A NEW DESIGN: *MODERN, CLEAN, AND SOPHISTICATED*

ASBMB today

February 2007

Sensing Frequency Modulated Cell Signaling

American Society for Biochemistry and Molecular Biology

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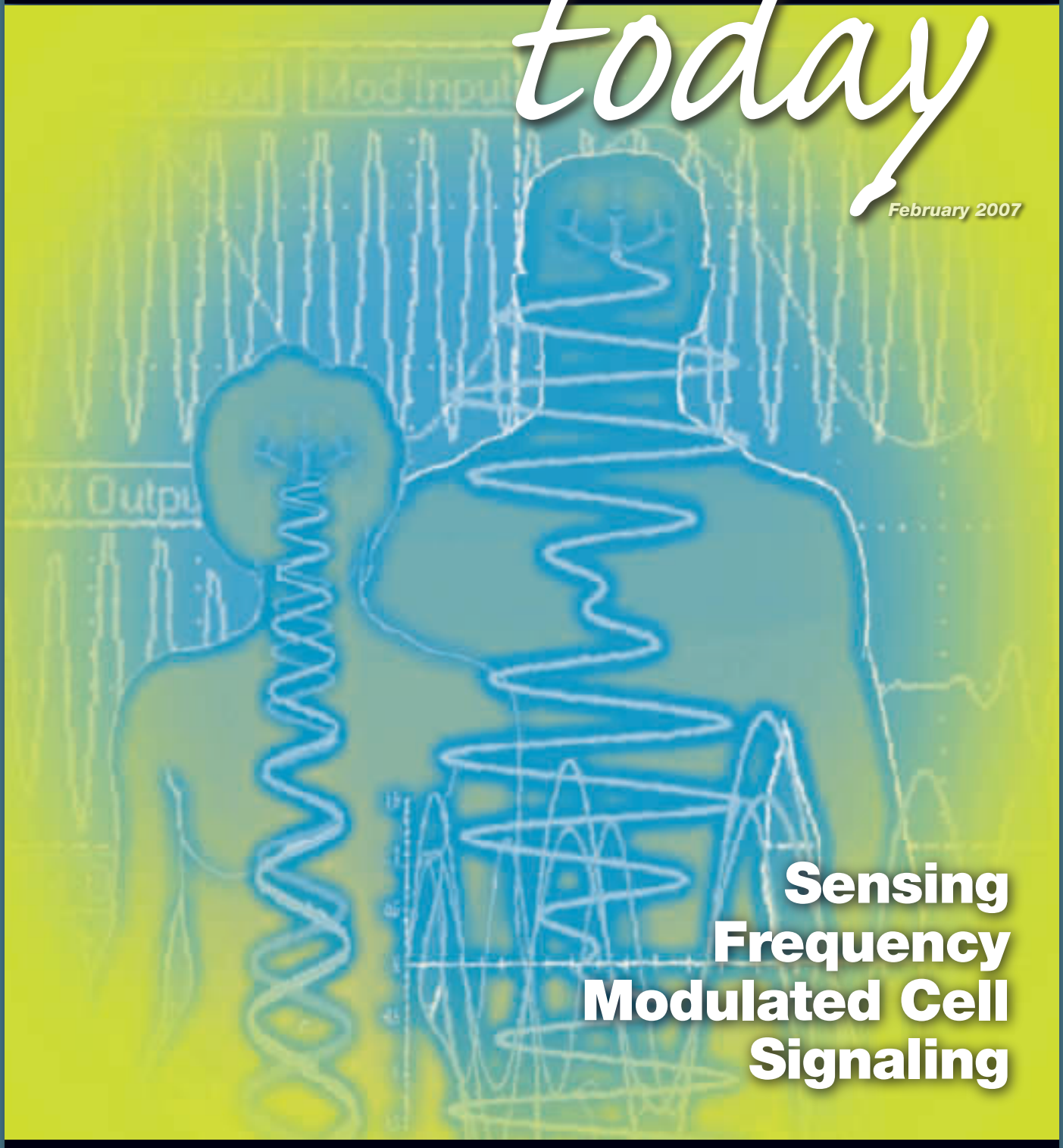

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American Society for Biochemistry and Molecular Biology

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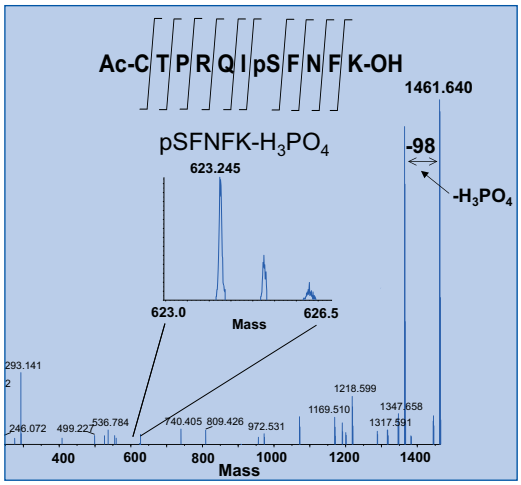

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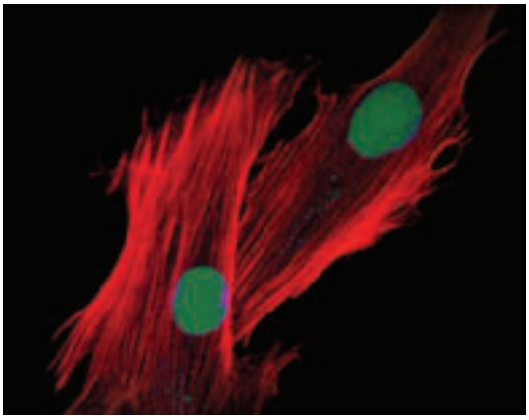

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Several receptor specializations have evolved to allow reception and transduction of frequency modulated signals. Image by Joel Ito and P. Michael Conn, Oregon Health and Sciences University. 23

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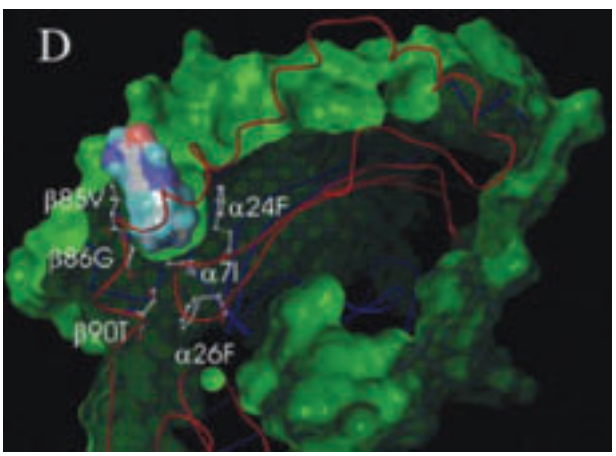

BioBits 30

A New *ASBMB Today*

BY NICOLE KRESGE

This issue of *ASBMB Today* marks the launch of a new, redesigned magazine. The magazine looks entirely different from the publication you've been seeing for the past five years because we've completely redesigned it from front to back, giving it a new modern look and feel.

The new design has been in the works for the past six months. It was created by Amy Phifer, who was also responsible for redesigning the *Journal of Biological Chemistry*. Building on her familiarity with ASBMB publications, Phifer has modernized *ASBMB Today*, creating a more compelling and consistent publication for our members. The redesign achieves a fresh, stylish look that we believe will appeal to both our readers and advertisers.

We have also brought in a new production partner, Cadmus Communications Corporation. Cadmus currently provides journal production services for *The Journal of Biological Chemistry* and *Molecular and Cellular Proteomics* and will be doing copyediting, composition, and printing for *ASBMB Today.*

Another subtle but noticeable change in the magazine is the increased thickness of the paper used for the magazine's cover. We have also decided to incorporate more scientific images in our cover art, and Phifer will be helping with the design of these covers. As a result, we welcome any cover figure submissions from our members.

Although it's the most obvious, this redesign is only one of many recent changes that *ASBMB Today* has experienced. 2006 brought many new columns and features to the magazine, including "Spotlight on Members," a brief listing of the latest achievements by our members; "Career Insights," a series of lively articles written by scientists who have embarked on different career paths; "ASBMB BioBits," brief summaries of recent articles from ASBMB's journals; and "Professional Development," a monthly column contributed by ASBMB's Education and Professional Development Committee.

There have also been editorial changes at *ASBMB Today*. Recently, I stepped up as editor of the magazine after spending the past 2½ years as the magazine's science writer/editor. In addition to my duties with *ASBMB Today* I also serve as ASBMB's science writer and am involved with various projects including writing Paper of the Week summaries and Classic article introductions for the *Journal of Biological Chemistry*, composing press releases for ASBMB and its journals, and editing the Society's Centennial history book. Prior to joining ASBMB, I received my Ph.D. from the Scripps Research Institute and spent several years as a postdoctoral fellow at the National Institute of Diabetes and Digestive and Kidney Diseases.

Nicole Kresge, *Editor*

Alex Toker

This summer, we also plan to bring on Dr. Alex Toker of Harvard Medical School as our new consulting editor. With his addition we hope to upgrade our science reporting by providing more articles targeted to our members' interests, publishing invited articles by prominent scientists, and increasing the number of *ASBMB Today* science articles contributed by our members.

The entire staff of ASBMB is excited about the magazine's new look and content. We hope you find it as attractive and engaging to read as we do to produce. Of course, we value your opinion and would like to know what you think about the changes. To give us feedback, to suggest things you would like to see in *ASBMB Today*, or to submit articles for publication in the magazine, e-mail us at asbmbtoday@asbmb.org.

Nicole Kresge

Nicole Kresge, Ph.D.
Editor

letters to the editor

RESPONSE

Benefits of NIH- and NSF-funded Research

In the January 2007 issue of *ASBMB Today,* reader Randy Morse, chief, Laboratory of Developmental Genetics, Wadsworth Center, Albany, noted that skepticism exists in various quarters about the supposed benefits of NIH- and NSF-funded research and suggested that it would be useful to have available ". . . a publicly accessible list of tangible benefits that have derived from NIH- and NSF-funded research. Maybe such a list already exists. Could the ASBMB help in some way with this?"

In fact, there is a wide variety of information about NIH- and NSF-funded research and the benefits that have flowed from it. By typing "Benefits of Biomedical Research" into the Google search engine, more than 800 hits appear almost instantaneously. Most of the early ones, however, include links to some of the sites below.

NIH Fact Sheets and Testimony

Moving to the National Institutes of Health, the best source of information on publicly funded research and its benefits for the public is the "Research Results for the Public" site at http://www.nih.gov/about/researchresultsforthepublic/index.htm.

This site includes more than a hundred fact sheets about "important medical discoveries that improve health and save lives." The fact sheets are listed alphabetically, from "age-related macular degeneration" to "uterine fibroids," and NIH promises more fact sheets to come.

NIH institutes also are fertile sources of information on research results in their own areas of specialization. They usually provide links to congressional testimony, in which institutes' directors discuss research progress funded through their own institutes as part of their annual congressional justifications.

NSF Discoveries

The National Science Foundation's Web site has a "discoveries" page, listing 192 discoveries and innovations that began with NSF support. This page is found at http://www.nsf.gov/discoveries.

A second (and slightly older) NSF site is the agency's discussion of the "Nifty 50," that is, 50 NSF-funded inventions, innovations, and discoveries that have become commonplace in our lives. From the biological world, these include edible vaccines, the sequencing of the *Arabidopsis thaliana* genome, and antifreeze proteins, to name a few. The list also includes development of fiber optics, Doppler radar, data compression technology, and bar codes. This list can be found at http://www.nsf.gov/about/history/nifty50/index.jsp.

FASEB

FASEB's Office of Public Affairs has a page for the public and for educators on its Web site. The site features links to resources about the benefits of biomedical research, FASEB's "Breakthroughs in Bioscience," publications, and other links on use of animals in research, evolution, and on stem cells. This page can be found at http://opa.faseb.org/pages/PublicEducators/.

Last but Not Least. . .

Finally, ASBMB itself has its advocacy page, accessible at http://www.faseb.org/asbmb/pa/advocacy/index.html.

This page has a plethora of links to articles on the economic benefits of biomedical research as well as numerous other links, both governmental and nongovernmental, about the benefits of federally funded biomedical research, NIH, and medical progress in general.

As this brief list indicates, there is no shortage of publicly accessible information on the Web and elsewhere on the value and benefits of federally funded biomedical research. In fact, there is an enormous amount of information on this subject—only a few mouse clicks away.

Peter Farnham
CAE, ASBMB Public Affairs Officer

ASBMB today

A monthly publicaton of
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president's message

2007 Gets Off to a Great Start, with More to Come

BY HEIDI HAMM

Happy New Year! I hope all of you had a great holiday season and are looking forward to 2007 as much as I am.

As the year gets underway, you will see ASBMB's efforts on behalf of biomedical research and science funding in general going in some new and innovative directions. As one example, U.S. members recently received via e-mail a copy of a full-page editorial that appeared on January 9 in *Roll Call*, a newspaper specifically focused on Congress and Capitol Hill. The editorial, entitled "Save NIH-Sponsored Biomedical Research," was written by Dr. John Kyriakis at Tufts University-New England Medical Center. He is a member of the ASBMB's Public Affairs Advisory Committee.

128 prominent scientists from universities, industry, and nonprofit voluntary health organizations signed this editorial. The editorial advocates funding the NIH at a level of $30.33 billion for 2007–the level specified in the NIH reauthorization bill (H.R. 6164), passed by the Congress late last year (which ASBMB also supported). The text of the editorial appears within this message (see the sidebar).

In addition to numerous members of the ASBMB leadership, other signers include several dozen members of the National Academy of Sciences and the Institute of Medicine, the presidents of 11 scientific societies, 12 Nobel laureates, CEOs or presidents of 8 life sciences companies, the president of the American Heart Association, the CEO of the American Cancer Society, and senior officials at several major universities and nongovernmental granting agencies.

The ASBMB Public Affairs Advisory Committee took on the project because of the serious shortfall in NIH funding since the doubling of the agency's budget was completed in 2003. As discussed in the editorial, success rates are declining and are now down to less than 20% overall at NIH, and first applications are often being funded at a rate in the single digits.

The editorial is one step in what will be a sustained effort to boost NIH funding over the next several years to restore the agency's purchasing power to at least what it was in 2003. While the Society staff has faxed a copy of the editorial already to all members of Congress and Senators, we strongly encourage all of you to send it to your own Representatives and Senators as well (this may well get more attention since it will come to them from constituents). It is still not too late to improve funding levels for FY 2007, as the NIH appropriations bill for FY 2007–which began on October 1, 2006–has still not been approved yet.

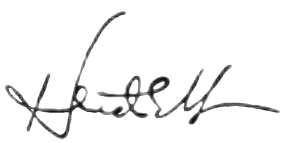
A Training DVD

Another project the Public Affairs Advisory Committeehas undertaken is

the production of a training DVD on how to lobby Congress. One of the common themes we heard from members is that many do not know how to get started as grass roots lobbyists, and so the committee decided that a good way to address that was to produce a training DVD. We will be working on this in February and into the spring. The DVD will feature a "meeting" between a legislator and a group of scientists to give the viewer an idea of how these events are conducted. Other training materials will also be included.

We hope to have the DVD available for distribution to members at the ASBMB Annual Meeting, coming up at the end of April in Washington, D.C., in conjunction with the annual Experimental Biology (EB) meeting. This will be particularly timely, since the Society will be participating in an EB-wide Congressional Visits Day. Staff from the EB-participating societies will be arranging Hill visits for any and all attendees. Watch your e-mails and this magazine for additional information on this event. We hope you plan to participate!

These are only a few of the events we have planned for 2007. While we expect them to be useful to the cause of promoting biomedical research, please don't forget the important role each of you plays as constituents and voters as well as scientists. We hope you will be in touch regularly with your representatives and Senators; get to know them and offer to serve as "science contacts" when they need expertise. Please contact the ASBMB's Public Affairs Officer, Pete Farnham, at pfarnham@asbmb.org if you would like some assistance.



The following editorial appeared in the January 9, 2007, issue of *Roll Call*.

Save NIH-Sponsored Biomedical Research

By John Kyriakis and Heidi Hamm

For most of a century, the National Institutes of Health (NIH) has supported some of the greatest advances in medical science. These include the identification of cholesterol as a risk factor for heart disease (and the subsequent identification of the protein targeted by statin drugs) and the discovery that cancer is a genetic disease. NIH-supported scientists helped discover and characterize the AIDS virus, and contributed substantially to the sequencing of the human genome. These advances have numerous medical applications.

Scientists throughout the U.S. receive NIH funding to support competitively awarded research grants. Both Andrew Fire and Craig Mello, this year's recipients of the Nobel Prize for Medicine or Physiology; as well as Roger Kornberg, this year's recipient of the Nobel Prize for Chemistry, have received substantial support from NIH for their research (as have many of the signatories to this letter). The future holds tremendous promise for continued progress towards conquering some of the most vexing diseases still facing humankind.

However, NIH-supported biomedical research is introuble. Continued erosion of the NIH budget since 2003 has begun to impair the U.S. biomedical research community's ability to make additional discoveries, which would lead to new treatments for major unmet medical needs such as diabetes, obesity and cardiovascular disease. If it continues, this erosion will have a substantial negative impact on the U.S. economy, not to mention its effect on the future health of the American people. The NIH funding crisis is relatively new. Beginning in 1999, and culminating in 2003, Congress doubled the NIH budget. Since 2003, however, inflation and recent budget cuts have shrunk the NIH budget by about 11%. This has been a huge blow to biomedical research, just when its future looked brightest. It has been an especially hard blow because due to the doubling, so many additional individuals have become productive scientists. But now it is harder than ever to get one's research funded. Under current budget constraints, and with the vastly increased-pool of capable researchers competing for scarce NIH dollars, NIH is funding less than 2 in 10 applications overall, with some programs funding about 1 in 10 applications. Thus, many promising young scientists are going without support, many outstanding grants go unfunded, and medical progress stagnates.

This has had a disastrous effect on the morale and productivity of biomedical scientists across the country. The NIH funding shortfall has also created additional pressure on nongovernment health agencies like the American Heart Association, American Cancer Society, and others as more investigators turn to these organizations for replacement funding. These organizations do not have the resources to match the shortfall.

The current situation even threatens U.S. economic security. Over the next ten years, health care will outpace manufacturing as the largest sector of the U.S. economy. Controlling health care costs in the face of an aging population will be severely hampered if medical innovation is slowed by a crippled biomedical research enterprise.

The NIH is an important driver of innovation and economic growth in the pharmaceutical and biotechnology industries. U.S. companies in these sectors of the economy are in business to make profit, and while much of their research is elegant and insightful, it is usually aimed at developing marketable products, not at uncovering basic biological information. Biomedical research is thus an essential first step to the development of new drugs and other life-saving therapies

NIH funding also supports thousands of small businesses throughout the country that provide services to institutions where research is conducted; it is estimated that each dollar invested in the NIH is leveraged 5-fold in the districts where they are spent. Thus, basic biomedical research is a key to the economic health of communities around the country. Given the central importance of NIH sponsored research to the health of the American people and to the US economy, the NIH budget must be restored. Congress will consider 2007 NIH funding this January when it convenes. **In keeping with the recent passage of the National Institutes of Health Reform Act of 2006 (H.R. 6164), an increase in the NIH budget to $30.33 billion for FY 2007 would begin to restore NIH's purchasing power lost since 2003.**

The public, as well as the biomedical research community, the NIH and the Congress should work together to make this happen.

3rd G Protein-Coupled Receptors Colloquium

April 27-28, 2007
Washington, DC

Organized by: Kim A. Neve, Ph.D. and Olivier Civelli, Ph.D.
Sponsored by the ASPET Division for Molecular Pharmacology
This is a Satellite Meeting to Experimental Biology 2007

These are exciting times in the GPCR field. Join us for the 3rd ASPET GPCR Colloquium. Continental breakfast and lunch will be provided both days. Registration deadline is April 6, 2007.

For more information visit: http://www.aspet.org/public/meetings/GPCR_07_Program.htm
Register online at: http://www.aspet.org/public/meetings/GPCR_regform.pdf

Friday, April, 27

Jonathan A. Javitch, *Columbia University College of Physicians and Surgeons* - The structural basis for GPCR oligomerization: Implications for activation.

Susan R. George, *University of Toronto* - Heterooligomerization of Class A GPCRs creates novel signaling units distinct from their constituent GPCR homooligomers.

David L. Farrens, *Oregon Health and Science University* - GPCR ligand binding and release: Insights and mysteries.

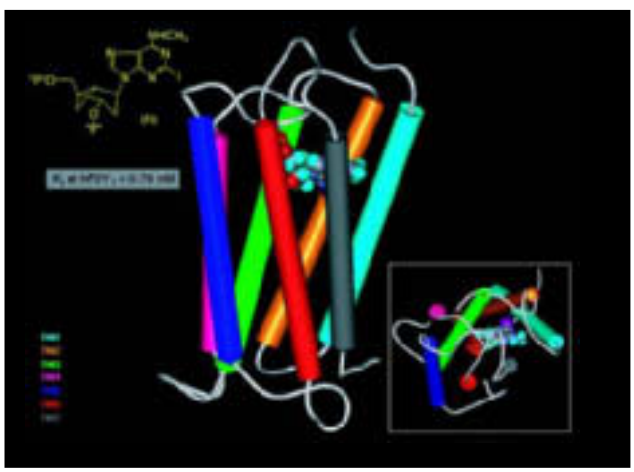
Stephen M. Lanier, *Medical University of South Carolina* - G proteins and their accessory proteins.

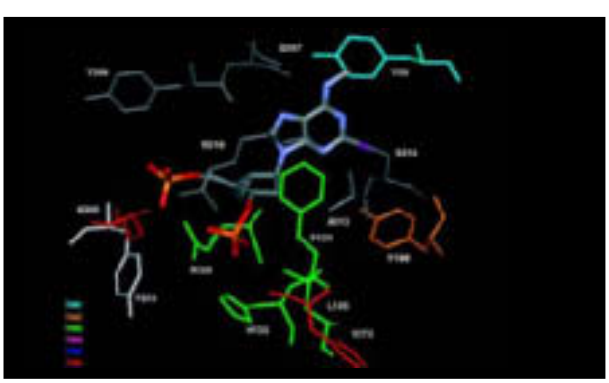
Kevin J. Catt, *NICHD, NIH* - Interactions between GPCRs and receptor tyrosine kinases.

Sudha K. Shenoy, *Duke University Medical Center* - GPCRs, arrestins, and ubiquitination.

Michel Bouvier, *University of Montreal* - Multiplexing resonance energy transfer approaches to study GPCR signaling complexes in living cells.

Emiliana Borrelli, *University of California, Irvine* - Use of genetically engineered mice to unravel the functions of dopamine receptors.





Saturday, April 28

Ursula B. Kaiser, *Brigham & Women's Hospital, Harvard Medical School* - Kisspeptin and GPR54 in the regulation of puberty and reproduction.

Rainer K. Reinscheid, *University of California, Irvine* - GPCRs in arousal and anxiety.

Eric R. Prossnitz, *University of New Mexico Health Sciences Center* - The role of GPR30 in estrogen signaling.

Gerard Le Fur, *Sanofi-Aventis* - Therapeutic benefits of inverse agonism at cannabinoid receptors.

Roger D. Cone, *Oregon Health and Science University* - Novel aspects of the melanocortin receptors.

Marc Parmentier, *Free University of Brussels* - Leucocyte chemoattractant receptors: New molecules and new concepts.

Special Lecture:
Shigetada Nakanishi, *Osaka Bioscience Institute* - The function and regulation of G protein coupled glutamate receptors in the neural network

ASBMB 2007: Signaling Pathways Controlling Cell Structure and Fate

ORGANIZER: MICHAEL B. YAFFE, MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Cell signaling is part of a complex system of communication that governs basic cellular activities and coordinates cell actions. The ability of cells to perceive and correctly respond to their microenvironment is the basis of development, tissue repair, and immunity as well as normal tissue homeostasis. Errors in cellular information processing are responsible for diseases such as cancer, autoimmunity, and diabetes. By understanding cell signaling, we can treat diseases effectively and, potentially, build artificial tissues.

This theme, organized by Michael B. Yaffe of the Massachusetts Institute of Technology, consists of four sessions, each covering an important aspect of signaling pathways

A diverse group of speakers at the leading edge of the cell signaling field has agreed to contribute to the Signaling Pathways Controlling Cell Structure and Fate theme at the 2007 ASBMB meeting in Washington, DC. This theme, organized by Michael B. Yaffe of the Massachusetts Institute of Technology, consists of four sessions, each covering an important aspect of signaling pathways.

The first session, Cytokine and Growth Factor Signaling, will be chaired by Joseph Schlessinger of Yale University School of Medicine. In the session, Mark Lemmon of the University of Pennsylvania will report on the activation and inhibition of the epidermal growth factor receptor. This will be followed with a presentation by Carl-Henrik Heldin of Uppsala University on signal transduction via receptors for platelet-derived growth factor (PDGF) and transforming growth factor β (TGF-β) and the use of PDGF and TGF-β antagonists as possible targets in tumor therapy. Dr. Schlessinger will round out the session with a talk on cell signaling by receptor tyrosine kinases and Sutent/SU11248, a new drug that blocks the actions of several tyrosine kinases.

Michael B. Yaffe

The second session, Signaling and Cell Cycle Progression, will be chaired by Rebecca Heald of the University of California, Berkeley. Tim Stearns of Stanford University will present a talk entitled "The Molecular Logic of the Centrosome Duplication Cycle." Susan Biggins of Fred Hutchinson Cancer Research Center will follow with a discussion of how the Ipl1/aurora protein kinase and Glc7 protein phosphatase regulate the metaphase to anaphase transition. Finally, Dr. Heald will close with her talk entitled "Mechanisms of Mitotic Spindle Assembly and Function."

The third session, Sensing and Signaling after DNA Damage, will be chaired by theme organizer Yaffe. In this session, Michele Pagano of New York University will discuss how two different ubiquitin ligases control the abundance of claspin at different phases of the cell cycle, and Wade Harper of Harvard University Medical School will talk about cell cycle and checkpoint control by the ubiquitin proteasome system. Yaffe will finish off with a presentation on a systems biology approach to protein kinase signaling after DNA damage. The session will be followed by a thematic reception.

The final session, Signaling to the Cytoskeleton, will be chaired by Dyche Mullins of the University of California, San Francisco. The first talk in this session will be by Annual Meeting organizer Michael K. Rosen of University of Texas Southwestern Medical Center. Rosen will report on his recent research on actin regulation by both the Wiskott-Aldrich Syndrome Protein (WASP) family members and the ubiquitous WAVE sub-group of WASP proteins. Next, Sandrine Etienne-Manneville of Institut Pasteur will discuss the control of polarity during cell migration by conserved proteins. And finally, Mullins will conclude the session with a talk titled "Reconstitution of Plasmid DNA Segregation from Purified Components."

ASBMB 2007: Systems Biology

ORGANIZER: TOBIAS MEYER, STANFORD UNIVERSITY SCHOOL OF MEDICINE

This theme was created to respond to the emerging realization that new techniques, concepts, and modeling strategies are needed to understand complex biological control processes. A main goal of this field is to develop quantitative experimental and theoretical strategies to understand protein machines, cells, and organisms. The theme has been organized in four sessions that cover exciting new developments in this important area of research: Mathematical Biology, Modeling of Cell Systems, Proteomics of Cell Systems, and Molecular Profiling of Cell Systems.

Tobias Meyer

The Mathematical Biology session will provide insight into how biochemical data from complex systems can be organized in mathematical models that produce computer simulations

The Mathematical Biology session will provide insight into how biochemical data (particularly large datasets) from complex systems can be organized in mathematical models that produce computer simulations. Unexpected, non-intuitive outcomes (a landmark of good functional models) can then drive more experimentation to validate or modify the mathematical model. Iterations of mathematics-driven experimentation and experimental data-driven modeling gradually produce a mechanistic understanding of a complex system based on theories expressed in mathematical form. These types of theories are often the prelude to revolutionary new technology. It is critical that mathematical approaches be appropriate for the biological scale they want to model.

Examples of modeling at the molecular, cellular, and tissue scale will be provided in the Mathematical Biology session. Vito Quaranta, Vanderbilt University, will introduce the concept of biological scales and relationships between scales. Ravi Iyengar, Icahn Medical Institute, and John Tyson, Virginia Tech, have pioneered modeling of signaling networks and will describe their approaches to modeling GPCRs and the cell cycle, respectively. Ed Munro, from the Friday Harbor Center for Cell Dynamics, will discuss models of cell polarization driven by Par proteins and cystoskeleton. Alexander Anderson of the University of Dundee will describe computer simulations of tumor growth that show how tissue properties may emerge from the cellular scale, and cellular properties may emerge from the underlying molecular scale.

The Modeling of Cell System Session focuses on control circuits and synthetic biology strategies and includes speakers James Ferrell (Stanford University), Wendel Lim (University of California, San Francisco), and Rustem Ismagilov (University of Chicago), all of who have made seminal contributions to these rapidly developing fields of research.

The Proteomics of Cell Systems session focuses on exciting new developments in mass spectrometry. Ruedi Aebersold (ETH Zurich) will talk about quantitative proteomics and systems biology, Michael Snyder (Yale University) will discuss the global analysis of biomedical activity in human disease using protein chips, and Anne-Claude Gavin (EMBL Heidelberg) will give a talk titled "Biochemical and Chemical Approaches to Biomolecular Networks."

The Molecular Profiling of Cell Systems session focuses on image-based short interfering RNA screening strategies for endocytosis and cell migration and developing and use of biosensors as well as on microarray and modeling strategies to understand cellular regulatory systems. Speakers included Peter Sorger (Massachusetts Institute of Technology), Elizabeth Winzeler (The Scripps Research Institute), Marino Zerial, (Max Planck Institute), and Tobias Meyer (Stanford University School of Medicine).

ASBMB 2007: MAC Sponsored Symposia

THEME ORGANIZER: MINORITY AFFAIRS COMMITTEE

The Minority Affairs Committee Sponsored Symposia at this year's annual meeting encompasses an interesting array of topics ranging from program assessment to infectious diseases.

The last two symposia will deal with hepatitis C and tuberculosis, two infectious diseases that are prominent in minority populations

The first symposium is titled "Best Practices in Program Assessment." The symposium will be moderated by Takita Sumter of Winthrop University, and the speakers scheduled to contribute are J. Lynn Zimmerman of the University of Maryland Baltimore County, A. James Hicks of the National Science Foundation, and John Matsui of the University of California (UC), Berkeley. Zimmerman will discuss the Meyerhoff Scholarship Program at University of Maryland Baltimore County and will analyze the elements of success of the program. Matsui will talk about the Biology Scholars Program, an undergraduate program at UC Berkeley designed to promote the success of students from economic, gender, ethnic, and cultural groups historically underrepresented in the biological sciences.

The second symposium, "Genetic Diseases in Minority Populations–Sickle Cell Anemia," will be chaired by Phillip A. Ortiz of Empire State College. In this session, Jane Hankins of St. Jude Children's Research Hospital will present a talk entitled "Current Issues in Sickle Cell Disease: Assessment of Iron Overload via a Noninvasive Method," William P. Winter of the Howard University Sickle Cell Anemia Center will give a talk entitled "Beyond Hemoglobin Polymerization: Multiple Molecular Mechanisms in Sickle Cell Disease," and Steven N. Wolff of Meharry Medical College will present the talk "Sickle Trait: A True Disease."

MAC Chairman George Hill

The last two symposia will deal with hepatitis C and tuberculosis, two infectious diseases that are prominent in minority populations. The "Infectious Diseases in Minority Populations–Hepatitis C" symposium will be chaired by Craig Cameron of Pennsylvania State University and will feature talks by Kouacou Konan of Penn State University, Antonio Estrada of The University of Arizona, and Gerond Lake-Bakaar of Weill Cornell University Medical Center and Rockefeller University. Konan will talk about new insights into the molecular and cellular biology of hepatitis C virus, and Estrada will discuss hepatitis B and C among minority drug injectors. Lake-Bakaar will round out the session with a look at the clinical aspects of hepatitis C virus infection and the racial disparities in treatment response.

The "Infectious Diseases in Minority Populations–Tuberculosis" symposium will be chaired by Marcos Milla of Roche Palo Alto. This session includes a talk by Harvey Rubin of University of Pennsylvania entitled "Enzymatic control in *Mycobacterium tuberculosis*: identifying new drug targets." Ujjini Manjunatha of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health will speak about the mechanism of action of 4-nitroimidazoles against *M. tuberculosis*. And finally, Bavesh Kana of the Center of Excellence in Biomedical Tuberculosis Research at the University of Witwatersand will present a talk entitled "The Role of Resuscitation Promoting Factors in the Virulence of *Mycobacterium tuberculosis*."

The Minority Affairs Committee will also be sponsoring a Minority Scientists Networking Mixer on Tuesday, April 1, from 12:30 p.m. to 2:00 p.m.

asbmb member spotlight

IN MEMORIAM

Frank W. Putnam 1917–2006

Frank W. Putnam of Bloomington, Indiana, and Cincinnati, Ohio, died November 29, 2006, at the age of 89. He received his B.A. from Wesleyan University (1939) and his M.A. (1940) and Ph.D. (1942) from the University of Minnesota. During World War II, while on the faculty of Duke University, he served as a civilian in the U.S. Chemical Corp at Camp Detrick, Maryland, as part of a team charged with defending against biological warfare.

He joined the Department of Biochemistry at the University of Chicago in 1947 and began his life long study of the proteins found in human blood. In 1955 he became professor and chairman of the Department of Biochemistry at the University of Florida College of Medicine where he developed new techniques for analyzing the sequences of proteins. In 1965, he founded one of the first programs in molecular biology at Indiana University in Bloomington. He published the first complete primary structure of human gamma globulin in 1967 and subsequently solved the structures of two additional classes of immunoglobulins, IgA and IgM. He became a Distinguished Professor of Molecular Biology in 1974 and a Distinguished Professor Emeritus in 1988. He was a beloved professor and teacher of medical students, graduate students, and scores of postdoctoral fellows with whom he continued to correspond professionally throughout his lifetime.

Barry Honig

Honig and Losick Honored by NAS

Richard M. Losick

Barry Honig, professor of Biochemistry and Molecular Biophysics at Columbia University, and Richard M. Losick, Maria Moors Cabot Professor of Biology and a Harvard College professor, were selected to receive awards from the National Academy of Sciences honoring their outstanding contributions to science. Both Honig and Losick are also investigators of the Howard Hughes Medical Institute.

Honig was chosen as the recipient of the 2007 Alexander Hollaender Award in Biophysics. The award, which consists of $20,000, is presented every three years for outstanding contributions in biophysics. The award was established by a bequest from Henrietta W. Hollaender in honor of her husband and was first presented in 1998.

Losick will receive the 2007 Selman A. Waksman Award in Microbiology. Supported by the Foundation for Microbiology, the award recognizes excellence in the field of microbiology and is presented every 2 years. It is considered the nation's highest award in microbiology.

Both awards will be presented at a ceremony in Washington, D.C., during the academy's annual meeting.

IN MEMORIAM

David L. Garbers 1944–2006

David L. Garbers died on September 5, 2006, in Dallas, Texas. He was a professor of pharmacology and director of the Cecil H. and Ida Green Center for Reproductive Biology Sciences at University of Texas (UT) Southwestern Medical Center.

Garbers grew up in La Crosse, Wisconsin, and earned a bachelor's degree in Animal Science in 1966, a master's degree in Reproductive Biology in 1970, and a doctorate in Biochemistry in 1972. He did postdoctoral research at the Vanderbilt University School of Medicine and became an assistant professor of Physiology at Vanderbilt in 1974. He was appointed a Howard Hughes Medical Institute investigator in 1976 and became a full professor in 1982. Garbers joined the UT Southwestern faculty in 1990 as a professor of Pharmacology and was named director of the Green Center in 1999.

Garbers devoted his scientific career to the study of reproductive biology. While at Vanderbilt, he discovered a novel family of receptors on the sperm cells of sea urchins that enable sperm to swim in the right direction. Garbers and his colleagues subsequently found these same receptors in higher organisms, including mammals. More recently, he identified proteins expressed only on sperm cells, including an ion channel that gives a sperm cell the motion it needs to penetrate the egg membrane. Garbers also served on the *Journal of Biological Chemistry* editorial board.

Mayor of NYC Declares

BY NICOLE KRESGE

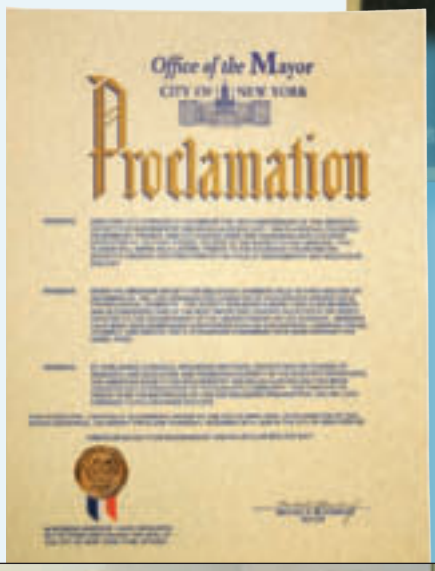
The year-long ASBMB centennial celebration concluded this past December with a commemorative ceremony and plaque dedication at the original site of the Society—the Belmont Hotel in New York City.

The ceremony, held on December 28, 2006, was attended by a delegation of officers, members, and friends of ASBMB to commemorate the founding of the Society 100 years ago. Dr. Judith Bond, immediate past president of ASBMB and professor and chair of Biochemistry and Molecular Biology at Penn State College of Medicine and Dr. Ralph Bradshaw, editor of ASBMB's *Molecular and Cellular Proteomics* and professor of Physiology and Biophysics at the University of California-Irvine, dedicated a commemorative plaque in the Altria Building, the successor to the Belmont Hotel.

As part of the festivities, a Proclamation from New York City Mayor Michael R. Bloomberg was presented to the Society, declaring December 28, 2006, as "American Society for Biochemistry and Molecular Biology Day." Mayor Bloomberg in his proclamation noted that ASBMB has made tremendous contributions to the scientific community through publication of journals, organization of meetings, advocacy for funding of research and education, and promotion of diversity in the scientific workforce.

At 4:30 p.m. on December 26, 1906, 29 scientists interested in physiological chemistry met in the second floor parlor of the Belmont Hotel and voted unanimously to form the American Society of Biological Chemists, which later became the American Society for Biochemistry and Molecular Biology. The meeting was organized by Professor John J. Abel of The Johns Hopkins University, who was a founder of the *Journal of Biological*

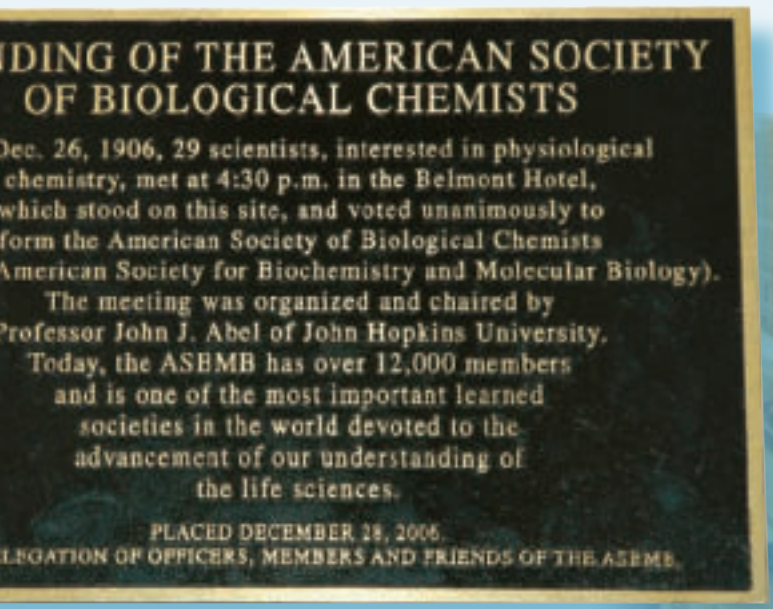
Drs. Ralph Bradshaw and Judith Bond with commemorative plaque (*also shown enlarged on righthand page*).

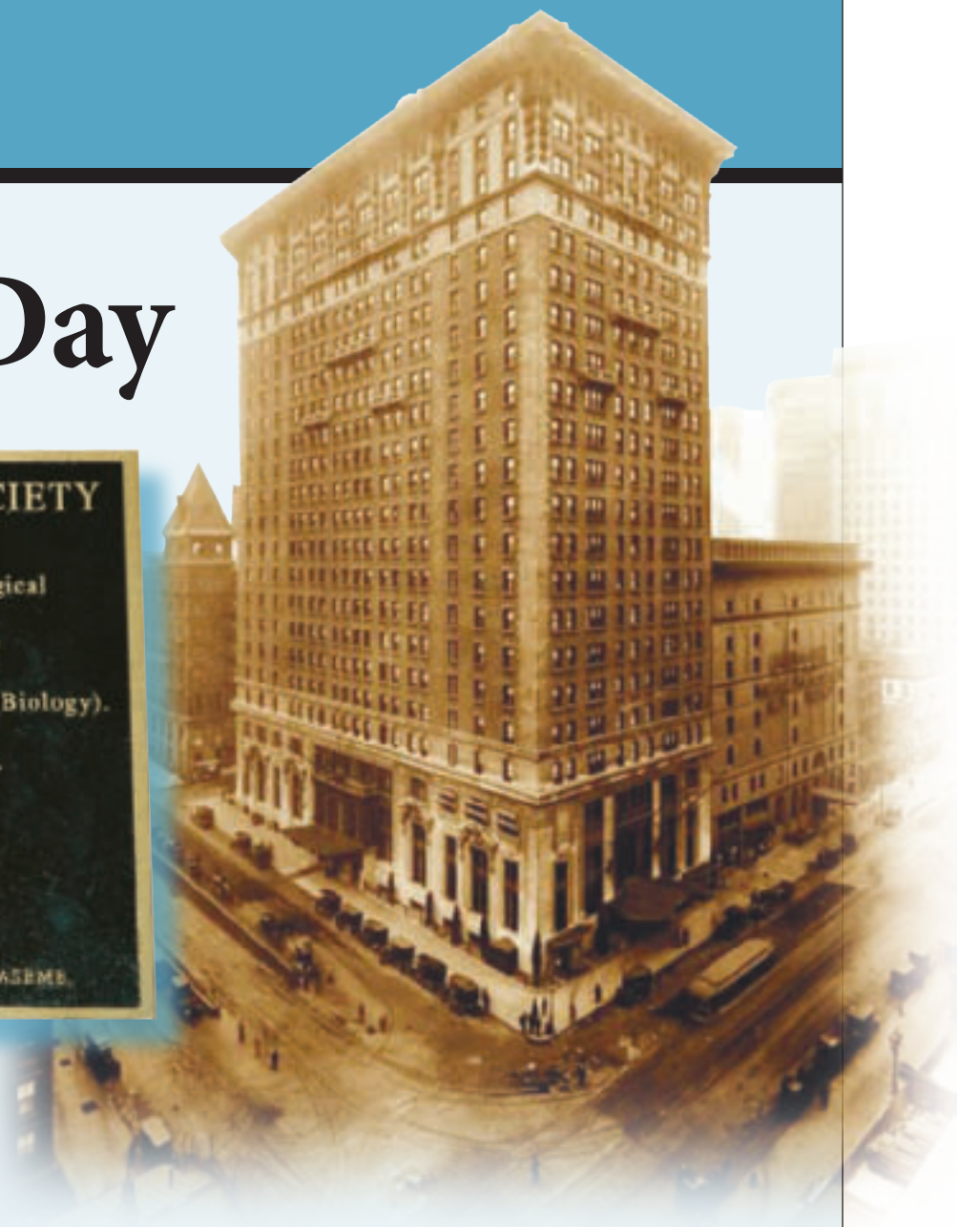


Left: Mayor Michael R. Bloomberg's ASBMB Day Proclamation.

The Centenary Plaque Dedication was attended by a delegation of officers, members, and friends of ASBMB, including (from left to right) Dr. Vern L. Schramm, Deanna Schramm, Dr. Ralph A. Bradshaw, Penny Bradshaw, Dr. Howard K. Schachman, Shelia Lennarz, Ethel Schachman, Dr. Judith S. Bond, Dr. William J. Lennarz, Chuck Hancock, Nancy Rodnan, Gerald L. Gordon, and Barbara A. Gordon.

ASBMB Day





The Belmont Hotel, where the American Society of Biological Chemists was formed, was built 1904–1908 and demolished in 1939. The 22 story hotel was the first superhotel to open around the new Grand Central Terminal.

Chemistry and later a founder of the American Society for Pharmacology and Experimental Therapeutics.

The Belmont Hotel had been completed only a few months prior to the meeting; it was the first of the new superhotels to open around the new Grand Central Terminal. The 94-meter-high, 22-story hotel was designed by Warren & Wetmore for the financier August Belmont. The construction started in 1904 and was complete in 1908. The hotel was demolished in 1939, just 31 years after it was built, to make way for an 85-story skyscraper, which was never built. The Altria building now stands on that site.

"We are thrilled to end our year-long celebration at the site where our Society began," said Dr. Heidi Hamm, ASBMB president. "To gather members, friends, and colleagues and acknowledge this day is a joy to us all. Our founders paved the way for ASBMB to begin in an era when biochemistry and molecular biology was considered a 'hybrid field.' Now, biochemistry and molecular biology is the keystone of life sciences. This dedication will be a lasting memorial to our founder's vision to embrace this 'new science' and give future biochemists and molecular biologists the foundation to explore technologies and medical breakthroughs that we now embrace."

Doctors Bond and Bradshaw were joined in the celebration by Barbara Gordon, ASBMB executive officer; Charles Hancock, past executive officer; Nancy Rodnan, director of publications; Dr. William Lennarz, professor and chair of Biochemistry and Cell Biology at SUNY-Stony Brook; Dr. Howard Schachman, professor of Molecular and Cell Biology at the University of California-Berkeley; and Dr. Vern Schramm, professor and Ruth Mems Chair of Biochemistry at Albert Einstein College of Medicine, by their spouses, and by representatives of Altria Corporate Headquarters.

FASEB

Science and Security Issues: Out with the Old, In with the New?

BY CARRIE D. WOLINETZ

Although the intersection of science and security has a long history, the involvement of the biomedical research community became more pronounced after the anthrax attacks of 2001. While many of the initial cultural clashes between the biomedical research and security communities have been resolved as the two groups have begun to work actively together, the final days of 2006 ended with a series of events related to science and security policy. Detailed below, it remains to be seen how these new laws, regulations, and reports will ultimately affect the scientific enterprise.

Bioterrorism

Shortly before recessing in December, both houses of Congress passed bills to establish the Biodefense Advanced Research and Development Authority (BARDA). BARDA was conceived by Senator Richard Burr (R-NC) as a way to bridge what he termed the "Valley of Death": the funding and regulatory gap between the initial research investment by the National Institutes of Health (NIH) or the biotechnology industry and the procurement funding available through the BioShield program. The initial proposals for BARDA included research functions that appeared to overlap substantially with NIH, and many in the research community, FASEB among them, objected strenuously. Our voices were heard, and Burr rewrote the BARDA bill, limiting its activities only to *advanced* R&D of vaccines and therapeutics related to biological attacks–a bill that was ultimately passed and signed by the President. The to-be-named director of BARDA will report directly to the Health and Human Services secretary, like the NIH director, and it is not yet clear how or when the fledgling agency will establish procedures to spend the $1 billion authority it was granted in the bill. Much of the funding is likely to be used as incentive to companies to develop BioShield-eligible products.

Deemed Exports

The scientific community celebrated a victory over the summer when the Department of Commerce withdrew an onerous proposal that would have required universities to license and monitor foreign nationals coming into contact with export controlled technologies, which includes many common pieces of laboratory equipment. "Deemed" exports refers to the knowledge about the technology possessed by the foreign national as opposed to the technology itself. In lieu of its proposed regulations, the Commerce Department established an advisory committee to examine the issue of "deemed" exports and scientific research. Interestingly, the co-chair of that committee, Dr. Robert Gates, is likely now thinking a bit beyond export control as the newly confirmed Secretary of Defense. However, just when it seemed like deemed exports was an issue to file under "reasonable solution," the Government Accountability Office (GAO) released a report in December on export control issues. The GAO report, compiled at the request of the House Judiciary committee, suggests that Commerce and State departments revisit the issue, particular in relation to assessing the vulnerabilities presented by foreign scientists and students at U.S. universities. The question remains as to whether Congress or the federal agencies will decide to revisit the issue in the upcoming year in light of the new report.

Visas

Issues related to the ability of foreign students and scientists to obtain a visa to visit, work, or study in the United States has been of the utmost concern to the scientific community. FASEB and other scientific organizations have been actively working with Congress, the State Department, Department of Homeland Security, and other federal agencies to try to alleviate many of the problems related to visas and scientists. The research community scored a quiet victory at the end of 2006 when the State Department announced it was extending the length of stay, from three to five years, for professors and researchers participating in the Visitors Exchange Program.

Carrie D. Wolinetz, Ph.D., is with the FASEB Office of Public Affairs.

NIH Launches dbGaP, a Database of Genome Wide Association Studies

This past December, the National Library of Medicine (NLM), part of the National Institutes of Health (NIH), announced the introduction of dbGaP, a new database designed to archive and distribute data from genome wide association (GWA) studies. GWA studies explore the association between specific genes (genotype information) and observable traits, such as blood pressure and weight, or the presence or absence of a disease or condition (phenotype information). Connecting phenotype and genotype data provides information about the genes that may be involved in a disease process or condition, which can be critical for better understanding the disease and for developing new diagnostic methods and treatments.

dbGaP, the database of Genotype and Phenotype, will for the first time provide a central location for interested parties to see all study documentation and to view summaries of the measured variables in an organized and searchable Web format. The database will also provide precomputed analyses of the level of statistical association between genes and selected phenotypes. Genotype data are obtained by using high throughput genotyping arrays to test subjects' DNA for single nucleotide polymorphisms (SNPs), areas of the genome that have been found to vary among humans.

The database was developed and will be managed by the National Center for Biotechnology Information (NCBI, www.ncbi.nlm.nih.gov), a division of NLM. dbGaP is located at www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gap.

The initial release of dbGaP contains data on two studies: the Age-Related Eye Diseases Study (AREDS), a 600-subject, multicenter, case-controlled, prospective study of the clinical course of age-related macular degeneration and age-related cataracts that was supported by the National Eye Institute (NEI, www.nei.nih.gov); and the National Institute of Neurological Disorders and Stroke (NINDS, www.ninds.nih.gov) Parkinsonism Study, a case-controlled study that gathered DNA, cell line samples, and detailed phenotypic data on 2,573 subjects. NEI and NINDS worked closely with NCBI in placing data from the two studies in dbGaP.

To protect research participant privacy, all studies in dbGaP will have two levels of access: open and controlled. The open access data, which can be browsed online or downloaded from dbGaP without prior permission or authorization, generally will include all the study documents, such as the protocol and questionnaires, as well as summary data for each measured phenotype variable and for genotype results. Preauthorization will be required to gain access to the phenotype and genotype results for each individual; these individual level data will be coded to protect the identity of study participants.

"The dbGaP project marks a new milestone in data sharing," said NLM Director Donald A. B. Lindberg, M.D. "Researchers, students, and the public will have access to a level of study detail that was not previously available and to genotype-phenotype associations that should provide a wealth of hypothesis generating leads," he said. "These data will be linked to related literature in PubMed and molecular data in other NCBI databases, thereby enhancing the research process."

NCBI expects to add database enhancements and a number of additional studies over the coming year. GWA studies that will be added encompass a broad range of disease areas and study models. The studies focus on heart disease, women's health, neurological disorders, neuropsychiatric disorders, diabetes, and environmental factors in disease. The Framingham SHARe Study, for instance, will provide data from the landmark Framingham Heart Study in which blood samples from approximately 7,000 subjects are being genotyped and linked to numerous types of phenotype data. Data from the Genetic Association Information Network (GAIN), a public-private partnership, also will be added to dbGaP. This project provides for genotyping DNA samples from participants in clinical studies that were already conducted.

House and Senate Pass Last Year's Stem Cell Bill—Again; Veto Expected—Again

BY PETER FARNHAM

On January 11, the House passed H.R.3, the Stem Cell Research Enhancement Act of 2007. The bill expands the number of embryonic stem cell lines available for federal funding by requiring the secretary of Health and Human Services to conduct and support research using human embryonic stem cells regardless of the date on which such cells were derived. H.R.3 had 211 cosponsors upon introduction.

Federal funding for a limited amount of embryonic stem cell research is legal under President Bush's policy announced in August 2001, when he decreed that stem cells derived from currently existing lines could continue to receive Federal funding, but those developed after August 9, 2001, could not. It soon became apparent that only about two dozen viable stem cell lines existed at the time, instead of the 60 or more said to exist. Thus, the House-passed bill would effectively overturn the ban on federal funding for research on embryonic stem cell lines derived after August 2001.

H.R.3 was one of six bills that House democrats vowed to pass within the first 100 hours of the new Congress. The bill is in fact the same as the Castle/DeGette bill that passed both the House and Senate last year, only to suffer the first veto offered by President Bush since he took office in 2001. Although H.R.3 passed the House with an even larger majority (253–174) than it did last year, it still lacks a majority large enough to override the expected presidential veto.

Newly elected Speaker Nancy Pelosi (D-CA) said shortly after the bill passed, ". . . We must unlock the promise for stem cell therapies to alleviate human suffering and to cure diseases, including diabetes, Parkinsons, Alzheimers, multiple sclerosis, and cancer. . . "With today's strong bipartisan vote, we now challenge President Bush to join members from both sides of the aisle in supporting the hope of stem cell research. Democrats and Republicans have joined together today to urge the President to sign this vital legislation into law." The Senate companion bill, S.5, was introduced on January 4 by Senate Majority Leader Harry Reid (D-NV). S.5 had 31 cosponsors upon introduction and is expected to be considered by the Senate in February.

Peter Farnham, CAE, is ASBMB's public affairs officer.

Industry Seeks Cheaper Ways to Develop Drugs

Pfizer and other drug companies have long justified the high prices they charge for new medicines by citing the staggering sums they must spend in the search for breakthrough discoveries.

But experts have said that Pfizer's decision to abandon what it hoped would be a blockbuster cholesterol drug after spending $800 million on its development suggests that this economic model may no longer be viable.

Put simply, the industry's approach to research is in desperate need of an overhaul, they say. Health plans are calling the shots about how much they'll pay for medicines, and they are very choosy about how much they'll spend. So drugmakers must find ways to produce new drugs more efficiently and cheaply.

The pharmaceutical industry's research system also isn't as productive as it once was. Despite a more than 6% rise in overall R&D spending last year to $39.7 billion, U.S. regulators approved only 20 drugs in 2005, down from 36 a year earlier.

"It is a tough time in the industry right now. Almost every company is having pipeline problems," said Kenneth Kaitin, director of The Tufts Center for the Study of Drug Development. "There has been no systematic change in the way companies bring products to market."

Drugmakers are trying to improve their performance, in part by conducting clinical trials and research in developing countries where costs are lower. They also are targeting niche diseases with small patient populations that don't require big drug trials. Plus, advances in technology and genetics are creating tools that streamline drug development.

But since health plans are unwilling to pay for "me-too" drugs or medicines that are similar to products already on the market, pharmaceutical companies have felt the need to explore unproven research paths in the quest for novel treatments.

"There is no low hanging fruit anymore," said Steven Nissen, a cardiologist at the Cleveland Clinic, who was conducting a trial on torcetrapib for Pfizer. "Companies are reaching farther than ever."

In 2006, Bristol-Myers Squibb scrapped a diabetes drug that treated the disease in a new way, and AstraZeneca dropped development of a novel stroke medicine. Kaitin said as companies take more bet-the-farm chances, more spectacular failures are inevitable.

Uwe Reinhardt, an economics professor at Princeton University, said he thinks eventually the industry will migrate to smaller organizations producing drugs that affect smaller segments of the population. There are signs of such changes already: Bristol-Myers cut its research areas to 10 from roughly 35 two years ago, in part to target the use of its research dollars.

In the meantime, new development strategies, aided by a better understanding of genetics and biology, are starting to be used.

Antimicrobial Chewing Gum Collaboration

Medical chewing gum specialist Fertin Pharma A/S announced a collaboration with the U.S. Army Dental Research and Trauma Detachment (USADRTD) for the development of antimicrobial chewing gum for the treatment and prevention of plaque, cavities, and gum disease. Dental emergencies represent an ongoing and significant challenge to the U.S. military as it tries to deploy troops overseas.

"Together, we will continue the USADRTD mission of developing a product that can improve dental health among first of all U.S. deployed military forces, but secondly it is a promising and highly interesting candidate for wide distribution to the public," says Lars Christian Nielsen, Fertin Pharma CEO.

The deal will see Fertin scientists formulate the USADRTD's antimicrobial decapeptide for controlled release in the oral cavity. The success of nicotine gums—Nicorette alone had 2005 sales of $171 million—has led to widespread acceptance of this form of drug delivery.

Scripps and Pfizer Make $100 Million Deal

The drug giant Pfizer Inc. announced that it will pay The Scripps Research Institute in La Jolla, California, $100 million over five years for the option to license nearly half Scripps' discoveries. The technology transfer deal will replace Scripps' 10-year partnership with Novartis, which expires at the end of this year.

The Scripps-Pfizer agreement is the latest of several over the years between Scripps and private industry that are structured to quickly turn biomedical discoveries into pharmaceutical drugs. Scripps is the one of the world's largest independent, nonprofit biomedical labs.

"Our goal is to cure people who are unhealthy, and our scientists are anxious that their work does move forward," said Scripps spokesman Keith McKeown.

Pfizer's partnership with Scripps is part of a company effort to increase collaborations with scientists outside the company, Pfizer chief executive Jeffrey B. Kindler said. "We want to find more ways to tap into the talent of the thousands of thousands of scientists who work outside the corporate structure," Kindler said.

Besides the $100 million over five years, Pfizer will pay Scripps royalties on profits it makes from the institute's discoveries as well as payments for reaching scientific "milestones" during its lab work.

Merck Bets $1 Billion on RNA interference

Looking to enhance its position in the nascent RNA interference (RNAi)-based therapeutics market, Merck announced it would acquire market leader Sirna Therapeutics. The $1.1-billion agreement will see the San Francisco-based biotech become a wholly owned subsidiary of the pharma giant.

In a prepared statement, Merck Research Laboratories President Dr. Peter Kim said, "We are delighted about our agreement to acquire Sirna Therapeutics, a company that has established a leading presence in the critically important area of RNAi."

Dr. Kenneth Krul, analyst for Kalorama Information, expressed surprise at the hefty price but notes that Merck appears to be banking on RNAi to bolster its pipeline. "I also think Merck is trying to lock up the technology, eliminating potential competition by taking the key stuff off the market," he adds.

Americans Uneasy about Biotech Food

Ten years after genetically engineered crops were first planted commercially in the United States, Americans remain ill-informed about and uncomfortable with biotech food, according to the fifth annual survey on the topic.

People vastly underestimate how much gene altered food they are already consuming, lean toward wanting greater regulation of such crops, and have less faith than ever that the Food and Drug Administration will provide accurate information, the survey found.

The poll also confirmed that most Americans, particularly women, do not like the idea of consuming meat or milk from cloned animals–a view that stands in contrast to scientific evidence that cloned food is safe.

Michael Fernandez, executive director of the Pew Initiative on Food and Biotechnology, which sponsored the survey, said that overall, Americans are "still generally uncertain" about genetically modified (GM) and cloned foods. "How the nex tgeneration of biotech products is introduced–and consumers' trust in the regulation of GM foods–will be critical in shaping U.S. attitudes in the long term."

In the five years since Pew began plumbing American views of genetically engineered food, U.S. acreage in such crops has grown substantially. Today, 89% of soybeans, 83% of cotton, and 61% of corn is genetically engineered to resist weed killing chemicals or to help the plants make their own insecticides.

Because most processed foods contain at least small amounts of soy lecithin, corn syrup, or related ingredients, almost everyone in the United States has consumed some amount of gene altered food.

Consuming cloned animals–addressed in the poll for the first time–popped up as a hot button issue. Even among those who said they had no objection to eating genetically engineered foods, 34% were comfortable with animal cloning, whereas 51% were not.

ANDREA DUINA:
Listen to Your Calling

Andrea Duina

Andrea Duina received his B.S. in Biology from the University of Illinois at Urbana-Champaign and his Ph.D. from the Department of Biochemistry, Molecular Biology, and Cell Biology at Northwestern University, in Evanston Illinois. He was a postdoctoral fellow in the Department of Genetics at Harvard Medical School before becoming an assistant professor of Biology at Hendrix College in Conway, Arkansas, in 2004. Duina is also an adjunct assistant research professor in the Department of Biochemistry and Molecular Biology at the University of Arkansas for Medical Sciences in Little Rock, Arkansas.

Many of my former graduate school and postdoctoral colleagues are often surprised when they learn that I did not follow the traditional career path expected of a scientist with a strong research background. "How did you know that you wanted to be at a small liberal arts college instead of a predominantly research-oriented academic institution?" they often ask. "I did not know!" is my usual answer.

That might seem like an odd response, but let me explain. Before I do that, however, let me put things into context by taking a few moments to introduce myself and my academic background. I received my Bachelor of Science degree in Biology from the University of Illinois at Urbana-Champaign and then went on to Northwestern University where I received my Ph.D. degree in the Department of Biochemistry, Molecular Biology, and Cell Biology. While in graduate school I met Reine, the person who would eventually become my wife. After receiving our Ph.D. degrees at Northwestern, Reine and I decided to go to Boston for our postdoctoral studies.

In Boston I was fortunate enough to join the laboratory of Dr. Fred Winston, a world renowned yeast geneticist at Harvard Medical School. After several years of productive research in the Winston laboratory, the time came to actually start looking for what some in the graduate school and postdoc world refer to as a "real job." That is to say, a job that was no longer shielded from the outside world but one that potentially had to deal with a number of unpleasant realities such as bureaucracy, stiff competition, and sink or swim work environments.

Although nowadays a "real job" following an academic postdoc can mean one of several things, the expected next step is still commonly one that involves setting up a research laboratory in a big academic research institution. In my particular case however, I knew for sure that I wanted to keep the "academic" part in my next job description, but I was not convinced that I wanted to limit my career to one that predominantly focused on research.

Let there be no misunderstanding, though: I knew I had a passion for research, and I absolutely wanted to remain immersed in it. How did I know this? While at the University of Illinois working on an undergraduate research project in the laboratory of Dr. David Nanney, I had an initial peek into what biological research was all about, and I thought I heard a calling in that direction, although I was not sure. However, that calling was the impetus behind my desire to pursue graduate studies. I kept my options open by telling myself that "if I don't love it, I can always try something else," but luckily, in part thanks to my ever passionate Ph.D. advisor, Dr. Richard Gaber, I did find meaning and purpose in research and that has shaped my career ever since.

However, while at Northwestern, I started to also hear a second calling that included the word "teaching" in it. This calling came as a result of several teaching assistantships I was fortunate to be part of, some of which included mini-lecture sessions involving undergraduate students. I greatly enjoyed sharing my passion for biology with others, and at the same time I realized that I was actually reasonably good at it.

So there I was, applying for that "real job," knowing that I wanted to be able to continue doing research but also having a sneaking suspicion that the second calling I heard while in graduate school might have been for real. It is therefore no great surprise that when I got the call from Hendrix College I jumped at the opportunity.

Hendrix is a highly regarded small liberal arts college in central Arkansas whose main mission is to offer undergraduate students from all over the country a top notch education. One of the characteristics that immediately attracted me to Hendrix was the fact that the administration and faculty clearly understand that hands-on learning experiences are absolutely crucial to the learning process of students. In my specific case, that would translate into ample opportunity and support for setting up a self-sustained, extramurally funded undergraduate research laboratory.

As in the case of my decision to go to graduate school, I was not absolutely positive that Hendrix was for me, and I kept my options open by telling myself that "if I don't love it, I can always try something else." However, I remember telling Reine, who admittedly was a bit apprehensive about a possible move from Boston to Arkansas, that "this might be EXACTLY what I am looking for."

I guess I would not be writing this if in fact it did not turn out that my current position as an assistant professor of Biology at Hendrix College was a perfect match for me. I have been able to confirm that my second calling was also in fact the real deal. At Hendrix, I find that I am able to pursue both of my passions, research and teaching, in a manner that I find extremely rewarding.

One bit of wisdom I would like to leave you with is the following: if you think you hear a calling, even though you might not be sure it is a real calling, pursue it nonetheless, keeping in mind that "if you don't love it, you can always try something else."

Teaching Interdisciplinary Science and Fostering Interdisciplinary Research: A Proposal

BY DR. J. ELLIS BELL

I've been attending educational symposia at scientific meetings for a good number of years, and probably the most frequent refrain I hear is that our students "don't learn very much in the 'allied fields' (i.e. physics and math courses) and don't seem to connect biology and chemistry courses to their biochemistry and molecular biology courses. I heard it again recently at the National Science Foundation in a conversation on the future of biology education. This brought up another comment I have heard in a number of contexts: our graduate students are not very well prepared to think in an interdisciplinary manner and take on interdisciplinary research. This comment can be equally applied to students and researchers making the transition from "basic" research to "translational" research. In a world increasingly focusing on interdisciplinary problems in science, these comments do not bode well for the future. We should be thinking of different approaches to education that will foster interdisciplinary science and lead to students who are better able to take on the challenges of the future.

The Compartmentalization of Science

The root of the problem, I suggest, lies in the way we teach science and the ways that we expect students to learn science. We compartmentalize science and put chemistry in one box, physics in another box, biology in yet another box, and math and computer science in still other boxes. And then we wonder why students compartmentalize. To make matters worse, even within the biology box or the chemistry box we compartmentalize even further in our teaching and further exacerbate the problem by "testing" our students in the same way. We do this in high school and in college and then suddenly in graduate school or medical school we want our students to think differently and respond to challenges differently. A few programs here and there over the last few years have tried to do something about the situation. David Botstein's program at Princeton, which was featured in last year's "Classroom of the Future" Symposium at the ASBMB Annual Meeting, is one of them, but maybe the time is right to think about whether such attempts should or could be more widespread and what the advantages and drawbacks of such an interdisciplinary, quantitative focus on science education might be.

An Interdisciplinary Science Course

So what are we talking about? Imagine a university or college where students taking science classes didn't take introductory chemistry, introductory biology, introductory physics, and introductory math or computer science courses but instead took a single, truly interdisciplinary course where the chemistry, physics, biology, and math were taught in a unified context so that students could not escape from the connections between the subjects and were held responsible for the connections between them, right from the start of their college education.

What would this look like for the average science major? Most science majors interested in the life sciences take 4 chemistry courses, 3–4 biology courses, 2 physics courses, and 2 math or computer science courses during their first two years in college. This results in a total of 11–12 courses out of a typical 16- to 20-course load over the two years. What if these individual courses were replaced by an Integrated Science core course that used the equivalent of 4 courses plus a year-long lab sequence in the first year and 2 courses plus a year-long lab sequence in the second year and was supplemented by 2 semesters of a more discipline-specific foundational course in the second year (most students have selected their major early in their second year and this course would be designed to anchor them in a department while still taking the interdisciplinary core)? Instead of taking the equivalent of 11–12 courses, students would be taking 8 courses with the goal of reaching the same coverage by the end of their second year as they would under current approach. The difference would be that 75% of their introductory science would be in the form of an interdisciplinary core.

So what would the result be? I believe that teaching an interdisciplinary core would not compromise coverage of topics. Instead it would make the underlying principles of the various disciplines more transparent to students and easier to relate to in an interdisciplinary manner. The course would also allow more time for other types of activities that a program might want to focus on. Some schools might use the time created to promote more formal research activities for first and second year students, others might use the additional time created in the major to require more advanced electives or further focus on interdisciplinary courses at a more advanced level, and still others might use these "extra" courses to broaden a liberal arts focus. Thus teaching an interdisciplinary core actually creates flexibility for degree programs and fosters "interdisciplinarity."

The course would also allow more time for other types of activities that a program might want to focus on

The Obstacles to Implementation

If it is such a good idea, why hasn't it been implemented in more than a handful of schools? There are many reasons. First and foremost, the departmental structure of most institutions and the ways of "counting" faculty teaching loads and assessing faculty effectiveness impede such initiatives. What is so wrong with team teaching a course with faculty from different departments? A good argument can be made that it benefits students to see collaborative teaching because it has become increasingly clear that collaborative research is here to stay, and my friends in industry tell me that one of the real skills necessary for industry is the ability to be a team player and work collaboratively. Young faculty often don't want to team teach because they fear that it might reflect badly on their "teaching evaluations." Maybe teaching effectiveness should be based upon demonstrable student outcomes and not on teaching surveys filled out by students. If student outcomes (such as the ability to understand and relate the foundational principles of different science disciplines to problems in the life sciences and to approach a problem from an interdisciplinary perspective) are better served by teaching an interdisciplinary core then we should be doing it in the most effective way we can.

The second objection often raised is that there are no textbooks to teach such a course. It's sort of a chicken and the egg type problem, and I suspect that major publishing companies would jump at the opportunity to help create such texts if it was clear that the science education community would support the concept of such interdisciplinary courses. I suspect, too, that the major funding agencies would also be supportive of a dialog between the disciplinary societies as to what aspects of physics, chemistry, biology, and math/computer sciences should be included in such a foundational core course and hence define the content of such a textbook.

There are currently no good ways of assessing student outcomes of such courses, but that doesn't mean that assessments cannot be created. The assessments must include a thorough foundation of disciplinary principles as well as emphasis on the students' ability to apply knowledge and skills in an interdisciplinary context. If both facets are not critically assessed, the whole premise of such a core falls. It is important that students at the end of the course are well prepared to go into any of the related disciplinary majors by making obvious connections between the sciences and emphasizing the necessity in today and tomorrow's world of approaching any of the sciences from an interdisciplinary perspective. (As an aside, such an interdisciplinary science core might also act to stop students "collecting" second and third majors in closely related subjects like biochemistry and chemistry–another aspect of our current education system that many dislike.)

Finally, when talking to people about such a core course I often hear, "but medical school admissions require all these courses." I believe that if the academic community were behind such a concept, and if they developed the appropriate assessments of student learning, the powers that govern medical school admissions criteria would not stand in the way. After all, they will be one of the main beneficiaries of such an innovation if it creates students that are better able to think across disciplines and in a more translational manner.

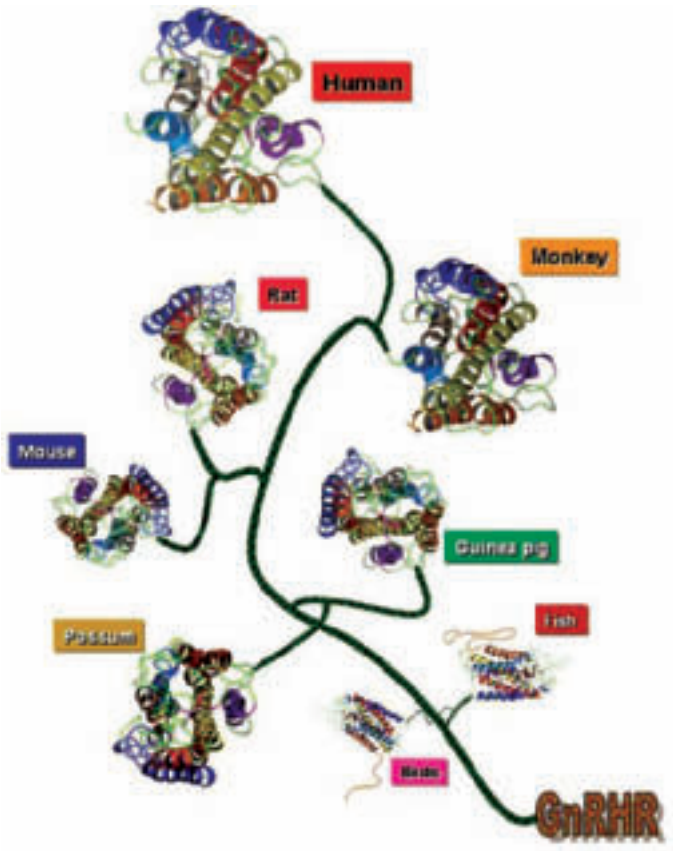
ASBMB, through its Education and Professional Development Committee, will open a dialog in the coming year with the appropriate disciplinary societies with the goal of defining the essential conceptual content such a core course should cover and developing suggestions for implementation and assessment. We will feature these in the 2008 Annual Meeting "Classroom of the Future" Symposium.

Receptor Specializations Aid in Frequency Modulated Signal Sensing

BY NICOLE KRESGE

A group of Oregon scientists has discovered specializations in a well characterized G-protein coupled receptor that appear to have evolved to sense frequency modulated signals. They were able to identify specific amino acid residues in the gonadotropin-releasing hormone receptor (GnRHR) that vary among primates and also differ when compared with pre-primate species. These residues regulate the plasma membrane expression of GnRHR and the binding interaction with its ligand.

GnRHR is a member of the seven-transmembrane, G-protein coupled receptor family. It is expressed on the surface of pituitary gonadotrope cells as well as on the membrane of lymphocytes and breast, ovary, and prostate cells. Following binding of gonadotropin releasing hormone (GnRH), GnRHR associates with G-proteins that activate a phosphatidylinositol-calcium second messen-



Stylized images of the GnRH receptor from different animals. Image by Dr. Alfredo Ulloa-Aguirre, Research Unit in Reproductive Biology, Instituto Mexicano del Seguro Social, Mexico City, Mexico.

P. Michael Conn is the associate director of the Oregon National Primate Research Center and of Cell Biology and Development at Oregon Health and Science University. He received his B.S. degree from the University of Michigan (1971), M.S. from North Carolina State University (1973), and Ph.D. from Baylor College of Medicine (1976). Conn joined the Department of Pharmacology at the Duke University Medical Center and was promoted to associate professor in 1982. In 1984, he became professor and head of Pharmacology at the University of Iowa College of Medicine, a position he held for 11 years before joining the National Primate Research Center.

Conn is best known for his research on the cellular and molecular basis of gonadotropin releasing hormone action in the pituitary and CNS and his vigorous support of the humane use of animals in research. He has been recognized with a MERIT award from the National Institutes of Health; the J. J. Abel Award from the American Society for Pharmacology and Experimental Therapeutics; the Weitzman, Oppenheimer, and Ingbar Awards of the Endocrine Society; the National Science Medal of Mexico (the Miguel Aleman Prize); the Oregon Medical Research Foundation Award for Discovery; and the Stevenson Award of Canada. Conn was president of the Endocrine Society, during which time he founded the Hormone Foundation. He has served as editor-in-chief for several scientific journals and is presently the editor-in-chief of *Endocrine, Methods, Contemporary Endocrinology,* and *Contemporary Drug Therapy*.

ger system. The receptor transduces both amplitude and frequency modulated signals. Slower GnRH pulses favor the release of pituitary follicle stimulating hormone, whereas faster pulses favor luteinizing hormone release. The need to distinguish the signals from background noise is especially critical if perception of pulse frequency is to be accurate.

"Neural, endocrine, and drug response systems typically respond to amplitude or frequency modulated stimuli," says P. Michael Conn, who headed the study. "Amplitude modulated systems have been well studied and typically achieve a graded response by summation of quantal responses from individual cells with different set points. The mechanism by which receptors transduce frequency modulated signals has been more elusive, however. This study reveals specializations of a well characterized G-protein coupled receptor that evolved in order to sense frequency modulated signals."

In their study, published in the February 2007 issue of *The FASEB Journal*, Conn and his colleagues (Jo Ann Janovick, Shaun Brothers, and Paul Knollman) used mutational analysis to determine the impact of evolved sequence specializations on GnRHR frequency modulated signal detection. They found that certain amino acid substitutions affect the plasma membrane expression of the receptor. For example, amino acids in the rat GnRHR result in more plasma membrane GnRHR expression than in primates.

The study reveals specific biochemical features of the primate GnRH receptor and explains how these features allow sensing frequency modulated signals by setting low level signal squelching and adjustment to signal sensitivity

"The observation that it has evolved (in the GnRHR) under strong convergent pressure and in spite of the metabolic 'waste' of unused receptor, along with added susceptibility to mutational disease, leads to the conclusion that it must have value," notes Conn. "One attractive possibility is that post-translational regulation might involve control by endogenous protein chaperones that may, themselves, be regulated by the steroidal milieu. In this manner, they might participate in the oscillation of the GnRHR through the reproductive cycle."

The scientists also found that unique modifications in the human and rhesus monkey GnRHRs are associated with decreased affinity for the GnRH agonist, as compared to rats. "The likely selective advantage of decreased affinity is clearer when one considers that the GnRHR in primates is governed by ligand frequency modulation, making the distinction of individual pulses important," explains Conn. "Decreasing the binding affinity is an effective strategy for ignoring low level stimuli, effectively squelching (suppressing) noise in the system, an advantage in a frequency modulated system.

"The study reveals specific biochemical features of the primate GnRH receptor and explains how these features allow sensing frequency modulated signals by setting low level signal squelching and adjustment to signal sensitivity," adds Conn. "Even among primates, subtle modifications at different amino acid positions are utilized to achieve the similar goal of squelching low level signals, suggesting that this is an important and convergent goal."

Silent Gene Mutation Changes Function of Anticancer Drug Pump

A genetic mutation that does not cause a change in the amino acid sequence of the resulting protein can still alter the protein's expected function, according to a new study conducted at the National Cancer Institute (NCI), part of the National Institutes of Health (NIH). The study shows that mutations involving single base changes in the multidrug resistance gene (MDR1) that do not affect the protein sequence of the MDR1 gene product can still alter the protein's ability to bind certain drugs. Changes in drug binding may ultimately affect the response to treatment with many types of drugs, including those used in chemotherapy. The results of this study appeared online in "Science Express" on December 21, 2006.

The genetic mutations examined in this research are known as single nucleotide polymorphisms (SNPs) and are very common. Some SNPs do not change the DNA's coding sequence, so these types of so-called silent mutations were not thought to change the function of the resulting proteins.

"This study provides an exception to the silent SNP paradigm by showing that some minor mutations can profoundly affect normal cell activity," said NCI Director John E. Niederhuber, M.D. "These results may not only change our thinking about mechanisms of drug resistance but may also cause us to reassess our whole understanding of SNPs in general, and what role they play in disease."

Despite success in treating some cancers with chemotherapy, many tumors are naturally resistant to anticancer drugs or become resistant to chemotherapy after many rounds of treatment. Researchers at NCI and elsewhere have discovered one way that cancer cells become resistant to anticancer drugs: they expel drug molecules using pumps embedded in the cellular membrane. One of these pumps, called P-glycoprotein (P-gp), is the protein product of the MDR1 gene and contributes to drug resistance in about 50% of human cancers. P-gp prevents the accumulation of powerful anticancer drugs, such as etoposide and Taxol, in tumor cells. The same pump is also involved in determining how many different drugs, including anticancer drugs, are taken up or expelled from the cell.

In this study, researchers led by Michael M. Gottesman, M.D, demonstrated that SNPs in the MDR1 gene result in a pump with an altered ability to interact with certain drugs and pump inhibitor molecules. To show that SNPs can actually affect pump activity, the researchers genetically engineered cells to contain either normal MDR1 or a copy of the MDR1 gene that contains one or more SNPs. Then, they used fluorescent dyes to track pump function based on the accumulation of dye in the cell or the export of dye out of the cell with and without various inhibitors of P-gp. This showed that although the SNPs did not change the expected P-gp protein sequence, the presence of one particular SNP, when in combination with one or two other SNPs that frequently occur with it, resulted in less effective pump activity for some drugs than normal P-gp without the SNP.

Michael M. Gottesman

Michael M. Gottesman obtained his M.D. from Harvard University Medical School. He did an internship and residency at the Peter Bent Brigham Hospital in Boston and was a postdoctoral fellow at the National Institutes of Health. After a year as an assistant professor in the Department of Anatomy at Harvard University, he moved to the NIH. He currently serves as the NIH deputy director for intramural research as well as chief of the Laboratory of Cell Biology in the National Cancer Institute.

Gottesman is the recipient of the Samuel G. Taylor III Award for Excellence in Cancer Research, the Rosenthal Foundation Award, and the NIH Director's Award. He has served on the editorial boards of several journals including that of the *Journal of Biological Chemistry*. *Photo: National Cancer Institute, Bill Branson, photographer.*

The P-gp protein sequences and production levels were normal in both the cells that received the normal MDR1 gene and those that received the mutant versions. Therefore, to determine how the SNPs affected pump function, the researchers used an antibody that could distinguish between different P-gp structural conformations. They found significant differences in antibody binding consistent with the existence of different protein conformations in the products of MDR1 genes with or without the SNPs. These results indicate that the shape of a protein is determined by more than its amino acid sequence.

"We think that this SNP affected protein function because it forced the cell to read a different DNA codon than it usually does," said Gottesman. "While the same exact protein sequence eventually got made, this slight change might slow the folding rhythm, resulting in an altered protein conformation, which in turn affects function."

Since silent SNPs are frequently found in nature, their biological role has largely been overlooked. However, this study raises the possibility that even silent mutations could contribute to the development of cancer and many other diseases.

Nobel Laureate Finds "Elegant" Explanation for DNA Transcribing Enzyme's High Fidelity

Last December, Roger Kornberg of Stanford University was awarded the Nobel Prize in Chemistry for his efforts to unravel the molecular basis of eukaryotic transcription. Now, Kornberg and his colleagues report in the December 1, 2006, issue of the journal *Cell* new structures that reveal another critical piece of the puzzle: how polymerase II discriminates among potential RNA building blocks to ensure the characteristic accuracy of the process.

The researchers found that a portion of the enzyme known as the trigger loop acts like a "trap door," swinging beneath a matching nucleoside triphosphate (NTP) building block, to close off the active center and form an extensive network of interactions with the NTP and other parts of the enzyme. Those interactions leave another side chain in the trigger loop precisely positioned, such that it may literally "trigger" the formation of the chemical bonds that link components of the growing RNA chain together. If the NTP is even slightly misaligned, Kornberg said, those critical interactions fail.

The trigger loop mechanism therefore couples NTP recognition and catalysis, ensuring the fidelity of transcription, they reported.

"Of all revelations from the structure [of the transcription machinery] since it was first solved, this is perhaps the most fundamental since it gets at the underlying mechanisms," Kornberg said. "It's long known that the enzyme operates with high fidelity—selecting the correct base and sugar—but it's been a mystery how that is accomplished."

These findings offer "an unexpected and elegant explanation that's both beautiful and simple, as nature invariably proves to be."

Kornberg's group captured the first picture of the polymerase II transcribing complex by x-ray crystallography in 2001. Those structures revealed the complex with a nucleotide still in the enzyme's addition site, just after it had been added to the RNA transcript.

Later x-ray structures revealed the transcribing complex with the addition site available for entry of a matched NTP. Those crystals uncovered a second NTP-binding site on the transcribing enzyme, dubbed the entry site. While all NTPs can bind the entry site, only an NTP matched for base pairing with the DNA template binds the addition site for attachment to the growing RNA strand, Kornberg said.

Yet the question of how the enzyme achieves such a high degree of discrimination between matched and mismatched NTPs remained unanswered.

The chemical attraction alone between RNA bases and their complementary bases on the DNA template strand is far from sufficient to account for the incredible selectivity of polymerase II, Kornberg said. And the scientists didn't know either how the polymerase avoids substituting the NTPs that constitute DNA for the cor-

Roger D. Kornberg

Roger D. Kornberg earned his B.A. from Harvard University and his Ph.D. from Stanford. He conducted postdoctoral research at the Medical Research Council Laboratory of Molecular Biology in Cambridge, United Kingdom. In 1976 he became an assistant professor in the Department of Biological Chemistry at Harvard Medical School. In 1978 he returned to Stanford as a professor in the Structural Biology Department and served as department chair from 1984 to 1992. Currently, Kornberg is the Mrs. George A. Winzer Professor in Medicine at the Stanford University School of Medicine.

In addition to the 2006 Nobel Prize in Chemistry, Kornberg received the 2002 ASBMB-Merck Award, the 2002 Pasarow Award in Cancer Research, and the 2005 Alfred P. Sloan Jr. Prize. He is a member of the National Academy of Sciences and the American Academy of Arts and Sciences.

rect RNA building blocks, molecules that differ by only one oxygen atom.

In search of an explanation in the current study, the researchers screened hundreds of crystals to achieve higher data quality and resolution than ever before.

"In the course of the work, we saw something that had never been noticed before—additional protein density beneath the matching nucleotide," Kornberg said. The team traced that protein density back to a portion of the polymerase II enzyme: the trigger loop.

"Of the 14 crystal structures now reported in which the trigger loop was observed, only in 2 is it seen in that location, directly beneath the NTP," Kornberg said. Those were the only two crystals in which the NTP was correctly matched to the DNA template, evidence of the trigger loop's "clear relationship to NTP selection," he explained.

Further study revealed that, when a matching NTP reaches the addition site, the trigger loop swings from its usual position some distance away until it rests parallel to the NTP. It then forms a network of interactions—some 20–30 in all—with components of the NTP, a process that serves to "recognize all features of the NTP in the addition site and detect its precise location," the researchers reported.

"The specificity is a result of the alignment with the NTP that is critically dependent upon the base, sugar, phosphate, and location when the trigger loop swings into position," Kornberg said. "If it is misaligned even slightly, that set of contacts cannot occur."

As a consequence of that alignment a histidine side chain of the trigger loop rests on the ß phosphate, the chemical constituent that must have its bond broken for the NTP to join the RNA chain through the formation of a phosphodiester bond, Kornberg said. The finding suggested the side chain acts as a trigger for bond formation.

"The basis for the extraordinary specificity with which RNA polymerases transcribe DNA lies in a structural element termed the trigger loop, which makes both direct and indirect contact with all features of the nucleotide in the polymerase active center," the researchers concluded.

Scientists Explore Function of "Junk DNA"

University of Iowa scientists have made a discovery that broadens our understanding of the rapidly developing area of functional genomics and sheds more light on the mysterious, so-called "junk DNA" that makes up the majority of the human genome.

The team, led by Beverly Davidson, Ph.D., has discovered a new mechanism for the expression of microRNAs–short segments of RNA that do not give rise to proteins but do play a role in regulating protein production. In their study, Davidson and her colleagues not only discovered that microRNAs could be expressed in a different way than previously known; they also found that some of the junk DNA is not junk at all but instead consists of sequences that can generate microRNAs.

Davidson and her colleagues, including Glen Borchert, a graduate student in her lab, investigated how a set of microRNAs in the human genome is turned on. In contrast to original assertions, they discovered that the molecular machinery used to express these microRNAs is different than that used to express RNA that encodes proteins. Expression of the microRNAs required RNA Polymerase III (Pol III) rather than RNA Polymerase II (Pol II), which mediates expression of RNA that encode proteins. The study was published in the December 2006 issue of *Nature Structural and Molecular Biology*.

"MicroRNAs are being shown to play roles in cancer and in normal development, so learning how these microRNAs are expressed may give us insight into these critical biological processes," said Borchert, who is lead author of the study. "Up to now it's been understood that one enzyme controls their expression, and we now show that in some cases it's a completely different one."

Genes that code for proteins make up only a tiny fraction of the human genome. The function of the remaining non-coding sequence is just beginning to be unraveled. In fact, until very recently, much of the non-coding sequence was dismissed as junk DNA. In 1998, scientists discovered that some DNA produced small pieces of non-coding RNA that could silence genes. This discovery won Andrew Fire and Craig Mello the 2006 Nobel Prize for Medicine or Physiology. Since their discovery, the field has exploded, and small, non-coding RNAs have been shown to play an important role in development and disease in ways that scientists are only just beginning to understand.

"Not so many years ago our understanding was that DNA was transcribed to RNA, which was then translated to protein. Now we know that the levels of control are much more varied and that many RNAs don't make protein but instead regulate the expression of proteins," Davidson explained. "Non-coding RNA like microRNAs represent a set of refined control switches, and understanding how microRNAs work and how they are themselves controlled is likely to be very important in many areas of biology and medicine."

Beverly Davidson

Beverly Davidson is the Roy J. Carver Professor in Internal Medicine at the University of Iowa and is professor in the Departments of Neurology, and Physiology & Biophysics.

She is also associate director of the Center for Gene Therapy for Cystic Fibrosis and Other Genetic Diseases and is director of the Gene Transfer Vector Core. She also holds the position of vice-chair for research in the Department of Internal Medicine.

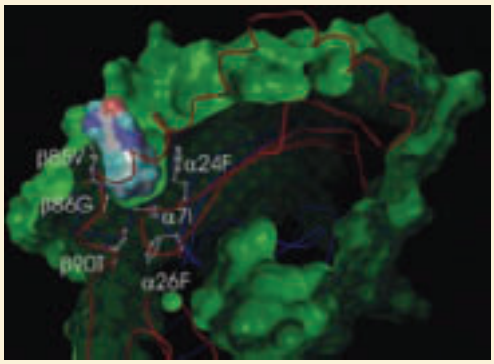
Prior to joining the faculty at the University of Iowa in 1994, Davidson received her Ph.D. in Biological Chemistry from the University of Michigan, where she also did postdoctoral training in Molecular Genetics. Davidson's research focuses on the development of molecular therapies for neurodegenerative diseases.

J. Biol. Chem. 2006 281: 38535–38542

Small Organic Compounds Enhance Antigen Loading of Class II Major Histocompatibility Complex Proteins by Targeting the Polymorphic P1 Pocket

Sabine Hopner, Katharina Dickhaut, Maria Hofstatter, Heiko Kramer, Dominik Ruckerl, J. Arvid Soderhall, Shashank Gupta, Viviana Marin-Esteban, Ronald Kuhne, Christian Freund, Gunther Jung, Kirsten Falk, and Olaf Rotzschke

Major histocompatibility complex (MHC) class II molecules are involved in presenting extracellular peptide antigens for surveillance by T cells. The peptides are loaded onto the molecules in the cytoplasm after which they migrate to the plasma membrane and present the peptides to T cells. Studies have shown that certain organic compounds, such as aliphatic alcohols and phenol derivatives, can accelerate peptide loading onto class II MHC molecules, thereby amplifying the immune response. In this paper, the authors screened a library of approximately 20,000 compounds to determine the molecular basis of this catalysis. They discovered that adamantine derivatives strongly accelerate the peptide-loading rate. The authors also elucidated both the structures of the catalytic compounds and the location of their target site, providing a structural framework for the rational design of new compounds to enhance vaccine antigen loading onto MHC class II molecules.



Adamantine derivatives bind to a pocket in MHC molecules.

jbc

J. Biol. Chem. 2006 281: 36944–36951

Novel Benzene Ring Biosynthesis from C_3 and C_4 Primary Metabolites by Two Enzymes

Hirokazu Suzuki, Yasuo Ohnishi, Yasuhide Furusho, Shohei Sakuda, and Sueharu Horinouchi

The shikimate pathway is the common route for the biosynthesis of aromatic amino acids and most biogenic benzene derivatives in bacteria, fungi, algae, and higher plants. However, studies indicate that 3-amino-4-hydroxybenzoic acid (3,4-AHBA), a benzene derivative that serves as a precursor for several secondary metabolites including grixazone produced by *Streptomyces griseus*, may be derived from a non-shikimate-type pathway. In this paper, the authors prove the existence of this new route from C3 and C4 precursors to a benzene ring. The pathway consists of two genes, *gril* and *griH*, that make benzene rings from the two primary metabolites, L-aspartate-4-semialdehyde and dihydroxyacetone phosphate. When expressed in *Escherichia coli*, the two genes caused the production of 3,4-AHBA. An analysis showed that *Gril* catalyzes aldol condensation between the two primary metabolites to form a 7-carbon product, 2-amino-4,5-dihydroxy-6-one-heptanoic acid-7-phosphate, which is subsequently converted to 3,4-AHBA by *GriH*.

pAYP26 carrying *griL* and *griH* produces a grixazone-like pigment.[c]

jbc

Mol. Cell. Proteomics 2006 5: 2252–2262

Quantitative Comparison of Caste Differences in Honeybee Hemolymph

Queenie W. T. Chan, Charles G. Howes, and Leonard J. Foster

The honeybee is an invaluable partner in agriculture around the world both for its production of honey and for its role in pollination. Like other eusocial insects, honeybees can be divided into several castes: the queen, workers, and drones. Each caste has different energetic and metabolic requirements, and each differs in its susceptibility to pathogens. Hemolymph, arthropods' equivalent to blood, distributes nutrients throughout the bee and contains components of the insects' innate immune system. In this study the authors applied qualitative and quantitative proteomics to gain a better understanding of honeybee hemolymph and how it varies among the castes and during development. They found large differences in hemolymph protein composition, especially between larval and adult stage bees and between male and female castes but also between adult workers and queens.

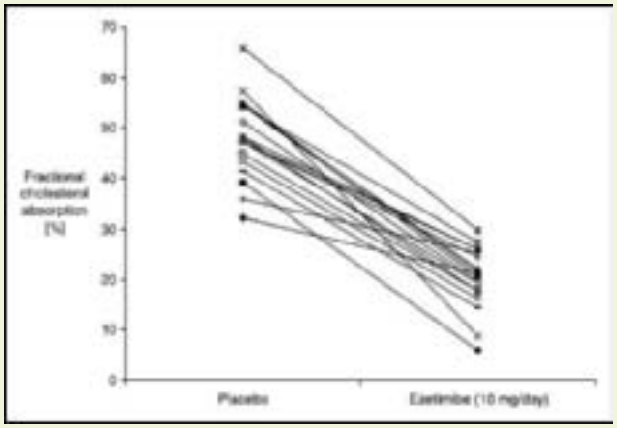
Hemolymph was drawn from adult bees.

J. Lipid Res. 2006 47: 2820–2824

The Lipid-Lowering Effect of Ezetimibe in Pure Vegetarians

Jacob J. Clarenbach, Michael Reber, Dieter Lütjohann, Klaus von Bergmann, and Thomas Sudhop

Studies have shown that ezetimibe (10 mg/day) reduces low density lipoprotein (LDL) cholesterol in patients with mild hypercholesterolemia on a normal-cholesterol diet by 16–22%. However, the LDL cholesterol lowering effect of ezetimibe in subjects with an extremely low dietary cholesterol intake such as vegetarians has not been studied. In this paper, the authors conducted a randomized, double-blind, placebo-controlled, two-phase crossover study in 18 healthy pure vegetarians to assess the effect of ezetimibe (10 mg/day) on plasma lipids, cholesterol absorption, and its synthesis. They found that fractional cholesterol absorption decreased by 58% during ezetimibe treatment. This change in intestinal cholesterol absorption was followed by a significant reduction in LDL cholesterol. From these results the authors conclude that the lipid lowering effect of ezetimibe is mediated mainly through a reduction of the absorption of endogenous (biliary) cholesterol.



Fractional cholesterol absorption decreases during ezetimibe treatment.

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Candidates should submit a cover letter, curriculum vitae, a description of research accomplishments, copies of three significant publications, a summary of teaching and curriculum development philosophy, a vision statement regarding leadership as chair of the department, and names and addresses of at least three references to:

Dr. Robert Lad, Chair of the Search Advisory Committee, College of Liberal Arts & Sciences, 100 Stevens Hall, University of Maine, Orono, ME 04469-5706 (e-mail: chemistry_chair_search@umit.maine.edu).

Application review will begin immediately and continue until the position is filled.

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Cleveland State University

GAANN PREDOCTORAL FELLOWSHIPS IN CELL AND MOLECULAR BIOLOGY

Cleveland State University (CSU) is now accepting applications for four GAANN predoctoral fellowships to begin in the fall 2007. These CSU GAANN Biology Scholars will join the Ph.D. program in regulatory biology, which is offered jointly by CSU and the Lerner Research Institute of the Cleveland Clinic. Research may be conducted at either institution. Fellowships provide tuition, some expenses, and a stipend of up to $30,000/year based on need. Applicants must be U.S. citizens or permanent residents; members of groups under-represented in the field are particularly encouraged to apply. For more information on the program and research faculty, see web.bges.csuohio.edu or contact:

Dr. Jeffrey Dean (216-687-2120 or j.dean@csuohio.edu).

meeting calendar

FEBRUARY 2007

Keystone Symposium on Ubiquitin and Signaling
February 4–9, 2007
BIG SKY RESORT, BIG SKY, MT
www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=860
E-mail: info@keystonesymposia.org
Tel.: 800-253-0685 or 970-262-1230

Keystone Symposium on PI 3-Kinase Signaling Pathways in Disease
February 15–20, 2007
HILTON SANTA FE/HISTORIC PLAZA, SANTA FE, NM
www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=864
E-mail: info@keystonesymposia.org
Tel.: 800-253-0685 or 970-262-1230

Keystone Symposium on Bioactive Lipids in the Lipidomics Era
February 20–25, 2007
TAOS, NM
www.keystonesymposia.org

MARCH 2007

Biophysical Society 51st Annual Meeting
March 3–7, 2007
BALTIMORE, MD
www.biophysics.org/

U.S. HUPO 2007
March 4–8, 2007
SEATTLE, WA
www.ushupo.org
E-mail: USHUPO@USHUPO.org
Tel.: 505-989-4876

2007 Deuel Conference on Lipids
March 6–9, 2007
BORREGO SPRINGS, CA
www.scripps.edu/imm/curtiss/deuel/index.html

Cell Signaling and Proteomics
March 22–27, 2007
STEAMBOAT SPRINGS, CO
www.keystonesymposia.org/Meetings/

RNAi2007: The Expanding Roles of Small RNAs
March 29–30, 2007
ST. ANNE'S COLLEGE, WOODSTOCK ROAD, OXFORD, UK
Organizer: Dr. Muhammad Sohail
www.libpubmedia.co.uk/Conferences/RNAi2007/Home.htm
E-mail: Muhammad.Sohail@bioch.ox.ac.uk
Tel.: 44-0-1865-275231

APRIL 2007

3rd European Symposium on Plant Lipids
April 1–4, 2007
YORK, UK
www.eurofedlipid.org/meetings/index.htm

Second Workshop on Biophysics of Membrane Active Peptides
April 1–4, 2007
LISBON, PORTUGAL
www.biophysicsmap.com

2nd International Congress on Prediabetes and the Metabolic Syndrome
April 25–28, 2007
BARCELONA, SPAIN
www.kenes.com/prediabetes2007
E-mail: prediabetes2007@kenes.com

ASBMB Annual Meeting in Conjunction with EB2007
April 28–May 2, 2007
WASHINGTON, DC
Contact: ASBMB 2007, 9650 Rockville Pike, Bethesda, MD 20814-3008
www.asbmb.org/meetings
E-mail: meetings@asbmb.org
Tel.: 301-634-7145

MAY 2007

7th International Symposium of the Protein Society
May 12–16, 2007
STOCKHOLM-UPPSALA, CA SWEDEN
www.proteinsociety.org/pages/page02b.htm
E-mail: cyablonski@proteinsociety.org
Tel.: 301-634-7277

National Lipid Association Annual Scientific Sessions
May 31–June 3, 2007
SCOTTSDALE, AZ
www.lipid.org/chapters/swla

Epistasis: Predicting Phenotypes and Evolutionary Trajectories
May 31–June 3, 2007
IOWA STATE UNIVERSITY, AMES, IA
www.bb.iastate.edu/%7Egfst/PSIframeset.html
Tel.: 515-294-7978

JUNE 2007

55th ASMS Conference on Mass Spectrometry
June 3–7, 2007
INDIANAPOLIS, IN
www.asms.org
Tel.: 505-989-4517

Mitosis Spindle Assembly and Function: A FASEB Summer Research Conference in Honor of Dr. B. R. Brinkley
Applications from students and post-docs are especially welcome!
June 9–14, 2007
HYATT GRAND CHAMPIONS RESORT AND SPA, INDIAN WELLS, CA
Organizers: Dr. Conly L. Rieder
E-mail: rieder@wadsworth.org
Dr. Robert E. Palazzo,
E-mail: palazr@rpi.edu

76th Annual European Atherosclerosis Society Congress
June 10–13, 2007
HELSINKI, FINLAND
www.kenes.com/eas2007
Tel.: 41-22-908-0488
Fax: 41-22-732-2850

JULY 2007

32nd FEBS Congress: Molecular Machines and Their Dynamics in Fundamental Cellular Functions
July 7–12, 2007
VIENNA, AUSTRIA
Registration is open until March 31
www.FEBS2007.org

Life Sciences 2007: The first joint meeting of the Biochemical Society, the British Pharmacological Society, and The Physiological Society
July 8–12, 2007
THE SECC, GLASGOW, UK
www.lifesciences2007.org/

Gordon Research Conference - Molecular and Cellular Biology of Lipids
July 22–27, 2007
WATERVILLE VALLEY, NH
www.grc.org

4th British Society for Proteome Research/European Bioinformatics Institute Proteomics Meeting
Integrative Proteomics: Maximizing the Value of Proteomics
July 25–27, 2007
WELLCOME TRUST CONFERENCE CENTRE, HINXTON, CAMBRIDGE, UK
www.bspr.org/
E-mail: meetings@bspr.org

Senescence, Aging, and Cancer Symposium
July 26–29, 2007
IOWA STATE UNIVERSITY, AMES, IA
www.bb.iastate.edu/%7Egfst/homepg.html
Tel.: 515-294-7978

FASEB Summer Research Conference
Lipid Droplets: Metabolic Consequences of Stored Neutral Lipids
Organizers: Dawn L. Brasaemle, Rutgers, The State University of New Jersey, and Rosalind A. Coleman, University of North Carolina
July 28–August 2, 2007
VERMONT ACADEMY, SAXTONS RIVER, VT
src.faseb.org

AUGUST 2007

13th International Conference on Second Messengers and Phosphoproteins
August 1–4, 2007
SAN DIEGO, CA
Abstracts must be submitted by July 1
www.smp-2007.com/

8th International Symposium on Mass Spectrometry in the Health & Life Sciences
August 19–23, 2007
FAIRMONT HOTEL, SAN FRANCISCO, CA
www.donatello.ucsf.edu/symposium/
E-mail: sfms@itsa.ucsf.edu
Tel.: 415-476-4893

13th Nordic Mass Spectrometry Conference
August 28–31, 2007
SAVONLINNA, FINLAND
www.nsms.no/moter.html

SEPTEMBER 2007

48th International Conference on the Bioscience of Lipids
September 4–8, 2007
TURKU, FINLAND
www.icbl2007.abo.fi

5th Euro Fed Lipid Congress
September 16–19, 2007
GOTEBORG, SWEDEN
www.eurofedlipid.org/meetings/goeteborg/index.htm

OCTOBER 2007

4th International & 2nd Asia-Pacific Peptide Symposium
October 21–26, 2007
CAIRNS, QUEENSLAND, AUSTRALIA
www.peptideoz.org
E-mail: mibel.aguilar@med.monash.edu.au
Tel.: 613-9905-3723

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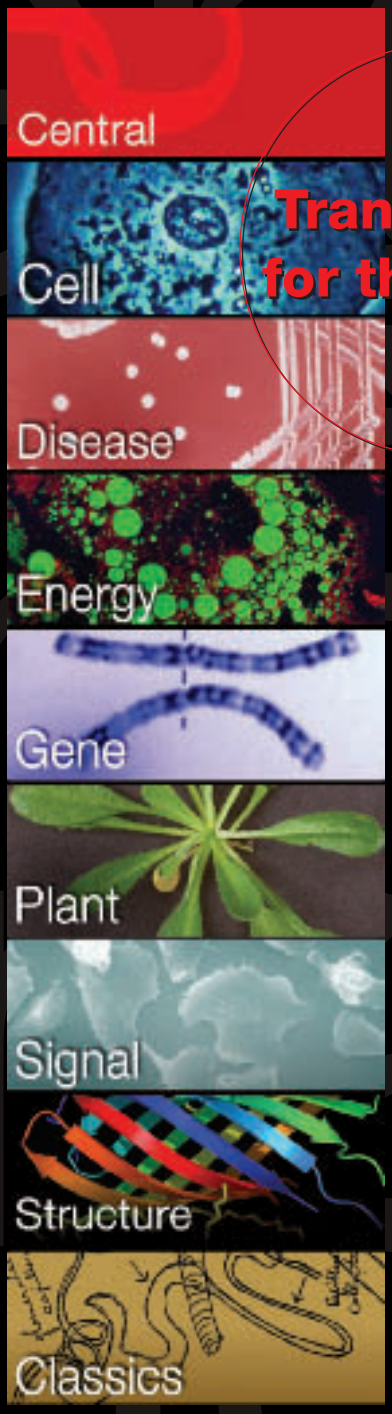

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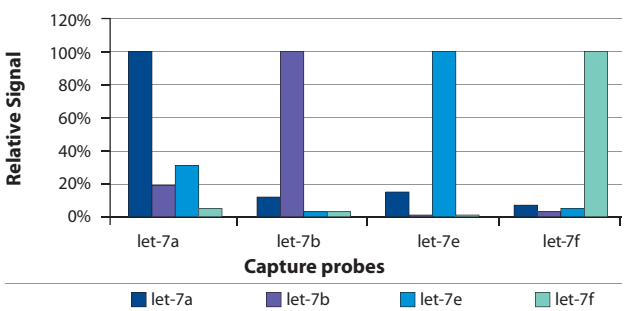

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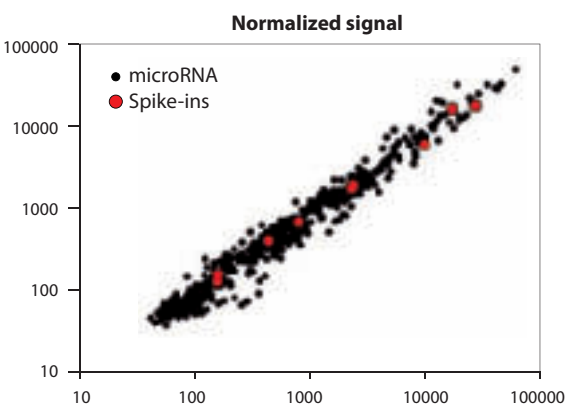

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