institution. We hope that you will keep Biological Chemistry in mind when you make charitable contributions this year.

As I come to the completion of my first year as chair of Biological Chemistry, I want to thank the faculty, staff, students and alumni for all their guidance and support. This is a wonderful institution and an exceptional Department, and I am certainly proud to be a part of it. I hope that those alumni who are attending the ASBMB Meeting in Boston this June will join me at the University of Michigan Department of Biological Chemistry Reception on Sunday evening June 13th from 8-10 p.m. at the Boston Marriott Copley Place Hotel.

Finally, let me end by asking you to continue to keep us informed of happenings in your world by completing the enclosed card in the back of this Newsletter. In coming years, we will be highlighting this information.

Best wishes to all of you for a happy and productive year.

Best personal regards,



William L. Smith

P.S. And please visit and bookmark our web site (www.biochem.med.umich.edu/biochem). This site has been recently updated and upgraded and provides an excellent way to keep up on what is happening in our Department.

Bernie Agranoff has been appointed to the Midwest Council of the American Academy of Arts and Sciences. Last September the UM Mental Health Research Institute inaugurated the Annual Bernard W. Agranoff Lecture in Neuroscience. The speaker was Professor Bruce McEwen of the Rockefeller University, and following the lecture he and MHRI and Biological Chemistry Department senior faculty were invited to a dinner at the University's Inglis House.

Jud Coon is a member of the Advisory Committee for the International Symposium on Microsomes and Drug Oxidations to be held in Mainz, Germany, in July.

David Engelke received the Distinguished Faculty Achievement Award from the University and will also receive this year's Distinguished Faculty Lectureship Award as recently announced by the Biomedical Research Council.

Daniel Goldman has received the prestigious Research Scientist Achievement Award of the Office of the Vice President for Research. The award recognizes outstanding scholarly achievements that lead to significant advances in science, education, health, and the arts and humanities.

Irwin Goldstein stepped down as Interim Chair with the arrival of Bill Smith, and returned to active Emeritus status. He continues to work in his laboratory with post-doctoral fellows and play an active role in the Department. His NIH grant on Protein-Carbohydrate Interaction, one of the longest running grants at the University, is up for renewal for years 38-41. Irwin continues to be a competitive runner, joining in the yearly Dexter/Ann Arbor run, and is a board member of the Peter Sparling Dance Gallery for Modern Dance.

Donald Hultquist, who recently retired, was presented with the Distinguished Service Award by the Medical Center

Alumni Society. His selection is particularly noteworthy since the Society rarely selects a PhD from the Basic Science Departments for this honor.

Daniel Klionsky, Professor of Biological Chemistry and of Molecular, Cellular and Developmental Biology and a charter faculty member of the Life Sciences Institute, has been named a Distinguished Teacher Scholar by the National Science Foundation and given a 4-year award to improve how introductory biology is taught. He has been teaching an honors-level introductory biology course to U of M undergraduates without textbooks or lectures. He is also the editor of a textbook titled "Autophagy" published by Landes Bioscience in January 2004.

Martha Ludwig was elected to the National Academy of Sciences. NAS members are elected in recognition of their distinguished and continuing achievements in original scientific research and act as official advisers to the federal government on questions involving science and technology. Election to membership in the Academy is considered one of the highest honors a scientist can receive.

Alex Ninfa presented a seminar recently at the Swammerdam Institute for Life Sciences of the University of Amsterdam as part of a signal transduction symposium. Other speakers at the symposium were Sir Michael Berridge (Cambridge), Laslo Bogre (London), and Peter J.M. Van Haastert (Groningen).

Geneva Omann, Associate Professor of Surgery and of Biological Chemistry, has received the Elizabeth Caroline Crosby Research Award, which supports a range of activities necessary for scholarly work in science and engineering fields. It was established in honor of Dr. Crosby, who began her long and distinguished career at the University of Michigan in 1920 and was the

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first woman to become a full Professor in the Medical School. The Award will support Geneva's research to develop high throughput assays for measuring G-protein-coupled receptor binding and processing.

Todd Porter (formerly Assistant Professor in our Department) is Associate Professor of Pharmaceutical Sciences, University of Kentucky College of Pharmacy in Lexington, where he is Director of Graduate Studies for the Graduate Center for Toxicology. Based on his earlier presentation in La Grande Motte, France, Todd has published a minireview, "Jud Coon: 35 Years of P450 Research, A Synopsis of P450 History," in *Drug Metabolism and Disposition* 32, 1-6 (2004).

Bill Smith received the 2004 State of Michigan Scientist of the Year Award, which is given as part of the Impression 5 Museum's Tribute to Science and Technology Award Program. He was elected as Fellow of the American Association for the Advancement of Science. Bill will also receive the prestigious Avanti Award from the American Society of Biochemistry and Molecular Biology, which recognizes outstanding research contributions in the area of lipids. He will present a lecture on "Prostaglandin Endoperoxide H Synthases/Cyclooxygenases" at the annual ASBMB meeting in Boston in June.

Zhaohui Xu has received the Basic Science Research Award from the University. This award honors scientists who have made outstanding contributions to the Medical School in biomedical research.

Erik Zuiderweg was elected as Fellow of the American Association for the Advancement of Science for the development of nmr methods for the determination of structure and dynamics of proteins.

ALUMNI/AE NEWS

Bob Blake (Postdoc with Coon) has accepted the Chair of Basic Pharmaceutical Sciences at Xavier University in New Orleans after almost two years as Interim Chair.

Diane Blake (Postdoc with Goldstein) has been promoted to full Professor at Tulane University School of Medicine and recently changed departments from Ophthalmology to Biochemistry.

Michael Cunningham (Postdoc with Kaufman) is now working for Bayer Corporation doing hemophilia-related research.

Lee Gorsky (PhD with Coon) carried out postdoctoral studies at the Cancer Center of Northwestern University Hospital and held positions at Abbott Laboratories and the U.S. Environmental Protection Agency before working in the field of Web development and multimedia technology-based training. As Vice-President of Operations at XBX Channel Media, he is involved in all aspects of Web and e-Learning projects, including analysis, design, development, implementation, and evaluation.

Fred Guengerich (Postdoc with Coon), Professor of Biochemistry and Director of the Center in Toxicology at Vanderbilt University, was given the 2003 North American Scientific Achievement Award of the International Society for the Study of Xenobiotics. He also received a Distinguished Faculty Award from Vanderbilt University.

Wei-Pang Huang (Postdoc with Klionsky) is an Assistant Professor at National Taiwan University.

Kyungho Lee (Postdoc with Kaufman) has moved back to Korea to take a position as Assistant Professor at Konkuk University in the Department of Biological Sciences.

Utpal Munshi (PhD with Menon) joined the laboratory of Dr. Eric Freed at the National Cancer Institute, NIH, for his postdoctoral fellowship starting in February 2004.

Chatchawan Srisawat (PhD with Engelke) is an Assistant Professor at Mahidol University in Thailand.

Donalyn Scheuner (Kaufman) was promoted to Technical Research Specialist in the Howard Hughes Medical Institute.

Martin Schroder (Postdoc with Kaufman) has taken a Lecturer position at the University of Durham in England in the Department of Biological and Biomedical Sciences.

Feng Shao (PhD with Dixon) was one of eight recipients of Racham's Distinguished Dissertation Awards of 2003 for his dissertation entitled: "Identification of a Novel Family of Cysteine Proteases and Their Functions in Bacterial Pathogenesis." He also received the Harold M. Weintraub Graduate Student Award.

Benbo Song (Kaufman) has moved to a research technician position in the Howard Hughes Medical Institute.

Per Strombhaug (Postdoc with Klionsky) has become an Assistant Professor at the University of Missouri.

Mingjia Tan (Postdoc with Kaufman) has taken a postdoc position in the Dental School at the University.

Martin Thompson (Postdoc with Kerppola and Engelke) is an Assistant Professor of Chemistry at Michigan Technological University.

Tetsufumi (Ted) Ueda (PhD with Coon), Professor of Pharmacology in our Medical School, lectured at the Teikyo University Faculty of Pharmaceutical

Sciences (in Tokyo), Tokyo University of Agriculture, Osaka University Medical School Department of Pharmacology, and Suntory Institute for Bioorganic Chemistry in Osaka.

Fred Woessner (Postdoc with Coon), who has retired at the Department of Biochemistry, University of Miami School of Medicine, is editing the second edition of the Handbook of Proteolytic Enzymes with A.J. Barrett and N.D. Rawlings in Cambridge, England, to be published by Elsevier - Academic Press. The original covered about 500 pages, but with the growth of the field two large volumes containing about 2400 pages are now required.

William Ziehler (PhD with Engelke) is attending law school at Michigan State University.

DISTINGUISHED GRADUATE LECTURESHIP

Our fourth annual Biological Chemistry Student Awards Ceremony and Distinguished Graduate Lecture was held on May 15, 2003. Dr. Nancy G. Nossal presented a lecture entitled "Interactions of Proteins and DNA at the Phage T4 Replication Fork." Dr. Nossal was a student with Bob Greenberg and received her PhD in 1963. She is Chief of the Laboratory of Molecular and Cellular Biology, National Institute of Diabetes and Digestive Kidney Diseases. Her research focuses on DNA replication, specifically on the mechanisms by which DNA synthesis on the two strands of the replication fork is controlled.



The next Student Awards Ceremony will be held on June 9, 2004, and the Distinguished Graduate Lecturer for 2004 will be Dr. Colleen Hayes. She was a student with Irwin Goldstein, and received her PhD in 1973. She is now Professor of Biochemistry at the University of Wisconsin and studies the diseases of the immune system to understand the molecular mechanisms that regulate immune system development and function.

LIFE SCIENCES INSTITUTE UPDATE

The Life Sciences Institute has moved into its new laboratory facilities on Washtenaw Avenue, just across the street from the Medical Center, and now counts 10 faculty toward its goal of an eventual 20 to 30 principal investigators. Four of these have joint appointments as faculty in our Department: Kun-Liang Guan, Rowena Matthews, Jeanne Stuckey, and Zhaohui Xu. The LSI building is also the

new home of the University's structural biology core, which used to be in Medical Science Building I. Dr. Stuckey, who runs the facility, will have room for a second beam line eventually. LSI, under the leadership of cell biologist Dr. Alan R. Saltiel, Professor of Physiology and Professor of Internal Medicine, as Director, is establishing itself as a hub for new collaborations between scientific disciplines.



Christensen Award

The Halvor N. and Mary Christensen Award for PhD Graduate Study in the Department of Biological Chemistry is presented annually to a second-year student on the basis of academic record. This award is given in memory of Professor Halvor N. Christensen, who was Chair of the Department from 1955-1970, and his wife Mary. The 2003 recipient of the award was Erin Rees, whose mentor is Dennis Thiele.



Christman Award

The Adam A. and Mary J. Christman Award 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 2003 recipient of the award was Jennifer Aurandt, whose mentor is Kun-Liang Guan.



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 2003 recipient of the award was Stephen Cary, whose mentor is Michael Marletta.



Dziewiatkowski Award

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 2003 recipient of the award was Claudia Figueroa, whose mentor was Anne Votjek.

Anthony and Lillian Lu Award

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 for a student who is a non-U.S. citizen. The 2003 recipient of the award was Yinnan Shen, whose mentor was Tom Kerppola.

Lee Murphy Memorial Prize

The Lee Murphy Memorial Prize 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 2003 recipient of the award was Feng Shao, whose mentor was Jack Dixon.

Halvor N. Christensen, former Professor and Chair of Biological Chemistry, died on October 2, 2003. A native of Nebraska, he took undergraduate studies at Kearney State Teachers College (now the University of Nebraska at Kearney). He then received his M.S. degree from Purdue University in 1937, and his PhD degree under the mentorship of Professor A. Baird Hastings from Harvard University in 1940. Upon completion of his doctoral studies, he accepted a position as a biochemist at Lederle Laboratories in Pearl River, New York. Four years later he became director of a chemical laboratory at Mary Imogene Bassett Hospital in Cooperstown, New York, and remained there until 1947. He returned to Harvard Medical School in 1947-48 as Assistant Professor and Director of the Department of Research Chemistry at Children's Medical Center in Boston, Massachusetts. He then went to Tufts University in Boston as Professor and Chairman of the Department of Biochemistry and Nutrition, where he served with distinction for eight years.

With this outstanding background and unusually broad experience, Halvor was recruited to the University of Michigan as Professor and Chair of Biological Chemistry in 1955. He vigorously addressed the needs of the Department at that time by recruiting faculty and graduate students interested in newer areas of research, planning the move from the West Medical building on main campus to the present Medical Science I building on the nearby medical campus, and emphasizing his deep concern about the quality of the teaching of biochemistry to medical students by his own personal involvement in lectures, demonstrations, and conference sections. In addition, Hal brought international attention to the department by his pioneering research in the area of biological transport, particularly that of amino acids. Thus, in many ways his leadership contributed to the present strength

of the Department. He stepped down from the chairmanship in 1970 and continued to carry out research and teach until he retired from active faculty status in 1986, when the Regents saluted him “for his dedicated service as a distinguished scientist and health educator” by naming him Professor Emeritus of Biological Chemistry.

Halvor and his wife Mayme (Mary) moved to La Jolla, California in 1989. She passed away on June 10 of last year and is remembered for her active participation in the Ann Arbor community, including the International Neighbors Club and the Faculty Women’s Club. In 1992, Hal and Mary, with assistance from their many colleagues and friends, generously established a graduate student award in their names. This ongoing award provides a very fine memorial to them for their dedication to graduate study by PhD candidates in Biological Chemistry at Michigan. Their daughter, Karen C. Gray, who lives in Stow, Massachusetts, can be reached by e-mail (kc3@juno.com).

Dale L. Oxender, formerly Professor of Biological Chemistry, died on December 11, 2003 after an extended illness. A native of Michigan, he took undergraduate studies at Manchester College in North Manchester, Indiana and then went to Purdue University, where he received his M.S. degree in 1956 and his PhD degree in Biochemistry with Professor H. C. Reitz as his mentor in 1959. Dale then joined our department as a postdoctoral research associate with Professor Halvor Christensen and a year later, in view of his many talents, was given a faculty position in Biological Chemistry. He soon became known internationally for his innovative research contributions in the areas of protein biochemistry, bacterial cell transport, and molecular genetics, and was promoted to the rank of full Professor in 1975. Dale spent a sabbatical leave with Professor Charles Yanofsky at Stanford University in

1978 and enjoyed it so much that he did the same again in 1985. He resigned from our Department and from the position of Director of the University’s Center of Molecular Genetics in 1990 to become Vice President of Biotechnology at the Parke-Davis Pharmaceutical Research Division of the Warner-Lambert Company in Ann Arbor. After ten years of service there he retired as Distinguished Research Fellow Emeritus from the company and Adjunct Professor from the University of Michigan. Dale had a continuing affection for his undergraduate school and was given the Manchester College Outstanding Alumni Award several years ago. His family and former colleagues have contributed to an annual scholarship in his name, to be given to an outstanding student majoring in science at the College. Dale’s wife, Jean, continues to live in Ann Arbor and can be reached by e-mail (djoxender@comcast.net).

Walter D. Block, former Professor in the School of Public Health with a joint faculty appointment in Biological Chemistry, died on January 5 at age 92. He attended the University of Dayton in Ohio, where he obtained his Bachelor’s degree in Chemical Engineering with highest honors. He then matriculated to the University of Michigan

Medical and Graduate Schools, where he obtained his Masters and Doctoral degrees. After graduation, he served as a Clinical Fellow at the Rockefeller Institute in New York City, where his interest in arthritis began. After this, he began his academic career at the University of Michigan Medical School as an Instructor in 1938. He was head of the Department of Human Nutrition in the School of Public Health and upon his retirement was named Professor Emeritus. He devoted his life to clinical research and teaching. Several of his more noted works were the first textbook on the treatment of arthritis with gold salts and the genetic study on amyloidosis in the Amish population in Bluffton, Indiana. The latter was considered to be one of the outstanding research studies of the decade. He also was a leading investigator in the Tecumseh project, which evaluated the effects of triglycerides and cholesterol in heart disease. Later in his career, he worked extensively in hypertension related to treating this disease. He also served as a Visiting Professor at Auburn University Medical School and the Tuskegee Institute and was the Clinical Director of the Caylor-Nickel Research Institute in Bluffton, Indiana. Walter’s wife, Thelma, still lives at 3000 Glazier Way, Ann Arbor, MI 48105.

TRANSITIONS

Dennis Thiele, Professor of Biological Chemistry, moved last September to Durham, North Carolina, where he is a Professor in the Department of Pharmacology and Cancer Biology at Duke University Medical Center. Dennis joined our Department in 1987 following postdoctoral training at Cornell University and the National Cancer Institute and developed an outstanding multidisciplinary research program, including genetics, molecular biology, and cell biology, as well as biochemistry. He has become one of the world’s experts on the metabolism and bioavailability of metals, using yeast as a eukaryotic model to study how cells respond to toxic metal ions. The honors he received while at the University of Michigan included the Burroughs Wellcome Toxicology Scholar Award, the George E. Connell Lectureship in Toronto, and the University’s Faculty Recognition Award and Distinguished Achievement Award. We wish Dennis much continued success in his new position.



Daniel Bochar

Dr. Bochar joined the Department as an Assistant Professor in September last year. He obtained his PhD degree in the laborato-

ry of Professor Victor W. Rodwell at Purdue University, where his research was on the understanding of enzyme catalysis using 3-hydroxy-3-methylglutaryl coenzyme A reductase as a model. In eukaryotes this enzyme catalyzes an early, rate-limiting reaction in isoprenoid biosynthesis that in humans is the target of drugs that reduce serum cholesterol levels. After the completion of his doctoral degree, he joined the laboratory of Dr. Ramin Shiekhataar at the Wistar Institute in Philadelphia, as a Postdoctoral Fellow. His research efforts in that group primarily concerned on one method of regulating gene transcription, controlling the access to nucleosomal DNA. His work resulted in the identification and purification of several novel protein complexes that can alter nucleosome structure in an ATP-dependent manner.

Dan's current research continues to focus on defining the mechanisms of transcriptional regulation through the modification of chromatin structure. The DNA of eukaryotes is packaged into chromatin by the wrapping of ~146 bp of DNA around a core histone octamer. This packaging serves to compact the DNA into the nucleus, but also presents a barrier to cellular processes, such as transcription, replication, and repair, that require access to the DNA. Therefore, controlling access to the chromosomal DNA represents an important regulatory point for these processes. Importantly, disruption of these chromatin remodeling events is critical to many pathologies, including neoplastic transformation and developmental disorders. Projects in his laboratory are concerned with

a class of enzymes that use the energy of ATP to alter the structure of chromatin. Using a combination of biochemistry, molecular biology, and cell biology, he aims to discover how these chromatin remodeling pathways are linked to development and neoplastic transformation.



Bruce Palfey

Dr. Bruce Palfey started a tenure-track position as an Assistant Professor in October of 2003. Bruce earned his B.S. in biochemistry

from Penn State University, worked for a couple of years as a technician doing developmental neurobiology research at the Wistar Institute in Philadelphia, and obtained an M.S. in synthetic organic chemistry from Drexel University prior to starting his PhD work in 1989 in the laboratories of David Ballou and Vincent Massey in our Department. During his doctoral work, he studied the mechanism of the flavin-containing enzyme p-hydroxybenzoate hydroxylase (PHBH) and defended his thesis in 1993. He continued studies on PHBH during his post-doctoral work, also in the Massey and Ballou labs, uncovering a novel control mechanism for a conformational change of the flavin that is important in catalysis by PHBH. He was appointed as Lecturer in the Department in 1996, and taught in graduate courses on kinetics, enzyme mechanisms, and calorimetry, as well as continuing his research in enzymology.

Bruce's current research is centered on the mechanisms of three flavin-catalyzed reactions in pyrimidine metabolism: the dihydroorotate dehydrogenases, the dihydrouridine dehydrogenases, and flavin-dependent thymidylate synthases. The dihydroorotate dehydrogenases are a family of enzymes that catalyze the only redox reaction in pyrimidine biosynthesis. Their critical role in pro-

viding the pyrimidines needed by rapidly growing cells makes them excellent drug targets. Current research is aimed at understanding in great detail the mechanism of flavin reduction by dihydroorotate, the origin of specificity for oxidizing substrates and their mechanisms of reaction with the reduced flavin, and the design of specific inhibitors. The dihydrouridine synthases are flavin-containing enzymes that reduce specific uracil residues to dihydrouridine during the maturation of tRNA. The importance of this wide-spread RNA modification is not yet understood. Thymidylate synthases convert dUMP to dTMP, which, upon conversion to the triphosphate, is incorporated into DNA. Recently, a flavin-dependent thymidylate synthase has been discovered and is being studied in order to elucidate its chemical and kinetic mechanisms and enable specific inhibitors to be designed that could potentially be used in treating a number of diseases.



Ray Trievel

Dr. Raymond Trievel joined the Department of Biological Chemistry as an Assistant Professor in September, 2003. Originally a native of

Pennsylvania, Dr. Trievel received his Bachelors training in biochemistry at the University of Delaware. While an undergraduate there, he developed an interest in enzymology while doing research on the mechanism of flavin-dependent acyl-CoA dehydrogenases in the laboratory of Dr. Colin Thorpe (a former post-doctoral fellow of Dr. Charles Williams in the Department). After graduating in 1995, Ray pursued doctoral research at the University of Pennsylvania and the adjoining Wistar Institute in the laboratory of Dr. Ronen Marmorstein, where he elucidated the structure and function of the histone N-acetyltransferase, GCN5. In 2000, he received his PhD in Biochemistry and Molecular Biophysics from

Penn and then joined Dr. Jim Hurley's laboratory at the National Institutes of Health where he solved the crystal structure of a lysine methyltransferase that belongs to a novel family of enzymes that regulate transcription and chromatin structure.

Ray is interested in studying enzymes that catalyze post-translational modifications of proteins in the nucleus. Among the most modified proteins in eukaryotes are histones, the major scaffolding proteins associated with nuclear DNA in chromatin. Histone post-translational modifications govern a wide range of nuclear processes including apoptosis, DNA repair, replication, and transcriptional regulation. Lysines are the most modified residues in histones and can be acetylated, methylated, ubiquitinated, or sumoylated. He is currently investigating the methylation of lysine residues, which can be mono-, di-, or trimethylated in vivo. Histone lysine methylation regulates transcription through recruitment of either transcriptional activators or silencers to discrete regions of chromatin. Histone lysine methyltransferases (HKMTs) catalyze the site-specific methylation of lysines in the amino-terminal tails of histones H3 and H4 and possess an evolutionarily conserved catalytic domain, termed the SET domain (named for three *Drosophila* gene regulators, Suppressor of Variegation 3-9, Enhance of Zeste, and Trithorax). He and his colleagues have solved crystal structures of a SET domain HKMT homolog bound to various substrates in order to investigate the mechanism of lysine multiple methylation by these enzymes. The structures have provided insights into the functions of these methyltransferases in chromatin remodeling and should aid in the development of inhibitors to specific SET domains, such as the oncogene EZH2, which is overexpressed in a variety of cancers including prostate and breast tumors. Future studies will focus on the roles of other nuclear enzymes in regulating transcription and chromatin remodeling.

DOCTOR OF PHILOSOPHY DEGREE GRANTED

The Department extends its congratulations to the following students who have completed their PhD degrees between April 1, 2003 and December 10, 2003.

Seonok (Sunny) Lee (Margolis)

"Discs Large and mLin-2/CASK: Evolutionarily Conserved Modulators of Epithelial Cell Polarity and Synaptic Junctions." Sunny will conduct postdoctoral research in the laboratory of Ulrike Heberlein at the University of California, San Francisco, where she will study the molecular mechanisms underlying *Drosophila* behavioral responses to alcohol and other various substances such as cocaine and nicotine.

Utpal Mayank Munshi (Menon)

"Activation and Internalization of the Luteinizing Hormone/Human Chorionic Gonadotropin Receptor." Utpal will conduct post-doctoral research in the laboratory of Dr. Eric Freed at the National Cancer Institute where he will study mechanisms of HIV assembly and release.

Augen A. Pioszak (Ninfa)

"Mechanism of Signal Transduction Through the *Escherichia coli* Two-Component System Transmitter Protein NRII (NTRB)." Augen has taken a position at the RIKEN Yokohama Institute in Yokohama, Japan. He will be concentrating on protein crystallography to study signal transduction proteins involved in cell growth and cell death pathways in mammalian cells.

Michael Roh (Margolis)

"The Role of the Crumbs Complex in Mammalian Epithelial Polarity." Michael will return to medical school to complete clinical clerkship requirements for the M.D. degree.

Xiaohua Shen (Kaufman)

"Unfolding the Unfolded Protein Response: Turn to the Worm!" Xiaohua will continue working in Dr. Kaufman's laboratory while pursuing postdoctoral opportunities in the areas of stem cell and developmental biology.

Dong Xu (Ballou)

"Studies of the Reaction Mechanism of Phenol Hydroxylase: Site-Directed Mutagenesis and 6-Azido-FAD." Dong will conduct postdoctoral research on cisplatin in Dr. Stephen Lippard's laboratory in Massachusetts Institute of Technology.

Hao Zhou (Thiele)

"Identification of Novel Copper Transport Genes in Eukaryotic Cells." Hao will conduct postdoctoral research in the laboratory of David Clapham at the Children's Hospital, Harvard Medical School, where he will study the role of ion channels and G protein coupled receptors in neuronal and cardiac cells.

NEW STUDENTS JOIN CURRENT PHD CANDIDATES

Andrew Budor is from Farmington Hills, Michigan and received his B.S. in Biochemistry from the University of Michigan. While attending the University of Michigan he was given the Regents Alumni Award.

Daniel Coughlin is from Royal Oak, Michigan and received his B.S. in Biology from Hillsdale College in Hillsdale, Michigan.

Blake Fausett, a Medical Scientist Training Program student, is from Ogden, Utah and received his B.A. in Biology from the University of Utah in Salt Lake City, Utah.

Rebecca Haesler is from Chelsea and received her B.S. in Biology from Massachusetts Institute of Technology in Cambridge, Massachusetts.

Chung-Han (Joe) Lee, a Medical Scientist Training Program student, is from Houston, Texas and received his B.S. in Biology at Stanford University in Stanford, California.

Brian Moore is from Cincinnati, Ohio and received his B.S. in Biochemistry and Biophysics at Rensselaer Polytechnic Institute in Troy, New York.

June Pais is from Tulsa, Oklahoma and received her B.S. in Chemistry from the University of Oklahoma in Norman, Oklahoma. She is to be congratulated for winning a National Science Foundation fellowship in 2003.

Leah Parkinson is from Pittsburgh, Pennsylvania and received her B.S. in Molecular Biology at the University of Pittsburgh in Pittsburgh, Pennsylvania.

Lance Rider is from West Lafayette, Indiana and received his B.S. in Biochemistry at Purdue University in West Lafayette, Indiana.

Ryan Sargeant is from Logan, Utah and received his B.S. in Chemistry from Utah State University in Logan, Utah. In 2003 he was a winner of a National Science Foundation fellowship.

Julie Williams is from Dearborn, Michigan and received her B.S. in Chemistry and her B.A.S. in Meteorology from Boise State University in Boise, Idaho.

Pamela Wong is from Ann Arbor, Michigan and received her B.S. in Biochemistry at the University of Michigan.

Qian Yang is from Chengdu, People's Republic of China and received his B.S. in Biochemistry and Molecular Biology at Peking University in Beijing, People's Republic of China.

Pamela Wong is from Ann Arbor, Michigan and received her B.S. in Biochemistry at the University of Michigan.

Qian Yang is from Chengdu, People's Republic of China and received his B.S. in Biochemistry and Molecular Biology at Peking University in Beijing, People's Republic of China.

We are extremely grateful to all of the individuals (and in some cases their organizations) whose recent gifts and donations have provided valuable discretionary funds to support a wide range of Departmental activities.

Mark E. Zaremba

Carol Ann Fierke

William & Diana Pratt

Tetsufumi & Yasuko Ueda

Anita H. Payne

Minor J. Coon

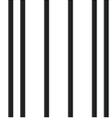
Audrey F. Seasholtz

Jane Ann Damren

Wilbur H. & Ellen R. Campbell

Your contribution to the Department, either designated for one of the following endowment funds or as an unrestricted gift, would be most welcome and sincerely appreciated. Checks may be made payable to the University of Michigan.

- Biological Chemistry Endowment Fund
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- Christman Fellowship Endowment
- Minor J. and Mary Lou Coon Graduate Student Fellowship in Biological Chemistry
- Departmental Gift Fund
- Dominic D. Dziewiatkowski Dissertation Award
- Graduate Program Endowment
- Anthony and Lillian Lu Professorship Endowment
- Vincent Massey Collegiate Professorship in Biological Chemistry
- Murphy Memorial Prize Endowment
- Smith-Coon Chair Professorship Endowment



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