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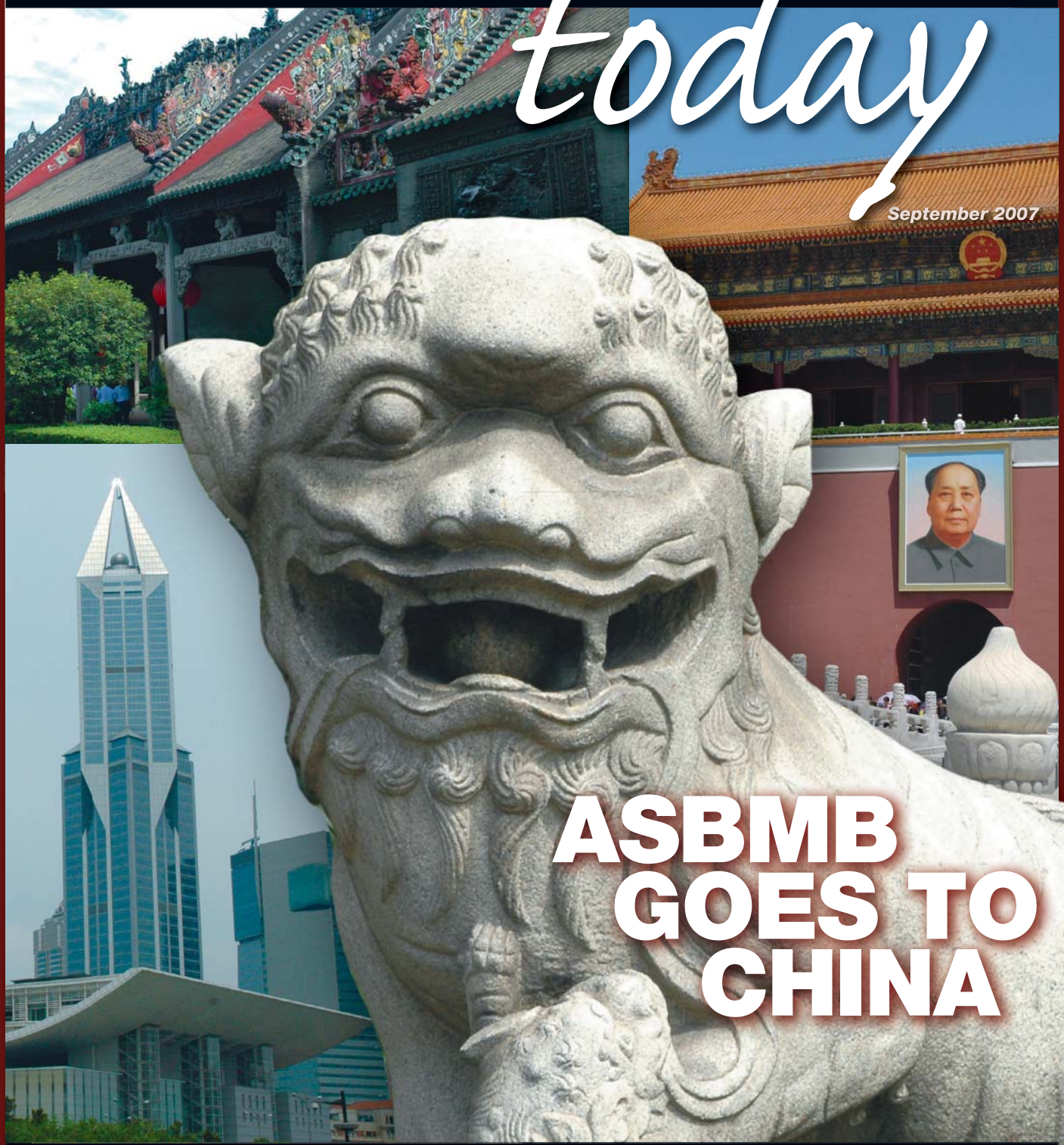
ASBMB today

September 2007



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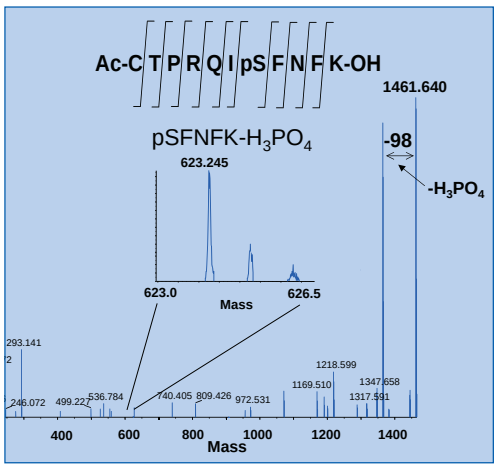

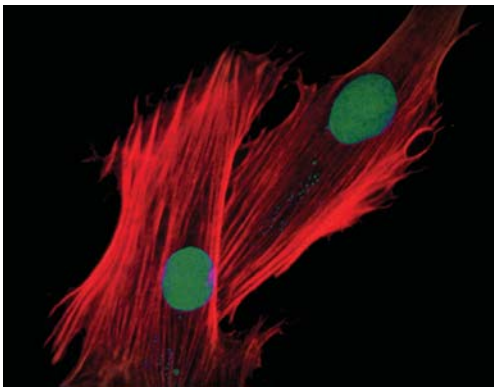

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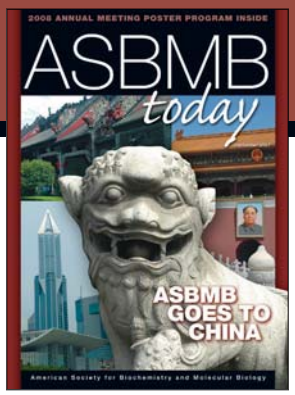

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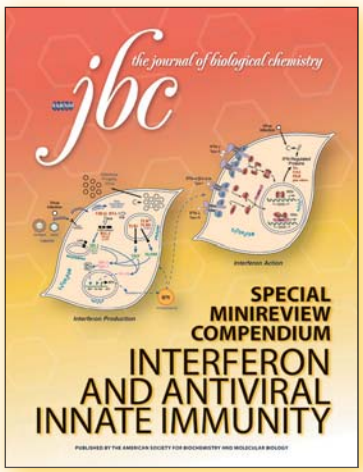

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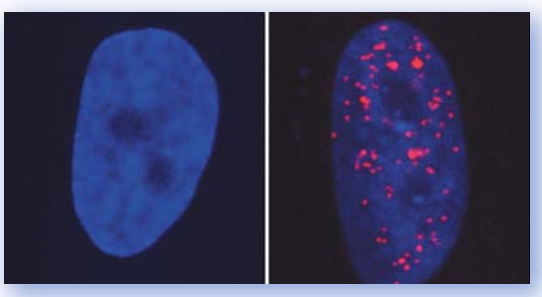

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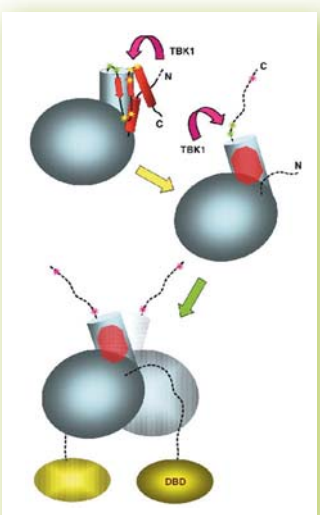

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president's message

Peer Review Front and Center

BY HEIDI HAMM

It's great to be back from a very productive and interesting trip to China with our ASBMB delegation. We met our goals of establishing a closer relationship with Chinese scientists in biochemistry and molecular biology, and we were delighted with the warm and enthusiastic welcome we received.

I am sure you have been hearing about the many calls for information from the National Institutes of Health (NIH) on many topics. One which is dear to our hearts is peer review. It's good to see that the NIH is making a major effort to examine the peer review process. This critical reexamination of the peer review system has been a high priority of ASBMB, prompted by the crisis in funding and resultant doubling of NIH grant applications over recent years. A key reason for this reassessment is to be sure the system is operating as it was meant to after the last major overhaul instigated by the Panel on Scientific Boundaries for Review almost 7 years ago. Of course, we hope that completely new ideas will emerge from this reexamination to help us overcome the real crisis in peer review that has resulted from the lack of investment in biomedical research over the last 5 years.

A number of activities to assess peer review are underway. Toni Scarpa, director of the Center for Scientific Review (CSR), announced a series of open houses to give the extramural community a chance to voice their views on the quality and expertise of various study sections and Integrated Review Groups (IRGs). (More information is given at cms.csr.nih.gov/AboutCSR/OpenHouses.htm.) The open house on Biomolecular IRGs, which is particularly relevant to ASBMB, will be held on December 18.

The Panel on Scientific Boundaries for Review, headed by Bruce Alberts, undertook the latest reorganization of study sections. I have been working closely with Bruce for a couple of years on the issue of how to influence the CSR to have more ongoing input from extramural scientists on how study sections are functioning. This ongoing interaction has led to a proposal for the two societies to work together to provide our input to the CSR. Thus, the two societies will jointly analyze the makeup and scope of the study sections that are of most interest to the two societies, determine whether there is sufficient breadth, expertise, and balance between basic and clinical investigators, etc. Our analysis will be provided to the CSR at this open house. If you are willing to be involved in this analysis, please let me or Mary Hendrix, chair of the Public Affairs Advisory Committee, know of your interest! In particular, we need ASBMB members who have served on these study sections recently, as they are the real experts on how well the study sections are working.

Additionally, a Working Group of the NIH Advisory Committee to the Director, focusing on a review of the current peer review system at NIH, met in Washington, D.C. on July 30 to hear

comments from the scientific community. ASBMB President-Elect Greg Petsko delivered ASBMB's comments, which covered 4 main points:

Oversight of study sections should be ongoing. The Center for Scientific Review must monitor the IRGs and study sections to ensure that they are functioning as they should, and make changes as appropriate based on feedback from both members of the study sections and those whose proposals are reviewed there.

Senior researchers should continue to serve on study sections. ASBMB also recommended that assistant professors not serve on study sections. Petsko recommended that senior researchers be compelled to serve on study sections, similar to serving on juries when called upon. As he noted, "holding a federal grant is a privilege, not a right," and thus those who hold them should be expected to pay back the system by study section service if called upon.

Study section membership must fit the charge of the study section. Care should be taken to ensure that individuals with all necessary expertise to carry out the reviews the study section is charged with are selected to serve.

Study section size should be manageable. Under the reorganization, many study sections have too many areas of science under their purview. ASBMB suggested that some of the sections should be broken down into smaller groups.

Petsko also recommended that the application package be redesigned so that it is only 15 pages long.

The comments were based on a survey conducted in March 2006 of ASBMB members on peer review. The above points synthesized the majority of the more than 1,000 comments received.

Working Group co-chairs Lawrence Tabak, director of the National Institute of Dental and Craniofacial Research, and Keith Yamamoto, University of California, San Francisco, noted in their July 12 letter to the community about the group that "With the increasing breadth and complexity of science, along with the rising number of research grant applications, we are

Critical reexamination of the peer review system is a high priority of ASBMB

taking a comprehensive look at our review process to ensure its continued strength for applicants and reviewers alike. We would like you to participate in this discussion." NIH Director Elias Zerhouni was in attendance the entire meeting.

NIH formed the Working Group to gather information from the external community to hear ideas on ways to improve the process. The July 30 meeting was the first in a series of meetings planned through the end of the year. A second meeting will be held in Washington to hear comments from the voluntary health community; three more meetings will be held in the fall—one each in New York, Chicago, and San Francisco. ASBMB will work to ensure that a few of our members attend each of these sessions and offer comments if possible.

A website has been established to keep the biomedical research community apprised of the activities of the Working Group. It can be accessed at enhancing-peer-review.nih.gov/.

We hope all of you with an interest in the NIH peer review system will bookmark this site and visit it regularly to keep abreast of what is going on. The Working Group will be accepting comments from concerned members of the biomedical research community; the NIH also currently has a request for information on the NIH System to Support Biomedical and Behavioral Research and Peer Review (grants.nih.gov/grants/guide/notice-files/NOT-OD-07-084.html).

In his opening remarks, Yamamoto noted that there had been many changes in peer review since he became involved in the mid-1980s. In 1987, there were only 1,800 people serving on study sections. Now, that figure has grown by an order of magnitude—18,000 scientists are currently serving. Furthermore, the nature of science is different; the scope of applications is much broader than 20 years ago.

Yamamoto went on to note that the review process must evolve and adapt to these changes. For example, there is currently too much emphasis on preliminary data and experimental detail. One way to deal with this might be to move toward an "editorial board" model of peer review, with permanent panels that evaluate applications as they come in. The technical details would be sent to panels of technical experts for review and the editorial board/study section would look at the proposal as a whole. This model would also avoid artificial competition.

This was only one of a number of ideas floated at the meeting; others will no doubt emerge in coming months. As Petsko noted in his closing remarks, the NIH peer review system "is the jewel of American science," and if it is going to be modified, it must be done deliberately and thoughtfully to maintain its luster.

Congress Leaves for August Recess with Veto Threats Looming

The 2008 appropriations bills currently being debated in Congress would provide $22 billion more in Federal spending than President Bush proposed in his FY 2008 budget. On August 2, the President reaffirmed his intentions to veto spending bills if this money remains in them.

ASBMB Today has learned that Senate Majority Leader Harry Reid (D-NV) met with the Democratic caucus on August 2 and told them he would not be scheduling a floor vote for the Labor/Health and Human Services (HHS) appropriations bill, which funds NIH. With the looming veto threat, expectation of another supplemental funding request in September for the Iraq war, and the likely need to respond to the report on progress in Iraq due in September, Reid did not see an opportunity to devote time to the bill. Thus, Hill staff expects the bill to be wrapped into either a giant omnibus appropriations bill or a "minibus" made up of two or three such bills. This is not likely to occur until the late fall, if then, thereby necessitating a continuing resolution, if not a series of them until final agreement is reached.

Therefore, it is very likely that most of the major science agencies, including NIH and NSF, will be on a continuing resolution once October 1, 2007, arrives. How long they will remain in this condition is anyone's guess.

NIH Spending and Policy Issues

On July 19, the House passed the FY 2008 Labor/HHS Bill by a vote of 276-140. The bill provides NIH with a $750 million increase (2.6%) in FY 2008. However, the actual NIH program increase is $549 million (a 1.9% increase) because the House would require that NIH transfer $201 million of its increase to the Global AIDS fund.

The Senate bill, passed in June, provides a $29.9 billion (3.5%) increase for NIH. However the bill also increases the amount of the transfer from NIH to the Global HIV/AIDS fund from $99 million in FY2007 to $300 million in FY 2008. As a result, the actual increase for NIH programs in FY 2008 is $799 million (2.8%), compared to $549 million (1.9%) in the House bill. Both the House and Senate bills fall short of the projected 3.7% increase in the Biomedical Research and Development Price Index (BRDPI) for FY 2008.

There may be some interesting discussions in conference about policy issues. First, the House approved a mandatory public access policy regarding scientific publications resulting from NIH-funded research.

The current NIH Public Access Policy asks researchers to submit their NIH-funded research articles to PubMed Central for online availability within 12 months of publication in a peer-reviewed journal. The House bill makes the submission mandatory. In recognition of copyright issues, however, a phrase was added requiring NIH to implement the policy "in a manner consistent with copyright law."

Publishers are not happy with this language, however. According to a statement by the Association of American Publishers, "mandatory submission of the final peer-reviewed manuscript cannot be implemented 'consistent with copyright law' because of its adverse impact on journal publishers' copyright interests in the version of the manuscript published as a journal article."

NSF Also Under the Gun

On July 26, the House voted to pass the FY 2008 Commerce, Justice, Science and Related Agencies Appropriations Act, which funds NSF and other science agencies as well as a host of other programs. The $53.8 billion bill provides NSF with $6.51 billion, a $592 million increase over its FY 2007 budget and $80 million more than the President proposed. House Commerce, Justice and Science Appropriations Chairman Alan Mollohan (D-WV) stated, "this increase would continue the goal of doubling NSF's funding in 10 years."

However, the President has said he will veto this bill as well, mainly

because of what the White House terms "an irresponsible and excessive level of spending" as well as "other objectionable provisions." These comments were made in a Statement of Administration Policy issued on July 24.

Regarding the NSF, the Statement of Administration Policy says, "the Administration supports neither the additional $72 million above the [President's budget] request allocated to NSF education programs that lack proven effectiveness, nor [Appropriations Committee] report language that seeks to allocate funds away from the NSF research programs that most directly contribute to America's economic competitiveness."

This is an apparent reference to report language instructing NSF to fund Biology, Behavioral, Social and Economic Science, and Geosciences at the agency at "comparable" levels to those enjoyed by the other research directorates. ASBMB supported this language when we became aware of it. It is highly unusual for the White House to single out such report language as a reason to veto an appropriations bill. Unfortunately, although the House passed the bill by a large majority, the margin of victory was several votes short of the two-thirds number needed to override the threatened veto.

The Senate Appropriations Committee approved an increase for NSF of $637 million or 10.8%, to $6.55 billion in FY 2008. The full Senate is expected to vote on the bill within the next two months, and then a conference committee will be appointed to reach a compromise between the House and Senate versions of the bill.

Go Visit Your Congressman

Congress left Washington on August 3 for the traditional August recess. They spend this time taking both vacations and the pulse of their constituents. In this latter capacity, please try to arrange to visit with your member this summer while he or she is home. Contact the ASBMB Public Affairs Office if you would like assistance. In addition, you might consider watching the training DVD the ASBMB Public Affairs Advisory Committee produced this spring, called *"Meeting with Your Congressman: A Guide for the Grass Roots Advocate."* You can watch this DVD on the ASBMB website (the link is on the home page at www.asbmb.org under "What's New")

Science Policy Fellow to Join Staff

Angela Noel Hvitved, a Ph.D. candidate in biochemistry and cell biology at Rice University, Houston, Texas, has been selected by the Public Affairs Advisory Committee as ASBMB's first science policy fellow. Ms. Hvitved, who defended her thesis in August, will be joining the ASBMB staff no later than October 1 after moving here from Houston.

As Hvitved told *ASBMB Today*, "Science and scientists should exert a much greater influence on our public policy than they currently do. One of my goals for this fellowship is to learn how career scientists can become actively involved in policy making. I wholeheartedly believe in the concept of the 'civic scientist' and hope to help scientists appreciate the civic responsibilities that accompany scientific training."

Hvitved received twin bachelor's degrees in Biochemistry and Philosophy from Iowa State University in 2000 and has been a graduate student at Rice since 2001. She notes that her degree in philosophy provided her with an extensive background in political theory and ethics and helped her cultivate a broader interest in the intersection of science and society.

She has worked as a teaching and research assistant at Rice and has received two training awards, including a Robert A. Welch Foundation Pre-doctoral Fellowship in July 2005. She has a long record of academic and community service, including a term as president of the Biochemistry and Cell Biology Graduate Student Association at Rice.

"Science literacy for all Americans," Hvitved says, "is critical for the health of our national science policy. A 2004 National Science Foundation (NSF) report on scientific literacy indicated that almost half of Americans believe that humans coexisted with dinosaurs and did not develop from earlier species. Each and every scientist should consider this a serious concern, not only because that 50% can elect policy makers with funding and oversight responsibilities, but also because it contradicts everything we spend our lives trying to accomplish—expanding the pool of human knowledge."

During her year-long fellowship, Hvitved wants to work on lifting the ban on federal funding for most human embryonic stem cell research, restoring funding increases to the National Institutes of Health (NIH), and raising awareness of the critical lack of scientific literacy among Americans. In addition, Hvitved will be helping the staff and Public Affairs Advisory Committee with various research projects, writing regularly for *ASBMB Today*, and generally helping to advance the ASBMB's policy goals. .

—Peter Farnham

FASEB Calls on Scientific Community to Endorse Common Guideline for COI, Unveils Toolkit

BY CARRIE D. WOLINETZ

FASEB has issued a call to the scientific community to adopt more consistent policies and practices for disclosing and managing financial relationships between academia and industry in biomedical research. This summer, FASEB unveiled a framework for a national guideline and held a meeting of more than 75 representatives of scientific societies and other key stakeholders to discuss the process of implementation. Participants in the meeting included industry leaders like Gail Cassell of Eli Lilly; government officials such as Norka Ruiz-Bravo, of the National Institutes of Health; and institutional groups ranging from the Association of American Medical Colleges (AAMC) to the National Association of State Universities and Land Grant Colleges (NASULGC) as well as more than two dozen scientific societies. In conjunction with the conference, FASEB launched the COI Tookit, a website designed to help researchers, institutions, publications, and industry put into practice FASEB's recommendations.

Leo T. Furcht, immediate past president of FASEB and chair of the committee that developed the program, described the challenge before the community: "FASEB is concerned that the lack of clarity and consistency in current conflict-of-interest policies may cause confusion by investigators and ultimately inhibit their ability to protect the integrity of research." According to Laura Brockway, FASEB's lead staffer on the project, "FASEB's recommendations articulate the issue from the investigators' perspective because they, as a group, determine the effectiveness of policies and practices."

Your Congress—Your Health

Research!America, the Albert and Mary Lasker Foundation, and several other partners recently released the results of a new Your Congress–Your Health public opinion poll. A similar poll was sent to all members of Congress. Responses from both polls can be found at www.yourcongressyourhealth.org/.

If your members of Congress have not yet submitted their responses to the Your Congress–Your Health questionnaire, please send them a message asking them to participate.

Delivering the keynote address, House Energy and Commerce Committee Vice-Chair Diana DeGette (D-CO), applauded FASEB's efforts and stated, "By creating a more consistent standard to the extent possible we are more likely to avoid ambiguity and confusion. Without such standards, we run the risk of further confusing the public about the integrity of research and exacerbating their distrust."

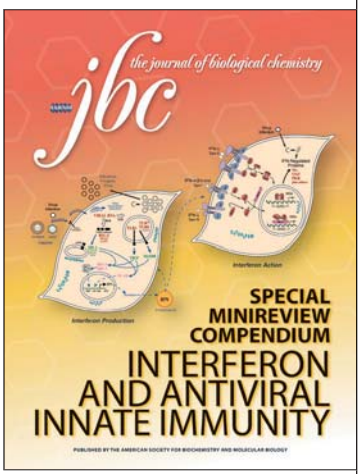
The FASEB framework is based on three guiding principles: investigators must conduct research activities objectively, operate with transparency, and be accountable to all stakeholders. To promote practices to achieve these principles, FASEB developed the COI Toolkit website containing recommendations to improve the management of academic-industry relationships and promote investigator education. Many of the recommendations were derived from guidelines FASEB published in 2006 (opa.faseb.org/pdf/FASEB_COI_paper_7x06.pdf). The Toolkit provides a platform for the community to share resources with the goal of moving toward a national guideline.

Participants in the meeting expressed enthusiasm for a set of common principles and guidelines that they could use to help better manage financial relationships between academia and industry. "It is essential that the various stakeholders work together to study the effectiveness of policies and practices and strive to balance the need for more common standards with preserving case by case analysis and situational driven decision making, when warranted," said Brockway. "While flexibility is needed, operating under more broadly agreed upon guidelines will benefit the public and ensure future public support for biomedical research."

The work was funded by a grant from the *Association of American Medical Colleges–Office of Research Integrity Responsible Conduct of Research Program for Academic Societies.* The FASEB COI toolkit may be viewed online at opa.faseb.org/pages/advocacy/coi/toolkit.htm.

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

New *JBC Minireview Compendium* on Interferons



Interferon (IFN), the first cytokine discovered, was identified by the British virologist Alick Isaacs and the Swiss researcher Jean Lindenmann in 1957 during their seminal studies on virus interference. They found that influenza virus-infected cells produced a secreted factor that transferred a virus-resistant state to previously uninfected cells. The factor was designated interferon because of its ability to interfere with virus growth.

To celebrate the 50th anniversary of the discovery of interferons, the *Journal of Biological Chemistry* (*JBC*) will release a compendium of eight *Minireview* articles published in the journal on this topic. The compendium is available for $22.00 on the *JBC* Web site (www.jbc.org/), and a summary of the compendium is available for free at www.asbmb.org/asbmb/site.nsf/main/publications?opendocument.

The compendium will also be distributed to the attendees of the Annual Meeting of the International Society for Interferon and Cytokine Research, September 16—19, in Oxford, United Kingdom.

"The *JBC* is pleased to provide this thematic compendium of *Minireviews* on interferon signal transduction and antiviral innate immunity," says Charles E. Samuel, editor of the *Minireview* section and associate editor of the *JBC*. "Much knowledge about interferons has been gained during the past 50 years, so it is important to assess the depth of that knowledge with a focus on recent advances and the new questions that yet need to be addressed."

Seven of the articles highlighted in the compendium were published in 2007 and were part of two *Minireview* series. The first series consisted of three articles on innate immunity and was published in the May 25 issue of the *JBC*. The second was composed of four articles on signal transduction and was part of the July 13 issue of the *JBC*. An eighth article from the January 9, 2004, issue of the *JBC* was added to these articles.

The first two *Minireviews* in the compendium, by Mitsutoshi Yoneyama and Takashi Fujita (Kyoto University, Japan) and Satoshi Uematsu and Shizuo Akria (Osaka University, Japan), provide updates on two kinds of nucleic acid sensors and the biochemical pathways by which they signal the production of interferon.

In the third *Minireview*, John Hiscott (McGill University, Montreal, Canada) focuses on the centrally important interferon regulatory factors (IRFs) involved in transcriptional activation of the type I interferon gene promoters.

Next, Sidney Pestka (Robert Wood Johnson Medical School, Piscataway, New Jersey) provides an account of the discovery of interferons, their purification and molecular cloning, and the biologic activities of IFNs.

In the fifth *Minireview*, Nicole de Weerd, Shamith Samarajiwa, and Paul Hertzog (Monash University, Melbourne, Australia) focus on recent developments in understanding the biochemical properties and functional activities of the type I IFN receptor proteins.

The combined biochemical and genetic studies of the mechanisms by which interferons induce transcriptional activation of new cellular gene expression led to the discovery of the Janus tyrosine kinase (JAK)-signal transducers and activators of transcription (STAT) signaling pathway by the Darnell and Stark laboratories. In the sixth *Minireview*, Christian Schindler (Columbia University, New York), David Levy (New York University School of Medicine), and Thomas Decker (University of Vienna, Austria) provide an overview of the JAK family of protein kinases and the STAT family of transcription factors.

Keiko Ozato, Prafullakumar Tailor, and Toru Kubota (National Institutes of Health, Bethesda, Maryland) then describe the mechanisms by which the IRF family of transcription factors plays critical roles in both innate and adaptive immunity, including the induction and action of the IFNs.

In the final *Minireview* of the compendium, Samuel Wormald and Douglas Hilton (Walter and Eliza Hall Institute of Medical Research and Cooperative Research Centre for Cellular Growth Factors, Parkville, Australia) describe the biochemical properties and mechanisms of action of three families of proteins that inhibit cytokine signal transduction, the SH2-containing phosphatases (SHP), the protein inhibitors of activated STATS (PIAS), and the suppressors of cytokine signaling (SOCS).

asbmb member spotlight

Please submit news about yourself to asbmbtoday@asbmb.org

Caruthers and Fedoroff Awarded National Medal of Science

CARUTHERS

FEDOROFF

Marvin Caruthers, professor of Chemistry and Biochemistry at the University of Colorado at Boulder, and Nina V. Fedoroff, the Verne M. Willaman Chair in Life Sciences and Evan Pugh Professor at Penn State University and an external professor of the Santa Fe Institute, are the recipients of the 2006 National Medal of Science, the nation's highest award for lifetime achievement in scientific research. They received their medals at a White House ceremony in July.

Caruthers was recognized for his lifetime accomplishments as a chemistry professor, researcher, and biotechnology innovator. He pioneered research in nucleic acid chemistry resulting in new methods that are used worldwide for the chemical synthesis of DNA and RNA.

Fedoroff received the medal for her pioneering work on plant molecular biology and for her being the first to clone and characterize maize transposons. She has also contributed to education and public policy pertaining to recombinant DNA and genetic modification of plants. U.S. Secretary of State Condoleezza Rice also recently named Fedoroff as her new science and technology adviser.

Jordan Awarded Pincus Medal

V. Craig Jordan, Alfred G. Knudson Chair of Cancer Research and vice president of the Medical Sciences Division at the Fox Chase Cancer Center, Philadelphia, is the co-recipient with Angela Brodie of the 2007 Gregory Pincus Prize and Medal from the Worcester Foundation for Biomedical Research at the University of Massachusetts Medical School, Worcester.

The international award recognizes outstanding research in endocrinology and honors Gregory Pincus, a co-founder of the Worcester Foundation in 1944 and the scientist responsible for the development of the oral contraceptive. Jordan is being honored for his pioneering research in developing the antiestrogenic drug tamoxifen for the treatment and prevention of breast cancer as well as the recognition of selective estrogen receptor modulators that lead to the subsequent development of the drug raloxifene for the prevention of both osteoporosis and breast cancer. Jordan started his research on tamoxifen at the Worcester Foundation in the early 1970s. Currently, Jordan is exploiting his discovery of the new biology of estrogen action that causes apoptosis in antihormonally resistant breast cancer cells.

Georgiou Is Amgen Biochemical Engineering Awardee

George Georgiou of The University of Texas (UT) at Austin has been honored with the 2007 Amgen Biochemical Engineering Award for his profound impact on protein therapy and other protein research.

Georgiou received the award and delivered a lecture on his research at the Biochemical Engineering IV conference in July in Quebec City, Canada. The bi-annual award was given in recognition of Georgiou's research excellence and leadership in biomedical engineering.

Georgiou holds the Cockrell Family Reagents Chair at the UT Austin, with a primary appointment in the Department of Chemical Engineering and further appointments in the departments of Biomedical Engineering and Molecular Genetics and Microbiology and in the Institute for Cell and Molecular Biology.

His research has had a profound impact in protein engineering, protein-based therapeutics, and on the fundamental understanding of protein biogenesis. His biochemical engineering contributions include the invention of numerous commercially important technologies for facilitating the discovery and manufacturing of protein therapeutics, and in particular therapeutic antibodies. He has also made seminal discoveries in the areas of oxidative protein folding and protein secretion.

Raines Receives Rao Makineni Lectureship

Ronald T. Raines, Henry Lardy Professor of Biochemistry and Professor of Chemistry at the University of Wisconsin-Madison, has won the 2007 Rao Makineni Lectureship award from the American Peptide Society (APS).

The award, one of only three bestowed by the APS, is given every other year to recognize "an individual who has made a recent contribution of unusual merit to research in the field of peptide science." Raines was honored for his "self-assembly of synthetic collagen triple helices, which provides new strategies for developing biomaterials for use in medicine and nanotechnology." His award address was delivered at the 20th APS symposium in June 2007 in Montréal, Canada.

Raines has made notable contributions to the exploration and exploitation of proteins. He demonstrated that mammalian ribonucleases can become potent cytotoxins and potential cancer chemotherapeutics. Raines discovered fundamental attributes of the collagen triple helix, enabling him to assemble triple helices that are stronger and longer than any found in nature. He and Laura L. Kiessling developed the traceless Staudinger ligation as a means to couple synthetic peptides and thus synthesize proteins.

Wells Presented with Medal of Friendship

Robert D. Wells, past president of the American Society for Biochemistry and Molecular Biology and of the Federation of American Societies for Experimental Biology (FASEB), received the Medal of Friendship (Universitatis Lodziensis Amico Medal) from the Rector (President) Professor Wojciech Katner of the University of Lodz, Poland, in June. This medal is provided to special friends of the university who have made substantial contributions to the education and/or well being of the institution.

Wells has trained a number of postdoctoral research associates at the University of Wisconsin-Madison, the University of Alabama at Birmingham, and the Institute of Biosciences and Technology, Texas A&M University System Health Science Center since 1979. At that time, Wells' first research associate joined his team to investigate non-B DNA structures in gene expression. This was quickly followed in 1986 by a second research associate, Adam Jaworski. Jaworski has been instrumental helping Wells identify young scientists to work in his laboratory as well as new professors to hire at the latter two institutions. Approximately 20 scientists have been hosted in the U.S. Furthermore, the total number of Polish citizens educated or trained in the U.S. in technical or scientific pursuits due to the Jaworski-Wells collaborations is 46.

Lefkowitz Lauded with Shaw Prize

Robert J. Lefkowitz, Howard Hughes Medical Institute investigator at Duke University Medical Center, has received the Shaw Prize in Life Science and Medicine for 2007 for his research into understanding the receptor system that controls the body's response to drugs and hormones. Lefkowitz will receive the award, which includes a $1 million prize, during a ceremony in Hong Kong in September.

The annual prize, which was first granted in 2004, was established by Run Run Shaw, a Chinese native who founded the film company Shaw Brothers Limited in Hong Kong in the 1950s. Shaw also serves as executive chairman of Television Broadcasts Limited, also in Hong Kong.

Lefkowitz received the award for his "relentless elucidation" of seven-transmembrane-spanning receptors. These receptors are the targets of almost half of the drugs on the market today, including antihistamines, ulcer medications, and beta blockers for heart disease. Lefkowitz first cloned the receptors in the 1980s.

"I am so deeply honored to be recognized like this," Lefkowitz said. "I am also proud that all I have accomplished happened while I was here at Duke. It is a very fulfilling feeling to have years of hard work recognized like this."

Borchardt Wins Biomolecular Science Award

Ronald Borchardt, Solon E. Summerfield Distinguished Professor of Pharmaceutical Chemistry at the University of Kansas School of Pharmacy, is the recipient of the PolyPops Development Foundation Award. He shares the award with Ismael J. Hidalgo, chief scientist and cofounder of Absorption Systems.

The researchers are being recognized for their discovery and development in the late 1980s and early 1990s of Caco-2 cells, a human colon carcinoma cell line that is widely used today in in vitro assays to predict the transport rate of drug candidates across the intestinal epithelial cell barrier.

The award is presented annually by the Society for Biomolecular Sciences to members of the scientific community who have shown innovation in the design and application of plastics and polymers in microplate development and design. The prize includes a $2,500 honorarium.

IN MEMORIAM:

Harry Rudney 1918–2007

Harry Rudney, chairman emeritus of the Department of Biochemistry and Molecular Biology at the University of Cincinnati College of Medicine, died on May 30, 2007.

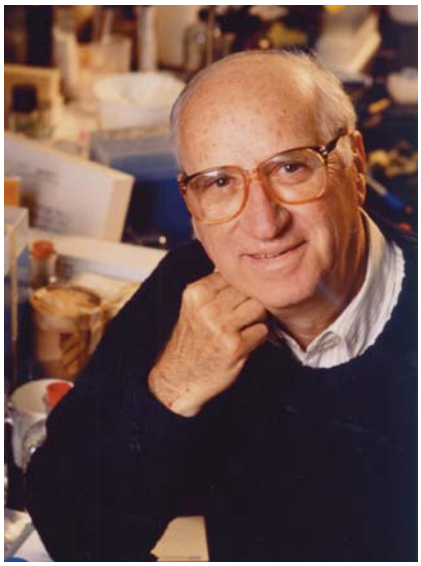
Born in Toronto, Canada, on April 14, 1918, Rudney was a member of a struggling Jewish immigrant family. Although he couldn't afford college, he attended public lectures offered by the University of Toronto. Among the lectures he heard was one given by Bruno Mendel, who worked at the Banting Institute. Rudney wrote to Mendel and suggested an experiment that he could do. Mendel was so impressed that he offered Rudney a job in his lab, which helped him pay his way through the University of Toronto.

Rudney went on to receive a master's degree from the University of Toronto in 1948 and a Ph.D. from Western Reserve University in Cleveland in 1952. He joined the faculty at Western Reserve before being recruited by the University of Cincinnati to be the chairman of the Department of Biochemistry and Molecular Biology. He was the Andrew Carnegie Professor of Biological Chemistry from 1967 until 1989. After his retirement, he returned to serve as interim chairman of the Department of Pharmacology for three years. He later served as chairman of the institutional review board.

Rudney was elected to the Fellows of the Graduate School at the University of Cincinnati in 1976 and received the George Rieveschl Jr. Award for distinguished research. He served as president of the Association of Medical School Chairmen of Biochemistry and was on the editorial board of the *Journal of Biological Chemistry*.

RETROSPECTIVE:
Daniel E. Koshland, Jr. (1920-2007)

Daniel E. Koshland, Jr., former ASBMB president and a tireless booster of the biological sciences, died on July 23 following a massive stroke. A long time professor of Molecular and Cell Biology at the University of California, Berkeley and a resident of Lafayette, California, Koshland was 87.



Koshland graduated from the University of California, Berkeley in 1941 and promptly joined the Manhattan Project, purifying plutonium for the atomic bomb. He received his Ph.D. from the University of Chicago in 1949. After a two-year postdoctoral fellowship at Harvard University, he accepted an appointment at the Brookhaven National Laboratory, where he remained for 14 years. He then joined the faculty of the University of California, Berkeley, where he also served as chair of the Molecular and Cell Biology Department from 1973 to 1978.

Koshland became editor-in-chief at Science magazine in 1984. He held the post for 10 years, during which time he was best known for his incisive and witty editorials. This was most evident in the character he created, "Dr. Noitall," who was intended to represent the many scientists who took narrow, overly simplistic views of important issues.

During his lifetime Koshland made major contributions to the fields of enzyme action, short- and long-term memory, and science education. In the 1950s, he proposed that the then popular lock-and-key theory of enzyme action was inadequate to explain all forms of enzyme action. To augment that theory, he proposed an induced-fit theory of enzyme action. In the 1970s, his interest turned to the mechanism by which cells "remember" situations and events. He demonstrated that bacteria have short-term memory and that purified mammalian cell lines show rudimentary memory.[1]

An heir to the Levi Strauss fortune, Koshland endowed the National Academy of Sciences with a $25 million gift to establish the Marian Koshland Science Museum, named for his late wife, an immunologist who did ground breaking work on a cholera vaccine and the behavior of antibodies.

We extend our sympathy and thoughts to Koshland's friends and family. Below, as a tribute, we offer thoughts and reflections from several of Koshland's friends and former colleagues:

I knew of Koshland's fame before I came to Berkeley, yet he was never intimidating even as he cast an imposing scientific presence. He made graduate school a thoughtful, rewarding and—importantly—enjoyable experience with his innovative ideas and charming wit. I am very proud to have passed through his lab, and I frequently reflect on his teachings as I develop my own scientific perspectives.

— Gideon Bollag, vice president, Plexxikon, ***former Koshland graduate student***

Dan loved to write limericks, and he would always write one for the students/postdocs on the occasion of their departure from the lab. He and I communicated in limericks after I left the lab. On the occasion of the ASBMB symposium in his honor, I presented him with the following limerick:

There once was a man named Koshland, D. E.
Who thought about things like enzymes with glee
From fits induced
To mechanisms deduced
He enraptured us all with his chemistry

— Alexandra Newton, University of California at San Diego, ***former Koshland postdoc***

With the death of Dan Koshland, biochemistry has lost a giant. He was a brilliant scientist whose research was characterized by its originality and boldness. As a teacher, he was outstanding—combining insight, rigor, and wit. He was a superb citizen devoting his energy and wisdom to problems in education and public policies affecting science. His contributions are inestimable.

— Howard K. Schachman, University of California at Berkeley, ***friend***

While working in the Koshland lab, I learned from a great scientist how to dare. He pushed us to think outside the box, to follow up on wild guesses and hunches and not worry about sticking our neck out with a speculation—as long as we label it as a speculation. This advice has guided me well throughout my career.

— Daria Mochly-Rosen, Stanford University, ***former Koshland postdoc***

Dan loved to play with names and puns, both to promote the research and to promote his postdocs. This story is one he used to tell on the lecture circuit in the early 1970s. A series of experiments were published on enzyme mechanisms that he would refer to as the "Neet-Koshland" experiments that were done in conjunction with Ken Neet. Shortly later he published studies on receptors (with Pete Lovely) that he referred to as the "Lovely-Koshland" experiments. He would laugh and say that he had to quit this approach when one day a new postdoc walked into his lab—Phil Strange.

— **Kenneth Neet,** Rosalind Franklin University of Medicine and Science, *former Koshland postdoc*

Dan and I were both past presidents of the American Society for Biochemistry and Molecular Biology. At the most recent meeting in Washington, D.C. we had a chance to visit for about half an hour before our past president's meeting started. I recall thinking to myself as we talked, what a wit he still has and what a sharp mind. He was an icon when I was a student in the 1960s, so just to see him functioning at such a high level at the ASBMB meeting was a real inspiration for an aging biochemist like myself. Dan was a true giant in the field of biochemistry. He will be missed.

— **Jack E. Dixon,** University of California at San Diego, *friend*

Dan always said that his ambition was to die young as old as possible. He succeeded: very few people, of any age, have had a younger heart or a more open mind. He went the way we should all go: suddenly, while still sharp and having fun. He managed to combine a gift for theorizing with a talent for clever but rigorous experiments—a feat that few have done so well. And throughout it all he gave the impression that he was just a kid playing with his favorite toy.

— **Greg Petsko,** Brandeis University and Harvard Medical School, *friend*

Dan used to say when we caught him with a Snickers bar that he ate as many preservatives as he could so that he could live as long as possible. My favorite Dan joke was about isocitrate dehydrogenase crystals—that they were so beautiful that he wanted to make a ring for his wife. She refused when she found out she had to sit in AmSO4 every time she wore it.

— **Susan Tsutakawa,** Lawrence Berkeley National Laboratory, *former Koshland graduate student*

FOOTNOTES:

More information on Koshland's research can be found in his *Journal of Biological Chemistry Classics* article (2007, 37, e29).

ASBMB Delegation T

Fuchu He and William Smith at the Beijing Proteome Research Center.

Heidi Hamm discusses ASBMB at Peking University.

Xiao-Fan Wang prepares for a talk at Guangzhou Institute of Biomedicine and Health.

A delegation of seven representatives from ASBMB recently met with Chinese scientists, students, and members of the Chinese Society for Biochemistry and Molecular Biology (CSBMB) as part of a scientific exchange between U.S. and Chinese biochemists and molecular biologists. This event was initiated and organized by Duanqing Pei, deputy director general of the Guangzhou Institute of Biomedicine and Health (GIBH) and supervisor of ASBMB's Guangzhou office.

The delegation included:

- **Heidi Hamm, president of ASBMB and chair of the Pharmacology Department, Vanderbilt University Medical Center, Nashville, Tennessee;**
- **Alma L. Burlingame, co-editor of the journal *Molecular & Cellular Proteomics* and professor of Chemistry and Pharmaceutical Chemistry at the University of California, San Francisco;**
- **William L. Smith, associate editor of the *Journal of Biological Chemistry* and professor and chair of Biological Chemistry at the University of Michigan, Ann Arbor;**
- **Xiao-Fan Wang, associate editor of the *Journal of Biological Chemistry* and professor of Pharmacology and Cancer Biology at Duke University, Durham, North Carolina;**
- **Xiaodong Wang, George L. MacGregor Distinguished Chair in Biomedical Science at the University of Texas Southwestern Medical Center, Dallas;**
- **Barbara Gordon, executive director of ASBMB.**

The delegation visited three cities from June 26 to July 3—Beijing, Guangzhou, and Shanghai. In each city, the ASBMB scientists presented their research, and the delegation described ASBMB and its journals.

The Beijing visit, which was coordinated by Zengyi Chang, a professor at Peking University's Center for Protein Science, included tours of Peking University, Tsinghua University, Tsinghua University's Peking Union Medical College, and the National Institute of Biological Sciences.

The delegation also visited a state of the art facility called the Beijing Proteome Research Center (BPRC), which is an international facility that will pursue research in proteomics.

In Guangzhou, the delegation commemorated the opening of the Society's office at GIBH with a plaque unveiling ceremony. This office will help raise ASBMB's visibility in China, promote the Society's Asian membership, and, we hope, increase submissions and subscriptions to the journals by Chinese scientists.

The plaque unveiling ceremony at the Guangzhou Institute of Biomedicine and Health.

Barbara Gordon, Alma Burlingame, Xiaodong Wang, and Heidi Hamm at the National Institute of Biological Sciences.

Tours China

The delegation meets with students and faculty at the Guangzhou Institute of Biomedicine and Health.

The ceremony was chaired by Hamm; Gordon; Pei; Xian-Min Ma, deputy director of the Department of Science & Technology of Guangdong Province; and Guang-Mei Yan, vice president of Sun Yat-sen University, Guangzhou.

After the ceremony, the delegation toured research laboratories at GIBH and met with Ling Chen, the founding director general of GIBH, and Huayu Qi, principal investigator at GIBH.

"I was really impressed by the talent and energy of the scientists we met and the superb facilities and state of the art instrumentation that we saw at some of these institutions," Hamm says. "It is clear to me that the Chinese government has significantly increased its investment in science and technology over the past decade."

In Shanghai, the delegation visited the Shanghai Institute for Biological Sciences (SIBS). Pei Gang, president of SIBS, first welcomed the delegation, which then toured the institute's research laboratories and met with Jia-Rui Wu, vice president of SIBS; Naihe Jing, deputy director of the Institute of Biochemistry and Cell Biology; and other SBIS scientists.

The ASBMB members also met with their Chinese counterparts from the CSBMB, a society that sponsors meetings and publishes two journals: the *Chinese Journal of Biochemistry and Molecular Biology* and the *Chemistry of Life*. CSBMB's president is Zhixin Wang, a professor at Tsinghua University's Department of Biological Sciences and Biotechnology and a member of the Chinese Academy of Sciences.

In Beijing, Guangzhou, and Shanghai, Burlingame noted that the Chinese Academy of Sciences has made major investments in mass spectrometry and proteomics. But, he adds, the leadership and current expertise involved in these investments vary with the levels of experience and scientific maturity of the research teams.

In all three cities, the delegation met with many young scientists who had completed Ph.D.s and/or postdoctoral fellowships in the United States but returned to China because the Chinese government is providing them with jobs and state of the art equipment.

"The Chinese government is stepping up its efforts to bring back its scientific talent, and, from what we have seen, it is working," Smith says.

Despite these efforts, the Chinese scientists who met with the delegation underscored the need for a change in the way Chinese scientists are hired, receive funding, and advance in their career. In all three situations, decisions are usually made based on the impact factors of the journals in which the scientists have published.

"The impact factor is currently an overriding criterion in making those decisions," Xiao-Fan Wang says. "Our discussions clearly showed that it was also a hot button issue for many scientists, and ASBMB offered to help define new criteria to better assess scientists' achievements."

"Overall, this visit went extremely well," Hamm says. "We have strengthened ASBMB's relationships with many top notch Chinese institutions and the Society's counterpart in China, opened our first international office in Guangzhou, and made ASBMB more broadly known among the scientists we met. These activities are clearly showing that ASBMB is growing and becoming more of a worldwide institution."

Early Medical Research Funding and the Evolution of Modern American Biochemistry

BY SEYMOUR S. COHEN

The United States did not develop an official national policy of financial support for medical research for almost a decade after World War II. Here I will describe how some financial support was developed in that period, *i.e.* 1946–1956, for what subsequently became the basis of the now large structure of American medical research. To do so it seems desirable to describe some personal experiences in developing a career in biochemistry before, during, and after American entrance into that War.

In 1937, I began graduate study in the Department of Biochemistry at Columbia University's College of Physicians and Surgeons and worked as a bottle washer for $40 a month. My fellowship in the last year of my graduate work was $800. Salaries for academic positions for new Ph.D.s were about $1,800 per year.

The Columbia Department of Biochemistry at that time, chaired by Professor Hans T. Clarke, has been described as one of the best in the country. Many of the faculty had been relatively recent European refugees, some of whom had obtained positions or consultative connections in clinical departments. Both postdoctoral fellows and graduate students were supported on absolutely minimal fellowships.

After receiving my Ph.D. early in 1941, I sought a postdoctoral position. Offers of a Naval position at Point Barrow, Alaska, and one at Peiping Union Medical College in China were not appealing. Curiously, pharmaceutical companies were not interested in my information on blood clotting. However an issue of *Science* in 1940 had pointed to new fellowships in virology for the National Foundation for Infantile Paralysis, and I applied for one of these to work with Wendell Stanley at the Rockefeller Institute in Princeton. I was interviewed by Homer Smith for the administering National Research Council and by Stanley, who was pleased by the notion of exploring the nature of the nucleic acid in tobacco mosaic virus. The awarded fellowship paid $2,100 per year, and I was excited at my good fortune.

In 1924 Franklin D. Roosevelt had been hit by disabling poliomyelitis and after a very difficult illness had traveled regularly to Warm Springs, Georgia, to attempt to regain some muscular strength. In 1934, his legal partner, Basil O'Connor, who led the Warm Springs Foundation since 1928, had begun fundraising to generate research funds to find a cure for the disease, and in 1938 President Roosevelt and O'Connor announced the formation of the National Foundation for Infantile Paralysis. In that year O'Connor appointed Tom Rivers, a leading virologist at the Rockefeller Hospital, to lead a Scientific Research Committee. One of the first decisions of the research committee was to expand knowledge in the field of virology by developing variously trained younger scientists, and this decision resulted in the announcement in *Science* to which I had responded.

In 1934 and 1935 Stanley published on the crystallization of tobacco mosaic virus, and very soon thereafter Bawden and Pirie discovered RNA in the virus. Having read these papers and the book of Bawden on plant viruses, I began my work at the Princeton laboratories in the spring of 1941. Early in 1942, shortly after the U. S. entered the war, Stanley and I were able to report on the isolation and existence of a viral RNA much larger than a tetranucleotide.

Soon after 1941, Rivers and many members of the Scientific Research Committee of the Polio Foundation went off to the armed forces until about 1947. Stanley's laboratory turned to the study of influenza vaccine, and I became involved in attempts of the Army and an academic Committee of Medical Research to improve the typhus vaccine, whose rickettsial antigens comprised less than 1% of the total protein in the vaccine. This work led me to the Childrens Hospital of Philadelphia and the University of Pennsylvania. By the end of the 1940s the rickettsia of typhus proved to be of bacterial structure and composition, but the discovery and use of antibiotics had revealed an inability of both penicillin and the known sulfa drugs to control infections by this fastidious microbe or indeed true viruses. In 1945 and 1946 the need for chemotherapeutic agents to control virus infections led me to begin to work on the biochemistry of bacteriophage multiplication.

It is important to realize that the National Institutes of Health (NIH) did not develop a system of funding medical research before 1955. In the period of 1946 to 1949 my work on phage was supported by remnants of funds through the Office of Naval Research to the Childrens Hospital. After my early studies on the biochemistry of phage multiplication appeared in 1946 to 1948, financial support was developed through the good offices of the Commonwealth Fund, and this was maintained until 1963, when this fund decided not to compete with NIH research funds.

In 1946 and 1947, the donation of funds through the March of Dimes had been sufficiently successful to encourage the Polio Foundation to renew the activities of its research committee, and under the O'Connor and Rivers leadership this body reviewed the status of virology. A key meeting of virologists in Madison, Wisconsin, in 1948 was held under the auspices of the research committee. In these few post-war years it had become clear that the phage systems permitted studies of the interaction of viruses and separate host cells, and these had included my own findings on the exaggerated synthesis of virus nucleic acids and proteins in infected bacteria as well as the dependence of such synthesis on host cell metabolism. After that meeting, the research committee pointed to the importance of similar experiments on virus-infected animal cells. The committee then attempted to encourage the development of animal tissue culture systems and of establishing virus-infection on plated tissue cultures as well as the isolation and characterization of several strains of polio virus from infected tissue cultures, etc. In addition to these steps, which became the basis of providing the killed virus in the Salk vaccine used in 1957, the research committee encouraged financially much of the work on the cytology, genetics, and composition of animal cells generally as well as on the structure, isolation, and enzymatic synthesis of the nucleic acids. It will be clear that the work and financial support via the Scientific Research Committee of the Polio Foundation in the decade from 1948 to 1956 functioned as essential anticipants of the NIH.

The National Institutes of Health (NIH) did not develop a system of funding medical research before 1955

The Cold Spring Harbor International Symposium in 1946 had stimulated the study of the growth, heredity, and metabolism of microbial cells. Those studies then occurred in a decade-long period in which American laboratories had been newly stocked with centrifuges, spectrophotometers, and the crude apparatus of paper chromatography as well as new useful analytical reagents. Also the application of isotopic techniques had created new techniques of chemical discovery in the many microbial systems. The decade was also marked by the extraordinary enzymology in the American laboratories of a few European refugees, such as the Coris, Lipmann, Szent-Gyorgi, and Ochoa, which revealed that phosphorylated intermediates were important in the metabolism of cells generally.

The relevance of these biochemical advances to the growth of knowledge in phage and other virus systems was accepted enthusiastically by the members of the research committee of the National Foundation for Infantile Paralysis who wanted to develop these new findings in animal cell systems. These scientists also contributed in major ways to the development of the structural biochemistry of the nucleic acids and proteins. The foundation was particularly active in encouraging and financing the study of the growth, cytology, and composition of animal cells that might serve as hosts for the polio virus and produce enough virus to serve as a vaccine for poliomyelitis by 1956–57. This development had been highlighted in 1953 by the Cold Spring Harbor Symposium on Viruses, which was supported by the National Foundation for Infantile Paralysis. A major section on the phages included the first American report of Watson and Crick on DNA structure, while the reports of Wyatt and Cohen described a new DNA pyrimidine whose synthesis required phage infection. The symposium concluded with a section on the multiplication of animal viruses in tissue culture, including the detection of phage-like polio virus-induced plaques in monolayers of animal cells by Dulbecco and Vogt.

In a very few years, *i.e.* the post-war decade from 1947 through 1956, the work on animal cells, stimulated by the National Foundation for Infantile Paralysis, had produced new data and directions in the study of their growth, behavior, and composition. These studies now pointed to approaches to the curbing of pathological cells, as in the growth of human cancers, and provided major incentives to research which might be undertaken by the American Cancer Society and the National Cancer Institute and other institutes of the NIH.

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Systems Biology: A Shared Goal with Diverse Views

BY FREDERICK P. ROTH AND BRENDA ANDREWS

In a well known Indian tale, blind men offer diverse descriptions of the same elephant ("…seizing on the swinging tail that fell within his scope, 'I see,' quoth he, "the Elephant is very like a rope!" (1)). Systems biology is the contemporary elephant in the room, and it is easy to wonder whether the diverse scientific views operating under this name are of the same beast. However, systems biologists do share a common ultimate goal: to produce a dynamic model that can predict the actions and internal workings of an entire organism.

Currently unachievable in any organism, a predictive dynamic model of an entire organism will require concerted effort on several fronts. Minimally, we must: 1) learn the "parts list" for organisms of interest; 2) obtain a basic understanding of the relationships between all parts; 3) observe system dynamics across time, space, and individuals; and 4) prepare for the global modeling challenge by first modeling small subsystems.

Global Systems Biology: Parts

Ultimate success in systems biology depends on the unfinished task of defining the parts—genes, gene products, and their basic functional role. Current challenges include gene/protein definition, post-translational modifications, phenotyping, epigenomics (*e.g.* heritable chromatin structure), and function annotation. It is clear that the parts list is far from complete. For example, recent work by Takashi Ito (University of Tokyo) and colleagues has expanded the list of *Saccharomyces cerevisiae* (the most extensively studied eukaryote) by dozens of introns, hundreds of new transcription units in regions previously thought to be intergenic, and hundreds of intragenic alternative transcriptional start sites (2). The connection of genes to basic cellular roles, *e.g.* determination of cell shape, also remains incomplete. In a single whole genome phenotyping screen in *Drosophila melanogaster*, Amy Kiger (University of California, San Diego) and colleagues expanded the list of genes affecting cell shape by one-third (3). It is clear that our most basic understanding of genes and gene functions remains vastly incomplete. A current challenge is the integration of disparate sources of data to roughly assign genes to functional roles, which can focus limited experimental resources on the most likely hypotheses (*e.g.* unpublished work by Frederick Roth (Harvard Medical School) and colleagues).

Global Systems Biology: Relationships

Before we can hope to simulate a global system, we must first have a general understanding of how the parts are related to one another. Current challenges include protein networks, genetic networks, gene regulatory networks, and chromatin networks. This area remains even less explored than the parts list. For example, Marc Vidal (Dana-Farber Cancer Institute/Harvard Medical School) and colleagues have roughly estimated that only ~1% of all interactions between human proteins are known (4). We have only begun to learn about genetic interactions (cases in which perturbations of two genes together yield a surprising result that often indicates a functional relationship). For example, Brenda Andrews (University of Toronto), Charlie Boone (University of Toronto), and colleagues are using an automated genetics platform to create a complete map of double-mutant genetic interactions that lead to a significant fitness defect in budding yeast. These groups have also begun to explore the effects of other genetic perturbations, particularly gene overexpression, with the aim of revealing unappreciated functional connections in *S. cerevisiae* (5). Furthermore, much of the dynamic control of biological systems is affected through transcriptional regulation. Unfortunately, we do not yet have a complete map connecting transcription factors to their DNA binding elements in any species. Tim Hughes (University of Toronto), Martha Bulyk (Harvard Medical School), and colleagues are systematically identifying DNA-binding specificity of transcription factors in mouse (unpublished work). In the meantime, it is clear that a comprehensive predictive model of any organism awaits a complete understanding of the relationships between components.

Global Systems Biology: Dynamics

We must also learn how the parts of an organism and their relationships change over time and space within an organism and between organisms and environmental stimuli. Current areas of interest include gene expression, signaling, development, genetic variation, and pathogenic systems.

For example, Jason Lieb (University of North Carolina, Chapel Hill) and colleagues are investigating how the occupancy and activity of human regulatory elements change in living cells (6). One class of circuit that affects dynamics and homeostasis in living organisms is feedback, and our knowledge of the existence of such circuits is incomplete. Rachel Brem (University of California, Berkeley) and colleagues are searching systematically for evidence of regulatory feedback (unpublished work). A major challenge for systems biology will be grappling with complexity and dynamics within multicellular organisms. As an example of current work in this area, Robert Waterston (University of Washington) and colleagues have developed technology for tracking the location and lineage of all cells in real time through the early development of the worm *Caenorhabditis elegans* (7), which they are now scaling up.

Local Systems Biology: Subsystems and Simulation

On the path towards modeling and simulating entire organisms, we can begin by modeling and simulating smaller modules and subsystems. For example, Trey Ideker (University of California, San Diego) and colleagues have been assembling knowledge about individual physical and genetic interactions to model cellular responses to DNA damage (see Ref. 8 for an example). In an example of dynamic subsystem modeling, Alexander Hoffmann (University of California, San Diego) and colleagues are developing temporal models of inflammatory signaling pathways (see Ref. 9 for an example). A major challenge in the modeling of subsystems is that many of our experimental measurements of cellular systems are derived from the study of ensembles of cells rather than individual cells. Alexander van Oudenaarden (Massachusetts Institute of Technology) and colleagues have been exploring stochastic phenomena, (*e.g.* Ref. 10), for which measurements on the single cell level will be critical.

In summary, systems biologists have a shared vision for where the field must ultimately go, but the scale of the challenge is immense and demands a diversity of vision as we proceed.

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Systems Biology Thematic Meeting

ORGANIZERS:
Brenda Andrews, *University of Toronto*
Fritz Roth, *Harvard Medical School*

Symposium: Global Systems Biology: Parts

Unexpected complexity of the budding yeast transcriptome, *Takashi Ito*

Functional genomic analysis of morphogenesis, *Amy Kiger*

Systematic function annotation in microbes and mammals, *Fritz Roth*

Symposium: Global Systems Biology: Relationships

Interactome networks and human disease, *Marc Vidal*

Genetic interaction networks in yeast, *Brenda Andrews*

Cracking the second genetic code, *Tim Hughes*

Symposium: Global Systems Biology: Dynamics

Genome-wide identification of active human regulatory elements by formaldehyde-assisted isolation of regulatory elements, *Jason Lieb*

Expression variation and regulatory feedback, *Rachel Brem*

Title TBD, *Robert Waterston*

Symposium: Local Systems Biology: Subsystems and Simulation

An integrated physical and genetic interaction map of genotoxicity, *Trey Ideker*

A temporal code to generate specificity in inflammatory signaling, *Alexander Hoffmann*

***Dynamics of signal transduction and gene expression in single cells: feedback*, inheritance and survival,** *Alexander van Oudenaarden*

The Diverse Aspects of Protein Synthesis and Degradation

BY MARK HOCHSTRASSER AND RACHEL GREEN


Mark Hochstrasser


Rachel Green

Biological systems devote considerable effort to the synthesis and subsequent folding of the enormous cellular repertoire of proteins. And, like all cellular processes, protein synthesis and folding are subject to many different levels of regulation to allow for the timely production of needed functional proteins. An understanding of the basic molecular mechanisms of protein synthesis and folding will be key for deciphering how these systems can be regulated. Just as overall protein synthesis is an enormously complicated and highly regulated process, so too is the controlled destruction of cellular proteins. Many important regulatory proteins are subject to rapid degradation as this allows tight control of their concentrations in the cell.

In addition, any protein made in the cell can suffer biosynthetic errors or post-translational mishaps such as incorrect folding or improper assembly. Accumulation of such defective proteins can be toxic and is linked to a variety of degenerative disorders such as Alzheimer and prion diseases. Much of this regulatory and quality control proteolysis falls under the province of the ubiquitin-proteasome system. Four sessions focusing on diverse aspects of protein synthesis and degradation will comprise the Protein Synthesis, Folding, and Degradation Theme.

Just as overall protein synthesis is an enormously complicated and highly regulated process, so too is the controlled destruction of cellular proteins.

In the Mechanisms of Protein Synthesis session, the speakers will focus on the molecular mechanisms of protein synthesis, principally in bacteria. Jamie Cate (University of California, Berkeley) will speak about recent structural advances detailing the interactions of the 70 S ribosome with ribosome recycling factor. These studies will illuminate key interactions that facilitate the poorly understood recycling step of protein synthesis that follows completion of the polypeptide chain. Scott Blanchard (Cornell University) will next discuss current advances in defining the thermodynamic and kinetic parameters of allosteric movements of the ribosome during elongation using single molecule approaches. Finally, Rachel Green (Johns Hopkins University) will describe recent biochemical studies focusing on the termination step of protein synthesis. Each talk will broadly focus on the theme of protein synthesis being a series of allosteric switches, dictating the specificity of each molecular event.

The Protein-Assisted Folding and Misfolding session will focus on discussion of diverse aspects of protein folding and misfolding. Judith Frydman (Stanford University) will talk about recent studies on the organization of the chaperone machinery in the eukaryotic cytosol and how it promotes folding of newly translated polypeptides and clearance of misfolded proteins. Jeff Kelly (The Scripps Research Institute) will discuss how the mechanisms of protein folding and misfolding are related to normal physiology and disease. Art Horwich (Yale University) will describe the mechanism of a complex ring-shaped folding machine, the chaperonin GroEL, which together with its detachable lid cofactor GroES uses ATP to bind and fold proteins within its central cavity.

In the Protein Turnover and Quality Control session, Brenda Schulman (St. Jude's Children's Research Hospital) will first describe the class of enzymes that provide the gateway into the ubiquitin system and closely related protein-conjugation systems. These so-called E1 or E1-like enzymes use ATP to activate the C terminus of ubiquitin or ubiquitin-like proteins (Ubls) for amide bond formation with target proteins. In the second talk, Randy Hampton (University of California, San Diego) will detail the fascinating mechanistic link between sterol-regulated degradation of HMG-CoA reductase and protein quality control at the endoplasmic reticulum (ER). HMG-CoA is a polytopic ER membrane protein and is the rate-limiting enzyme in the synthesis of cholesterol and related sterols. A specific ubiquitin-protein ligase (E3) functions both in

HMG-CoA degradation and quality control of a subset of aberrant ER proteins. Mark Hochstrasser (Yale University) will describe another set of ubiquitin- and Ubl-dependent reactions that occur at the ER membrane and inner nuclear membrane. These include ubiquitin ligation to specific abnormal ER membrane proteins and to certain nuclear regulatory proteins. The Ubl known as SUMO is also subject to attachment and removal at the nuclear membrane, and a new link between SUMO dynamics and RNA quality control will be described.

For the Protein Turnover in Cell Regulation session, a series of diverse regulatory mechanisms subject to control by protein turnover will be outlined. The first speaker, Michael Rape (University of California, Berkeley), will describe the intricate control of cell cycle progression through mitosis by what is probably the most complex E3 ubiquitin ligase, the anaphase-promoting complex (APC). How different substrates are targeted by the APC at defined stages of cell cycle progression will be a central topic. In the next talk, Ning Zheng (University of Washington, Seattle) will lay out the remarkable story of how the simple plant hormone auxin regulates plant growth by binding to a specific subunit of another ubiquitin ligase. Crystallographic data from Zheng reveal an elegant mechanism by which auxin binding stimulates subsequent substrate binding. In the last talk, Sinisa Urban (Johns Hopkins University School of Medicine) will discuss the unusual ability of certain proteases to cleave transmembrane proteins within the plane of the membrane. How hydrolysis reactions can occur in the hydrophobic interior of lipid bilayers has been a long standing puzzle, but biochemical and structural data from Urban and others on the rhomboid proteases have now shed considerable light on this problem.

Protein Synthesis and urnover Thematic Meeting

ORGANIZERS:
Mark Hochstrasser, *Yale University*
Rachel Green, *Johns Hopkins University School of Medicine*

Symposium:
Protein Turnover and Quality Control

Structural insights into ubiquitin-like protein transfer cascades, *Brenda Schulman*

Sterol regulation and protein quality control at the ER, *Randy Hampton*

SUMO and ubiquitin at the nuclear envelope and ER, *Mark Hochstrasser*

Symposium:
Protein Turnover in Cell Regulation

Ubiquitin ligase machinery: from plant biology to human diseases, *Ning Zheng*

The multiple roles of ubiquitin in orchestrating mitosis, *Michael Rape*

Structure and function of rhomboid intramembrane proteases, *Sinisa Urban*

Symposium:
Mechanisms of Protein Synthesis

Ribosome function is modulated by built in switches, *Rachel Green*

Single-molecule observations of allostery in translation, *Scott Blanchard*

Structures of E. coli ribosome with ribosome recycling factor, *Jamie Cate*

Symposium:
Protein-Assisted Folding and Misfolding

Chaperone-mediated protein folding in the eukaryotic cytosol, *Judith Frydman*

Amyloid diseases, *Jeffery W. Kelly*

Chaperonin structure and function, *Art Horwich*

A Renaissance for Metabolism Research

BY MARK JOHNSTON

Metabolism is pretty much figured out, right? One need look no farther than the remarkably well annotated metabolic chart taped to the wall in most every the lab to see that. Most steps in most metabolic pathways of the major experimental organisms, as well as humans, have been characterized. What more is there to know? Less and less, it might seem, by one (admittedly unscientific) measure: the number of papers in the *Journal of Biological Chemistry* (*JBC*) with the word "metabolism" in the title declined steadily over the last 50 years, from 606 in the 1950s to only 270 in the 1990s. So why attend sessions on metabolism at the ASBMB meeting? It's an area that's all but wrapped up, isn't it?

Certainly not! Important, novel, and often surprising discoveries continue to be made about the mechanisms, meaning, and momentousness of metabolism. And because of that well annotated metabolic chart, the questions being asked are incisive, and the answers are penetrating. Indeed, metabolism research is in something of a renaissance: *JBC* is on a pace to publish in this decade 474 papers with the word "metabolism" in the title, the most since the 1950s. The golden age of metabolism research may be upon us!

And we're seeing that discoveries in the field of metabolism relate more and more directly to human disease. If the "translational research" that we are increasingly urged (sometimes badgered) to pursue is to come to fruition, I suspect that some of the first and most significant successes will be won in the arena of metabolism. It seems fitting, then, to focus the Metabolism sessions at the ASBMB meeting on important human diseases. These sessions promise to provide an early window into a field whose impact only stands to increase.

The unusual metabolism of many types of tumor cells has been recognized since the early 1930s, when Otto Warburg (and, independently, Herbert Grace Crabtree) discovered that those cells tend to "ferment" glucose (producing lactate) rather than oxidize it, even though they harvest less energy in doing so. There has been renewed interest in this phenomenon in recent years. In the Metabolism and Cancer session, Doug Wallace (University of California, Irvine) will present his intriguing ideas for the role of the mitochondrion and hexokinase in the "aerobic glycolysis" of cancer cells. But long before Warburg and Crabtree, the ancient Egyptians found that yeasts metabolize glucose in the same way, producing ethanol rather than lactate (which made the Egyptians very happy). I (Mark Johnston) will describe the basis for this lifestyle of yeasts, which provides a paradigm for understanding the metabolism of cancer cells (and continues to provide us with bread and beverages that make us happy). Contributing to the unorthodox metabolism of tumor cells is the increasing hypoxia they must endure, which is possible because of the hypoxia-inducible factors (HIFs) that mediate the cells' response to this stressful condition. Celeste Simon (University of Pennsylvania) will provide insight into how HIFs modulate metabolism and promote tumor proliferation.


Mark Johnston

One of the best known and most prevalent metabolic diseases is diabetes. It is not a coincidence that the prediabetic condition is known as the "metabolic syndrome." Despite many years of intensive investigation, diabetes remains enigmatic and difficult to treat, so there is a thirst for new insight into the disease. In the Metabolism and Diabetes session, Grahame Hardie (University of Dundee) will describe new findings on a central sensor of cellular energy status: the AMP-activated protein kinase (AMPK). This "fuel gauge of the cell" is the target of antidiabetic drugs and a focus of efforts to find new therapies. The endpoint of the progression towards diabetes is chronic high levels of glucose in the blood, ultimately caused by failure of the devices for its disposal. Barbara Kahn (Harvard University) will discuss the importance of glucose sensing and transport in the maintenance of metabolic harmony. The other side of the diabetic coin is glucose starvation, and Pere Puigserver (Harvard University) will describe how cells adapt to this condition by increasing fatty acid oxidation. What he has to say will prove relevant to obesity and ageing.

Some surprising connections between altered metabolism and neurodegeneration that have surfaced recently will be described in the Metabolism and Neurodegeneration session. Who would have thought that defects in glycolysis might contribute to Parkinson disease? Barry Ganetzky (University of Wisconsin, Madison) was as surprised as anyone when his studies of a *Drosophila* mutant with neurological

problems led him to that conclusion. A role for metabolic defects in epilepsy should not surprise anyone, however, because it has long been known that certain forms of epilepsy can be controlled with diet. But Avtar Roopra's (University of Wisconsin, Madison) observation that an inhibitor of glycolysis blocks certain types of epilepsy was a surprise and opens the door for a new class of anticonvulsant drug. Jeff Milbrandt (Washington University) will describe his discovery that increasing the NAD^+ level in damaged neurons delays---and in some cases prevents---axonal degeneration and death. Maybe there's some hope for us ageing baby boomers after all!

Although that metabolic chart tacked to the wall in the lab represents a remarkable scientific accomplishment, we must admit that it's somewhat superficial: it doesn't really describe the highly interconnected and dynamic metabolic network. How do all those pathways coordinate with each other, and how do they adjust in harmony when the cell's circumstances change? The speakers in the Metabolic Networks session will begin to provide some of the answers. Bernhard Palsson (University of California, San Diego) will present integrated metabolic and regulatory network models that enable predictions of cell growth phenotypes of mutants missing certain transcription factors. Christina Smolke (Caltech) will discuss work from her lab integrating molecular switches into synthetic and endogenous cellular networks. And James Liao (University of California, Los Angeles) will describe his efforts to design intracellular oscillators that interface with metabolism with the goal of predicting cellular behavior and designing gene metabolic circuits for novel functions.

Even though we have that comprehensive metabolic chart—indeed because we have it—research on metabolism is alive and well, and more exciting than ever! Come see for yourself at the 2008 ASBMB meeting.

Metabolism Thematic Meeting

ORGANIZER:
Mark Johnston
Washington University School of Medicine

Symposium: Metabolism and Diabetes

AMPK: the fuel gauge of the cell, *Grahame Hardie*

Nutrient control of gluconeogenesis through PGC-1-alpha/SIRT1 deacetylase complex, *Pere Puigserver*

Glucose transport and sensing in the maintenance of glucose homeostasis and metabolic harmony, *Barbara Kahn*

Symposium: Metabolism and Cancer

The Warburg effect in yeast, *Mark Johnston*

Mitochondria and cancer: stochastic genetics and energetic pathophysiology, *Doug Wallace*

Hypoxia-inducible factors: central regulators of the tumor phenotype, *Celeste Simon*

Symposium: Metabolism and Neurodegeneration

NADH, AMPK, and neurodegeneration, *Jeff Milbrandt*

TPI deficiency and neurodegeneration in Drosophila: an AGE-dependent link to a common mechanism? *Barry Ganetzky*

Glycolysis and epilepsy, *Avtar Roopra*

Symposium: Metabolic Networks

Identification of genome-scale metabolic network models, *Bernhard Palsson*

Integration of molecular switches into synthetic and endogenous cellular networks, *Christina D. Smolke*

The design of intracellular oscillators that interact with metabolism, *James Liao*

RNA: From Atom to Organism

BY FRANK SLACK AND ROBERT T. BATEY

The past decade has brought discoveries that have revolutionized our thinking about gene regulation and cell biology. The emergence of a role for RNA in almost all aspects of biology has resulted in a paradigm shift in how biologists view the subcellular world. In the past, RNA was primarily viewed as a messenger shuttling information from DNA to proteins or the structural components of translation. We now understand that RNA plays many more important roles in the cell, from gene regulation to catalysis. In this ASBMB meeting theme we have tried to capture a few snapshots of this very exciting scientific frontier in four sessions that present views of the RNA world that span from atomic to organismal levels.

The Riboregulation session will focus upon recent work uncovering the mechanisms by which RNA regulates gene expression inside the cell. This session will by chaired by James Goodrich (University of Colorado, Boulder), who will present data on how non-coding RNAs that are induced by heat shock are able to repress transcription by RNA polymerase II. Ronald Breaker (Yale University) will describe how cis-acting regulatory elements in mRNAs called riboswitches are able to regulate gene expression through their ability to specifically bind a range of small molecule metabolites. Finally, Gisela Storz (National Institute of Child Health and Human Development, National Institutes of Health) will describe the role of small non-coding RNAs in bacteria and how they serve to regulate a number of processes.

The session on Dynamic RNA Structures chaired by Robert Batey (University of Colorado, Boulder) will center upon the atomic level structure of RNA and functional conformational changes that they undergo. Batey will describe x-ray structures of the metabolite binding domain of riboswitches and how binding induces conformational changes in the RNA that allow it to control gene expression. Julie Feigon (University of California, Los Angeles) will focus upon developing atomic resolution models of RNA using NMR spectroscopy to understand how they function in a biological context. Nils Walter (University of Michigan) will focus upon the use of single molecule fluorescence experiments to reveal the mechanisms by which ribozymes are able to achieve catalytic activity.

The Emerging Non-coding RNA World session will be chaired by Tom Gingeras (Affymetrix). This session aims to introduce the audience to the large amount of newly discovered transcription and RNA species present in the cell. John Mattick, (University of Queensland, Brisbane, Australia) will kick off the session with a discussion of the complexity of non-coding RNA species found in eukaryotic cells and how this might be proportional to species complexity. Tom Gingeras (Affymetrix) will describe the recent discovery of massive transcriptional output in animal cells. Then, recent Nobel laureate Andrew Fire (Stanford University) will discuss new aspects of RNA interference.

The Roles for Small Non-coding RNAs session will be chaired by Frank Slack (Yale University). This session will focus on functions for some of the newly discovered RNA species. First Slack will introduce microRNAs and their roles in development and cancer. Next, Anastasia Khvorova (Dharmacon/Thermo) will discuss recent advances in small interfering (siRNAs) technology. This will be followed by a discussion on the roles of miRNAs in plants by Marja Timmermans (Cold Spring Harbor Laboratory).

Small RNAs and Dynamic RNA Elements Thematic Meeting

Organizers: Frank Slack, *Yale University* **and Robert T. Batey,** *University of Colorado-Boulder*

Symposium: Riboregulation

Small Non-coding RNAs in bacteria, *Gisela Storz*

Gene regulation by riboswitches, *Ron Breaker*

Role of B2 and Alu RNAs in regulation of transcription, *Jim Goodrich*

Symposium: Dynamic RNA Structures

Probing conformational changes in riboswitches, *Rob Batey*

NMR studies of dynamic RNA elements in telomerase, *Julie Feigon*

Single molecule studies of RNA dynamics, *Nils Walter*

Symposium: The Emerging Non-Coding RNA World

New RNA species in animals, *John Mattick*

Massive transcriptional output, *Tom Gingeras*

New endogenous siRNAs, *Andrew Fire*

Symposium: Roles for Small Non-Coding RNAs

MicroRNAs in cancer, *Frank Slack*

siRNAs, *Anastasia Khvorova*

MicroRNAs in plants, *Marja Timmermans*

ASBMB Taps 8 Scientists and 1 Politician for Top Awards

The American Society for Biochemistry and Molecular Biology (ASBMB) has announced the recipients of its annual awards competition. Eight scientists and one politician were singled out for their outstanding achievements and contributions to science. The awards will officially be presented at the Experimental Biology 2008 meeting, April 5–9, 2008, in San Diego.

I. Robert Lehman of Stanford University will give the Herbert Tabor/*Journal of Biological Chemistry* Lectureship. Lehman received the award for his outstanding scholarly contributions to the field of DNA metabolism, his admirable track record as a mentor, and his unparalleled service to the *Journal of Biological Chemistry.*

C. David Allis of the Rockefeller University will be honored with the ASBMB Merck Award for his seminal contributions to the field of chromatin biology. The Merck Award is given to a researcher who makes outstanding contributions to research in biochemistry and molecular biology.

Alexandra C. Newton of the University of California, San Diego will be presented with the Avanti Award in Lipids. Newton has worked for over two decades on molecular aspects of lipid signaling and as a result has been able to elucidate the molecular controls that regulate the function of protein kinase C. This award honors outstanding scientists whose research interests are in the field of lipids.

The FASEB Excellence in Science Award will go to **Mina J. Bissell** of the Lawrence Berkeley National Laboratory. The award recognizes outstanding achievement by women in biological science. Bissell is a world renowned leader in the area of the role of extracellular matrix (ECM) and microenvironment in regulation of tissue-specific function with special emphasis in breast cancer, where she has changed some established paradigms.

S. Walter Englander of the University of Pennsylvania School of Medicine will give the Herbert A. Sober Lectureship. This lectureship, which is awarded every two years, recognizes outstanding biochemical and molecular biological research with particular emphasis on development of methods and techniques to aid in research. Englander has been a central figure in the development and application of hydrogen exchange-base methods that revolutionized insight into the biochemistry and biophysics of proteins.

The Honorable **Michael N. Castle**, (R-DE), member of the U. S. House of Representatives, will receive the Howard K. Schachman Public Service Award. The award recognizes an individual who best demonstrates dedication to public service in support of biomedical science. Castle was selected in recognition of his repeated efforts to boost the budget of the National Institutes of Health since 2003 and for his efforts to promote a more rational Federal policy regarding use of human embryonic stem cells.

The Schering-Plough Research Institute Award will be presented to **Scott A. Strobel**, a Howard Hughes Medical Institute professor at Yale University. The Schering-Plough Award was established to recognize young investigators for outstanding research at an early stage of their careers. During his short career, Strobel has become a major leader in the study of the structure, function, and mechanism of RNA molecules involved in catalytic processes.

John D. Scott a Howard Hughes Medical Institute investigator at Vollum Institute, Oregon Health & Science University, will be honored with the William C. Rose Award. The award recognizes outstanding contributions to biochemical and molecular biological research and a demonstrated commitment to the training of younger scientists. Scott's work on the AKAP family of scaffold proteins has transformed the field of intracellular signaling. He has also been an exemplary trainer of graduate students and postdoctoral fellows who have gone on to make their own contributions to the field of signal transduction.

The ASBMB Award for Exemplary Contributions to Education will be presented to **Michael F. Summers**, a Howard Hughes Medical Institute investigator at the University of Maryland, Baltimore County. Summers has pioneered efforts to recruit and retain students traditionally lost to science and aided in broadening the diversity of students engaged in science. The award, administered annually by the ASBMB Education & Professional Development Committee, is given to a scientist who encourages effective teaching and learning of biochemistry and molecular biology through his or her own teaching, leadership in education, writing, educational research, mentoring, or public enlightenment.

A Generalist Finally Finds Her Place

BY SYDNEY C. GARY

Strong generalist tendencies are not that helpful when you are supposed to be attending to one molecule acting on one specific cell type during a tiny window of development in a mouse brain. "Focus, Sydney!" my postdoctoral advisor would say encouragingly (or was it frustratedly?). I found it near impossible to do this, especially with all the interesting things going on outside of the cell culture dishes I stared into day after day.

I had switched research areas between graduate school and my postdoctoral training, from studying gene expression in leukemias at the Medical College of Virginia to developmental neurobiology at Yale University. This was because I found the brain fascinating and wanted to learn all I could about neurobiology, and going into a new field seemed exciting.

My first two postdoctoral years were fantastic, full of learning everything I could about neurobiology, applying new techniques, and just enjoying the opportunity to grow scientifically. Around year three, though, my research project was sputtering, and my publication record was far from robust. I needed to rein in my "diverse" interests a bit and follow my advisor's urging to be more focused on my research project.

I tried, I really did. But it just wasn't working for me. I hate to resort to tired metaphors, but as my postdoc years kept accruing, I was feeling more and more like "a fish out of water," or "a fish on a bicycle," or something involving a fish. It wasn't good.

Like most of us in this growing fraternity of alternative career holders, I forced myself to endure a self-assessment exercise, which revealed that my strengths and interests were not being maximized as a laboratory scientist. I liked to teach, write, create graphics and figures, design websites—even troubleshoot and fix faulty lab equipment or computer problems. Also, I realized I lacked the drive and personality evident in those of my peers who were succeeding at the academic research game. I finally accepted that I should be doing something else that would capitalize on my strengths.

So, after four years as a postdoc, I took that first difficult step away from the bench. I applied for and was offered a one-year visiting assistant professor job at Haverford College, a small liberal arts college outside of Philadelphia. This appeared to be my dream job, and I loved it there. Unfortunately, when the year was up, I was back on the job market. But at least I had experience teaching undergraduates, so I was ready to send in my CV and teaching philosophy to all the small, liberal art colleges reasonably close to the northeastern city I had adopted as home and watch the next dream job fall into place. That particular academic job cycle, there was one tenure track position advertised in my area of expertise and in my admittedly narrow target geographical area. I—along with another 300 dream job seeking hopefuls—applied. One of those other 300 got it.

I spent the next two years back at Yale, in the nether world of the "associate research scientist" (non-tenure track faculty), which was a strange existence. I was fortunate that my postdoc advisor was willing to keep me around while I was looking for the next opportunity to come sweep me away, and I enjoyed keeping my

Sydney Gary

Sydney Gary is the assistant director of the Banbury Center at Cold Spring Harbor Laboratory (CSHL). She received a B.S. in Biology from Southwestern University in Georgetown, Texas, and received a Ph.D. in Pharmacology/Toxicology from the Medical College of Virginia in Richmond. In the 9 years between her Ph.D. and her current position at CSHL, she was a postdoctoral fellow at Yale University, a visiting assistant professor at Haverford College in Haverford, Pennsylvania, and a medical editor and writer at Manisses Communication in Providence, Rhode Island.

research project going. But it did seem a bit like treading water.

At this point, I decided that rather than wait around for the perfect small-college position that fulfilled my very restrictive criteria, I would instead focus on applying my generalist tendencies to become a science writer/medical writer. I started applying for all sorts of different positions, from academic journal editor to medical education specialist with a small biotech firm. Everyone seemed to be looking for someone with demonstrated writing or editing experience, and my volunteer column for a quarterly magazine, paltry number of research papers, and various grant writing exercises just didn't cut the mustard. It was a very frustrating time.

After almost two years of searching, I finally landed a job as an associate editor for a group of clinical psychiatry publications based in Providence, Rhode Island. The main reason I got the job was that I had met the editor during a pickup basketball game, and we started talking about our jobs and my desire to get into writing/editing—and she took a chance on me. So after all my high tech job searching using the array of Internet career websites and search capabilities, it all came down to just meeting someone on the basketball court and having a discussion about what I wanted to do. I spent two years as an associate editor, learning how to write for a deadline, conduct interviews with researchers, design and layout a publication, and manage freelancers. I also learned a lot about clinical psychiatry, adding a useful medical slant to my basic science training. It was exhausting work but also fantastic experience that was critical for my next career move.

This seemingly meandering career path had provided me with the CV of an authentic generalist.

This seemingly meandering career path had provided me with the CV of an authentic generalist. People suddenly took me seriously when I applied for non-research jobs, including the position I now hold at Cold Spring Harbor Laboratory—finally my dream job. Cold Spring Harbor is a high caliber research institution that also runs some of the top scientific meetings and postgraduate courses in the world. As assistant director of the Banbury Center at Cold Spring Harbor Laboratory, I am involved in developing new programs, meetings, and courses, focusing on the areas of neuroscience and mental health. Amazingly, I get to interact almost every day with highly respected international scientists who come to Cold Spring Harbor as meeting participants, course lecturers, and sometimes even course students. I also am fortunate to get to work closely with many of the scientists here as well as other fellow "generalists" who have made their way to Cold Spring Harbor to contribute their various skills as directors of programs, editors of books, etc. We can all thrive here in this unique and wonderful place.

When I saw the advertisement for the position at Cold Spring Harbor Laboratory, it seemed to be tailored for my patchwork background of neurobiology, clinical psychiatry, teaching, and writing. It was the easiest cover letter I ever wrote for a job application, everything just came together. My generalist tendencies finally paid off.

Mentoring of Postdoctoral Scholars Attracts National Attention

BY KEITH J. MICOLI AND LUCIA MOKRES

The training of current and future scientists in the United States has been an area of increasing concern for the past decade as the number of postdoctoral scholars has grown without an increase in the number of independent academic positions into which they may transition. Although there have been tremendous advances in technology and in the way in which science is performed, there has been little change in the training of postdoctoral scholars in the past century. As job markets and grant pay-lines have tightened, the average first time National Institutes of Health (NIH) R01 recipient is now over 40 years old. Funding agencies, universities, and individual mentors are now recognizing that to maintain a dynamic and creative workforce and to encourage the best and most capable students to enter science, there must be more effort applied to making the postdoctoral period more effective as a means of transitioning to independence.

Great strides have been made towards enhancing postdoctoral training in the last five years with the creation of the National Postdoctoral Association (NPA), the expansion of institutional Postdoctoral Training Offices, and the increased attention paid to new and young investigators by the NIH and the National Science Foundation (NSF). One major area of focus for these organizations has been the development and endorsement of effective mentoring policies and programs for postdoctoral fellows. Mentorship in laboratory management and research skills is crucial for the development of young scientists if they are to become competent investigators and managers of independent laboratories, and principal investigators must be encouraged to emphasize this key aspect of postdoctoral training.

Regrettably, for some time there has been debate whether the time spent mentoring postdoctoral fellows could be counted towards the percent of effort on a research grant. By allowing principal investigators to bill for time spent mentoring as part of effort reporting, they may be more likely to ensure that appropriate mentorship is provided during the postdoctoral training period. To this end, the NIH has clarified its position regarding mentoring and effort reporting, in response to a request by the NPA. The NIH now states that time spent mentoring postdoctorates can be counted toward percent effort reported on a research grant "to the extent that mentoring activities are not readily separable from activities related to supervising the participation of students and postdoctorates in the funded research project" (see OMB circular A-21 and the NIH clarification at grants1.nih.gov/training/q&a.htm#post).

In a similar effort to foster appropriate mentorship of postdoctorates, the U.S. Congress and President Bush recently approved a new provision on postdoc mentoring as part of the America Competes Act, reauthorizing the National Science Foundation. According to SEC. 7008, entitled "Postdoctoral Research Fellows:"

a. MENTORING—The Director shall require that all grant applications that include funding to support postdoctoral researchers include a description of the mentoring activities that will be provided for such individuals, and shall ensure that this part of the application is evaluated under the Foundation's broader impacts merit review criterion. Mentoring activities may include career counseling, training in preparing grant applications, guidance on ways to improve teaching skills, and training in research ethics.

b. REPORTS—The Director shall require that annual reports and the final report for research grants that include funding to support postdoctoral researchers include a description of the mentoring activities provided to such researchers.

The NIH clarification and the NSF reauthorization represent major steps towards the development of policies that will foster more comprehensive and effective mentoring practices for postdoctoral fellows. The U.S. research enterprise will benefit greatly from the addition of young scientists who have received top quality training in all aspects of their investigative careers. ASBMB continues to advocate for such improvements in postdoctoral training policies, working in collaboration with NPA and other scientific organizations to achieve this goal.

Maurice Swanson: Finding New Cures for Muscular Dystrophy

BY PAT PAGES

Marice S. Swanson

Genes can go wrong in many different ways. Most known genetic diseases are directly caused by mutations in specific genes, but in some neuromuscular diseases the cause is indirect and the mutant gene produces an abnormal mRNA that attaches itself to proteins essential for normal adult development.

Maurice S. Swanson, professor of Molecular Genetics and Microbiology at the University of Florida, Gainesville, has spent the past 15 years understanding how these RNA-binding proteins work and finding ways to prevent their damaging effects. Recently, Swanson has also tested chemical compounds that have showed promise in the treatment of muscular dystrophy, a disease that weakens and ultimately wastes away muscles.

> ***"Scientists should now be able to design drugs that may cure many important neuromuscular diseases in the near future"***

"The knowledge that diseases can be caused by sequestration of RNA-binding proteins is relatively new," Swanson says. "But so much research has been done on this topic that scientists should now be able to design drugs that may cure many important neuromuscular diseases in the near future, which is very encouraging."

Swanson's interest in nature and science started when he was a child growing up in Seattle. He remembers particularly enjoying his biology and chemistry classes. He also remembers being fascinated by a surgical operation that he attended at a relatively young age. His father, an obstetrician-gynecologist, had allowed Swanson to watch the entire operation—a hysterectomy, or surgical removal of the uterus—that he was conducting. The operation gave Swanson a first-hand, practical look at surgery and may have prompted him to specialize in the biomedical field later in life.

Swanson attended Colorado College, a liberal arts college in Colorado Springs, where courses are taken one at a time. Every semester, students would take an average of four courses, one after the other. "I really enjoyed this way of learning," Swanson says. "In other colleges, students take concurrent classes in multiple subjects. At Colorado College, I was able to focus on one topic at a time, which was an early taste of what it would be like to be a scientific researcher."

After graduating with a bachelor's degree in Biology, Swanson pursued a master's degree in Biology at the University of California, Santa Barbara, where his interest in biochemistry and molecular biology was fostered. He worked on mRNA translation in Euglena, a pear-shaped, one-celled organism that, like a plant, makes its own food by photosynthesis, but when in darkness acts like an animal by eating tiny plants and animals. During this period, he also became intrigued by the process of cellular senescence and aging, and this interest prompted him to transfer to the University of California, Berkeley, for his doctoral studies.

For his Ph.D. thesis, Swanson began working on the free radical theory of cell aging, which transitioned to studies on mitochondrial bioenergetics and the regulation of electron transport chain components. During this period, he enjoyed being surrounded by a large number of Ph.D. students, postdoctoral students, and scientists from many countries. He notes that "the lab was quite diverse with biochemists, biophysicists, and physiologists working closely together—it was a wonderful interplay of scientists who approached problems from different

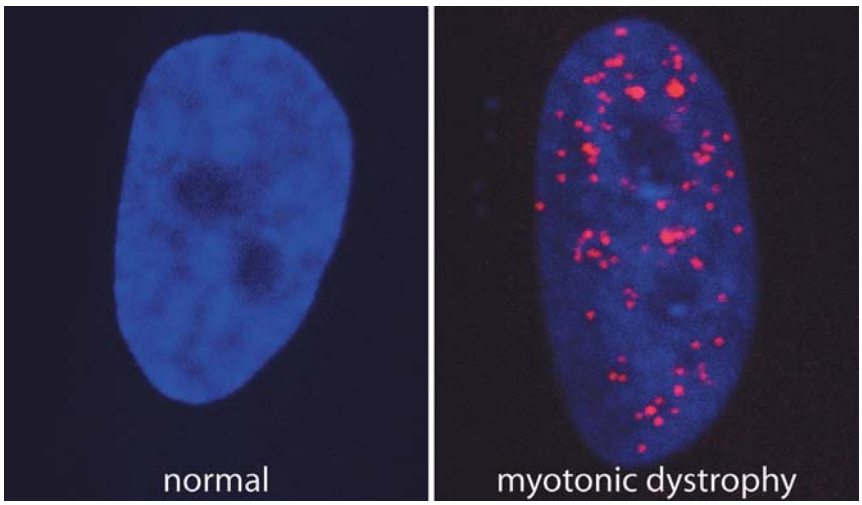

Fig. 1. Nuclear RNA foci (*red*) in normal (*left*) and myotonic dystrophy (*right*) cells viewed in a microscope by fluorescence *in situ* hybridization. The nucleus is stained *blue*.

perspectives but often came to similar conclusions about which experiments needed to be done to answer the relevant question."

After completing his Ph.D. in 1980, Swanson initially went to Northwestern University, Evanston, Illinois, to work with Emanuel Margoliash, now emeritus professor of Biochemistry and Molecular and Cellular Biology at Northwestern, to continue his studies on mitochondrial bioenergetics. His interest in RNA biology was later rekindled by his interaction with another Northwestern professor, Gideon Dreyfuss, who is now a Howard Hughes Medical Institute investigator and Isaac Norris Professor of Biochemistry and Biophysics at the University of Pennsylvania School of Medicine, and Swanson started working on nuclear RNA processing.

"Our work centered on how RNA is processed in a cell nucleus, especially how RNA binds to a very abundant class of RNA-binding factors called the heterogeneous nuclear ribonucleoproteins, or hnRNPs," Swanson says. "We discovered that these and many other types of RNA-binding proteins contain a structural motif—now called the RNA recognition motif—that allows these proteins to recognize specific RNA sequences."

In 1989, Swanson moved to the University of Florida to set up his own laboratory, where he investigated how nuclear RNA processing and mRNA export are coordinated in yeast. The scientists found that yeast also expresses hnRNPs, and one of these proteins, Nab2p, is involved in both polyadenylation—the addition of adenine nucleotides to the 3' end of mRNA—and mRNA export from the nucleus to the cytoplasm.

Later, Swanson and colleagues found a related protein in human cells, which they called CUGBP1 because it prefers to bind to CUG repeats in mRNA. This discovery led them to work on myotonic dystrophy, a neuromuscular disease caused by the expansion of a CTG repeat in the Dystrophia Myotonica Protein Kinase *(DMPK)* gene and, in turn, results in the production of a mutant RNA with tandem CUG repeats. Another research team then discovered that a less common form of the disease, called myotonic dystrophy 2, is caused by a series of between 80 and 11,000 CCTG repeats in the first intron of the zinc finger protein 9 (*ZNF9*) gene.

Both forms of myotonic dystrophy cause skeletal muscles to lose the ability to relax once they contract and affects one of every 8,000 people. "One of the principal manifestations of the disease is muscle hyperexcitability," Swanson says. "When patients with myotonic dystrophy contract one of the muscles in their arm, it's very difficult for them to release that contraction."

The muscles progressively weaken and eventually waste away. The disease also affects the heart muscle and is associated with irregular heart rhythms that can lead to sudden death. It also can result in cataracts, premature hair loss, and mild to moderate mental retardation. These symptoms worsen with each generation as ever increasing copies of a malfunctioning RNA repeat sequence are produced.

Swanson and colleagues discovered that, after the repeats are transcribed into mRNA, the resulting CUG (from the *DMPK* gene) and CCUG repeats (from the *ZNF9* gene) fold into an unusual hairpin structure, and the contorted mRNAs accumulate in areas of the nucleus called foci. The hairpin structures then bind to proteins called muscleblind-like 1 (MBNL1), which bind to both CUG and CCUG repeats.

"When viewed in the microscope by fluorescence *in situ* hybridization (Fig. 1), the nuclei of these cells look like they have measles," Swanson says. "You can also see that these CUG repeats colocalize with MBNL1 proteins."

In people not affected with the disease, CUGBP1 and MBNL1 are involved in RNA alternative splicing, the process that regulates the removal of introns from pre-RNAs as well as the removal of some exons from coding sequences. This splicing is often regulated according to cell type and developmental stage. In the case of muscle cells, some exons that are leftovers from the fetal developmental stage are removed, so that only exons coding for adult muscle proteins are activated.

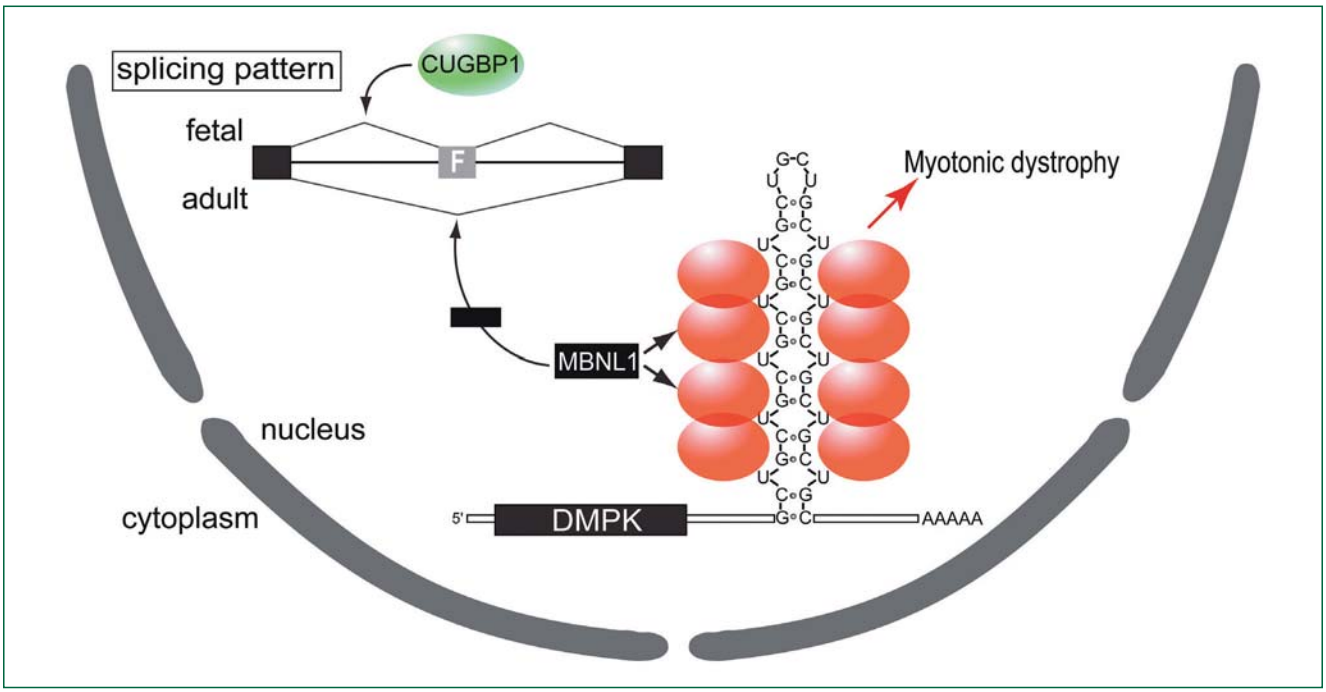

Fig. 2. Schematic representation of the sequestration of MBNL1 (*red ovals*) in myotonic dystrophy (coding regions, *black boxes*; untranslated regions, *smaller open boxes*; fetal alternative exon, *gray box*; CUG repeat shown as a *double-stranded RNA*).

In myotonic dystrophy, because MBNL1 is sequestered by the CUG and CCUG repeats, it cannot remove certain fetal exons anymore, and the resulting mRNAs are then translated to produce fetal muscle proteins, which are unable to work in adult muscle tissues (Fig. 2).

"Newborn muscle is very different than adult muscle; muscle proteins must undergo multiple changes between the time we are newborns and the time we become adults," Swanson says. "But in adult patients with myotonic dystrophy, the fetal forms of proteins that are expressed during embryonic and neonatal life are present, and these are incompatible with adult muscle function."

Because MBNL1 proteins are inactivated in myotonic dystrophy, Swanson and colleagues recently decided to inject a surplus of MBNL1 in mice carrying the genetic flaw underlying the disease, so that even if some proteins bind to mRNA, others can still splice out the fetal exons. The experiment worked: the mice recovered after a few weeks.

"We simply flooded the muscle with extra copies of the muscleblind protein," Swanson says. "We were able to correct the myotonia as early as four weeks after injection, and at 23 weeks it was completely eliminated in the muscle that was injected with the virus carrying this muscleblind protein."

Encouraged by these results, the scientists are now planning to inject MBNL1 directly into the bloodstream. "About 30% of myotonic dystrophy patients succumb to heart problems, so theoretically systemic injections might also prevent that," Swanson says.

Swanson and colleagues eventually hope to find out whether correcting myotonia early by restoring normal levels of MBNL1 might prevent at least some of the muscle loss that characterizes the adult onset disease.

Swanson is very excited about the therapeutic prospects of his latest results. "Our work provides proof of principle that the approach is effective, at least in mice," Swanson says. "Our hope is that this strategy will ultimately lead to an effective treatment of myotonic dystrophy and possibly other neuromuscular and neurodegenerative diseases in humans."

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Matthias Mann: Using Proteomics to Understand Protein Interactions

BY PAT PAGES

Understanding how all the proteins in a cell work together may soon be a reality, thanks to new technologies pioneered in part by Matthias Mann, director at the Max Planck Institute for Biochemistry in Martinsried (near Munich), Germany. Mann has spent his 25-year career developing these techniques with the hope of better understanding how drugs work at the cellular level and finding ways to improve current drugs while minimizing their side effects.

"To understand what proteins do in cells, scientists used to study them one at a time, but with current technologies, we can look at thousands of proteins at a time," Mann says. "If you think of a cell as a factory, we used to study every worker separately, but now we can look at the factory in one shot, which is much more interesting."

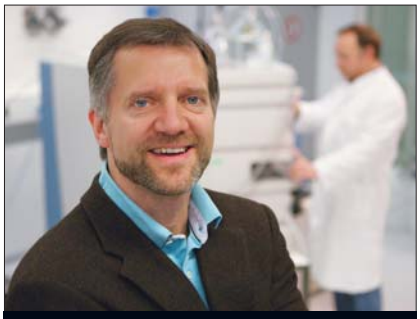
This new perspective on proteins, called proteomics, is generating an increasing amount of research on the inner workings of cells and is being used to design new drugs against a wide variety of diseases, including cancer, diabetes, and neurodegenerative diseases. Mann, in particular, was among those who created and developed this field and has trained dozens of scientists in it, both in Denmark and Germany.

Mann's early interests were in physics and mathematics. He graduated from the University of Gottingen in 1982 with a major in physics and then pursued a master's degree in physics. For his master's thesis, he worked on a device that produced a beam of atoms or molecules to study how they formed dimers in the gas phase.

In 1983, he met with John Fenn, a professor of chemical engineering at Yale University, New Haven, Connecticut, who was developing a new technique to identify the chemical composition of molecules. Until then, the most common technique to do so was by vaporization and "electron impact" mass spectrometry (MS), in which a molecule was broken down into ions and the various ions were separated by mass and charge, leading to knowledge of the molecule's chemical composition. But the new technique, called electrospray ionization, was easier to use and more accurate than mass spectrometry and could be used to analyze larger molecules.

Until the early 1980s, physicists and chemists had been the main users of mass spectrometry, because the molecules they were studying were relatively small. Biologists, who usually work with larger molecules—such as organic molecules, proteins, and DNA—used another technique called the Edman degradation method. This technique determined the amino acid sequence of a protein by removing the amino acids one by one and then analyzing them, but this method was very slow and laborious.

Electrospray ionization—for which Fenn received the 2002 Nobel Prize in Chemistry—offered the potential to replace the Edman method. So when Mann heard about it, he quickly became interested. While working with Fenn, Mann was so excited about the electrospray technique that Fenn invited him to work as a Ph.D. student in his team.



Matthias Mann

Unlike traditional mass spectrometry, electrospray MS does not break a molecule into ions and look at the chemical nature of each ion. Instead, it ionizes the entire molecule and determines its chemical composition at once. Then the technique identifies different molecules present in a sample by separating them by charge and mass (see figure). During his Ph.D. years, Mann showed that electrospray lived up to its promise by successfully identifying peptides and proteins.

After receiving his Ph.D. in 1988, Mann became a postdoctoral fellow at the University of Southern Denmark in Odense, where he worked on another technique called matrix-assisted laser desorption and ionization (MALDI). The technique, which worked like electrospray ionization but was much faster (see figure), had been introduced in 1988 by German scientists Michael Karas and Franz Hillenkamp. Eager to test this new technique, Mann converted an existing mass spectrometry machine into a MALDI machine.

In 1992, Mann moved to the European Molecular Biology Laboratory, where he set up his first research team. At that time, the first DNA-sequencing

databases started to become available, which was an opportunity for Mann and his colleagues to match the information they had collected on proteins with that of a database's DNA. The scientists were able to study many proteins at a time, leading to their first proteomics studies.

Mann's team used the DNA information as follows. First, an unknown protein was cleaved into peptides by a protease such as trypsin, and the masses of the peptides were measured by using either electrospray or MALDI. Then, a computer program converted the DNA information into proteins and determined the peptides that they would produce if cleaved by trypsin. The computer program compared the masses of the peptides of the unknown protein to the peptide masses of each protein encoded in the genome, and the results were statistically analyzed to find the best match.

"By combining the mass spectrometry techniques with DNA databases, we boosted our research considerably," Mann says. "We were suddenly able to work on proteins that were relevant to a wide range of biomedical problems, including cancer, aging, and diabetes. There was a lot of pressure, too, because we had pledged to show that mass spectrometry could outperform the old chemical methods."

The proteins Mann and his team identified were mostly regulatory—those switching on other proteins or those interacting with genes to control their transcription, of which there are about 20 families. These proteins are particularly relevant to medical applications, Mann says, because they can cause diseases when they are defective.

In 1998, Mann went back to the University of Southern Denmark, where he set up his second research team and later developed a technique to detect differences in protein abundance between two samples. Called stable isotope labeling with amino acids in cell culture (SILAC), this technique compares the protein composition of two populations of cultured cells to understand differences between, say, normal and cancerous cells, or cells that respond differently to the same drug.

In this technique, one cell population is fed with a growth medium containing normal amino acids, while a second population grows on a medium containing "heavy" amino acids, which contain a non-radioactive isotope, such as carbon 13 instead of carbon 12 or nitrogen 15 instead of nitrogen 14. When the cells of the second population grow, they incorporate the isotope into their proteins, making them heavier than their counterparts. The two populations are then combined and analyzed together by electrospray, MALDI, or other similar techniques.

SILAC—which is now a popular proteomics technology—is being used by many scientists to study cell signaling and protein-protein interactions.

Mann and the 40 scientists and students working in his third team at the Max Planck Institute of Biochemistry are now actively pursuing research on a variety of topics, which include refining the current proteomic technologies, developing techniques to analyze the protein composition of body fluids---including blood, urine, and cerebrospinal fluid---to diagnose the early symptoms of various medical conditions, and studying epigenetics, changes in genes not caused by mutations but by proteins interacting with genes.

"I feel privileged to be part of such an interesting and growing field of study," Mann says. "I couldn't have imagined that my original work on mass spectrometry would have led me to such a large number of interesting problems. And it's only the beginning: Now that we have developed all these proteomics technologies, we can expect a lot of promising results, especially in the pharmaceutical area."

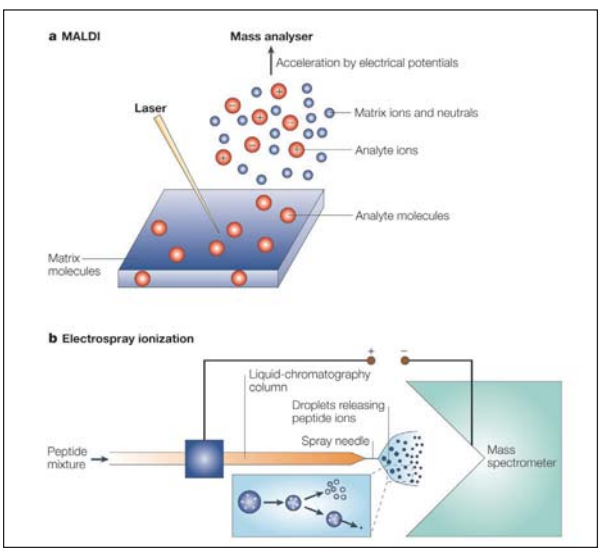


Fig. 1. Simplified representations of the electrospray and MALDI techniques when used to identify various peptides.

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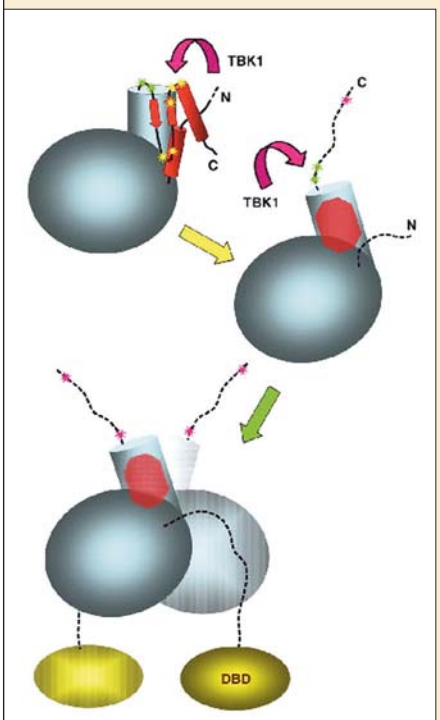
The Transcription Factor Two-step

The interferon regulatory factor 3 (IRF-3) transcription factor is a key component of the innate antiviral response. It is activated by phosphorylation mediated as part of a signaling cascade by the kinases TBK1 and IKKε. Phosphorylation results in IRF-3 dimerization and removal of an autoinhibitory structure, allowing interaction with the co-activators CBP/p300. In this *JBC* paper, the authors provide evidence for a two-step model for the mechanism of IRF-3 activation by phosphorylation. Using purified proteins they show that TBK1 can directly phosphorylate full-length IRF-3 *in vitro*. Phosphorylation at residues in site 2 (Ser-396 to Ser-405) of IRF-3 alleviates autoinhibition to allow interaction with CBP and facilitates phosphorylation at site 1 (Ser-385 or Ser-386). Phosphorylation at site 1 is, in turn, required for IRF-3 dimerization.



Two-step model of IRF-3 activation.

Interferon Regulatory Factor 3 Is Regulated by a Dual Phosphorylation-dependent Switch

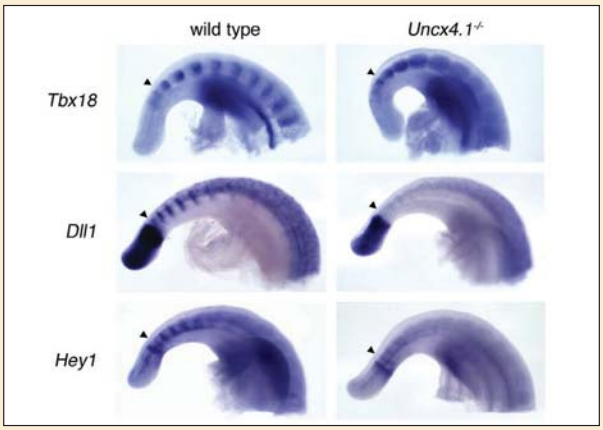
Daniel Panne, Sarah M. McWhirter, Tom Maniatis, and Stephen C. Harrison

J. Biol. Chem. 2007 **282,** 22816–22822

jbc

Looking Inside T-Box

T-box (*Tbx*) genes encode a family of transcription factors that regulate a variety of developmental processes. *Tbx18* and *Tbx15* encode a closely related pair of T-box proteins that, together with *Tbx22*, form a subgroup of the Tbx1 subfamily in vertebrates. Functional analyses in mice have shown that *Tbx15* is needed for skin and skeletal development, and *Tbx18* is required for the formation of the vertebral column, the ureter, and the posterior pole of the heart. In this *JBC* paper, the authors characterize the subcellular localization, DNA binding specificities, protein interactions and transcriptional properties, and the structural prerequisites of the two proteins. They show that both proteins homo- and heterodimerize, bind to various combinations of T half sites, and repress transcription by interacting with proteins in the Groucho family of corepressors. The authors also provide evidence that competition with activating T-box proteins constitutes a possible mode of regulation of the promoters for *Nppa* and *Dll1 in vitro* and *in vivo*.



Overexpression of Tbx18 coincides with downregulation of Dll1 and Hey1.

Transcriptional Repression by the T-box Proteins Tbx18 and Tbx15 Depends on Groucho Corepressors

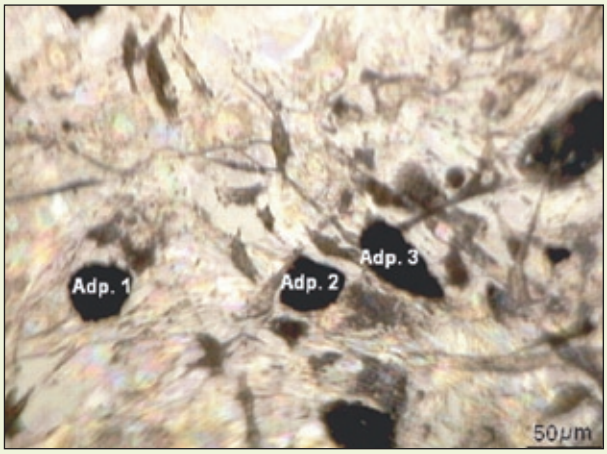
Henner F. Farin, Markus Bussen, Martina K. Schmidt, Manvendra K. Singh, Karin Schuster-Gossler, and Andreas Kispert

J. Biol. Chem. 2007 **282,** 25748–25759.

jbc

Lipid Transfer in Prostate Cancer

Several studies have shown that a high intake of dietary fatty acids can increase the risk of prostate cancer. Moreover, circulating prostate cancer cells metastasize in the bone marrow, which harbors a rich source of lipids stored inside adipocytes. Although prostate cancer cells exhibit higher levels of lipid in the presence of adipocytes, there has been no data that unequivocally establish that this increase is the result of adipocyte-to-tumor cell lipid transposition. In this *JLR* paper, the authors use Fourier transform infrared (FTIR) microspectroscopy to demonstrate that human prostate cancer cells do indeed uptake isotopically labeled fatty acids from an adipocyte. This study is significant not only because it demonstrates lipid-specific translocation between adipocytes and tumor cells but also because it uses FTIR microspectroscopy to characterize various biomolecular features of a single adipocyte without the need for cell isolation and lipid extraction.



Adipocytes transfer lipids to surrounding cancer cells.

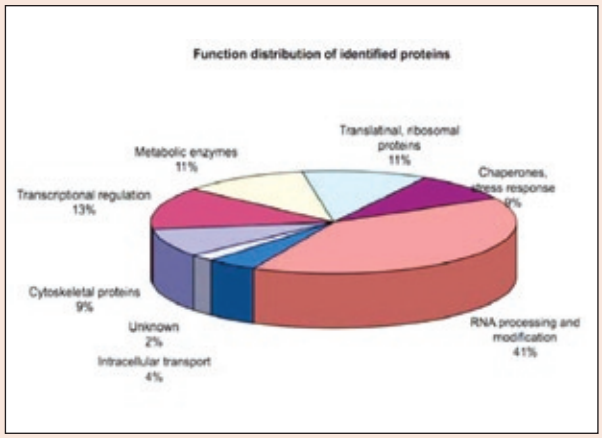
Direct Evidence of Lipid Translocation between Adipocytes and Prostate Cancer Cells with Imaging FTIR Microspectroscopy

Ehsan Gazi, Peter Gardner, Nicholas P. Lockyer, Claire A. Hart, Michael D. Brown, and Noel W. Clarke

J. Lipid Res. 2007 **48,** 1846–1856

Trading a Phosphate for a Sugar

Many cellular and nuclear proteins add *O*-GlcNAc to serine and threonine side chains in response to environmental and biological stimuli. Some of the known *O*-GlcNAc sites are the same as or adjacent to phosphorylation sites, and it is thought that the addition of the sugar might occur directly in competition with that of the phosphate. In this *MCP* paper, the authors examined O-GlcNAc perturbations in response to inhibition of glycogen synthase kinase-3 (GSK-3). Using stable isotope labeling with amino acids in cell culture (SILAC)-based quantitative mass spectrometry they identified 45 potentially *O*-GlcNAcylated proteins. Ten of these proteins showed increased *O*-GlcNAcylation, and 19 showed decreased *O*-GlcNAcylation upon GSK-3 inhibition. They also mapped the O-GlcNAc site of vimentin, which showed increased O-GlcNAcylation upon GSK-3 inhibition.



45 potentially *O*-GlcNAcylated proteins were identified

Dynamic Interplay between O-GlcNAcylation and GSK-3-dependent Phosphorylation

Zihao Wang, Akhilesh Pandey, and Gerald W. Hart

Mol. Cell. Proteomics 2007 **6,** 1365-1379

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Susan.Wallace@uvm.edu
or:
Dr. Sylvie Doublié, Associate Professor, Department of Microbiology and Molecular Genetics, University of Vermont
Sylvie.Doublié@uvm.edu

University of Wisconsin–Madison

TENURE-TRACK POSITION IN BIOCHEMISTRY

The Department of Biochemistry at the University of Wisconsin-Madison (www.biochem.wisc.edu) invites applications for a position in biochemistry at the Assistant Professor level. Applications in *all areas of biochemistry* will be considered. The Department is particularly interested in candidates working with cutting edge technologies (nanotechnology, cellular imaging, proteomics/metabolomics/lipidomics) in animal, plant or model organisms in research areas related to the chemistry of protein or nucleic acid function, regulation of metabolism, or neurobiology. The University and Department provide an excellent environment for the development of an outstanding research program. The successful candidate will be expected to develop a vigorous, extramurally-funded, independent research program, and to participate in the undergraduate and graduate teaching programs of the Department. PDF applications should include a curriculum vitae, a list of publications, and a brief summary of accomplishments and directions of future research and be sent to facultysearch@biochem.wisc.edu. Three letters of reference should be forwarded to the same address with applicant's name in header. Applications should be completed by *October 15, 2007*.

facultysearch@biochem.wisc.edu.

scientific meeting calendar

SEPTEMBER 2007

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

Disorders of Lipid Metabolism
SEPTEMBER 6–7, 2007
SAN DIEGO, CA
www.biosymposia.org/content23119.html

Second International Meeting on the Role of Nitrite in Physiology, Pathophysiology, and Therapeutics
SEPTEMBER 6–7, 2007
BETHESDA, MD
www.strategicresults.com/nitrite2/

British Mass Spectrometry Society Meeting
SEPTEMBER 9–12, 2007
EDINBURGH, SCOTLAND
www.bmss.org.uk/meetings.htm
E-mail: bmssadmin@btinternet.com
Tel.: 44-(0)-1480-880-669

Mass Spectrometry in Clinical Chemistry and Molecular Diagnostics
SEPTEMBER 14–18, 2007
PACIFIC GROVE, CA
www.asms.org
E-mail: office@asms.org
Tel.: 505-989-4517

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

ISICR Annual Meeting: 50th Anniversary of the Discovery of Interferons
SEPTEMBER 16-19, 2007
OXFORD, UK
www.isicr.org/2007meeting/

10th International Conference of the Eicosanoid Research Foundation: Bioactive Lipids in Cancer, Inflammation, and Related Diseases
SEPTEMBER 16–19, 2007
MONTREAL, CANADA
bioactivelipidsconf.wayne.edu/

The 7th Annual Meeting of the Safety Pharmacology Society
SEPTEMBER 19–21, 2007
EDINBURGH, SCOTLAND
209.183.221.48/am2007/index.asp

OCTOBER 2007

XVI International Symposium on Drugs Affecting Lipid Metabolism
OCTOBER 4–7, 2007
NEW YORK, NY
www.lorenzinifoundation.org/download/dalm2007.pdf

HUPO 6th Annual World Congress
OCTOBER 6–10, 2007
SEOUL, KOREA
www.hupo2007.com
E-mail: Wehbeh.Barghachie@mcgill.ca
Tel.: 514-398-5063

GERLI: 4th Lipidomics Meeting: Lipoproteins and Lipid Mediators
OCTOBER 9–11, 2007
TOULOUSE, FRANCE
www.gerli.com/toulouse2007ter.htm

5th Annual World Congress on the Insulin Resistance Syndrome
OCTOBER 11–13, 2007
NEWTON, MA
This scientific meeting will bring together national and international leaders as well as researchers in the clinical practice of the syndrome.
E-mail: insulinresistance@pacbell.net/metabolicinst@pacbell.net
Tel.: 818-342-1889
Fax: 818-342-1538

Society for Advancement of Chicanos and Native Americans in Science National Conference: *Stretching the Imagination to Support Leadership and Sustainability*
OCTOBER 11–14, 2007
KANSAS CITY, MO
www2.sacnas.org/confNew/confClient/

Second International Conference on Anchored cAMP Signaling Mechanisms
OCTOBER 12–14, 2007
PORTLAND, OR
www.akap2007.com

Protein Misfolding and Neurological Disorders Meeting
OCTOBER 17–19, 2007
DUNK ISLAND, NORTH QUEENSLAND, AUSTRALIA
www.proteinmisfolding.org

5th General Meeting of the International Proteolysis Society (IPS2007)
OCTOBER 20–24, 2007
PATRAS, GREECE
www.ips2007patras.gr/

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

Cytokines in Health and Disease: Fifteenth Annual Conference of The International Cytokine Society
OCTOBER 26–30, 2007
SAN FRANCISCO, CA
www.cytokines2007.org

NOVEMBER 2007

HIV/AIDS Research at the National Cancer Institute: A Record of Sustained Excellence Symposium
NOVEMBER 1–2, 2007
BETHESDA, MD
web.ncifcrf.gov/events/hivaidsresearch2007/

The Liver Meeting 2007 Annual Meeting of the American Association for the Study of Liver Diseases
NOVEMBER 2–6, 2007
BOSTON, MA
https://www.aasld.org/eweb/DynamicPage.aspx?webcode=07am

44th Japanese Peptide Symposium
NOVEMBER 7–9, 2007
TOYAMA, JAPAN
peptide-soc.jp/english/engindex.html
E-mail: jps@peptide.co.jp

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Sincerely,

Surendra Gupta

Surendra Gupta, Ph.D.
President

ARC

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