Contents

Comments from the Chair ............................................................... 5
Progress and Prospects at the Medical Center ................................. 6
Faculty News ................................................................................. 8
Alumni News ................................................................................. 10
Transitions .................................................................................. 12
1997 Entering Students .................................................................. 13
Degrees Granted ........................................................................... 14
Gifts 1996-97 ................................................................................. 14
Research Activities:
  Philip Andrews, Ph.D. ................................................................. 15
  William Jourdan, Ph.D. ............................................................... 18
  Ron Taussig, Ph.D. ..................................................................... 21
  Debra Thompson, Ph.D. ............................................................ 23
Social Hour in Washington, DC .................................................... 25
Student Awards ............................................................................ 26

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From the Chair....

I would like to highlight several items that have taken place in our teaching efforts our past year or so. Then I will comment on a couple of awards that our faculty have received for their distinguished research efforts. I should also indicate that the University and the Medical School Administration has undergone considerable change in the past year or so. Irwin Goldstein, a member of our faculty who also serves as the Associate Dean of Research, details some of these changes in his section in this Newsletter. Briefly, Lee Bollinger, Nancy Cantor, and Gil Omenn our are new president, provost and executive vice president of medical affairs, respectively. I have had a chance to get to know each of them, and I think we are really fortunate to have people of this caliber leading a great institution like ours.

We have made substantial changes during the past few years in our course offerings. A new course for our graduate students focuses on helping them critically analyze research results and aids them in designing new experiments. This was an effort originally developed by Laurence Mathews and is now taught by both Laurence and Ron Taussig. In addition, four years ago we completely reorganized the Medical School’s first-year curriculum. Biochemistry’s Cell and Molecular Biology course directed by Don Hultquist and Claudia Kent has been a major success. It is a team taught course which includes faculty from Biochemistry, Physiology, Pathology, and Microbiology. This integrated course has become a model that is widely copied inside the University as well as at other institutions. In addition to the conventional lecture format, medical students also participate in small group sessions and in clinical correlations. We have also completely redone our teaching efforts in biochemistry courses given to the dental and nursing students. Renny Franceschi and Carolyn Worby are directors of these two courses respectfully. These courses now include clinical correlations which are relevant to dentists and nurses. Finally, Alex Ninfa and David Ballou have just published a biochemistry laboratory textbook. This was a product of their efforts in teaching our laboratory course for undergraduates on campus. I am particularly pleased with the dedication and hard work that our faculty puts forth in their teaching efforts.

Now I would just like to comment on a couple of the major awards that our faculty have received during the past year. First, Michael Marietta was appointed a senior investigator of the Howard Hughes Medical Institute. This is a very prestigious honor which follows a national competition for these positions. We are currently renovating space on the fifth floor to accommodate Michael. With the completion of this construction, Michael’s laboratory will be located in Biological Chemistry and this will bring several of our investigators interested in enzymology together. Michael will join several HHMI investigators in our department. They are: Randy Kaufman, Tom Kerppola, Ben Margolis, and Gary Nabel. In February, Vince Massey received notification that he is being honored as the Michigan Scientist of the Year. Each year the State of Michigan recognizes a distinguished scientist, a distinguished teacher, and an industrialist with this honor. Congratulations to Vince! These are only two of the many highlights of our faculty and students. Highlighted in other sections of this Newsletter are described additional honors, awards, and recognition of both the students and faculty.

I again hope to see all of you at the American Society for Biochemistry and Molecular Biology meeting in Washington, DC this year. We will be having our annual University of Michigan Biochemistry Reception on May 19, 1998. I hope all of you can join us at this event.
Progress and Prospects at the Medical Center

by Irwin Goldstein Professor of Biological Chemistry and Associate Dean for Research and Graduate Studies

Last year I described the structural and physical changes in the Medical School and Center — the dedication and opening of the new Cancer Geriatrics Center, renovations in the Medical School, etc. In this note I will concentrate on personnel and programmatic changes and innovation in the Medical School and Central Campus.

Our new President, Lee Bollinger, has been busy assembling his new executive management team. Among these are the appointment of Nancy Cantor as Provost and Executive Vice President of Academic Affairs. You may recall that Nancy, a Professor of Psychology, was brought back to campus from Princeton University, where she was Chair of Psychology, to be Dean of the Rackham Graduate School. She has a good appreciation of our Medical School graduate programs and served us well while she was in Rackham, but President Bollinger tapped her for Provost and Vice President for Academic Affairs. She now resides in the Fleming Building.

Nancy’s replacement, the top candidate of the search committee, is Earl Lewis, Professor of History and Afro-American and African Studies, who was already serving as Interim Dean of the Rackham Graduate School. He also is acquainted with our Medical School graduate programs.

Additionally, Fred Neidhardt has agreed to a one-year extension as Vice President for Research during which a national search for a successor will be instituted.

Gilbert Omenn, the new Executive Vice-President for Medical Affairs, has been involving himself in all aspects of the Medical School and our Health Care System — academic programs, hospital affairs, technology transfer, forging new relationships with industry and other health care systems. He also announced the formation of a search committee for Dean of the Medical School and indicated his preference for a clinical chair nominee.

Several exciting, new, programmatic initiatives have been announced by A. Lorris Betz, the Medical School Interim Dean. These are: Basic Science Research Partnership Fund ($1.5 million) — to support collaborative basic research projects involving PIs who devote the majority of their effort to basic science research and co-investigators who devote the majority of their effort to patient care. Preference will be given to newly established collaborations between junior investigators and established investigators who are pursuing research beyond their area of expertise, and also to applications for short-term interim support between funded grant periods. Up to $25,000/year is available. New research ventures may be funded for 1-2 years; interim support may be funded for up to 1 year. Applications will be reviewed and funding decisions made by the Biomedical Research Council.

Clinical Research Partnership Fund — to support collaborative patient-based research projects involving clinical faculty PIs and co-investigators who spend the majority of their effort in basic research, either within the same or a different department in the Medical School or other academic units of the University. Preference will be given to new collaborations involving PIs who are new clinical investigators or established investigators pursuing research in new areas. Up to $50,000/year for 1-2 years is available. Funds may be used in part to support the academic salary of faculty provided the requested amount is matched by an equal commitment from the department. Applications will be reviewed and funding decisions made by the Advisory Council on Clinical Research which was established in October 1997.
**Technology Venture Fund** ($0.5 million) — to provide “gap” funding for research and development to increase the transfer potential of concepts that have already demonstrated promise through basic research, but are not yet ready for venture capital investment. Up to $50,000 total to be spent over 1-2 years. Funds may be used in part to support the academic salary of faculty provided the requested amount is matched by an equal commitment from the department. Applications will be reviewed and funding decisions made by the Technology Transfer Advisory Council which was established in October 1997.

**Medical Education Scholars Program** ($0.5 million) — to improve the teaching skills and prepare Medical School Faculty for leadership roles in medical education through participation in a structured curriculum of study involving one half-day per week and completion of a guided independent study project. An average of 12 faculty will be admitted to the program each year. Funds will be used to provide seed money for projects (up to $5,000/project) for program administrative support, and for faculty salary support of up to $7,500 provided the requested amount is matched by an equal commitment from the department. Up to two faculty may be nominated by each department chair. Applications will be reviewed by the program steering committee with input from the Curriculum Policy Committee. Funds for these programs come from the efforts of our clinical faculty and staff in reducing clinical expenses during the past year.

Additional programs announced by the Executive Vice-President for Medical Affairs include a **Biomedical Sciences Scholars Program** ($2,000,000). The purpose of this program is the creation of a strategic plan with corresponding dedicated funds to recruit outstanding scientists in key areas of investigation across multiple departments and schools. The goal of this program is to develop a whole new generation of leaders in biomedical research at our institution. This program will provide an attractive package of institutional resources for academic units within the University and will include a funding pool of $2 million for distribution over and above usual departmental commitments. Facilitation of recruitment opportunities for such individuals will accomplish the following:

- Enhance the University’s visibility in key areas of biomedical science through the successful recruitment of high profile scientists;
- Enable the University to compete effectively with peer institutions for investigators likely to be in significant demand;
- Help build strong interdisciplinary research initiatives in areas such as cell biology, structural biology, molecular genetics, neuroscience, and immunology.

The nomination process for the Biological Sciences Scholars Program will be coordinated and overseen by an interdisciplinary research committee, which also serves as the Howard Hughes Medical Institute Dean’s Advisory Committee. This committee includes representation from the College of Literature, Science & Arts, College of Pharmacy, and the Medical School. It is chaired by Jack Dixon.

Additional monies have been allocated to establish two centers: **Gene Therapy**, and **Organogenesis**. The first, under the leadership of Gary Nabel, a Howard Hughes Investigator and member of the Department of Biological Chemistry, involves basic research in molecular virology, stem cell biology, gene expression, and gene targeting. Clinical disorders targeted for application include cancer, cardiovascular disease, HIV and immune disorders. The Center for Organogenesis is an interdisciplinary, cross-campus program, organized to investigate the growth and development of organ systems. It is under the current leadership of Deborah Gumucio, Department of Anatomy and Cell Biology. Search for a permanent Director is underway.
Of significant interest to our Department of Biological Chemistry and all of the other departments is the development of a plan for a new administrative structure for the recruitment and admission of graduate students at the University of Michigan Medical School. At issue is a complete revision of the manner in which the departments recruit, admit, and provide stipends and tuition for graduate students. The first year curriculum is also under scrutiny. As you can imagine, there is heated debate regarding the merits of such a system. The program allows students complete flexibility in their choice of laboratories for rotation and final choice of mentors and Departments or Programs for matriculation for the Ph.D. degree. Several schools (Vanderbilt, UCLA, Washington University (St. Louis)) claim great success in attracting excellent students in this way. Several “Town Meetings” to discuss the administration and merits of the new system are planned. We would be very interested in any comments our former students would like to make.

After almost twelve years in the Dean’s Office, I intend to “step down” from my administrative duties this coming September. It has been a rewarding experience and one which has enabled me, and the colleagues in my office, to bring enhanced recognition and support to our biomedical research (enterprise) community and to the contributions of the Basic Science Departments.

During my tenure, the title of the office I occupy was changed to include graduate studies: The Office of Research and Graduate Studies. The Ph.D. programs of the Basic Science Departments were given the importance they deserve: there was additional financial support for graduate student tuition and stipends (although still insufficient); a new graduate student medical insurance program; the establishment of a $1 million dollar graduate student endowment as well as a 2:1 matching Basic Science Departmental endowment program ($250,000); the appointment of an Assistant Dean with primary responsibility for Graduate Student Programs; and the establishment of a very active Graduate Student Council with representatives from each of the Departments and Graduate Programs and an Association of Multicultural Scientists. Awards for outstanding graduate student teaching were also established.

During my term in office, we have succeeded in consolidating a collection of world class biomedical research core facilities on a single floor of the new Medical Research Building II; and in obtaining a generous annual subsidy to operate the facilities. These include a Biopolymer Core (protein characterization - amino acid analysis, N-terminal sequence, molecular mass, polypeptide and DNA synthesis, and carbohydrate compositional analysis); DNA sequencing core; transgenic animal facility with knockout capabilities; and NMR facility.

I leave with the satisfaction of knowing the next Associate Dean for Research and Graduate Studies will have a firm groundwork on which to build further support for our Research and Graduate Studies in the Medical School.

Faculty News:

Bernie Agronoff: was made a Fellow of the American Association for the Advancement of Science.

Dave Ballou: received a National Institutes of Health MERIT award.

Jud Coon: was made an Honorary Member of the Society of Toxicology in recognition of outstanding and sustained research contributions to biochemical toxicology and was given a commemorative plaque at the Society’s annual meeting in Seattle. He continues to be Foreign Adjunct Professor at the Karolinska Institute, Stockholm, and is on the Advisory Committee for the 12th
International Symposium on Microsomes and Drug Oxidations to be held in Montpellier, France, in July.

**Jack Dixon:** was honored by election as Fellow of the American Academy of Arts and Science.

**Bill Folk:** after nine years as Chair of Biochemistry at the University of Missouri-Columbia, is now returning to the laboratory. He reports that Sarah Scanlon, who managed his labs in Ann Arbor, Austin, and Columbia, says she is looking forward to his being back in the lab. He collaborates with several former students, including Shelley Berger and **Steve Triezenberg**, from his U-M days. His wife **Martha** is practicing landscape architecture, and his children Jennifer and Torrey are pursuing sustainable farming and olympic rowing, respectively.

**Renny Franceschi:** is Associate Dean for Research at the University of Michigan Dental School.

**Bob Fuller:** is Vice Chair of the 1998 Gordon Conference on Hormonal and Neural Peptide Biosynthesis.

**Ari Gafni:** was made a Fellow of the Gerontological Society of America.

**Amiya Hajra:** received the Distinguished Research Scientist Achievement Award of the University of Michigan.

**Claudia Kent:** is co-organizer of a Satellite meeting for the 1998 ASBMB National Meeting.

**Benjamin Margolis:** recipient of the 1997 Young Investigator of the Year Award from the American Society of Nephrology/American Heart Association.

**Michael Marletta:** in addition to his appointment as a senior investigator in the Howard Hughes Medical Institute, is co-chair of the ASBMB’s 1998 Annual Meeting Program Committee and chair of the ACS Biological Chemistry Division’s Annual Meeting Program Committee.

**Vincent Massey:** will be honored with the 1998 Michigan Scientist of the Year award at the Impression 5 Science Museum in Lansing.

**Rowena Matthews:** received a 1997 Distinguished Faculty Achievement Award from the University of Michigan. She is a Senior Fellow of the Michigan Society of Fellows and has received a MERIT award from the National Institutes of Health.

**Alexander Ninfa** and **David Ballou** (picted above): have written a textbook combining basic theory, techniques, and applications of biochemistry and biotechnology with laboratory exercises that reinforce scientific principles, entitled *Fundamental Laboratory Approaches for Biochemistry and Biotechnology*, published by Fitzgerald Science Press in April, 1998.

**Alan Price:** since 1990 has been Chief, Investigation Branch, Office of Research Integrity, for the U.S. Public Health Service. He visited our department in February and spoke at the U-M/Office of Research Integrity Conference on “Managing Integrity in Research.”

**Audrey Seasholtz:** received an NARSAD Young Investigator Award.

**Dennis Thiele** and **Ron Taussig** have initiated a weekly Postdoctoral Seminar series to showcase the work of our postdoctoral fellows, which now number over seventy.

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9
Alumni News:

Kagehiro Amano (postdoc with Randy Kaufman) is now an Assistant Professor in Clinical Pathology at the Tokyo Medical College.

Ruma Banerjee (postdoc with Rowena Matthews) has been promoted to Associate Professor of Biochemistry at the University of Nebraska.

Pimchai Chaiyen (Ph.D. with Dave Ballou and Vince Massey) has returned to Thailand, where she is now an Assistant Professor in the Department of Biochemistry at Mahidol University, Bangkok.

Eric Coulter (postdoc with Dave Ballou) is now at the University of Georgia in the Department of Chemistry, with Dr. Don Kurtz.

Louis DeFilippi (Ph.D. with Don Hultquist) has left Allied Signal Inc. He is presently a consultant and co-editor (along with Gordon Lewandowski of the New Jersey Institute of Technology) of "Biological Degradation of Hazardous Wastes," a Wiley Interscience book.

Jim Drummond (Ph.D. with Rowena Matthews) is now an Assistant Professor of Biology at Indiana University.

Brian Ernsting (Ph.D. with Rowena Matthews and postdoc with Jack Dixon) is an Assistant Professor of Molecular Biology at Evansville University.

Jim Fessenden (Ph.D. with Jochen Schacht) is now a postdoctoral fellow working with Dr. Isaac Pessah in the Department of Molecular Biosciences in the School of Veterinary Medicine at the University of California-Davis.

Verna Frasca (Ph.D. with Rowena Matthews) is now working with the Technical Support group at Pharmacia Biotech - now Amersham Pharmacia Biotech. She provides technical support for the molecular biology and chromatography media product lines and also has her own research program. Recently, she was promoted to Supervisor for Sequencing (automated and manual) technical support.

John French (Ph.D. with Jud Coon) is Professor of Chemistry and Biochemistry at the University of Alaska Fairbanks.

Elizabeth Gottlin (postdoc with Jack Dixon) is now a Scientist at Navalou Pharmaceuticals in Durham, North Carolina.

Hebe Guardiola-Diaz (Ph.D. with Audrey Seasholtz and postdoc with Jack Dixon) is an Instructor at the University of Michigan in the Department of Biology. She has accepted the position of Assistant Professor of Biology at Trinity College in Hartford, Connecticut, beginning next fall.

Fred Guengerich (postdoc with Jud Coon), was made a Fellow of the American Assoc. for the Advancement of Science and will succeed Jud as Chairman of the International Scientific Committee for the International Conferences on Cytochrome P450: Biochemistry, Biophysics, and Molecular Biology.

Chris Harris (Ph.D. with Vince Massey) is spending a year as postdoctoral fellow at the University of Varese, Italy, working with Professor Mirella Pilone.

Paul Hollenberg (Ph.D. with Jud Coon), Professor and Chair of the University of Michigan's Department of Pharmacology, is Co-director of the Cancer Pharmacology Program in the University's new Comprehensive Cancer Center and has joined the Editorial Board of the Journal of Pharmacology and Experimental Therapeutics.

Yulong Hong (postdoc with Kun-Liang Guan) is now a Scientist at Warner-Lambert Parke-Davis.

Joe Jarrett (postdoc with Rowena Matthews) has taken a position as an Assistant Professor in the Department of Biochemistry and Biophysics at the University of Pennsylvania.
Simon Labbé (postdoc with Dennis Thiele) was the recipient of a Centennial Fellowship from the Medical Research Council of Canada. This fellowship is only awarded to eleven young scientists throughout Canada.

Jane Larson (Ph.D. with Jud Coon) is living in Durham, NC, where she is Technical Sales Representative for Stratagene, whose headquarters are in La Jolla, California.

Erlund Larson (Ph.D. in Chemistry and M.D. at U of M, and postdoc with Jud Coon) is a Resident in Internal Medicine at the University of North Carolina Medical School in Chapel Hill.

Dan Lohse (postdoc with Jack Dixon) is now an Assistant Professor of Pharmaceuticals in the College of Pharmacy and Health Services at Drake University.

Anthony Lu (postdoc with Jud Coon), who recently retired from his position as Executive Director of Drug Metabolism at Merck Research Laboratories, will be honored by a colloquium entitled "Drug Metabolism in the New Millennium," to be held in April at the ASPET National Meeting. The speakers and session chairs include others with a connection to Michigan biochemistry: Jud Coon, Fred Guengerich, Paul Hollenberg, and Ron White.

Dermot McGinnity (postdoc with Jud Coon) has taken a position at Astra Charnwood, Loughborough, Leics, England.

Kevin Morano (postdoc with Dennis Thiele) was the recipient of a postdoctoral fellowship from the National Institutes of Health for his project entitled "Heat Shock Factor: Stress and the Cell Cycle.

Edward Morgan (postdoc with Jud Coon), Associate Professor of Pharmacology at Emory University, has been elected to the Executive Committee of the Drug Metabolism Division of the American Society for Pharmacology and Experimental Therapeutics.

Yerramilli Murthy (postdoc with Vince Massey) has been appointed as a Research Scientist with IDEXX Laboratories in Maine.

Youichi Niimura (frequent visiting scientist in the Massey lab) has been made a full professor at the Tokyo University of Agriculture.

Kyuichiro Okuda (visiting professor with Jud Coon) has retired from his faculty position at Hiroshima University and is now carrying out research in the Department of Surgery at Miyazaki Medical College in Japan.

Julian (Bill) Peterson (Ph.D. with Jud Coon) is President of the Faculty Senate at the University of Texas Southwestern Medical Center and Chair of the NIH Physical Biochemistry Study Section.

Eric Priuska (Ph.D. with Jochen Schacht) is now working at IA Inc., in Ann Arbor.

Chris Rohlman (Ph.D. with Rowena Matthews and postdoc with Dave Engelke) has been promoted to Associate Professor of Chemistry at Pomona College.

Richard Slaeter (postdoc with Jud Coon) is now Senior Program Director of the Pharmaceutical Products Development market sector at Battelle in Columbus, Ohio.

Toshiro Sugimoto (postdoc with Kun-Liang Guan) is now at Shega University in Japan.

Quinn Vega (postdoc with Jack Dixon) is now an Assistant Professor at Montclair State University.

Tetsufumi (Ted) Ueda (Ph.D. with Jud Coon), Professor of Pharmacology at Michigan, gave an invited lecture at the Excitatory Amino Acid Symposium held in Waterville Valley, New Hampshire, as a satellite to the 1997 Meeting of the International Society for Neurochemistry.

Zhiwu Zhu (postdoc with Dennis Thiele) is now an Assistant Professor in the Department of Biology at the University of California, Santa Cruz.
Transitions

Isadore A. Bernstein, Professor Emeritus of Biological Chemistry and of Environmental and Industrial Health, died January 11, 1998, at the age of 78. He was actively engaged in research to the very end. Is graduated with a Ph.D. degree in Biochemistry (under the mentorship of Harland G. Wood) in 1952 from Western Reserve University after serving as an officer in the army during World War II. Immediately thereafter, he accepted a joint appointment with the Institute of Industrial Health and the Department of Biological Chemistry at the University of Michigan, rising to the rank of Professor in 1968.

Is Bernstein’s research interests focused on cutaneous metabolism, encompassing molecular mechanisms in epidermal carcinogenesis, DNA repair, regulation of protein synthesis and keratinization. These studies resulted in the development of techniques for cultivating an “epidermis” in vitro, which enabled him to study terminal differentiation and how it might be affected by exposure to environmental chemicals and toxins. The investigations ran in parallel with his interests in biochemical mechanisms of accommodation to chemical, physical, and environmental stressors, leading to the development of predictive tests for human susceptibilities to environmental chemical agents. Innovatively, he used the in vitro epidermis to test pharmaceutical and cosmetic derivatives, thus avoiding the use of experimental animals. This approach was more cost-effective and humane. Moreover, using the patient’s own skin to initiate the epidermis, the procedure has been applied to burn therapy. More recently, autologous fibroblasts have been successfully tested as a protective covering over mechanical devices used in patients with congestive heart failure prior to implantation, thereby avoiding rejection.

During his 40-year career at the University, Dr. Bernstein trained and befriended many students of different nationalities, taking a paternal interest in their development and well-being, a task he undertook in partnership with his devoted wife, Claire. This interest in and encouragement of his students was recognized in 1989 by the Kunming Medical College, People’s Republic of China, which in 1988 conferred upon him an Honorary Professorship. Covering yet another facet of his activities, in 1989 he was awarded the Kussho, the Order of the Rising Sun, Gold Rays with Neck Ribbon, by the Government of Japan for his continuing service to further Japanese-American relationships in the field of epithelial cell differentiation.

Both Is and Claire were founding members of a committee of volunteers who came together to assist in the absorption of New Americans from the former Soviet Union. An active citizen of the University at large, Is served on, and indeed chaired, many committees beyond the boundaries of department and school covering a spectrum of topics which truly reflected his wide interests and commitments.

He will be remembered fondly by friends and colleagues for his kind, gentle, but persistent persuasive talents. Those seeking further information on Is Bernstein may access the webpage set up by his West Coast colleagues at www.psrc.ucsf.edu/PSRC/bome-page.htm. Contributions in memory of Dr. Bernstein may be made to the Isadore Bernstein Lectureship Fund and sent to Ms. Terri Mellow, Director of Development, School of Public Health, 3508 SPH I, University of Michigan, Ann Arbor, MI 48109.

— By David Aminoff

Beverly Dale-Crunk (Ph.D. in this Department, 1968), who works in the area of epithelial biology and is Professor of Oral Biology and Director of the Dental Scientist Program at the University of Washington in Seattle, has commented, “Isadore Bernstein’s influence extended far beyond his own laboratory work and that of his group. He brought together scientists working on skin proteins and dermatologists at a series of meetings that he organized at Boyne Mountain, Michigan. The result was that this field was moved to a new level with these intensive yet enjoyable meetings that eventually led to the long running Gordon...
Conference that remains a central focus of those committed to the field of epithelial differentiation. He will live on the memory of the many scientists whom he influenced.

**Bimal Bachhawat** (postdoc with Jud Coon) died in 1996, as reported in last year's Newsletter. In recognition of his many accomplishments, including a major impact on the development of science in India, contributions may be made to the "Professor B.K. Bachhawat Memorial Fund" and sent to Dr. Arabinda Guha, 111 Iden Ave., Pelham, NY 10803. The funds will be used for a postdoctoral fellowship to be administered by the Christian College and Hospital in Vellore, India, where Bimal was a faculty member early in his career.

Professor **Naba K. Gupta** (1934 - 1997) an alumnus of our department, passed away on September 16, 1997. The cause of his untimely death was pancreatic cancer.

Naba did his undergraduate studies (B. SC. with honors in Chemistry, 1954) at Calcutta University, India, where he also obtained his M. SC. degree in Applied Biochemistry in 1957. In 1958 he joined this department as a graduate student and did his Ph.D. thesis research under the late Prof. William Robinson. After graduating from the University of Michigan in 1963 he did his postdoctoral research first (1963-65) with Prof. Birgit Vennesland, at the University of Chicago, and next (1965-68) with Prof. Har Gobind Khorana, at the University of Wisconsin (Madison, WI). In 1968 he joined the faculty of the Chemistry Department, at the University of Nebraska (Lincoln, NE) as an Associate Professor, and he was promoted to full Professor in 1972. In 1994, in recognition of his meritorious research on protein biosynthesis, he was appointed as the Marshall Professor of Biotechnology at the University of Nebraska.

Naba's research was mainly on the enzymology and regulation of eukaryotic protein biosynthesis, especially the initiation of mRNA translation. He was the first to show that the eukaryotic translation initiation factor 2 (eIF-2) binds to the initiator met-tRNA in the presence of GTP, and the complex is then trans-ferred to the 40S ribosomal subunit for starting translation. In recent years he also showed that eIF-2 is regulated by phosphorylation (inhibition), and that a glycoprotein, p67, protects it from phosphorylation, thus keeping it active. Naba’s contribution in this area of research is well recognized internationally.

I have personally known Naba since our college days in India, and through our time as fellow graduate students sharing the same apartment in Ann Arbor in the early sixties. He was a warm-hearted, ebullient person who was utterly dedicated to scientific research. I, his friends and colleagues, family members and his many former students and postdoctoral fellows who are now carrying on his teachings both here and in India will dearly miss him.

— By Amiya Hajra

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### 1997 Entering Class of Graduate Students

**Heidi Campbell** is from Kaysville, Utah. She received her B.S. in Chemistry from Utah State University. Heidi received the James E. Casey Merit Scholarship of the National Merit Scholarship Corporation, and the Superior Student Scholarship from Utah State University.

**Chia-En Chen** is from Lansdale, Pennsylvania. She received her B.S. degree in Biochemistry at Union College in New York.

**Deborah John** is from Salt Lake City, Utah. Her undergraduate degree is from the University of North Carolina at Chapel Hill, where she was awarded the Miles Academic Scholarship and the Nancy Jo Abeys Scholarship.

**David Karnak** is from Parma Heights, Ohio. He received his B.S. (Biochemistry) degree from the University of Dayton, where he was a recipient of the President's Scholarship and a member of the Golden Key National Honor Society. *(Continued p. 26)*
Degrees Granted:

The Department extends its congratulations to the following students who completed their Ph.D. degrees since June of 1997:

David A. Ammar (Thompson) “Cloning of a Type 2 Neuropeptide Y Receptor and Characterization of Neuropeptide Y Responses in the Retinal Pigment Epithelium of the Eye.”

Pimchai Chaiyen (Ballou/Massey) “2-Methyl-3-hydroxypyridine-5-carboxylic Acid Oxigenase: Thermodynamics, Kinetics, Substrate Analogs and Gene Cloning.”

Jim Fessenden (Schacht) “The Characterization of the Nitric Oxide/Cyclic GMO Pathway in the Auditory System.”

Christopher M. Harris (Massey) “Transient and Pre-Steady-State Kinetic Analyses of Xanthine Oxidoreductase.”

Christian H. Weber (Ludwig) “The X-Ray Structure of CTP:Glycerol-3-phosphate Cytidylyltransferase from Bacillus Subtilis.”

Don “Buddy” Edward Wiese (Matthews) “Interactions of the Leucine-Responsive Regulatory Protein with the Promoter Region of the GLTBDF Operon of E. coli Specifying Glutamate Synthase.”

Gifts

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

Biological Chemistry Endowment Fund • Jo-Anna, Allen, and Thomas Spector • Paul P. Fan • David A. and Evelyn Tyner • Kenneth A. Epstein and his wife • Pharmacia & UpJohn, Inc. • Smith Kline Beecham Foundation • The Proctor & Gamble Foundation • Monsanto Fund • Warner-Lambert Company • Jewish Community Foundation

Dominic D. Dziewiatkowski Dissertation Award • Sam & Jane Ann Damren

Minor J. and Mary Lou Coon Graduate Student Fellowship in Biological Chemistry • Vincent Massey • Margaret E. Gutowski and Michael Marletta • Dennis Thiele and Maria Sippola-Thiele • Merle and Shirley Mason • Bristol-Myers Squibb Foundation • Estate of Lila Miller

Gerard Summer Fellowship Program • Ralph Colton

Other Gifts • Minor J. and Mary Lou Coon • Thanks also to our anonymous donors.

We make every attempt to ensure the list is accurate and complete. Please let us know if there are errors. Information about specific gift opportunities is available from:

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Post-translational processing events play a central role in control of cell physiology and make a major contribution to the overall complexity of cells. These events are characterized by their broad chemical range, from simple disulfide bond formation to phosphorylation, hydroxylation, glycosylation, and highly controlled proteolytic cleavage events, among others. Our laboratory is interested in the contribution of post-translational modifications to cell complexity and patterns of cell control. We will initially use a survey approach to this field of study to identify common patterns both within and between cells.

Existing technologies are not well suited for the kind of high-throughput survey approach that we have envisaged for the early stages of this work, so we have undertaken development of new technologies with the necessary capabilities. We have taken as a starting point the currently available genome sequences, and used this information in concert with high-resolution separation and mass spectrometry techniques to develop new methods for genome (and proteome) analysis.

It has been estimated that the genomes of at least 50 organisms will be completed and released for public access by January 1, 2000. The rate of completion for new genomes will continue to accelerate in the same manner that DNA sequence information has accelerated exponentially. The sheer volume of available sequence data is staggering and has given bioinformatics a dramatically increased importance in biomedical research. The increasing amount of genome sequences becoming available to investigators is beginning to revolutionize experimental approaches to a variety of problems in Biology and Medicine.

We have developed a surface-scanning approach to high-throughput analysis of proteomes. The method involves desorption directly from the gel surface by a UV laser (MALDI) followed by mass analysis by time-of-flight mass spectrometry (TOFMS). The nature of the gel and its processing are critical factors in the success of this technology. Thin layer gels are preferred for their better physical stability under vacuum, but also because their short diffusion paths allow rapid processing of the gels and ready access of the analytes to the gel surface.

The very large amount of data resulting from scanning a single one-dimensional gel can be processed into a two-dimensional image of the proteins in which one dimension is gel position and the other is m/z, while ion intensity is represented as optical density or color scaling (Fig. 4). When an isoelectric focusing gel is scanned, we refer to the resulting image as a virtual 2-D gel since it is directly analogous to a classical 2-D gel, except that the second dimension is mass spectrometry instead of an SDS gel.

An example of the resolution of this method and its application to identification of post-translational modifications is shown for Braun's lipoprotein in Figure 5. Braun's lipoprotein is the major lipoprotein of the E. coli membrane. The heterogeneity of the covalently-attached fatty acids (C13, C14, C15, etc.) is clearly apparent with the characteristic mass separation of 14 Daltons corresponding to one methylene group.

*Figure 1. MALDI mass spectrum of 150 mm long BB gel at 107.4 nm. Note the ion observed at 51,372 Daltons. The spectrum in this figure was internally calibrated against insulin (5,734 Da) and myoglobin (16,953 Da).*
Figure 2. MALDI mass spectrum at 106.9 m/z. Note the increase in the mass at approximately 40,956 Daltons relative to Figure 1 and the weak ion near 71,156 Daltons. The spectrum was not internally calibrated, yet the mass at 40,956 differs from Figure 1 by only 30 Daltons. These spectra may be aligned to generate a contour map of the proteins present in the mixture as shown in Figure 3.

Figure 3. Portion of a virtual 2-D gel image for proteins having pl values from 5.2 to 5.6 and masses from 15 to 55 kDa. The thin-layer gel was MALDI-scanned at approximately 0.5 mm increments over a mass range of 300 to 85,000 Daltons. The largest mass observed was 78,000 Daltons (not shown). The sample was 10 micrograms of a total E. coli extract. Note that the position increment of about 0.5 mm was coarse enough that most mass peaks are represented in single scans only, while a few of the broader (or taller) peaks exhibited a regular increase and decrease as the laser beam scanned across the band.

systems, it is necessary to understand the role(s) of each individual gene product in that system. This is a massive undertaking when the system is as complex as a living cell. The thousands (to tens of thousands) of component proteins present in a cell may change with the cell cycle, environmental conditions, developmental stage, or metabolic state. The post-translational modifications associated with these proteins may also change. The gene products define the functionality of the cell and changes in the protein complement distinguish a cell spatially and temporally.

It has been clear for several years that large improvements in methods for protein structure analysis were necessary to keep pace with the avalanche of information produced by DNA sequencing efforts. Previous methods available for protein analysis (Edman degradation, amino acid analysis, etc.) have had relatively small, incremental improvements. The development or rediscovery of new ion sources for mass spectrometry has led to its widespread use for analysis of proteins. Mass spectrometry, with the advantages of accuracy and sensitivity has held the promise for provid-
ing the necessary dramatic increase in throughput required for large-scale protein mapping. This promise has not yet been realized because it has not been possible to effectively link high-throughput protein purification methods with mass spectrometry.

Imagine being able to break open a population of cells and having the tools to determine the amount of each protein in the cell and also being able to determine what gene encodes each of these proteins. This is the aim of our current major project.

There are numerous applications for proteome projects in pharmaceutical research. Proteome projects in the pre-clinical area of anti-bacterial chemotherapy will have an edge over other pre-clinical areas because of the advanced state of genomic information for bacterial systems. We think that this application is the ideal one to serve as a model for other therapeutic areas.

George (Bill) Jourdian, Ph.D.
Research Profile

For the past 30 years, our research program has focused on the remodeling of connective tissue during development and in disease. Initially, these efforts emphasized the biosynthesis of the carbohydrate portion of connective tissue-associated glycoconjugates.

However, the direction of the research program changed dramatically in the late 1970s. We found, serendipitously, that the exogenous addition of β-galactosidase, a lysosomal hydrolase, to generalized gangliosidosis fibroblasts resulted in the "correction" of abnormal levels of lipid- and protein-carbohydrate complexes to the levels present in the mutant cells, i.e., reduced the intracellular levels of the lipid- and protein-carbohydrate complexes to those present in normal fibroblasts. The enzyme was taken up in a saturable manner, internalized and transported rapidly to the lysosomal compartment. Enzyme uptake required the presence of mannose 6-phosphate (Man-6-P) residues contained on N-linked "mannose rich" oligosaccharides covalently-bound to the peptidic core of this and other lysosomal hydrolases. This novel finding was unexpected. Even more unexpected was the observation that this recognition system was not restricted to the endocytic pathway but participated in the intracellular transport of newly synthesized lysosomal enzymes as well (Fig. 1).

Characterization of Mannose 6-phosphate receptors

Subsequently, binding of Man-6-P containing lysosomal enzymes to liver membrane preparations was demonstrated. These results suggested the presence of a putative Man-6-P receptor. Shortly thereafter, a "soluble" protein was extracted with detergent from bovine liver membrane preparations and isolated in homogeneous form by affinity chromatography. The protein, a type I transmembrane glycoprotein (~ 275 kDa), contains two Man-6-P binding sites per molecule and is present in most mammalian tissues, being found in highest concentrations in brain, testes and liver. Maximum ligand binding occurs at ~ pH 6.8 in the absence of cations. The effect of the structure and location of the Man-6-P residues, contained on naturally occurring and chemically synthesized "mannose-rich" ligands, has been examined in depth with this receptor and a small molecular weight, membrane-associated Man-6-P receptor (described below). The presence of a single, terminal, non-reducing Man-6-P residue on each ligand is essential for uptake and/or intracellular transport of each Man-6-P receptor. Recognition, though to a lesser degree, extends to the position of substitution of the mannose residues, the nature of the glycosidic linkages and whether the oligosaccharide chains are linear or branched. Biantennary oligosaccharides that contain a terminal Man-6-P residue on each branch exhibit an approximate 10-fold stronger binding to each receptor than oligosaccharides carrying a single Man-6-P residue. The relationship between intracellular trafficking and the processing and trimming of the oligosaccharide portion of lysosomal enzymes and the addition of Man-6-P residues is summarized in Fig. 2. Others have demonstrated that the Man-6-P receptor polypeptide core also contains a distinct insulin growth factor II binding site (CI-MPR/IGF-II).

Interestingly, in vitro, and putatively in vivo as well, lysosomal hydrolases partially inhibit binding of IGF-II and vice versa. These results suggest a highly regulated, dual role for this
receptor. Others have cloned and expressed functional CI-MPR/IGF-II.

Several laboratories have isolated a soluble form of CI-MPR/IGF-II from the serum of several animal species (Sol CI-MPR/IGF-II). The soluble receptor lacks the membrane and cytosolic domains present in CI-MPR/IGF-II but still contains two functional Man-6-P binding sites. In contrast to CI-MPR/IGF-II which contains largely mannose rich oligosaccharides, the soluble receptor contains elevated levels of highly sialylated oligosaccharides. These results suggest that the oligosaccharides of the soluble receptor are processed in a manner distinct from the membrane-associated receptor. The soluble receptor is developmentally regulated, i.e., the receptor is present in elevated amounts in fetal calf serum and after parturition its level rapidly decreases. In adult serum, the soluble receptor is present only in low concentrations. It is tempting to hypothesize that the soluble receptor arises from the action of an ER-associated proteinase that specifically cleaves misfolded membrane-associated CI-MPR/IGF-II. Alternatively, the putative proteinase may regulate the levels of membrane-associated receptor in the developing fetus. Studies are currently in progress to address these issues.

In 1985, the Kornfeld group at Washington University (St. Louis) and this laboratory reported the isolation of a novel, low molecular weight (41-46 kDa) membrane-associated Man-6-P receptor from bovine liver and testes, respectively (CD-MPR). In contrast to CI-MPR/IGF-II, the low molecular weight receptor exists as a dimer in membranes, and as oligomers in "solution". In its monomeric state, but not in higher oligomeric forms, the receptor requires cations for ligand binding. Several laboratories have cloned and expressed CD-MPR from a number of mammalian tissues and species. The expressed proteins exhibit a high degree of homology. In contrast to CI-MPR/IGF-II, which contains 19 potential N-glycosylation sites only two of which are glycosylated, CD-MPR contains five glycosylation sites, four of the sites are glycosylated. Testes CD-MPR is comprised of two major isoforms. One isoform contains complex oligosaccharide chains with poly- N-acetylglucosamine sequences terminated by sialic acid residues; the second isoform contains largely mannose rich chains, some of which terminate in galactose residues. The isoform containing complex chains binds Man-6-P ligands poorly suggesting that the structure and charge on the oligosaccharide chains may play a role in the regulation of binding of Man-6-P ligands. The ability of mutant cell lines containing variable levels of each Man-6-P receptor (CI-MPR/IGF-II and CD-MPR) to differentially distinguish proteins carrying Man-6-P residues suggests that the receptors interact with distinct subgroups of lysosomal hydrolases. The results of immunochemical studies demonstrate that CD-MPR and CI-MPR/IGF-II have been highly conserved during evolution. Each receptor is highly folded. The luminal portion of CD-MPR contains a single copy of a cysteine-rich segment (domain) containing approximately 145 amino acid residues whereas CI-MPR/IGF-II contains 15 homologous cysteine-rich domains.

Characterization of the Man-6-P Binding Sites: Ongoing Studies

In a collaborative effort with the Lehmann group (Freiburg, Germany), a series of diazirine compounds containing one, or two, Man-6-P residues were synthesized. These photo-labile affinity reagents are currently being used to probe the nature of the ligand binding sites of each Man-6-P receptor. In related studies, in collaboration with the Saper group, we have initiated efforts designed to establish the three dimensional structure of Sol-MPR/IGF-II. In addition, in an attempt to define the nature of the Man-6-P binding sites, we have cloned and expressed a functional 56 kDa fragment containing the Man-6-P binding site near the amino terminus of CI-MPR/IGF-II (domains 1-3). Each of these proteins have been crystallized. Preliminary X-ray diffraction studies are in progress.

Summary

The isolation and characterization of the Man-6-P receptors, the increasing availability of
novel mutant cell lines, procedures for the crystallization and structural modeling of proteins, and an increasing armamentum of genetic and molecular tools suggests that rapid progress in our knowledge of the function and regulation of the Man-6-P receptors as they participate in the endocytic and intracellular transport of lysosomal hydrolases may be anticipated. This information will enhance our understanding of the role of lysosomal glycosidases in the remodeling of glycoconjugates in normal development and in disease.

Acknowledgment

The scientific contributions of the pre- and postdoctoral students who have participated in these and other research efforts in this laboratory during the past thirty years are gratefully acknowledged. Their ideas, efforts and friendship have made my scientific career at Michigan an enjoyable and rewarding experience.

Selected references for further reading:


Modulation of intracellular cyclic AMP (cAMP) levels has been shown to impact on a number of cellular processes underlying changes in protein phosphorylation state, regulation of ion channel conductance, and gene expression. Regulation of intracellular cyclic AMP concentrations is principally controlled at the level of its synthesis, through the hormonal regulation of adenyl cyclase, the enzyme responsible for the conversion of ATP into cyclic AMP. The adenyl cyclase system is comprised of three components (figure 1): heptahelical, G protein-coupled receptors for a variety of hormones, neurotransmitters, and autacoids; heterotrimeric G proteins; and the catalytic entity itself. This architecture is common to all G protein-regulated systems, for example, hormone-regulated effectors such as phospholipases, ion channels, and phosphodiesterases (in the visual system).

Central to the regulation of G protein coupled signaling systems, is the specificity of the G proteins to recognize and couple an appropriate receptor to the correct downstream effector. A major aim of my research is directed at determining the precise molecular signals underlying the specificity of recognition of adenyl cyclases by G protein subunits. Towards this goal, my lab has developed a genetic system to examine this problem using the hormone regulated adenyl cyclase system as a model.

We are using yeast, Saccharomyces cerevisiae, as a genetic tool to select for mutants of both adenyl cyclases and G protein a subunits that will allow us to probe the molecular basis of G protein recognition and regulation of adenyl cyclase. Yeast require cAMP for growth, which is normally supplied by the yeast adenyl cyclase encoded by the Cyr gene. We have been able to rescue the lethality associated with a deletion of the Cyr locus by expressing mammalian adenyl cyclase and G protein subunits and have used these engineered strains of yeast to isolate mutant forms of both adenyl cyclase and G protein subunits with altered regulatory properties. Among the mutants isolated, we have obtained cyclases defective in their coupling to G protein subunits, constitutively active mutants, and mutants defective in their binding of metal cofactors necessary for catalysis. Sequence analysis, structural mapping studies, and biochemical characterization of these mutants have identified residues in both cytoplasmic domains of the cyclase that are involved in the specific binding of and regulation by Gsa, coordination of magnesium ions, and amino acid residues important for allosteric activation of the enzyme. Additional screens are being used to isolate adenyl cyclase mutants unresponsive to regulation by inhibitory G proteins, Gia, G protein bg subunits, or the activator forskolin. Similarly, this genetic system is being used to isolate mutants in the G protein a subunits that are defective in their coupling to the adenyl cyclase protein.

Defects in the receptor and G protein components of the adenyl cyclase system that render the system constitutively active, have been shown to be causative to a number of human diseases including McCune-Albright syndrome and some hypersecreting endocrine tumors. Our ability to select for
constitutively active mutants of adenylyl cyclases with our genetic system, will greatly facilitate the examination of human disease states correlated with adenylyl cyclase mutations. A long term goal of this project is to initiate a survey of human tumors (having elevated intracellular cAMP levels) for oncogenic mutations in genes encoding adenylyl cyclases. These studies will have a significant impact on the understanding of the mechanisms underlying the regulation of adenylyl cyclases and in general, G protein-coupled effector systems. In addition, these studies will provide the basis for elucidating possible defects in adenylyl cyclase structure or function as the basis for abnormal signal transduction in humans.

Over the last year, we have initiated a program to investigate a family of mammalian proteins, named RGS proteins (for Regulators of G protein Signaling) which constitutes a fourth, recently discovered component of G protein signaling systems. Twenty mammalian family members have been identified in the sequence data bases and are characterized by a 150 amino acid long region of the protein (termed the RGS box) evolutionarily conserved to yeast and C. Elegans where they were initially discovered. We and others have demonstrated that many of these RGS box proteins bind to and negatively regulate G protein alpha subunits of the Gi class. This is brought about by stimulating the intrinsic GTPase of the G protein, therefore accelerating the return to the inactive GDP form.

Many of the RGS family members possess large amino or carboxy terminal extensions of the core RGS box. It is thought that these extensions play a role in targeting these RGS proteins to specific subcellular locations, or specify their interactions with other proteins, possibly G protein effector molecules. Using both genetic and biochemical approaches, we have isolated several novel signaling molecules that were identified by their ability to specifically bind to the amino terminal extension of one of the RGS proteins. We are currently characterizing the interactions of these proteins with members of the RGS family, and examining the roles of G protein in regulating these proteins.

References
Debra A. Thompson, Ph.D.
Research Profile

We are studying the vertebrate visual system to understand the complex biology that sustains the rod and cone photoreceptors, the light detecting cells of the retina. These fragile and highly specialized cells are easily damaged by trauma, disease, aging, and inherited defects, resulting in a number of blinding conditions that are currently not amenable to treatment or cures. Our research focuses on molecular studies of the retinal pigment epithelium (RPE), a polarized monolayer of cells whose function is intimately linked to photoreceptor viability. The RPE acts as the outer blood-retina barrier, carrying out activities essential for visual processing and photoreceptor renewal. Our approach has been to develop strategies to identify tissue-specific genes likely to subserve RPE-specific functions. This focus has resulted in a new appreciation of neuropeptide Y signaling in the physiology of the RPE. In addition, it has led directly to the cloning of a unique gene that we have determined is responsible for an inherited form of childhood blindness.

We began our studies by targeting the identification of genes likely to be involved in regulating key signaling pathways in the RPE. Our initial focus was on the characterization of G protein-coupled receptors, since it is known that second messenger responses in the RPE regulate both water transport and phagocytosis. As the result of an intensive screening effort, we identified sequences encoding a number of G protein-coupled receptors, three of which represented newly identified proteins. We established that one of these, found preferentially expressed in eye and brain, is activated by neuropeptide Y and corresponds to the type 2 neuropeptide Y receptor previously characterized only by pharmacological assays. We characterized the bovine and human cDNAs, deduced the human gene structure, and identified the second messenger signaling pathways in the RPE activated by neuropeptide Y using biochemical and electrophysiological assays. We also established that neuropeptide Y receptor subtypes are differentially expressed throughout ocular tissues, and that neuropeptide Y is synthesized by the amacrine cells of the inner retina. Our findings lead to us to predict an important role for neuropeptide Y in the physiology of the RPE, and suggest that neuropeptide Y release from the retina serves as a paracrine signal in this system. Our future interests lie in defining the role of neuropeptide Y in the coordinate physiology of the photoreceptors and RPE in vivo.

Our second approach involved screening for tissue-specific proteins using monoclonal antibodies that we raised against preparations of RPE membranes. As a result, we identified cDNAs encoding an abundant 61-kDa protein (official gene name, RPE65) whose sequence lacks significant homology to any other known protein and is without recognizable functional motifs. Although the function of RPE65 has not been established, it has been proposed to play a role in the synthesis of the visual pigment chromophore, 11-cis retinal. Our initial studies of RPE65 focused on characterization of the human gene intron/exon structure, chromosomal localization, and intragenic polymorphic markers, representing the first structural analysis of a gene transcribed specifically in the RPE. In addition, this analysis provided the tools to investigate RPE65 as a candidate disease gene involved in inherited degenerations of the retina.

To evaluate RPE65 in human disease, we established a collaboration with Professor Andreas Gal, a retinal geneticist at the Universitäts-Krankenhaus Eppendorf in Hamburg who studies patients with autosomal recessive childhood-onset severe retinal dystrophy (arCSRD). arCSRD designates a heterogeneous group of disorders that destroy rod and cone function. The most severe cases result in blindness at birth and are termed congenital amaurosis of Leber,
while less severe cases are considered juvenile retinitis pigmentosa. Using polymorphic markers present within the RPE65 gene sequence, we established linkage of the disease gene responsible for arCSRD to the RPE65 locus in two consanguineous families from the Indian subcontinent. Subsequent sequence analysis of RPE65 in these families, as well as a cohort of over 300 patients with autosomal recessive retinal dystrophies, resulted in the identification of 13 different and most likely pathogenic mutations. The inactivating nature of the mutations found (predicted to cause defects in protein folding, splicing, and premature termination of translation) and the autosomal recessive mode of inheritance, suggest that RPE65 mutations result in complete or partial loss of protein function. In contrast to other genes whose defects have been implicated in degenerative retinopathies, RPE65 is the first disease gene in this group of inherited disorders that is expressed exclusively in the RPE. This finding creates a new emphasis on the RPE in the study of the causes of inherited retinal degenerations.

The discovery of the involvement of RPE65 in human disease underscores the fundamental importance and medical relevance of molecular studies of the RPE. Our current interests are to better understand the normal function of RPE65, as well as the ways in which RPE65 dysfunction contribute to arCSRD. In addition, we are studying the regulation of RPE65 expression in an effort to identify the mechanisms involved in its tissue-specific expression. Our goals are to identify the promoter elements and trans-acting factors responsible for RPE-specific expression, and to understand the relationship of these regulatory mechanisms to those involved in the neurosensory retina.

We hope this work will result in the identification of additional functionally important RPE genes, as well as aid in developing strategies for genetically manipulating the RPE in a selective and controlled manner. These steps should bring us closer to future therapies for retinal degenerations involving survival factor expression and gene replacement in the RPE.

*Selected Publications*


*Figure 1. RPE65 gene structure and mutations that cause arCSRD.*
Biochemistry Social Hour in Washington DC

The 1998 meeting of the American Society for Biochemistry and Molecular Biology will be held May 16-20, 1998 in Washington, DC. Four satellite meetings will be held in conjunction with this meeting. Please plan to join us at the Michigan Social Hour.

Date: Tuesday, May 19, 1998
Time: 5:30 p.m.
Place: Grand Hyatt Washington
Room: Constitution E

Two complimentary beverage tickets are on the back cover.
Jeeyong Lee is from Seoul, Korea. He received his Master's degree in Biochemistry from Oregon State University, and his undergraduate degree at Yonsei University in Seoul.

Seonok Muecke is from Urbana, Illinois. She received her R.N. degree from the Margaret Pritchard Nursing College in Korea and worked as a nurse for five years. She then received her B.S. degree in Biochemistry from the University of Illinois.

Augen Pioszak is from Grand Rapids, Michigan. As a Biochemistry major he received the B.S. degree from Michigan State University.

Vladimir Ramirez-Carrozzi is from San Francisco, California. He received his B.S. in Biochemistry and Molecular Biology at the University of California - Santa Cruz. He was a recipient of the Minority Biomedical Research Support Fellowship at UCSC and of the National Hispanic Scholarship Fund.

Haris Vikis is from Manitoba, Canada. At Queen’s University in Kingston, Ontario he received his B.S. degree in Biochemistry. Haris was a recipient of the Queen’s Appeal Undergraduate Scholarship.

Dong Xu is from the People’s Republic of China. He received his B.S. degree in Biological Sciences and Biotechnology at Tsinghua University in Beijing where he was given the Scholarship of Progress on Study.

his wife Mary. The 1997 recipient of the award was Lauren Stegman from the Brian Ross Laboratory. Lauren, who is from Scottsdale, Arizona, is in our Medical Scientist Training program.

Christman Award
The Adam A. and Mary J. Christman Fellowship is presented to a third-year Department student who is judged to be the most outstanding in that class. The award is dedicated to the memory of Professor and Mrs. Christman. The 1997 recipient of this award was Gregor Zimmerman from the Ron Taussig Laboratory.

Murphy Memorial Award
The Lee Murphy Memorial 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 1997 Murphy Award was presented to Brett Lennon from the laboratory of Dr. Charles Williams.

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 recipient of the 1997 Award was Eileen Pagan-Ramos, who trained in the laboratory of Dr. David Engelke.

Faye A. Bradbury was the recipient of the Endocrine Society’s Quest Diagnostic, Inc. New Investigator Travel Award. This award was bestowed for exceptional research presented at the 79th Annual Meeting of the Endocrine Society in Minneapolis, Minnesota, June 13, 1997.

Yunde Zhao (Marletta) and Gregor Zimmerman (Taussig) are both recipients of the Rackham Predoctoral Fellowship competition. The Rackham Predoctoral Fellowship Program supports outstanding students during the completion of their dissertation.
Dr. Christensen (center) with Dr. Brian Rose (left) and Lauren Segman.

Dr. Jack Dixon (right) presenting Lauren Segman the Christensen Award.

Gregor Zimmerman (right) with Dr. Ron Tressler (center) and Dr. Halvor Christensen.

Dr. Jack Dixon (right) congratulating Gregor Zimmerman on receiving the Christensen Award.

Elkyn Pagan-Ramos holding her winning thesis with mentor Dr. David Engelter.

Dr. Jack Dixon giving Elkyn Pagan-Ramos the Dzienkowski Award.

Brett Womans (right) receiving the Murphy Award with his mentor, Dr. Charles Williams.

Brett Womans (right) being given the Murphy Award by Dr. Jack Dixon.
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