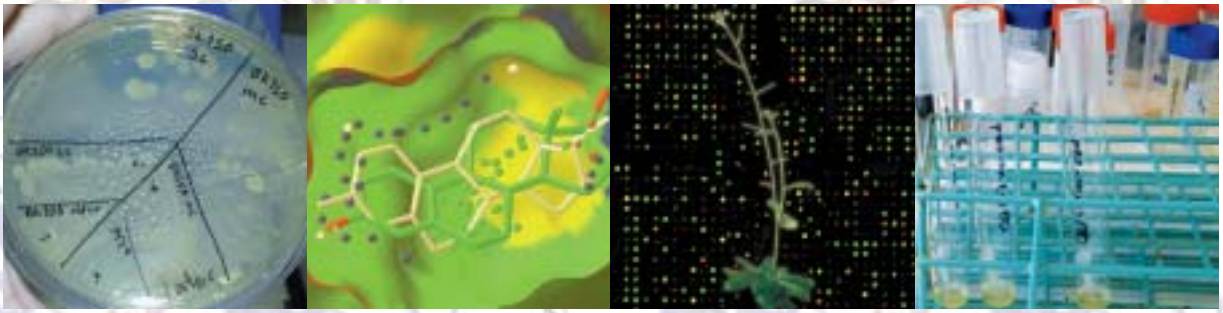
MICHIGAN STATE UNIVERSITY

BIOCHEMISTRY & MOLECULAR BIOLOGY



2001

MICHIGAN STATE UNIVERSITY

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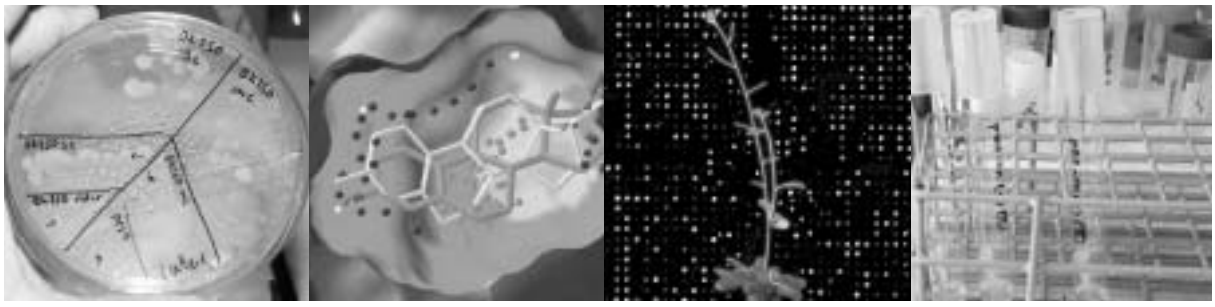

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Contents

A Message From the Chairperson

William L. Smith, Professor and Chair
Web Site: http://www.bch.msu.edu
Email: bchalumn@msu.edu

Dear Friends and Alumni,

I imagine you have all had the same experience this past year: It has not been boring. For starters and as promised, we became the Department of Biochemistry and Molecular Biology (BMB) on July 1, 2000. This more modern designation fits more closely with our academic and research mission and is in line with the name of the national society.

At the time of this writing, BMB, along with its companion basic biomedical science departments (Microbiology and Molecular Genetics, Pharmacology and Toxicology, and Physiology), is undergoing a comprehensive external review. This started with an internal review, and BMB came out exceptionally well in this first phase. For example, 95% of our faculty currently have extramural funding—a remarkable number for any department anywhere and particularly for a department with a major focus on undergraduate education. Indeed, a total of 51 undergraduates worked in BMB laboratories in 1999-2000, continuing a longstanding tradition in the Department of providing hands on, individualized training to our undergraduate majors. Notable activities of our undergraduates are featured later in this magazine.

A final comment regarding the departmental review. There has been considerable emphasis over the last several years on two terms: "interdisciplinary" and "thinking outside the box." One of the purposes of the departmental reviews is to determine if the basic biomedical science departments are performing well on these fronts. It was interesting to see the preliminary data that indicated that most of our funded faculty are interacting actively with faculty from other disciplines. However, we need to keep in mind, as I am reminded by my departmental colleagues, that "in order to have interdisciplinary, we need to have disciplines." Indeed, one of the very constructive outcomes of the review is likely to be a clearer definition of what information, culture and approaches define the discipline of "Biochemistry and Molecular Biology" and an improved perception of how we can best convey the elements of our discipline to our students.

The new Bio-Physical Sciences Building (see page 7) will connect via 5th floor and basement corridors to the west side of the Biochemistry Building. The new building is on schedule for completion in December, 2001, and occupancy by mid 2002. You can imagine the mess (or see it first hand *via* a link found at **http://www.msu.edu:80/~neils**). Adding to this, the Chemistry parking ramp on Shaw Lane has been torn down and is being rebuilt; in the meantime, we have to deal with the parking problem. We are continuing with our own set of Biochemistry Building renovations ($500,000 generously provided by the Provost), also scheduled for a December completion. This includes paint-

BMB Mission Statement: The goal of the Department of Biochemistry and Molecular Biology is to improve the research stature of the department while maintaining quality instruction in our undergraduate, graduate, and medical school programs.

Continued on page 2

ing the hallways and laboratories, replacing outdated furniture and generally trying to modernize the building. Dr. Bieber has been shepherding this effort and deserves considerable praise. Present and future students and faculty will derive long term benefits from this renovation. Next up will be repairs to the building ventilation system which will also involve replacing all the ceiling tiles and fluorescent fixtures. The anticipated cost is $11-13 million, but the University has placed this as the highest priority in its most recent capital equipment request to the State of Michigan.

I mentioned in my letter last year that BMB has defined three major research focus areas and has spent the last five years working to develop these areas: Structural Biology, Biochemistry of the Cell Nucleus, and Plant Biochemistry. As you will read in more detail later, our efforts are already beginning to pay substantial dividends. The State of Michigan has been very forward looking in investing its tobacco settlement windfall. One area being targeted is the life sciences under the umbrella designation of the Michigan Life Sciences Corridor (MLSC). Expected funding is $50 million per year for 20 years. One of the five areas initially targeted for development is Structural Biology. MSU has been designated as the hub for this research area. The co-Directors of this Center for Structural Biology are Drs. Ferguson-Miller and Preiss, and major contributors include Drs. DeWitt, Garavito and Kuhn, also from the BMB faculty. Dr. Kuhn has also been a leader in development of the MLSC Bioinformatics Center, while Drs. Gage and Zacharewski have been instrumental in establishing the MLSC Proteomics and Genomics Centers, respectively. Drs. Jon and Laurie Kaguni are principal investigators on one of the individual research grant awards from MLSC, while Dr. Gregg Howe is principal investigator on another MLSC research award. To further enhance our efforts in Structural Biology, BMB is in the midst of recruiting a new faculty member in this area, and we hope to have this new colleague join us later this year. Additionally, as you will read later in this magazine, there has been considerable development of centralized research service facilities under the auspices of the Vice President for Research; major contributors from the BMB faculty have included Dr. Loran Bieber and Drs. DeWitt, Fraker and Gage. Joseph Leykam and Dr. Padmanabhan, affectionately known as Pappan ("Poppin"), have also been key players.

BMB has defined three major research focus areas and has spent the last five years working to develop these areas: Structural Biology, Biochemistry of the Cell Nucleus, and Plant Biochemistry.

In the New Things and Changes category, we have welcomed two new faculty during the past year. Dr. Dean DellaPenna, who is an internationally recognized expert in nutritional genomics, engineering plants to enhance their production of micronutrients (an example is vitamin E), has joined BMB, coming from the University of Nevada, Reno. Dr. John LaPres, now our youngest faculty member and a Michigan native, comes to us from the University of Wisconsin; Dr. LaPres is investigating the biochemical basis for the toxicity of certain metals like nickel. He has a joint appointment in the National Center for Food Safety and Toxicology. Dr. Glenn Davis has just recently been named Dean of the College of Human Medicine and will come to MSU later this year. You may recall that BMB is jointly supported and administered by four units including the Colleges of Natural Science, Human Medicine, and Osteopathic Medicine and the Michigan Agricultural Experiment Station. Although most of you are unlikely to have spent much time dealing with deans, the financial, academic and moral support from our deans over many years has been essential

for enhancing the quality of the department. Next, I am pleased to note that Professor Zachary Burton assumed the position of Director of Undergraduate Programs on January 1, 2001. Dr. Burton has taught in our undergraduate molecular biology laboratory (BMB 472) for a number of years and has additional experience from mentoring the BMB Undergraduate Club and our summer undergraduate research training program in recent years. Dr. Burton has also achieved prominence for his research on the regulation of gene transcription. He takes over for Dr. Kindel who did an excellent job as Director but chose to retire this past year; a feature on Dr. Kindel is presented later in this magazine. And most sadly, Dr. Jerry Babcock, former chairperson of the Department of Chemistry and a close friend and colleague of many of the BMB faculty, passed away December 22, 2000. In addition to his creative, insightful science, Dr. Babcock set a wonderful personal tone and was admired by everyone with whom he came in contact; he is missed and will continue to be missed.

In the Special Recognition category, Dr. Tony Serianni is our Boezi Award winner for 2001 (see article below). We will welcome back his mentor, Dr. Bob Barker, who was Chair of BMB from 1974-1980, for the awards dinner in April; Dr. Barker will give the traditional after dinner speech. I encourage you to forward nominations for Boezi Award candidates to me, and I will refer them to our Awards Committee. I am also pleased to note that Assistant Professor David Arnosti has been recognized by Sigma Xi with its Young Investigator for the Life Sciences Award.

Dr. Keith Yamamoto from the University of California at San Francisco will be our first endowed William W. Wells Lecturer in April and Dr. John Shanklin of Brookhaven National Laboratories will deliver the first N. Edward Tolbert Lecture this May. The contributions made by many of you have provided the initial funding for these endowed lectureships. We in BMB benefit enormously from visits of distinguished scientists such as these individuals, and we are very grateful to our alumni for the financial contributions that make this possible. The State of Michigan has been unusually supportive of the universities in the state, including MSU. However, funding from the state is not adequate to cover many of the activities that add so much to the quality of the department, such as undergraduate research support, travel support for graduate students, and endowed lectureships (see description of established endowment funds and related funding opportunities later in this magazine). Your contributions provide support for such activities and are absolutely essential for maintaining and improving the quality of the Department. Accordingly, we hope that you will keep BMB in mind when you make charitable contributions this year.

We also hope you will keep us informed of happenings in your world by completing the enclosed card (do not worry—we will *not* call you!). We highlight this information in the back of this magazine each year, and this is one of our most popular features.

I wish you all a happy and prosperous year.

Best personal regards,

William L. Smith

P.S. And please visit and bookmark our web site **(http://www.bch.msu.edu/)**. It is a good site and an excellent way to keep up on what is happening in MSU Biochemistry and Molecular Biology.

An Overview

Department of Biochemistry and Molecular Biology, Michigan State University

Administration (% funding): College of Natural Science (Lead Dean; 51%), College of Human Medicine (18%), Michigan Agricultural Experiment Station (17%), College of Osteopathic Medicine (14%)

Faculty: 28 wholly appointed in Biochemistry and Molecular Biology, and 12 jointly appointed in other departments
5 University Distinguished Professors
9 MSU Distinguished Faculty Awardees
2 NIH MERIT Awardees

Specialists: 3 (Laboratory, Bioinformatics and Structure Facilities)

Staff: 14 (secretarial, accounting, Biochemistry Instrument Shop, Biochemistry Stores, Animal Room)

Undergraduate Majors: 220

Graduate Students: 45

Postdoctoral Fellows: 45

University Facilities: Macromolecular Structure, Mass Spectrometry, Genomics, Bioinformatics/Computer Graphics, Flow Cytometry

Centers: REF Center for Biological Modeling
MLSC Center for Structural Biology

Research Emphases: Structural Biology
Plant Biochemistry
Biochemistry of Cell Nucleus

'00 Grant Support (66): 25 NIH, 7 NSF, 3 USDA, 3 DOE, 2 ACS, 2 AHA, 24 Other
Approximately $7.5 million in extramural support

Teaching: Undergraduates (lectures, labs, independent study)
Graduate students (core Biochemistry, Mol. Biology)
Medical Schools (BCH521, PBL, Systems)

Construction on Schedule

Progress continues on the Bio-Physical Sciences Building, which is being built just west and north of Biochemistry. This will link the present Biochemistry and Chemistry Buildings into a contiguous space housing several basic science departments. For information about the new building, including live camera shots showing construction progress, go to: **http://www.msu.edu:80/~neils**. Construction is proceeding on schedule, with completion planned for December, 2001. Faculty in the Departments of Microbiology and Molecular Genetics, Physics and Astronomy, and Physiology are looking forward to moving into the new structure early in 2002.

Status in March, 2000.

View the final phases of the Bio-Physical Sciences Building construction at ***http://www.msu.edu:80/~neils.***

Status in March, 2001.

Tony Serianni Named Recipient of the 2001 John A. Boezi Memorial Award

Dr. Tony Serianni has been named as the recipient of the John A. Boezi Memorial Award for 2001. The award will be presented at the annual departmental Awards Banquet to be held in April, 2001.

Tony is currently Professor of Chemistry and Biochemistry at the University of Notre Dame and Chief Executive Officer of Omicron Biochemicals, Inc. He received his Ph.D. in Biochemistry from MSU in 1980, with Dr. Robert Barker, Professor and Chair of Biochemistry, as his mentor. When Bob Barker moved to Cornell University in 1980, Tony moved with him as a postdoctoral research associate. In 1982, Drs. Barker and Serianni co-founded Omicron Biochemicals, a company specializing in the synthesis of stable isotopically-labeled carbohydrates and carbohydrate derivatives (e.g., nucleosides) for applications in a wide range of chemical, biochemical, biomedical, and clinical studies; further information about Omicron Biochemicals is available at the company's web site: **www.omicronbio.com**. Also in 1982, Tony joined the faculty at Notre Dame as an Assistant Professor of Chemistry, and moved the operations of Omicron Biochemicals to South Bend.

In his academic research, Tony has focused on exploiting the use of stable isotopes in carbohydrate and nucleic acid chemistry, biochemistry, and structural biology. Nuclear magnetic resonance (NMR) methods play a major role, and Tony Serianni and his coworkers have pioneered development of NMR methodologies that permit determination of structure and dynamics of isotopically-labeled biomolecules with increased precision and detail. Tony notes that this research is interdisciplinary in nature, requiring the development of new synthetic strategies for incorporation of stable isotopes into biomolecules, the application of advanced multidimensional NMR methods to decipher the inherently complex NMR spectra, and the development of new experimental approaches for relating NMR parameters with molecular behavior and new theoretical approaches for obtaining information not readily obtainable by direct experimental methods. Further information about Tony's research, and a listing of more than 90 publications describing his work, can be found at **www.nd.edu/~aseriann**.

Tony has played an active role in various professional organizations, including service as Chairman of the American Chemical Society's Division of Carbohydrate Chemistry, as well as editor and/or member of the editorial board of *Carbohydrate Research* and the *Journal of Carbohydrate Chemistry*. He currently serves on NIH committees evaluating Shared Instrumentation grants and NIH-funded research facilities.

A "faculty profile," written by Tony himself, appeared in a recent issue of the newsletter from the Department of Chemistry and Biochemistry at Notre Dame. It provided a highly personal and insightful account of Tony's interests and accomplishments. The concluding paragraph of that profile provides an especially nice summary of Tony's success in blending a career in both academia and business:

Tony Serianni

"I have had a unique opportunity over the years to experience firsthand both academia as a professor and the business world as founder of a small and successful business. The two worlds are often viewed as antagonistic, the former idealistic and altruistic and the latter pragmatic and sometimes tainted by the constant drive for profitability. I have found these common descriptions narrow and stereotypic. The assets of each can, under the right conditions, be harnessed to drive research and knowledge forward in a manner not possible by each entity working alone. What is necessary to make the synergy work well is open communication, clearly defined goals, and strong research and business ethics to guide the day-to-day challenges of personnel, finances and information management. It has been exciting and challenging to explore this synergy over the past 18 years, and I have learned a great deal from the experience."

-Tony Serianni, 2001 John A. Boezi Memorial Award Recipient

Past Recipients of the Boezi Award

Professor John A. Boezi joined the newly formed Department of Biochemistry in 1963. Together with colleagues like Fritz Rottman and Allen Morris, John represented the emerging field of "molecular biology" and played a major role in shaping the research and teaching program in the early days of the Department. John's sudden death in 1980 was deeply felt by his students and faculty colleagues alike. In his memory, they established an award to be given annually to a recipient of a B.S., M.S., or Ph.D. degree from this department who had gone on to a distinguished career that reflects the qualities personified by John Boezi.

In the many years that have passed since establishment of this award, the number of degree recipients from this department has continued to grow steadily. Communications being imperfect, the Department recognizes that it may not be aware of some graduates whose accomplishments since leaving MSU would make them worthy candidates for the Boezi Award. We thus solicit your assistance in identifying past graduates of this department, undergraduate or graduate, who would merit consideration. Please send suggestions and pertinent information to Dr. William L. Smith, Chairperson, Department of Biochemistry and Molecular Biology or e-mail us at bchalumn@msu.edu.

1983	Donald W. Carlson	Ph.D.	1961
1984	Allen T. Philips	Ph.D.	1964
1985	John A. Gerlt	B.S.	1969
1986	George H. Lorimer	Ph.D.	1972
1987	Lawrence B. Dumas	B.S.	1963
1988	Douglas D. Randall	Ph.D.	1970
1989	Ronald C. Desrosiers	Ph.D.	1975
1990	George M. Stancel	Ph.D.	1970
1991	Raymond J. Dingledine	B.S.	1971
1992	Howard C. Towle	Ph.D.	1974
1993	A. Stephen Dahms	Ph.D.	1969
1994	Sherwood R. Casjens	M.S.	1967
1995	Friedhelm Schroeder	Ph.D.	1973
1996	Philip L. Felgner	Ph.D.	1978
1997	Arlyn Garcia-Perez	Ph.D.	1984
1998	Ann E. Aust	Ph.D.	1975
1999	Peter Steck	Ph.D.	1981
2000	Sally Camper	Ph.D.	1983

Department of Biochemistry and Molecular Biology Faculty Play Prominent Role in Bringing Life Sciences Corridor Funding to MSU

A significant portion (an expected $50 million per year for the next 20 years) of the funds coming to Michigan as this state's share of the tobacco lawsuit settlement will be used to support research in the life sciences and related business developments under the initiative called the Life Sciences Corridor (LSC). The "corridor" refers to the geographical relationship of Wayne State University on the east and the Van Andel Institute on the west, with Michigan State University, the University of Michigan, and the pharmaceutical firms of Pfizer (formerly Warner-Lambert Parke-Davis, in Ann Arbor) and Pharmacia-Upjohn (Kalamazoo) in between. These represent the major research institutions in Michigan. A requirement for funding under the LSC is that the research must involve collaborators at two or more institutions in Michigan, preferably including industry. The LSC is administered by the Michigan Economic Development Corporation.

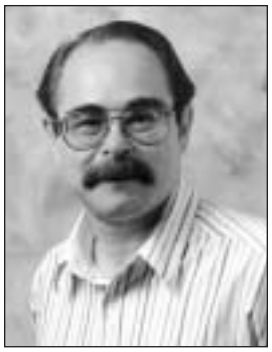
Funds from the LSC initiative are of two basic types. One category provides for development or enhancement of research infrastructure. Core facilities offering state-of-the-art instrumentation and technology will be established. While these will be physically located at particular institutions, they will be available for use by researchers from universities, private research institutions, and biotechnology or pharmaceutical firms throughout Michigan. The other type of funding under LSC will be for specific collaborative research projects.

The initial grants made under the LSC initiative were announced at a meeting of the LSC Steering Committee, Dec. 13, 2000. BMB Professors Shelagh Ferguson-Miller and Jack Preiss were co-principal investigators on a proposal that will bring $26 million over five years to establish the Michigan Center for Structural Biology (CSB) at MSU. Headed by Ferguson-Miller and Preiss, the successful proposal for establishment of the Structural Biology facility also involved major collaborative efforts with investigators at the University of Michigan, Wayne State University, and the Van Andel Institute. Though administered in East Lansing, this facility includes satellites at these other institutions and will be available to investigators state-wide. The Center for Structural Biology will house a 900 MHz nuclear magnetic resonance (NMR) spectrometer at MSU, providing state-of-the-art capability for determination of the structure of biomolecules using NMR. Funding through the Center for Structural Biology will also allow construction of beam lines at the Advanced Photon Source (Synchrotron) at Argonne


Dave DeWitt


Shelagh Ferguson-Miller


Doug Gage


Mike Garavito


Gregg Howe

National Laboratory (Argonne, IL), to be used for structural determinations by x-ray crystallographic methods. The synchrotron beam line proposal was led by BMB Professor Mike Garavito, who brings unique expertise in membrane protein crystallography, which will be a focus of CSB research. Another important part of the CSB is establishment of a protein expression facility, to provide the substantial amounts of protein required for structural studies; this effort is led by BMB Associate Professor Dave DeWitt. The Michigan Center for Structural Biology will give Michigan researchers access to the most sophisticated instrumentation available for biomolecular structural determinations.

Other infrastructure proposals funded by LSC will permit establishment of Centers for Bioinformatics, Proteomics, and Genomics. The Centers for Bioinformatics and Proteomics will be located at UM, and the Center for Genomics at Wayne State. These operations will provide services at MSU through nodes designed by BMB faculty members Leslie Kuhn (Bioinformatics), Doug Gage (Proteomics), and Tim Zacharewski (Genomics).

LSC funding was also awarded for collaborative research projects involving two other BMB faculty members. Gregg Howe, jointly appointed as Assistant Professor in the Department of Biochemistry and Molecular Biology as well as the MSU-DOE Plant Research Laboratory, received $1 million in funding for research aimed at identifying the molecular and biochemical basis of plant defenses against insects. Working with Howe will be Mark Whalon (MSU Department of Entomology) and Eran Pichersky (UM Department of Biology). One aim of these investigators will be to identify volatile compounds that either deter insect attack or attract natural predators of the insect. Howe and his collaborators further propose to define the biochemical basis for the effects of these compounds, and to characterize the genes involved in their synthesis and the mechanism by which these genes are regulated. The proposed research may lead to novel non-transgenic approaches to crop protection against insect pests.

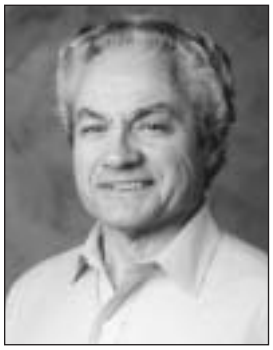
Together with investigators at UM and at Pfizer, BMB Professors Jon and Laurie Kaguni received $660,000 to support studies on the process of DNA replication as it pertains to diseases, with the ultimate goal of developing drugs that may act through effects on DNA replication of pathologically important organisms.

Total LSC funding awarded to these and other MSU scientists was $40.4 million, to be received over the next 3-5 years. Dr. Robert Huggett, Vice President for Research and Graduate Studies, noted that "The Life Sciences Corridor is a perfect model for how to conduct modern day, cutting-edge research. It will definitely lead to more jobs, more businesses and a better quality of life for Michigan's citizens. Michigan State is proud to be a major part of this effort."


Jon Kaguni


Laurie Kaguni


Leslie Kuhn


Jack Preiss


Tim Zacharewski

Thank You!

The Department of Biochemistry and Molecular Biology is grateful to the following donors for contributions received from 4-1-00 to date:

Mr. Thomas A. Abraham and Mrs. Judith A. Abraham

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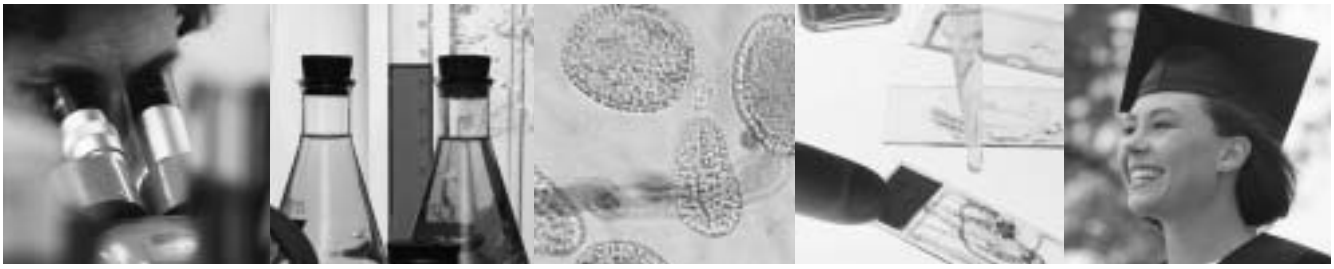


PROFILES

Paul K. Kindel, Professor Emeritus

Paul Kindel was one of several young faculty members, including Clarence Suelter, who were recruited during that period and subsequently played critical roles in developing the programs of the Department.

Last year's issue of this magazine carried the news of the retirements of Professors Clarence Suelter and Bill Wells. The changing-of-the-guard continued when Professor Paul K. Kindel joined the ranks of emeritus faculty on January 1, 2001. Paul became a member of the faculty in 1963, as an Assistant Professor. Some of you will recall that those were the days in which the fledgling department was growing under the leadership of founding Chairperson R. Gaurth Hansen. Paul Kindel was one of several young faculty members, including Clarence Suelter, who were recruited during that period and subsequently played critical roles in developing the programs of the Department. Dr. Kindel was particularly noted for his involvement with the undergraduate program. For many years, he taught the undergraduate biochemistry laboratory course, now known as BMB 471, relinquishing this responsibility only last year. He also served as Undergraduate Program Director for the past several years, bringing his famed concern for organization and detail to the task. Along with his more senior colleagues, Harold Sell and Ed Tolbert, Paul was one of the pioneer "plant biochemists" in the department, his primary interest being in chemical characterization of cell wall constituents and elucidation of their biosynthetic pathways. His many contributions to the department are recognized by his colleagues, who wish him well as he and his wife, Judy, begin what we hope will be a long and enjoyable retirement. Knowing Paul and Judy, retirement will continue to include a fair share of travel, hiking, biking, and gardening, but we will count on them to show up periodically at departmental social events to renew old ties.

Core Facilities Support Research

Dave DeWitt

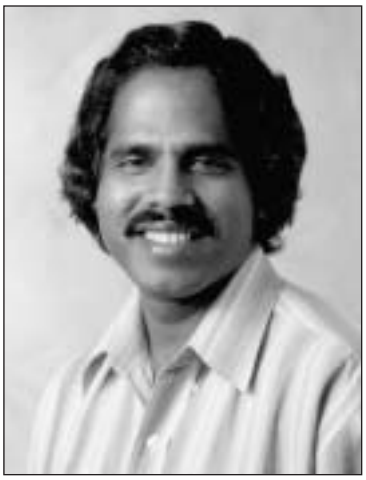
Much of present-day research in biochemistry and molecular biology relies on sophisticated instrumentation and technology. In most cases, the cost is such that it is impractical to have the instrumentation in individual labs. Moreover, most of these instruments have the capability for running many more samples than are likely to be generated by an individual research group. The obvious solution, seen at virtually all research universities, is to establish central facilities that provide these support services to many research groups, both on– and off– campus. Costs are thus shared among several users, making access to state-of-the-art instrumentation fiscally possible. Detailed information about these "core facilities" at Michigan State can be found at **http://www.msu.edu/unit/vprgs/analytical_core_facilities.htm.**

Several of the core facilities are physically housed in the Biochemistry Building, and provide critical support services to faculty and students in the Department of Biochemistry and Molecular Biology as well as many other departments. Others, also used extensively by BMB faculty and students, are located in adjacent buildings. All core facilities are maintained by highly skilled personnel who play a critical role in making this instrumentation and technology available to MSU researchers.

The Genomics Technology Support Facility (GTSF) recently began operations in Room S18, Plant Biology Laboratory (right across Wilson Road from the Biochemistry Building). The GTSF is so new that, at the time this is being written, it is not yet included in the web site (see above) describing other core facilities at MSU. BMB Associate Professor Dave DeWitt is Director of the GTSF, with Joe Leykam serving as Deputy Director for Operations. Joe is also manager of the Macromolecular Structure, Sequencing, and Synthesis Facility (MSSSF), another core facility described below. Assisting Dave and Joe in getting the GTSF up and running is Annette Thelen (Ph.D. in Biochemistry from MSU, 1992). MSU researchers are most grateful to Loran Bieber, Professor of Biochemistry and Molecular Biology, who has spent an enormous amount of time over the past year or so in organizing the GTSF, securing the funding and necessary laboratory space, and overseeing the purchase of instrumentation. The GTSF offers a variety of gene analysis services including custom and high throughput DNA sequencing, DNA fingerprinting and genotyping, quantitative PCR, and DNA array analysis. "Custom DNA sequencing" is done with an automated system capable of running 64 samples simultaneously, while "high throughput sequencing" generates sequence information from as many as 384 DNA samples at a time, arranged in 96 well ("microtiter plate") formats. In the latter case, preparation of the DNA samples, conduct of the sequencing reactions, and electrophoretic analysis of the sequencing products is highly automated through robotics. DNA fingerprinting and genotyping techniques include AFLP (amplified fragment length polymorphism) analysis and SSR (simple sequence repeats) analysis, and are also highly automated using the Perkin Elmer ABI GeneScan Analysis System.

Also available in the GTSF is instrumentation for analysis of "gene chips." The latter are arrays of known DNA sequences that are spotted at high density (approximately 20,000 discrete spots within a 1" square) and then simultaneously hybridized with cDNAs synthesized from mRNA isolated from two different samples (e.g., cells grown

Joe Leykam



Kaillathe Padmanabhan ("Pappan")

"Custom DNA sequencing" is done with an automated system capable of running 64 samples simultaneously, while "high throughput sequencing" generates sequence information from as many as 384 DNA samples at a time, arranged in 96 well ("microtiter plate") formats.

under two different conditions); the cDNAs synthesized from the different mRNA samples are labeled with distinct fluorescent nucleotide analogs (e.g., red and green). Thus, genes that are expressed in both mRNA samples (e.g., under both growth conditions) will hybridize to both the "red" and "green" cDNA (≈ mRNA), producing yellow fluorescence. However, genes preferentially, or exclusively, expressed under one or the other experimental conditions being compared will hybridize preferentially to the corresponding mRNA, producing either red or green fluorescence. Thus, analysis of the resulting fluorescence provides information about the relative expression of the various known genes under the two experimental conditions being compared. While relative expression levels can also be obtained by methods such as Northern blotting, this typically provides information on one, or perhaps a few, genes at a time. Gene chips permit simultaneous determination of the relative expression levels of ***thousands*** of genes! Commercially available gene chips provide DNA arrays representing the genomes of a number of different organisms (human, rat, mouse, yeast, E. ***coli***, ***Arabidopsis***), and gene chips can also be prepared in the GTSF using robotic apparatus that produces arrays of DNA sequences of particular interest to an investigator.

Arabidopsis Gene Array (See cover for color image.)

As one could readily imagine, the methods discussed above produce an ***enormous*** amount of data. Analyzing it in a manner that leads to useful conclusions is well beyond the capability of the individual investigator just sitting down at his/her desk with the "raw data" — just imagine trying to interpret the results from a single gene chip experiment, which provides information about the relative expression of thousands of genes, and deducing what genes are coordinately expressed or repressed under the different experimental conditions. Or imagine trying to analyze and detect similarities between the 384 different sequences generated in a single high throughput sequencing experiment. Analysis and management of such huge amounts of data requires sophisticated computer methodology, and this is what is now generally called the realm of "bioinformatics." Development of bioinformatics capability is well underway and will continue; this is integral to the role of both the GTSF and the Macromolecular Computing Facility (see below) as core facilities supporting the efforts of MSU researchers.

The Macromolecular Comput-

Core Facilities Support Research

Continued from page 15

ing Facility, also known as the Computer Graphics Facility, is located in 218 Biochemistry, with Dr. Kaillathe Padmanabhan ("Pappan") as Manager. Pappan interacts closely with the BMB departmental Computer Committee, chaired by Dave DeWitt. The result has been development of a first class facility that provides access to Silicon Graphics Workstations, with supporting software that permits visualization and modeling of the 3-dimensional structures of proteins, nucleic acids, and other biomolecules. Also available are several IBM-based PCs as well as a MacIntosh, all with an array of software for word processing as well as graphics capabilities. These computers are linked to printers (black and white as well as color, including a high quality dye sublimation printer which provides photographic quality color prints), and also to slide makers, permitting direct production of slides from computer images. The most recent acquisition in the printer category is a large format inkjet printer that can output posters, which have become a popular format for presenting work at scientific meetings. Thus, the Computing Facility provides the capability for the entire process of transforming raw experimental data into finished presentation, as figures for manuscripts, or as slides or posters for presentation in other venues. The Macromolecular Computing

Doug Gage

Pamela Fraker

Facility also houses two SUN Microsystems servers that provide for sequence analysis (nucleotides, amino acid) with either the widely used "GCG" (Genetics Computer Group) program suite or the sequence analysis package from Lasergene. These sequence analysis services are web-based and thus make this capability available in the laboratories and offices of individual faculty and students across campus. The sequence analysis functions are directly relevant to the fast-developing field of genomics/bioinformatics, and this part of the Macromolecular Computer Facility's operations has been closely integrated with the most recent core facility to appear on campus, the GTSF.

The Macromolecular Structure, Sequencing and Synthesis Facility (MSSSF) was recently relocated and now resides in 110 Biochemistry. Manager Joe Leykam oversees the facility, which provides an array of services including oligonucleotide synthesis with both standard and modified (e.g., fluorescently labeled or biotinylated) bases, protein sequencing, peptide synthesis, molecular weight determinations by electrospray mass spectrometry, and mass mapping (e.g., of protein digests) by HPLC-mass spectrometry. Several capillary or microbore HPLC instruments are available for separation and analysis of complex samples such as protein digests. In addition to the analytical and synthesis services provided, the MSSSF houses instrumentation for phosphor-imaging and chemiluminescence imaging, permitting quantitative analysis of autoradiograms and immunoblots. Also available is a BIACORE 2000 which can be used for real-time monitoring of protein-protein or protein-nucleic acid interactions without the use of fluorescent or isotopically labeled molecules. The MSSSF staff also assist with database searches, oligonucleotide design, and development of experimental protocols to optimize chances for successful sequencing of sample proteins or peptides.

The Mass Spectrometry Facili-

Louis King

ty, located in 11 Biochemistry, has several different types of mass spectrometers. The basic principle of mass spectrometry is the same with all instruments, i.e., separation of molecules or molecular fragments based on their molecular mass (actually, it's based on charge/mass ratio, but under the experimental conditions, this is effectively determined by mass). However, the specific method by which this fractionation on the basis of mass is attained and the method by which samples are introduced into the mass spectrometer differ with the various instruments. This provides researchers an opportunity to utilize the method that is most efficacious for their particular sample. Dr. Doug Gage, Associate Professor of Biochemistry and Molecular Biology, serves as Director of the Mass Spectometry Facility, with Professor John Allison, Department of Chemistry, as Co-Director.

The Flow Cytometry Facility, recently relocated to 419 Biochemistry, is directed by Professor Pamela Fraker, with the assistance of Dr. Louis King, an expert in the operation of the "**FACS** machine" - fluorescence-activated cell sorting. Heterogeneous cell populations can be labeled by various (and multiple) fluorescent markers, e.g., fluorescent antibodies against specific membrane proteins, DNA-binding dyes with fluorescence intensity that corresponds to DNA content, dyes with fluorescent properties reflecting intracellular pH or [Ca^{++}]. The FACS machine analyzes the heterogeneous cell population, quantitatively categorizing cells based on the relative intensity of the various fluorescent signals, which in turn reflect the corresponding biochemical/physiological properties of the cells. In the "sorting" mode, the FACS machine actually fractionates the cells, providing highly purified populations of cells with defined biochemical/physiological characteristics, which can then be cultured or further analyzed. The Flow Cytometry Facility is one of three "optical imaging" core facilities. The others are the Center for Electron Optics, which provides electron microscopy services, and the Laser Scanning Microscopy Laboratory, which provides confocal microscope imaging and 3-D graphics reconstruction.

Visit Our Web Site

http://www.bch.msu.edu

Point your browser to **http://www.bch.msu.edu** and you will find information about many aspects of the department. Get current information about faculty members you may remember, and meet faculty members who have joined the department since your time with us. Find out about ongoing research activities, and about departmental support facilities such as the computer graphics facility, transgenic D*rosophila* facility, and others. Information about current graduate and undergraduate programs is available through the web site. Should you have a specific question, you may e-mail the Department at bchalumn@msu.edu, which will quickly provide the answer to your question.

Toxicogenomics Activities in BMB:

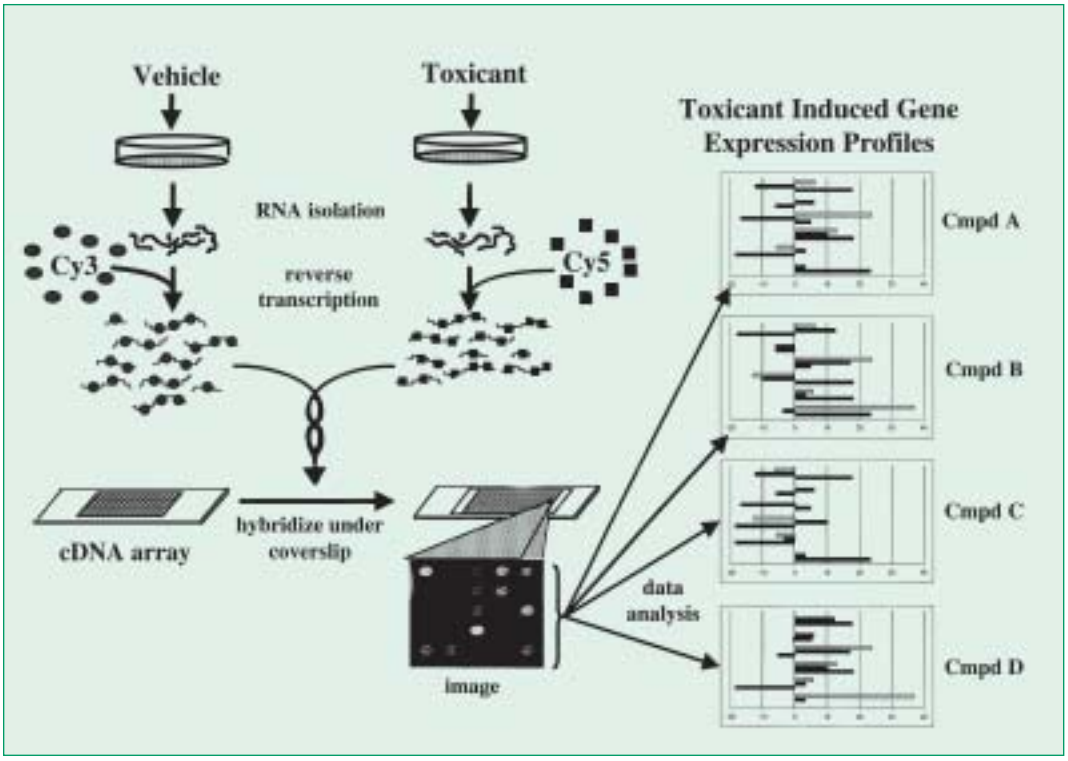
Investigating the toxicity of natural and synthetic chemicals by monitoring global changes in gene expression

by John LaPres, Assistant Professor and Tim Zacharewski, Associate Professor

John LaPres Tim Zacharewski

Sometime during the summer of 1973, the Michigan Chemical Corporation of St. Louis, Michigan, inadvertently substituted FireMaster, a persistent and lipophilic mixture of polybrominated biphenyls (PBBs) that is used as a fire retardant, for NutriMaster, a magnesium oxide animal feed nutritional supplement. It was not until April of 1974 that the primary source of PBBs was discovered. Another 18 months passed before the PBB contaminants were removed from the food distribution chain. This tragic event resulted in the widespread contamination of dairy and poultry products, and livestock in Michigan. Estimates indicated that approximately 85% of the residents of Michigan were exposed to PBBs, which prompted public concern regarding possible adverse health consequences in the exposed population. Michigan State University responded to this unfortunate incident by forming the multidisciplinary Institute for Environmental Toxicology (IET), and more recently, by establishing the National Food Safety & Toxicology Center (NFSTC). IET and NFSTC rely on the support and participation of faculty within many departments, institutes, centers and colleges at MSU. Over the years, a number of faculty within the Department of Biochemistry and Molecular Biology (BMB) have been actively participating in toxicology-related research programs through affiliations with IET and NFSTC. More recently, the complement of biochemical toxicology oriented faculty within the department has been bolstered by the recruitment of Drs. John LaPres and Tim Zacharewski, both of whom hold joint appointments with NFSTC.

Toxicology concerns the study of the adverse effects of chemical, biological and physical agents on living organisms. It combines elements of many scientific disciplines to assess the likelihood that harmful health effects will occur following exposure to a toxic agent. In order to fully assess the adverse effects of exposure to synthetic and natural toxic agents, a more comprehensive understanding of their molecular, cellular and



Toxicant Induced Gene Expression Profiles. Fluorescently labeled cDNAs are prepared with RNA extracted from control or toxicant-treated cells; cDNA from control cells is labeled with Cy3 while cDNA from treated cells is labeled with Cy5. The labeled cDNA probes are simultaneously hybridized to arrays of known cDNAs printed on glass slides. Fluorescent emission intensity ratios (Cy3:Cy5) are calculated for each cDNA in the array and analyzed to identify characteristic changes in gene expression, also referred to as a gene expression profile. Compounds A and C have comparable gene expression profiles, suggesting that these chemicals elicit changes in gene expression through a similar mechanism of action. Significantly different gene expression profiles are seen with compounds B and D, suggesting different mechanisms of action.

tissue level effects is required. Moreover, this understanding must extend to all levels of organization within an organism, including its genome and proteome. The rapid advancement of the Human Genome Project, as well as other genome projects, has generated full or partial sequence data for thousands of genes. With this wealth of sequence information, researchers have begun to evaluate and assign function to these genes, resulting in the emergence of a new field, termed Functional Genomics, that encompasses many new approaches to mine and interpret data on a genomic and proteomic scale. The various genome projects have significantly increased the availability of cDNAs and promoted the development of novel experimental and computational tools that have provided innovative strategies for investigating the impact of toxic agents on living organisms.

Toxicogenomics is an emerging field that utilizes these tools within predictive and discovery toxicology paradigms. It merges the enormous potential of bioinformatics and genomics with toxicology to assess and elucidate the mechanisms of action of known and suspected toxicants as well as drug candidates, thus providing a more comprehensive safety or toxicity evaluation. It is anticipated that toxicogenomics will revolutionize the field of toxicology by uncovering novel mechanisms of toxicity, help identify individuals with specific drug and chemical sensitivities, and assist in the development of safer and more effective compounds such as drugs, pesticides and industrial chemicals.

Collaborations within BMB and the establishment of core service facilities at Michigan State University have been instrumental in the incorporation of toxicogenomics into the research programs of Drs. LaPres and Zacharewski. The Arabidopsis Functional Genomics Consortium, lead by Dr. Pam Green (DOE - Plant Research Laboratory, BMB), and other plant functional genomics projects (Christoph Benning, BMB; Dean DellaPenna, BMB) have provided valuable expertise in the development of cDNA microarray technology. Funds from MSU and the Michigan Life Sciences Corridor have been used to establish the Genomics Technology Support Facility (GTSF) and develop

Continued on page 20

bioinformatics capabilities that are critical to analysis of the massive amounts of data generated by microarray experiments (see preceding article).

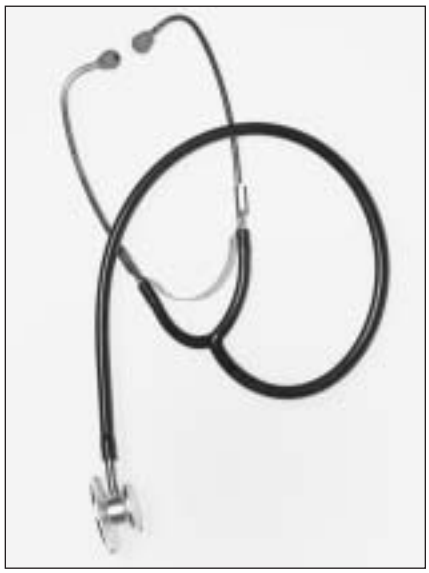
The LaPres and Zacharewski laboratories are currently using cDNA microarrays to investigate the effects of toxicants on gene expression in mammalian models. Microarrays allow investigators to examine the expression of thousands of genes within cultured cells or tissues in a single experiment. It has been proposed that each chemical or drug that acts through a particular mechanism of action will induce a profile or signature of characteristic gene expression changes. Therefore, microarrays can be used to compile expression profile data that is elicited following exposure to various compounds. Consequently, gene expression profiling may be used to classify chemicals with respect to their mechanism of action by virtue of their similarity to expression profiles generated from chemicals with known mechanisms of action. It is anticipated that gene expression profiling may also assist in the discovery of novel roles for genes involved in both toxicity and cellular defense, and in the identification of individuals who may be sensitive to certain drugs or chemicals.

The LaPres laboratory (**http://www.bch.msu.edu/faculty/lapres.htm**) is interested in using microarray technology to elucidate the mechanisms of action of metals such as nickel, lead and cadmium. These metals have been linked to several adverse effects, including birth defects, decreased intelligence quotients, erythropoietic abnormalities and cancer. Currently, it is believed that some of the toxic effects attributed to metals stem from their ability to increase levels of reactive oxygen species (ROS) within target cells. The toxicity of these metals, therefore, could be attenuated by treatment with ROS scavengers such as vitamin E and C. Many genes induced by metals are also involved in angiogenesis, which plays a critical role in promoting tumor growth. Understanding the role of these genes is therefore important for the understanding of tumor development. The LaPres laboratory is currently investigating genes involved in angiogenesis that are induced by metals using microarrays, cell culture and *in vivo* models.

Zacharewski and coworkers (**http://www.bch.msu.edu/~zacharet/zachar.htm**) use an integrated approach that includes ***in silico*** (bioinformatics), ***in vitro*** and ***in vivo*** models to investigate the mechanisms of toxicity of chemicals that interact with steroid hormone receptors. Studies have shown that some chemicals, commonly referred to as endocrine disruptors, can interfere with the normal functioning of the endocrine system by mimicking the activities of steroids such as estrogen and androgen. There is increasing concern that exposure to endocrine disruptors may increase hormone-dependent cancers, compromise fertility, increase reproductive tract abnormalities and impair cognitive abilities. Microarray technology is being used to characterize the gene expression profile of estrogenic and androgenic steroids, drugs, natural products, environmental contaminants and industrial chemicals. More specifically, microarrays are being used to: 1) evaluate the ability of ***in vitro*** assays to predict ***in vivo*** toxic responses, with the ultimate goal of minimizing animal use in testing chemicals for endocrine disruption, 2) examine the effects of estrogenic and androgenic substances on gene expression in various steroid responsive target tissues, 3) investigate the effect of endocrine disruptors on human brain cell differentiation, and 4) compare the effects of endocrine disruptors, alone and in combination, on gene expression.

Drs. LaPres and Zacharewski derive their current research support from various sources including the National Institutes of Health, the United States Environmental Protection Agency and the American Chemistry Council. Currently, Drs. LaPres and Zacharewski are collaborating on a project to establish models that can be used to investigate the effects of food-borne chemicals and environmental pollutants on child development. Future efforts include establishing national and international collaborative projects in toxicogenomics with other academic institutions, research centers, government agencies, and pharmaceutical and chemical industries.

Biochemists Make Good Docs!



Perhaps one of the first things that pops into your head when you hear "biochemistry" is "research." Indeed, virtually everything we currently know in this discipline rests firmly on experimental observations made in the laboratory, and further expansion of our biochemical knowledge is directly dependent on continued research. While biochemistry is properly viewed as a laboratory science, training in biochemistry can provide entrée into many careers other than that of a research scientist. In fact, probably most of us are familiar with people who have obtained undergraduate or graduate degrees in biochemistry, and then moved on to satisfying careers outside the laboratory. In future issues of this magazine, we plan to highlight some past graduates from this department who have established such careers. In the present issue, we introduce you to two former undergraduate biochemistry majors who went on to successful and fulfilling careers in medicine.

At MSU and elsewhere, "premeds" frequently have a reputation, justified or not, for being more concerned about their grade point than about many other aspects of undergraduate life. Admission to most professional schools is highly competitive, and certainly the "GPA" is a significant factor in determining admission. The undergraduate biochemistry degree is not generally considered the least strenuous route to a B.S. degree. Upper level organic chemistry? Not for me! Calculus? Oh my! Physical chemistry? Horrors! But then there are the strong-of-heart who recognize the biochemistry undergraduate program as an excellent basis for subsequent training in medicine. Two of these are Robert J. Holmes, M.D. (B.S. Biochemistry, 1974) and David K. Young, D.O. (B.S. Biochemistry, 1977).

Robert J. Holmes, M.D.

Robert J. Holmes, M.D.

After his graduation with high honors from MSU, Bob Holmes attended Wayne State University, from which he received the M.D. in 1978. He did a surgical residency at Wayne State from 1978-1983, and then a second residency, in cardiothoracic surgery, at Yale University School of Medicine from 1983-1985. He is board certified in both surgery and thoracic surgery. After a brief association with a thoracic and cardiovascular surgery practice in Lorain, Ohio, Bob returned to Michigan in 1986. Initially, he was an Associate, then partner, in a thoracic and cardiovascular surgery practice in Detroit, but since 1998 he has been associated with Michigan Cardiothoracic Surgeons in Pontiac, MI. Bob is a member of numerous professional organizations, has been a staff surgeon at several hospitals in the

Continued on page 22

Biochemists Make Good Docs!

Continued from page 21

Detroit area, and is currently staff surgeon at St. Joseph Mercy Hospital in Pontiac. Despite the hectic schedule of a busy cardiovascular surgeon, Bob has found time to return to MSU for the occasional visit and has, in fact, actually been sighted within the halls of his old stompin' grounds, the Biochemistry Building. Like many of our undergraduates, Bob was involved in undergraduate research during his time at MSU, and his subsequent regular contributions to the Biochemistry Undergraduate Endowed Scholarship Fund have benefitted other students who have followed in his footsteps.

David K. Young, D.O.

David K. Young, D.O.

Dave Young received the B.S with high honors in 1977. He then returned to his birthplace, Kirksville, Missouri, where he attended the legendary Kirksville College of Osteopathic Medicine, receiving the D.O. degree in 1981. His internship and residency in internal medicine were done at Grandview Hospital in Dayton, Ohio, followed by fellowships in sleep disorders (Henry Ford Hospital, Detroit, 1985-1986) and pulmonary medicine (Grandview Hospital, Dayton, 1986-1988). Dave is board certified in internal medicine and pulmonary medicine, and a diplomat of the American Board of Sleep Medicine. The pull of the East Lansing area was apparently quite strong. Since 1989, Dave has been in practice in Lansing, and he and his family currently live in East Lansing. He is a partner in Pulmonary and Critical Care Consultants, a practice concentrating on pulmonary and critical care medicine and sleep disorders. Dave is currently the Co-Director of the Sleep Disorders Center at Sparrow Hospital in Lansing, and is also Medical Director of the Respiratory Therapy Department at Sparrow. He is an active member of many professional organizations, and serves on the American Osteopathic Board of Internal Medicine and the American Board of Sleep Medicine. He also has re-established a formal association with MSU, no longer as a student but as an Associate Clinical Professor of Internal Medicine, College of Osteopathic Medicine. But it is not all work and no play - among his credits, Dave lists being a "band certified percussionist." Dave's unrestricted contributions to the department have been most helpful in enhancing the undergraduate and graduate experience of students who have followed him here at MSU.

The Biochemistry and Molecular Biology Undergraduate Club:

Pop, Pizza and Science

Undergraduate Biochemistry and Molecular Biology majors can get together and expand their horizons, both personal and professional, in a series of activities organized by the BMB Undergraduate Club. Hughes Scholar and Biochemistry major Janel Funk serves as President of the club during the current academic year. Through the efforts of Dr. Zach Burton, Associate Professor of Biochemistry and Molecular Biology and Undergraduate Program Director, a variety of events provide the opportunity to meet with BMB faculty members and outside speakers, as well as to learn about the research activities of other undergraduates. The program for Fall Semester 2000 was centered around a series of lectures by BMB faculty members that comprise a course, BCH 101, commonly called "Meet the Profs" (see **http://www.bch.msu.edu/courses/BCH101.htm** for a schedule of speakers and their topics). This course was initiated a few years ago and was intended primarily as a mechanism by which incoming biochemistry majors (mostly freshmen and sophomores) could learn more about their chosen field as well as become familiar with faculty members of the Department and their research interests. The lectures were open to BMB Club members and other interested undergraduates, even if they were not enrolled in the course.

In addition, Club President Janel Funk organized a Genomics Symposium in which BMB faculty members Christoph Benning, Pamela Green, John LaPres, and Dean DellaPenna discussed the increasingly important field of genomics and its applications. Also on the Fall Semester program was Greg Zeikus, Professor of Biochemistry and Molecular Biology and President of the Michigan Biotechnology Institute, presenting his well-informed opinions on the current activities and future trends in biotechnology. Dr. Zeikus' talk was co-hosted by the International Society of Pharmaceutical Engineers, another club on campus. Both the Genomics Symposium and Dr. Zeikus' talk were well-attended, reflecting the current interest in these topics.

Activities scheduled for Spring Semester 2001 include a Career Fair that took place on Jan. 30; this has been a popular activity, which provides a means for students to explore various career options that might be open to them with an undergraduate degree in biochemistry. Other Spring Semester activities are largely focused on undergraduate research, including a poster session at which undergrads can present their results in the poster format and discuss them with others informally. More formal presentation of research reports will occur in a Biochemistry Undergraduate Research Forum as well as a university-wide Research and Creative Arts Forum. The annual departmental Awards Banquet is scheduled for April 19 and will include presentation of the Boezi Award to Dr. Tony Serianni (see above) as well as recognition of the accomplishments of undergraduate and graduate students, including presentation of the Outstanding Graduate Student and Outstanding Undergraduate Student Awards.

Zach Burton

While, ideally, one might hope that interest in the program would be sufficient inducement to draw undergraduates to these activities, reality, as always, wins out. Thus, it has become customary that many of these events include the added attraction of free pizza and pop.

REF Center for Biological Modeling Is Established

The Research Excellence Fund Center for Biological Modeling was established on July 1, 2000. The purpose of the Center is to foster interdisciplinary research between the biological and physical/computational sciences in modeling important biological processes. Faculty from several departments are affiliated with the Center, including faculty from the Departments of Biochemistry and Molecular Biology, Chemistry, Computer Science and Engineering, Crop and Soil Science, Epidemiology, Microbiology and Molecular Genetics, Physics and Astronomy, and Zoology. Leslie Kuhn, Associate Professor of Biochemistry and Molecular Biology, serves as Director of the Center, with Bob Cukier, Professor of Chemistry, as Associate Director. Shelagh Ferguson-Miller, Professor and Associate Chair of the Department of Biochemistry and Molecular Biology, is another BMB faculty member involved with the Center.

The Center for Biological Modeling is developing a range of programs emphasizing interdisciplinary approaches toward modeling of biologically important processes such as protein folding, biomolecular catalysis, the spread of disease, rational development of drugs, and the evolution of organisms and molecules. These programs include a graduate/postdoctoral research awards program, new courses in biological modeling, a seminar series as well as annual conferences and workshops, and an incoming visitors program which provides support for short (several days) to long-term (year-long sabbatical) visitors who collaborate with MSU faculty members on research in the general area of biological modeling. For more information, see the Center's web site (**http://biomodel.msu.edu**) or contact the Center's Administrative Assistant, Helen Geiger (geiger@msu.edu).

Shelagh Ferguson-Miller

Leslie Kuhn

The Center for Biological Modeling is developing a range of programs emphasizing interdisciplinary approaches toward modeling of biologically important processes such as protein folding, biomolecular catalysis, the spread of disease, rational development of drugs, and the evolution of organisms and molecules.

Graduates Spring 2000 - Spring 2001

Ph.D. and M.S.

Spring 2000

Fan, Li	Ph.D.
Lakkides, Karen	M.S.
Mao, Yifan	M.S.

Summer 2000

Thuresson, Elizabeth	Ph.D.

Fall 2000

Binderup, Kim	Ph.D.
Ichikawa, Hiroshi	Ph.D.
Laakko, Tonya	Ph.D.
Smith, Timothy	Ph.D.
Tonukari, Nyerhovwo John	Ph.D.

B.S. - Undergraduates

Spring 2000

Agrawal, Ritesh	BCH
Almy, David	BCH
Boehm, Melissa	BCH
Booms, Jon	BCH
Fruner, Darcy	BCH
Itkin, Yana	BCH/BT
Jones, Stephanie	BCH
Lopez, Santiago	BCH
Mahajerin, Ali	BCH
Michalik, Brian	BCH
Micielli, Renee	BCH
Paddock, Troy	BCH
Sanborn, Marla	BCH/BT
Sanderson, Todd	BCH
Saziru, Tiriza	BCH
Schaefer, Kevin	BCH

Summer 2000

Miller, Sarah	BCH
Littlepage, Eric	BCH/BT
Okonkowski, Jessica	BCH
St. Charles, Amy	BCH
Walsh, Matthew	BCH

Fall 2000

Boyce, Adam	BCH
Eastman, Jeffrey	BCH
Hindash, Ammar	BCH/BT
Nyquist, Otto	BCH/BT
Rowbottom, Christopher	BCH
Tadesse, Dawit	BCH

Spring 2001*

Alhumaidi, Fauzi	BCH
Barnafo, Emma	BCH/BT
Bewernitz, Mark	BCH
Book, Catherine	BCH
Carbeno, Stacey	BCH
Carlson, Tiffany	BCH
Cha, Keith	BCH
Domzalski, Alison	BCH
England, Kristen	BCH
Kachel, C. Alan	BCH
Kehrer, Robert	BCH
Kidd, Stephen	BCH/BT
Lito, Piro	BCH
Losiniecki, Andrew	BCH
Pickering, Curtis	BCH
Ranke, Sarah	BCH
Rosenlund, Nina	BCH/BT
Russell, Ryann	BCH/BT
Smith, Stacey	BCH
Woolley, Brook	BCH/BT
Wright, Kevin	BCH

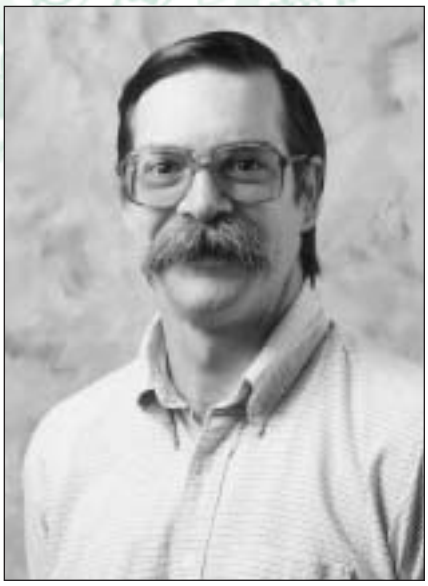
As of the date this is written. There may be other students applying for graduation later this semester.

The Hughes Undergraduate Research Scholars Program

With support from the Howard Hughes Medical Institute, a specialized program has been developed for highly motivated MSU undergraduates with a strong interest in research in the biological sciences. The Hughes Undergraduate Research Scholars Program (HURSP) will provide undergraduate research training for 15 to 20 new participants each year, with special focus on minorities underrepresented in science. The primary emphases in the training program are biochemistry, cell and molecular biology, and molecular genetics, areas in which there is a strong research base at Michigan State University. There is a major laboratory component to the program, which provides students with experience in using sophisticated experimental methods required for contemporary research in the biological sciences.

Funding for the program resulted from a proposal written by Estelle McGroarty, Professor of Biochemistry and Molecular Biology and Associate Dean in the College of Natural Science. Dr. McGroarty serves as Director for the program, and is assisted by a Scholars Committee comprised of: Bill Henry and Jack Preiss, both Department of Biochemistry and Molecular Biology faculty members; Dr. Neil Bowlby, a Specialist who serves as coordinator of the undergraduate laboratory courses in the Department of Biochemistry and Molecular Biology; Larry Snyder, Professor of Microbiology and Molecular Genetics; and Dorothy Reed, Coordinator of the Charles Drew Science Enrichment Laboratory. The Scholars Committee serves as a source of advice on both the operation of the program as well as the selection of students to be admitted.

Estelle McGroarty



Neil Bowlby

Research training is initiated with a ten week Workshop during the summer following the student's sophomore year. The Summer Workshop is organized and run by Dr. Bowlby, and prepares the Hughes Research Scholars for advanced undergraduate research experiences, conducted in the laboratories of faculty mentors during their junior and senior years. Hughes Research Scholars are provided a research stipend of $4,000 per year and devote at least 8-10 hours per week to their research projects. The Scholars also attend bi-weekly meetings, during which there is discussion of topics in molecular biology and genetics. A major strength of the program is that

Andrew Antczak and Jon Kaguni

Janel Funk and Zach Burton

students work on an original research project that may lead to publication(s) in a high quality peer-reviewed journal. In addition to being a valuable research experience, this also enhances the credentials of the student seeking entrance into graduate or professional school.

Hughes Research Scholars who are currently seniors in the Department of Biochemistry and Molecular Biology are listed below, along with their faculty mentors and a brief description of their research project.

Andrew Antczak, working in the laboratory of Jon Kaguni, Professor of Biochemistry and Molecular Biology. Andrew is working with DnaA protein, a DNA binding protein involved in replication of the E. *coli* chromosome. Analysis of the predicted secondary structure of DnaA suggests that the DNA binding domain of DnaA does not resemble any of the known DNA binding motifs: helix-turn-helix, helix-loop-helix, leucine zipper, or zinc finger. Thus, the DNA binding domain of DnaA could represent a fifth and novel DNA binding motif. Andrew has shown that DNA binding is associated with the C-terminal region of DnaA. A polypeptide representing this region binds to oriC, the region of the DNA to which DnaA binds, with affinity and specificity similar to that seen with the intact DnaA protein. Andrew is now attempting to solve the structure of this polypeptide by NMR spectroscopy. He also hopes to co-crystallize the peptide with a 23-bp oligonucleotide representing the sequence bound by DnaA. Other planned studies include genetic experiments aimed at determining whether the C-terminal polypeptide is lethal at high doses in DnaA-dependent bacteria.

Janel Funk, working in the laboratory of Zach Burton, Associate Professor of Biochemistry and Molecular Biology. Janel's research project is to complete a mutagenic analysis of the N-terminal domain of human RAP74, the larger subunit of transcription factor IIF (TFIIF). She constructed 22 novel mutants in the region from amino acids 1-136. Mutant proteins were isolated and assembled with the RAP30 subunit for analysis in transcription assays. To date, seven mutants have been analyzed for the ability to assemble a

Continued on page 28

The Hughes Undergraduate Research Scholars Program

Continued from page 27

Doug Luckie and Errett Hobbs

preinitiation complex containing TATA-binding protein (TBP), TFIIB, RNA polymerase II and TFIIF. Each of the mutants was able to bring RNA polymerase II into the preinitiation complex, as does wild type TFIIF. Presently she is testing the accuracy of transcription by these mutants from the adenovirus major late promoter. The activity of RAP74 mutants in elongation rate stimulation will also be determined. Of particular interest is testing the hypothesis that TFIIF stimulates elongation by affecting the functional dynamics of RNA polymerase II. These studies are expected to provide new insight into the structure and function of TFIIF and the role of this factor in regulating transcription.

Errett Hobbs, working in the laboratory of Doug Luckie, Assistant Professor of Physiology and in Lyman Briggs School. Cystic fibrosis is an autosomal recessive disease that affects approximately 1 in 2000 white Caucasians. Previous studies have indicated that CF cells (cells that have the mutant protein causing cystic fibrosis) exhibit increased rates of extracellular acidification. Errett and others in the Luckie laboratory are attempting to lower the expression of the normal CF protein, called CFTR, in a stepwise manner in order to determine if extracellular acidification is dose-dependent with respect to the expression of CFTR. Initial experiments aimed at decreasing expression of CFTR will be done by stably transfecting Calu-3 cells with plasmids that constitutively express mRNA transcripts antisense to exons 1-6 of CFTR. Successful transfectants will be identified by performing Northern blots to quantitate the expression of antisense CFTR transcript. The expression of CFTR may be further decreased by incubating the stably transfected Calu-3 cells in media containing antisense CFTR oligonucleotides.

Jason Jens, working in the laboratory of Steve Triezenberg, Professor of Biochemistry and Molecular Biology. *Arabidopsis thaliana* responds to cold temperatures by activating several genes (called COR genes) to effect a survival mechanism for itself. This activation is done by the transcription factor, CBF1. It is hypothesized that CBF1 activates the COR genes by a mechanism homologous to the yeast ADA genes. Through yeast and human studies, the ADA proteins have been found to exist in large complexes (ADA2, GCN5, GAL4, among

Steve Triezenberg and Jason Jens

Andy Losiniecki and Honggao Yan

others). In addition, the ADA proteins are highly conserved from yeast to plants and even to humans. From these studies, it has been shown that ADA2 and GCN5 interact with each other. With this established, the question becomes "What other proteins might interact with ADA2?" Jason is exploring the hypothesis that other components of the ADA complex and/or transcription factors might bind ADA2.

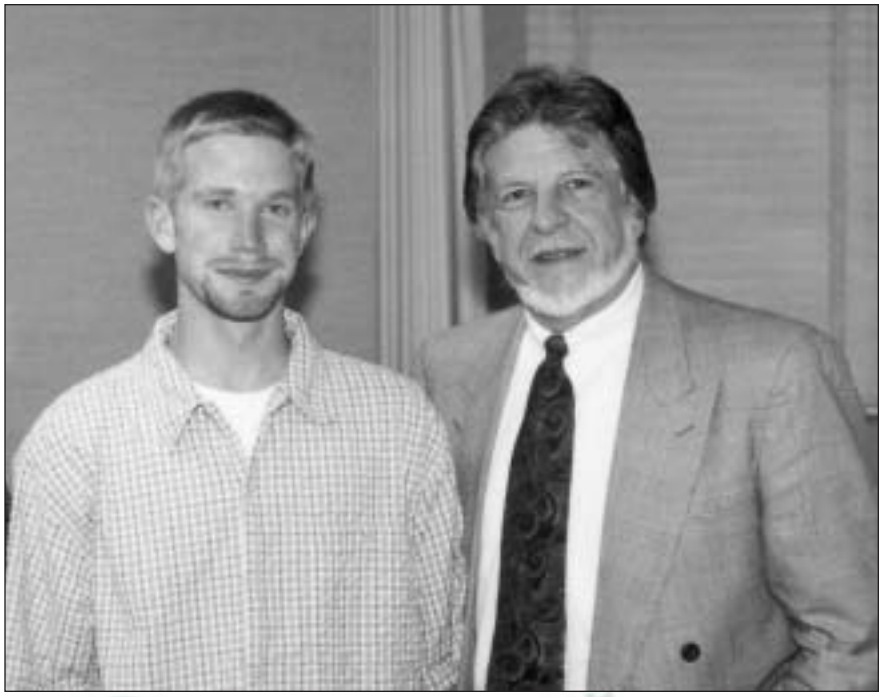
Andrew Losiniecki, working in the laboratory of Honggao Yan, Associate Professor of Biochemistry and Molecular Biology. Andrew is continuing work with the human dUTPase, the enzyme that catalyzes the hydrolysis of dUTP to dUMP. The focus of Andrew's work is on the flexible C-terminal arm of this protein molecule, which is believed to be involved in the catalytic activity of the enzyme. He has been investigating a mutant form of the human dUTPase, which has been found to have an activity only about 0.5 % of that seen with the wild type enzyme. However, since an even larger reduction in activity was expected, he hypothesizes that contamination may still be present. Two types of contamination are possible. One would be the presence of trace amounts of the wild type human enzyme, which is considered quite unlikely. The other might be the presence of dUTPase from E. *coli*, the organism in which the mutant human enzyme is expressed, in amounts great enough to account for the activity measured. If these possible contaminants can be ruled out, studies with the mutant enzyme can proceed with confidence that results obtained truly reflect properties of the mutant protein.

Continued on page 30

The Hughes Undergraduate Research Scholars Program

Continued from page 29

Curtis Pickering, working in the laboratory of Jim Trosko, Professor of Pediatrics and Human Development. Curtis has been investigating the effects of the signal transductant nitric oxide (NO) on gap junctional intercellular communication (GJIC). He has found that NO transiently inhibits cell-cell communication via gap junctions while activating the MAPK pathway ERK1/2. He hopes to use an ERK1/2 inhibitor to determine if GJIC inhibition occurs through ERK1/2 activation or through a separate pathway. He plans to determine if the gap junction protein is nitrosylated during NO induced inhibition as this may be another factor in its inhibition. He is also working on another project aimed at purifying the gap junction protein, connexin 43 (Cx43), for mass spectrometric analysis.



Curtis Pickering and Jim Trosko

News from Past Graduates

The concluding section in the last issue of this magazine provided some information about several past graduates of this department. Since that time, several other alums have responded to the request to let us know what life has brought to them since they left MSU, and we thank them for that. Their responses are collated below. Look them over and you might see a familiar name, and perhaps the opportunity to renew contact with a friend from your days at MSU. If you don't see your name below (or even if you do), we invite you to use the form attached to this publication to bring us up-to-date on your post-graduation activities and current position. You can use the postage-paid envelope to return the form to us or, if you prefer, send the information by e-mail to bchalum@msu.edu. We look forward to hearing from you!

McKenna, Timothy M. - BS '73:

Tim also received his DO degree from MSU in 1976. He is board certified in general surgery and is in a general surgery practice in the Lansing area. He currently serves as Vice-Chair of the Department of Surgery for Sparrow Health Systems and can be contacted by mail to 1209 Windale Place, East Lansing, MI 48823.

Cichy, Michael G. - BS '78:

Mike is Environmental Technology Manager for Rohm & Haas, and can be contacted by mail to 7449 Leonard, Manistee, MI 49660.

Rogers, Clare E. - BS '81:

Clare has been working in research since her graduation in '81, first at the Michigan Cancer Foundation in Detroit, and subsequently in the Departments of Internal Medicine and of Chemical Engineering at UM in Ann Arbor. She is currently a research specialist in the Howard Hughes Medical Institute at UM. She received an MS in Bioengineering from UM in 1990. For the past 14 years her speciality has been in operation of flow cytometry instrumentation, first as manager of the core flow cytometry facility at UM and now for the Howard Hughes Medical Institute. Clare tells us that she married in 1983 and currently has two school-age daughters. Clare can be contacted at the Howard Hughes Medical Center, 1150 W. Medical Center Drive, Ann Arbor, MI 48109.

Weston, Matthew - BS '84:

Matthew is Director of Technical Services for Resinall Corp. He can be contacted by mail sent c/o Resinall Corp., P.O. Box 195, Severn, NC 27877.

McCoy, Andrea J. (Titlow) - BS '95:

After graduation, Andrea spent a year in the graduate program in medicinal chemistry at the University of North Carolina - Chapel Hill, then switched to the Department of Biochemistry and Biophysics where she worked on the effects of the HA-fusion peptide on membrane fusion. After marriage in 1998, she moved to the Texas Health Science Center in San Antonio where she worked on mechanisms of bacterial resistance to antimicrobial peptides. Currently, Andrea is in the Molecular and Cell Biology graduate program at the Uniformed Services University of the Health Sciences in Bethesda, MD; her research interests are in the area of bacterial pathogenesis. Andrea can be contacted at her home address, which is 6546 Creek Run Drive, Centreville, VA 20121, or by e-mail at ajmccoy8@hotmail.com.

Hoard, Heidi M. - BS (Lyman Briggs) '96:

Heidi is currently completing her Ph.D. work at the Mayo Clinic in Rochester, MN. Her thesis

"I haven't mastered the Minnesotan accent yet and I don't get the Norwegian jokes, but I've managed to avoid Lutefisk and enjoy Minnesota hot dish."

work is focused on the interactions of electron transferring flavoprotein with dimethylglycine dehydrogenase, sarcosine dehydrogenase, and the acyl-CoA dehydrogenases, and involves the use of both mass spectrometry as well as traditional enzymological approaches. She states that her education and research experience at MSU have helped her be an independent, successful graduate student. Heidi also notes that she has been involved with the Upward Bound program, helping high school students enrolled in the program improve their math and science skills. The Minnesota winters have also been occasion for her to learn to enjoy snowshoeing, cross-country skiing and quilting. Heidi states: "I haven't mastered the Minnesotan accent yet and I don't get the Norwegian jokes, but I've managed to avoid Lutefisk and enjoy Minnesota hot dish." Heidi can be contacted at 1006 N. Broadway, Apt. 3, Rochester, MN 55906, or by e-mail at hoard.heidi@mayo.edu.

Fruner, Darcy L. - BS, '00:

Since her recent graduation, Darcy has been a Laboratory Professional with Pharmacia & Upjohn in Kalamazoo. She can be contacted at 3215 Stonebridge Court, Apt. 7, Portage, MI 49024, or by e-mail at frunerda@msu.edu.

Kubinec, Mark G. - BS, '87:

After completing his degree at MSU, Mark went on to graduate work and received a Ph.D. Chemistry from the University of California, Berkeley. He can be contacted at 6039 Park, Richmond, CA 94805.

Melcher, Ulrich - PhD, '70:

In May of 1999, Ulrich was named as the first incumbent of the Robert J. Sirny Professorship in Agricultural Biochemistry at Oklahoma State University. Ulrich's research interests are focused on plant viruses and their molecular evolution. Ulrich can be contacted at the Department of Biochemistry and Molecular Biology, 246 NRC, Oklahoma State University, Stillwater, OK 74078, or by e-mail at umelcher@biochem.okstate.edu.

Desrosiers, Ronald C. - PhD, '75:

Ron Desrosiers sent us a nice note expressing his satisfaction with the previous issue of this departmental magazine. Ron has had a distinguished career since his days at MSU, and his achievements were recognized with the Boezi Award that he received in 1989. Ron is currently Professor of Microbiology and Molecular Genetics at Harvard Medical School and Director of the New England Regional Primate Research Center. He can be contacted at Harvard Medical School, New England Regional Primate Research Center, One Pine Hill Drive, Box 9102, Southborough, MA 01772-9102, or by e-mail at ronald_desrosiers @hms.harvard.edu.

Norris, Joanna (Hanks) - PhD, '82:

Joanna is currently Associate Professor and Health Professions Advisor at the University of Rhode Island. She can be contacted at Department of Biological Sciences, Ranger Hall, University of Rhode Island, Kingston, RI 02881, or by e-mail at jnorris@uri.edu.

Washburn, Michael P. - PhD, '98:

Mike was the last graduate student who worked under the mentorship of Professor Bill Wells, who retired last year. Mike moved to Seattle to begin postdoctoral work with Dr. John Yates at the Univ. of Washington, but Professor Yates soon moved his lab to the Scripps Research Institute in San Diego, where he also accepted a position as Director of Proteomics at the Novartis Agricultural Discovery Institute. Mike and several other members of the Yates laboratory also made the move to San Diego, and Mike currently holds a position as Staff Scientist, Protein and Metabolite Dynamics, with the Novartis Agricultural Discovery Institute. He can be contacted by mail to 1571 Avenida de los Linios, Encinitas, CA 92024.

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Contributions from past students and other supporters of the Department of Biochemistry and Molecular Biology provide funding for several departmental awards and developmental activities. Endowment funds have been established to provide support for the William W. Wells and N. Edward Tolbert Lectureships and the John A. Boezi Memorial Alumnus Award. Additional endowment funds are the Biochemistry Undergraduate Endowed Scholarship Fund and the Biochemistry Enrichment Fund. Unrestricted financial gifts to the Department are also used for these activities.

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We want to hear from you!

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What have you been up to since graduation? Please include any information about research projects, awards, personal events, etc., that you would like to share with fellow alumni and former classmates.

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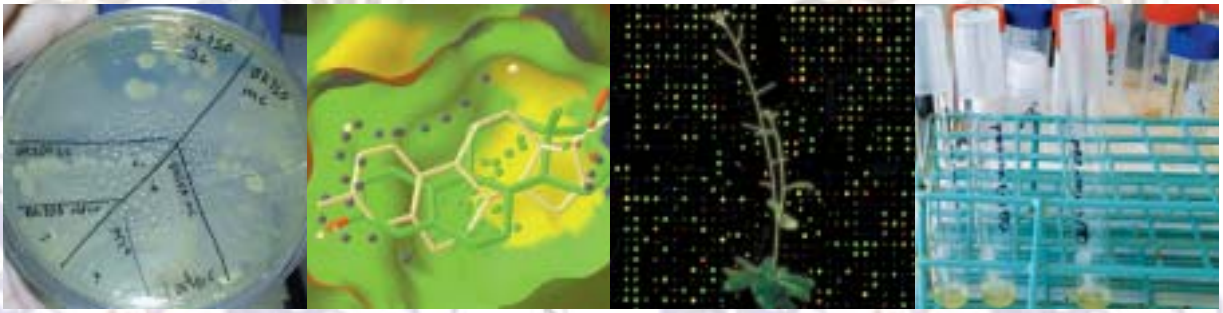

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