



## NSF Gets 8.4 Percent Increase This Year; NIH Bill Also Moving Ahead

By Peter Farnham  
Public Affairs Officer

**T**he conference committee on VA/HUD appropriations reported out a final FY 2002 appropriations bill on November 6, with an 8.4 percent increase for the National Science Foundation. NSF's budget went up to \$4.789 billion, a total of \$373

million over the FY 2001 level of \$4.416 billion. This increase, about what had been expected by the life sciences community for some months now, is only about half the amount needed to keep NSF on the 5-year doubling track, a policy position that ASBMB adopted last year.

The major line items under NSF received the following totals: Research and Related Activities, \$3.598 billion (with almost \$509 million going to the Biological Sciences Directorate); Major Research Equipment, \$138.8 million; Education and Human Resources, \$875 million; Salaries and Expenses, \$170 million; and the Office of the Inspector General, \$6.7 million.

In other good news, the L/HHS appropriations bill finally cleared the Senate on November 6, and includes an increase for the National Institutes of Health of \$3.4 billion, to a total of \$23.7 billion. This sets up an item of contention in conference as the House version of the bill provides about \$22.9 billion for NIH, some \$800 million less than the Senate.

In other appropriations news, the House adopted its fourth continuing resolution, this one to fund the government through November 16. The previous resolution expired at the end of October.

Senior House and Senate Democrats are also trying to increase the \$40 billion in supplemental defense/security funding agreed to by the Congress and the White House in the wake of the September 11 attacks. Budget hawks are dead set against this, claiming it goes against an agreement to limit to \$40 billion any extra spending to respond to the attacks.

However, the war in which we are engaged is going to get expensive. This was made clear in late October when

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**Comments**

Please direct any comments  
or questions concerning *ASBMB  
News* to:

**John D. Thompson**

*ASBMB News* Editor

9650 Rockville Pike

Bethesda, MD 20814-3996

Phone: 301-530-7145

Fax: 301-571-1824

E-mail: [jthompson@asbmb.faseb.org](mailto:jthompson@asbmb.faseb.org)

**NSF Expecting 8.4% Increase . . . from page 1**

the House Appropriations Committee approved a \$317.5 billion defense bill. During markup, Committee Chairman Bill Young (R-FL) said that this overall number was not big enough and would likely get bigger as the bill moved toward final passage. A figure at least \$20 billion higher is considered likely.

All this of course spells bad news for biomedical and other life sciences research funding next year, as increased efforts to fight terrorism both at home and abroad will make large increases for research even more difficult to attain than they have been up to now.

**ASBMB President Praises Action On NIH Budget**

The letter below was sent by ASBMB President Robert Wells to Senator Tom Harkin (D-IA), Chair of the Senate Appropriations Committee Subcommittee on Labor, Health and Human Services, and Education, to express ASBMB's appreciation of the panel's efforts on behalf of the NIH budget. Copies were also sent to Senators Arlen Specter (R-PA), ranking minority member of the subcommittee; Robert Byrd (D-WV), chair of the Senate Appropriations Committee; and Ted Stevens (R-AK), ranking minority member of the Appropriations Committee.



American Society for Biochemistry and Molecular Biology

ROBERT D. WELLS  
President

Institute of Biosciences and Technology  
Texas A&M University  
Texas Medical Center  
2121 West Holcombe Blvd.  
Houston, TX 77030-3303  
Tel: (713) 677-7651  
Fax: (713) 677-7689  
Email: [rwells@ibt.tamu.edu](mailto:rwells@ibt.tamu.edu)

October 22, 2001

The Honorable Tom Harkin  
United States Senate  
Washington, DC 20510

Dear Senator Harkin,

On behalf of the 10,000 members of the American Society for Biochemistry and Molecular Biology, please accept my heartfelt thanks for your tireless efforts to bring about an increase this year in the National Institutes of Health budget of \$3.4 billion. This increase will keep the NIH on-track to double in five years. The ASBMB members are very aware of the efforts and hard work that must have gone into the recent decision by the Appropriations Committee to approve this increase for FY 2002. I just wanted to drop you a note to let you know that all of us at ASBMB deeply appreciate your effective work.

More important, however, is the benefit that will be gained for many years in the future by those suffering from crippling or life-threatening diseases. It is actually for these people that we in biomedical research do our work, and your contributions to keeping this work moving forward are invaluable.

Again, thank you very much for your enormous contribution to the health of the citizens of our country.

Sincerely,

*Robert D. Wells*

Robert D. Wells

# Conflict of Interest Issues Aired at Institute of Medicine Meeting

*We are indebted to Debra Aronson, of FASEB's Office of Public Affairs, for the following report on conflict of interest issues that were discussed during the public session of the recent Institute of Medicine meeting here in Washington, DC. Ms. Aronson's report follows.*

**T**he program focused on managing the relationships between industry, academia and the investigator. David Blumenthal, MD, Professor of Medicine and Health Policy at Harvard, offered the following definition of a conflict of interest:

"A conflict of interest exists when two or more goals are opposed such that the pursuit of one impedes the other." For example, a conflict of interest might exist between the pursuit of knowledge and the interests of research subjects.

The program was limited to a discussion of the issues that arise from individual conflicts of interest of a financial nature. However, there was consensus that problems arising from institutional conflicts cannot be overlooked and need to be addressed separately. Currently there has been very little exploration of institutional conflicts of interest. There was also consensus that nonfinancial conflicts of interest, such as those that might arise from an investigator's interest in professional advancement or from conflicts in commitments, could also impair the integrity of biomedical research. There has been no ongoing discussion about taking these nonfinancial conflicts out of the hands of academic self-governance where they presently reside.

## Background

According to David Korn, Vice President for Research at the Association of American Medical Colleges, the conflict of interest issue arose in the early '80s as a result of several widely publicized episodes of scientific misconduct dealing with falsification of research data. This resulted in a congressional review of financial conflicts of interest. In 1995, the National Science Foundation and the Public Health Service required that federally supported investigators engaged in research funded by PHS or NSF disclose to their institutions significant financial interests that would reasonably appear to affect their research. If institutions then determined that a conflict of interest existed, the institutions were required to determine how the conflict of interest could be managed. In 1998, FDA also

established regulations dealing with financial conflicts of interest. These several federal requirements resulted in a variety of individualized practices at the same time that industry/academic relationships were growing. There has been an increasing concern that the requirements of 1995 and 1998 are not sufficient. Intense scrutiny of financial conflicts of interest is undoubtedly linked to increasing concern about protecting human participants in research, particularly after the death of Jesse Gelsinger. There was also discussion of the profound changes to academic medicine, prompted in large part by the success of recombinant DNA technology and the 1980 Bayh-Dole Act which allowed the biotechnology industry to flourish.

## How Prevalent are Financial Conflicts of Interest?

The amount and proportion of funding from private corporations has increased for clinical research, while the proportion of industry funding has remained stable for nonclinical research. According to Dr. Blumenthal, 43% of faculty received gifts from industry in the form of honoraria, consulting fees, equity interests and royalties. Conditions on those gifts included prepublication review by industry.

Joseph Martin, Dean of the Faculty of Medicine at Harvard Medical School, pointed out that in 2001, \$100 billion was spent on research and development. Following is a breakdown of the sources:

- \$26 billion came from federal funding (a decreasing percentage of total R&D),
- \$7.5 billion came from foundations and universities,
- \$12 billion came from biotech companies, and
- \$50 billion came from large pharmaceutical companies.

*The New England Journal of Medicine* reported that it hadn't found any authors who did not report financial conflicts of interest since 1999.

Dr. Martin noted that aside from the real concern that financial considerations negatively impact the integrity of the research, additional consequences of these industry/academic relationships include delays in publication in order to patent and changes in research direction that follow the dollar.

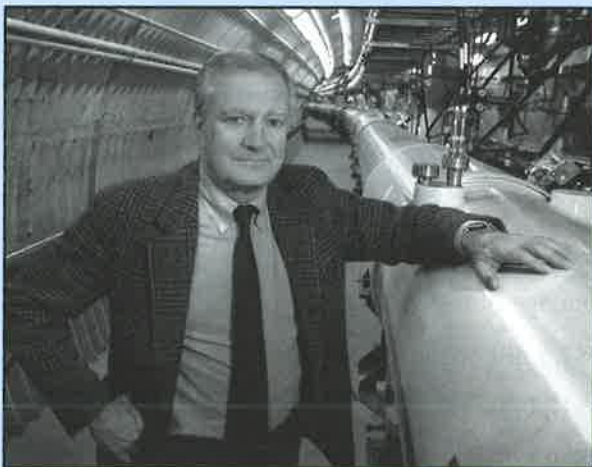
Thomas Bodenheimer, MD, Clinical Professor, Family and Community Medicine, University of California, San Francisco School of Medicine highlighted another concern. He pointed out that 21% of the results of a sample of 156 research investigations were never published because of pressure not to publish negative results. This failure to publish has a tremendous influence on clinicians because clinicians rely on what is published. Sometimes this pressure is in the form of a lawsuit.

## What Can Be done?

There has been a lot of activity within the research advocacy community to strengthen voluntary measures to address these conflicts, both to assure research integrity and also to preempt federal regulation in this arena.

Harvard Medical School convened leaders from 15 medical schools and academic hospitals and they proposed a set of principals and guidelines focusing only on individual conflicts.

### **John Marburger Confirmed as President's Science Adviser**



*Nominated by President Bush in June, Dr. John Marburger was finally confirmed by a voice vote by the Senate in October. Dr. Bob Park, Director of the American Physical Society's Washington office, noted that: "With a Ph.D. in Physics from Stanford (1962) and experience as a physics professor, university president, and Director of Brookhaven National Lab, there was never a question of whether Marburger is qualified to serve as the President's science adviser and head of OSTP."*

The Association of American Universities' Guidelines just came out, and the American Association of Medical Colleges also has a Task Force that is expected to issue a report on the subject. The International Committee of Medical Journal Editors adopted a policy that researchers submitting manuscripts for publications should disclose any financial interest they have which are related to the research.

The Office of Human Research Protection issued guidelines in January and there is a question as to whether these guidelines will become regulations or whether researchers will be allowed to continue to manage their own conflicts.

There was some discussion about forbidding conflicts of interest. Dr. Korn feels an absolute prohibition would be an overreaction and could be contrary to public interest. He noted that many communities have expectations that research institutions will lead to increases in economic development. While academic/industry partnerships might be the only way of accomplishing this, the public has a puritanical intolerance of any possible conflicts of interest. This intolerance might be minimized by enhancing the public's understanding of how research is funded. Also, Congress has been generous with the research community because it is anxious for cures which are dependent on these partnerships. There was also some concern that in the zeal to "retain an ideal state of virtue," by prohibiting conflicts we will drive the best researchers out of research universities. Dr. Bodenheimer suggested that we can reduce the risk that industry funded research will impair research integrity by having steering and publication committees with nonindustry members who design and report on trials.

## **NIAAA Director Gordis Announces Retirement**

At the end of August, the Director of the National Institute on Alcohol Abuse and Alcoholism, Enoch Gordis, M.D., informed NIH Acting Director Dr. Ruth Kirschstein of his intention to retire at the end of this year.

Dr. Gordis, who will turn 71 in February, has been with the Institute for 15 years. In announcing his retirement, he stated, "This decision did not come easily or quickly. These years have been the most rewarding of my career, and I have been fortunate to have worked with so many of you across the various disciplines that make up our field. Your support, advice and friendship have been invaluable as we have worked to foster progress in alcohol research."

# A Is for Anthrax and Asymmetrical

By John D. Thompson  
Editor, ASBMB News

**A** isn't for apple anymore, it's for anthrax and asymmetrical; anthrax to assassinate and asymmetrical for attacking the underpinnings of this nation in new and unforeseen ways.

In the weeks since September 11, we have come to know a new horror. Having just witnessed the potential of an airliner as a weapon of mass murder, we are now seeing the Postal Service used to deliver death by disease.

Much has, and will continue to be, written about these new additions to twenty-first century warfare, but two publications are of particular interest. At the heart of *Nature* magazine's November 8 issue and released in advance on *Nature's* website is a report on the threat of biological warfare and what is being done to counter it, and scientific papers about the bacterial toxin that causes anthrax, its structure, and the human receptor for anthrax. In October, an article in *The Economist* raised the question of whether the real goal of the bioterrorists is mass murder or mass panic.

Writing for *Nature*, Claire Fraser, of the Institute for Economic Research in Rockville, Maryland, and Malcolm Dando, of the University of Bradford in the UK, noted, "There is an increasing concern in both the scientific and security communities that the ongoing revolution in

biology has great potential to be misused in offensive biological weapons programs."

Those possibilities for misuse were highlighted in another article, which told how two Australian scientists seeking to make a contraceptive vaccine by altering the genes of the mousepox virus inadvertently created an unusually virulent strain of mousepox. If a similar genetic manipulation were applied to smallpox, they realized, this feared killer could be made even more dangerous.

*Nature* reported that advances in genomics have greatly increased the possibilities of mixing and matching traits from different microorganisms. Some researchers, it said, are concerned about potential abuses of DNA sequence data.

The information being generated by genome projects is not the only concern. According to *Nature*, several companies are developing techniques of "directed" molecular evolution that can be used to accelerate the evolution of desired traits by introducing genetic variation and then applying artificial selection.

Other approaches that might be used to develop bioweapons include the deliberate hybridization of

## IOM Outlines Plans to Counter Bioterrorism

Speaking at the Institute of Medicine's Annual Meeting in mid-October, IOM President Kenneth Shine outlined plans of the IOM and National Academies of Science regarding bioterrorism.

Initiatives planned or in progress at the NAS/IOM are:

- **Peer Review of Enabling Technologies:** Questions have been raised as to where the appropriate place is to conduct research on bioterrorism. Are national labs or universities the proper place? The NAS/IOM will evaluate this issue. In addition, if the government identifies technologies that need to be pursued, the NAS/IOM will identify experts in these or related technologies who could peer review the proposed research.
- **National Security Science and Technology Initiative:** An IOM committee co-chaired by Richard Klausner (formerly NCI) and Lewis Branscomb (Harvard/MIT) will be responsible for information gathering on issues related to bioterrorism and terrorism security issues and sending a report to President Bush, Tom Ridge, and John Marburger.

• **International Cooperation:** especially with Russia and Saudi Arabia

Longer term projects include:

- IOM committee on Information, Technology, and Civil Liberties to evaluate ideas such as a national identity card, data analysis, and information management of suspected terrorists and terrorism activities.
- Outreach activities to industry, universities, and the public.

related viral strains. Although most crosses of viruses are less potent than the parent strains, sometimes virulence increases — some virulent strains of flu, for instance, arise as naturally occurring recombinants between different influenza viruses.

Potential bioweapons designers might also be watching developments in gene therapy. Attempts to introduce therapeutic genes into patients' tissues rely mostly on weakened forms of various viruses. These vectors have yet to introduce genes efficiently and reliably. But if researchers can make them do so, similar vectors might also be used to ferry harmful genes into unsuspecting victims.

## Building Defenses

Increased security at airports, mailing centers, and other government facilities is underway, and conceivably might be expanded to places where research is being conducted on projects that might inadvertently have implications for biological warfare.

Also working to develop defenses against bioterrorism are institutions such as Sandia's Center for National Security and Arms Control in California, which is developing an Internet-based system to detect early signs of bioweapon exposure, irrespective of the agent responsible. At the same time, the U.S. Defense Advanced Research Projects Agency (DARPA) is developing biosensors based on living tissues that should provide physiological responses to a wide spectrum of both known and unknown pathogens.

DARPA is also investing in the development of new antibiotics and vaccines that could target a broad range of pathogens. Some of DARPA's strategies target common mechanisms of bacterial growth, such as genes essential to cell division and those encoding enzymes central to evolutionarily conserved metabolic pathways. One company with funding from DARPA, Maxygen, in Redwood City, California, is applying DNA shuffling technology to combine proteins from related pathogens in the hope of developing vaccines that could provide broad protection.

Fraser and Dando report that in addition to these activities, companies such as Maxygen, are developing technologies to carry out directed molecular evolution, in which genes are broken down into smaller pieces and then shuffled during reassembly to create "daughter genes" with new properties. This has serious implications for biowarfare, but at the same time it must be recognized that advances that could be used to produce biological weapons can also be used to set up countermeasures for defense.

In their conclusion, the authors wrote:

"The genomics revolution holds great promise for the advancement of basic biology, medicine, and agriculture. Unfortunately, the threat of biological warfare and terrorism, though limited today, is real, and the genomics revolution has the potential to have major impacts on this most chilling threat during the twenty-first century. To ensure that the benign potential of genomics is realized, biologists will have to overcome their reluctance to discuss the implications of their work in the context of biowarfare and terrorist activities."

## The Terror Factor

Panic, not death, surmised *The Economist*, may be the primary goal of the bioterrorists.

It noted that using biological or chemical materials as weapons of mass destruction is difficult, and recalled a 1995 incident when an apocalyptic Japanese cult, Aum Shinrikyo, released a nerve agent called sarin on the Tokyo subway. The intention was to kill thousands, but in spite of spending more than \$30 million on research, the cult attack only killed 12 people.

That attack was not a great success, but now we appear to be dealing with more sophisticated terrorists. Where Aum Shinrikyo attempted, but failed, to develop anthrax spores as a weapon, we are now confronted with enemies who have succeeded. And, as we have seen, the resulting deaths have been accompanied by disruption in the mails and in the working of government and private sector offices.

Since the September 11 attacks, American officials have stressed that not only the terrorists involved in any future assaults—biological, chemical, or otherwise—but also any states that shelter them, will be targeted. Such threats, however, may not be so effective against shadowy terrorist networks. Where do you aim the retaliatory missiles? And it is not clear whether terrorist states, which show little regard for international law, can be deterred from lending a secret helping hand to a group such as Osama bin Laden's. Whatever the source, the anxious reaction across America in the wake of the anthrax incidents has shown that the difficulty of delivery on a large scale is not a barrier to biological terrorism's effectiveness if the aim is not mass murder, but to create panic and disrupt business and government services.

While government agencies and the military work to strengthen our security and the scientific community seeks antidotes for biological warfare, for those on what in simpler times was called "the home front" the need is to cultivate the spirit that kept London going about its business during the Blitz of World War II. ☸

# Satellite Meetings Offer Special Opportunities for Younger Scientists

**T**he ASBMB Satellite Meetings on the Friday and Saturday, April 19 and 20, preceding EB2002 offer special educational opportunities in three separate sessions that will more than justify an early arrival in New Orleans.

As Drs. Joan and Ronald Conaway of the Stowers Institute for Medical Research, and Ali Shilatifard, Ph.D., St. Louis University, the organizers of Satellite I, said:

“The 2002 ASBMB Satellite Meeting on Transcriptional Regulatory Mechanisms will cover a broad area of transcriptional regulatory mechanisms in both eukaryotic and prokaryotic organisms. We believe that a cross pollination of ideas from eukaryotic and the prokaryotic model systems would be very beneficial to both the lecturers and the attendees at this meeting. In so doing, we have invited two keynote lecturers, Drs. Robert Roeder and Richard Losick, who will present their studies on mechanisms of transcriptional regulation in eukaryotic and prokaryotic organisms, respectively.

“In addition to the keynote lectures, the Satellite I meeting will include sessions on Basic Transcription Mechanisms, chaired by Dr. Shilatifard; Activation Mechanism, chaired by Dr. Barbara Graves, Huntsman Cancer Institute; Repression Mechanisms, chaired by Dr. Ron Conaway; and Chromatin and Transcriptional

Regulation, chaired by Dr. Sharon Y. R. Dent, Anderson Cancer Center. Each session will include two or three invited speakers, with the remainder to be chosen from submitted abstracts. This meeting should provide an excellent opportunity for younger scientists, including post-doctoral fellows and graduate students, to showcase their work through platform lectures and posters and to interact with more senior colleagues.”

The title of the lecture by Professor Jean-Marc Egly of the University of Strasbourg will be “Transcription Coupled to DNA Repair. Where We Are.”

“In the course of our investigations to understand mechanisms of gene expression,” explained Professor Egly, “our lab has focused on the role of the various enzymatic activities of TFIID, a key factor involved in both transcription and DNA repair. Distortion in the current activity of TFIID such as mutations in the XPB and XPD helicases, two of its subunits originate the rare genetic disorder Xeroderma pigmentosum (XP). Establishing a genotype/phenotype relationship allow us to explain the various roles of TFIID in both transcription and DNA repair.

“UV-sensitivity and high skin cancer susceptibility can easily find explanations in a faulty DNA repair due to a defect of the XPB and XPD helicases to open DNA

## **ADVICE FOR FEDERAL EMPLOYEES:**

### ***Don't Wait; Get Your Travel Plans OK'd Now***

If you are a scientist employed by the federal government and you want to attend EB 2002 and the ASBMB Satellite Meetings, the time to get your travel plans approved is now.

New rules issued by Department of Health and Human Services (HHS) Secretary Tommy Thompson stipulate that advance approval is required before any HHS employee can attend a meeting, if five or more of that agency's employees will be attending.

The rule requires that federal scientists apply for approval to attend such a meeting at least 45 days—and for some agencies 8 full weeks—in advance of the meeting.

A report on the BioMedNet website said that the rule might dramatically reduce the number of government scientists who can travel to any one meeting, and stated, “If the restrictions are not reversed, scientists complain, they will adversely affect the quality of conferences and, in the long term, of government science.”

Scientists from the National Human Genome Research Institute at NIH are normally a large presence at the American Society of Human Genetics' Annual Meeting. This year, however, BioMedNet reported that while nearly 200 NIH scientists requested permission to attend, HHS approved only two-thirds of the requests and did not release details until just 10 days before the meeting.

around a lesion. The severity of the phenotypes, as well as the restricted number of XP-B patients, identified, could be explained by the crucial role of XPB in gene expression; we demonstrated that the XPB patients' mutations, as well as mutation in its ATP-binding site, abolish DNA opening that normally allows reading of the coding strand by RNA pol II.

"The role of the XPD helicase in transcription is still unclear. On the one hand, preventing the XPD helicase activity does not abolish transcription and is not lethal as deduced from yeast or human studies. On the other hand, analysis of the phenotypes of XP-D patients, varying from neurological abnormalities to growth retardation, plead for a defect in gene expression. We demonstrated the indirect role of XPD in allowing the function of the cdk7 kinase another subunit of TFIIH towards the nuclear receptors, the phosphorylation of them being a prerequisite in any transactivation process. Whether or not such phosphorylation is required to allow activators to regulate DNA repair is an interesting question?"

## Satellite II

Scientific and Technical Challenges in the Human Proteome will be the theme of this satellite, organized by Al Burlingame, Ph.D., University of California, San Francisco, and John Stults, Ph.D., Genentech, Inc.

"This satellite meeting," said Dr. Stults, "will examine state-of-the-art technologies that are currently in use in key areas of proteomics: sample preparation, particularly subcellular fractionation; protein separation, identification, and quantitation, with and without gels; determination of post-translational modifications; and automation and informatics.

"Leaders in the field will present the important techniques in these areas, and describe their utility for the study of protein interactions, signaling pathways, and the molecular basis of disease. Significant time will be given to discussions of how well these technologies meet the needs of the biological community, what challenges remain, and how these additional needs might be addressed."

One of the keynote lecturers in Satellite II will be Professor Ruedi Aebersold, of the Institute for Systems Biology in Seattle. His topic will be Quantitative Proteome Analysis: New Technology and Applications.

"A number of powerful technologies now permit the determination of complete genome sequences as well as the systematic and quantitative measurement of gene expression," says Dr. Aebersold. "The systematic measurement of gene expression at the protein level is commonly referred to as proteomics. It is the premise of proteomics, particularly if applied for quantitative measurements, that new protein markers diagnostic for

specific disease and new therapeutic targets will be discovered. It is furthermore expected that proteomics will significantly contribute to the mechanistic understanding of biological processes if the technology is either applied by itself in a discovery mode, or in combination with traditional hypothesis-driven research approaches.

Dr. Aebersold's presentation, he explained, "will discuss standard proteomics technologies and recent technical advances. The applicability of proteomics and its impact on basic biological sciences and biomedical research will also be discussed."

"Analytical Proteomics for Clinical and Research Use: Combining Mass Spectrometry, 2D Gels, and Antibody Arrays" will be the topic for the keynote lecture by Leigh Anderson, Ph.D., Chief Scientific Officer at Large Scale Biology Corporation.

"Three streams of technology will play major roles in quantitative (expression) proteomics over the coming decade," said Dr. Anderson in discussing his lecture topic.

"Two-dimensional electrophoresis and mass spectrometry represent well-established methods for, respectively, resolving and characterizing proteins, and both have now been automated to enable the high-throughput generation of data from large numbers of samples. These methods can be powerfully applied to discover proteins of interest as diagnostics, small molecule therapeutic targets, and protein therapeutics.

"However, neither offers a simple, rapid, routine way to measure many proteins in common samples like blood or tissue homogenates. Antibody arrays do offer this possibility, and thus complete the triumvirate of technologies that will deliver the benefits of proteomics to both research and clinical users.

"Integration of efforts in all three approaches will be discussed, highlighting the application of the Human Protein Index database as a source of protein leads for pharmaceutical and diagnostics development."

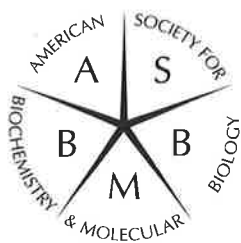
## Satellite III

Combinatorial Signaling will be the focus of Satellite III, organized by Doctors Ralph Bradshaw, University of California, Irvine, and Sarah Parsons, University of Virginia Health Sciences Center.

"The past 20 years have witnessed an explosion of information regarding intracellular signaling pathways that cells use to respond to environmental cues or factors," noted Dr. Parsons. "Sometimes these factors

*Continued on page 20.*





## ASBMB Satellite Meetings April 19-20, 2002 Sheraton New Orleans, Louisiana

### Satellite I - Transcriptional Regulatory Mechanisms

Organized by Ronald C. Conaway, *Stowers Inst. for Med. Res., Kansas City, MO*, Joan W. Conaway, *Stowers Inst. for Med. Res., Kansas City, MO*, and Ali Shilatifard, *Saint Louis University*

#### Keynote Lecturers

Robert G. Roeder      Richard Losick

#### Symposia

##### Activation

\*Barbara J. Graves, Peggy Farnham, Robert Schleif,  
Dale Dorsett

##### Chromatin

\*Sharon Y.R. Dent, Karolin Luger, Ed Seto

##### Repression Mechanisms

\*Ronald C. Conaway, Elke Krueger, Don Ayer

##### Fundamental Mechanisms

\*Ali Shilatifard, Jean-Marc Egly, Robert Landick

### Satellite II - Scientific and Technical Challenges in the Human Proteome

Organized by Al Burlingame, *UCSF* and John T. Stults, *Genentech, Inc.*

#### Keynote Lecturers

Ruedi Aebersold      Leigh Anderson

#### Symposia

##### Cellular and Subcellular Fractionation in Scientific and Technical Challenges of the Human Proteome

\*John J. M. Bergeron, Michel Desjardins,  
Peter McPherson

##### Proteomic Approaches to Protein Modifications

\*Al Burlingame

##### Protein Separation and Quantitation in Proteomics

\*John T. Stults, Ruth A. VanBogelen, John R. Yates, III

##### Proteomics on Scale: Translating Capacity into Knowledge

\*Steven A. Carr, Marc Vidal, Scott Patterson

### Satellite III - Combinatorial Signaling

Organized by Ralph A. Bradshaw, *UC, Irvine* and Sarah J. Parsons, *Univ. of Virginia Hlth. Sci. Ctr.*

#### Keynote Lecturers

Ralph A. Bradshaw      Natalie G. Ahn

#### Symposia

##### Receptor Crosstalk

\*Sarah J. Parsons, Corinne M. Silva,  
Louis Lattrell

##### Receptor Oligomerization

\*Steve Hubbard, Melissa Starovasnik,  
Moosa Mohammadi

##### Growth Factor/Integrin Signaling

\*John T. Parsons, Alan Wells, Michael Schaller

##### Non-Genomic Steroid Signaling

\*Margaret A. Shupnik, Kathryn Horwitz,  
Stavros Manolaga

#### Abstract Deadline—November 7, 2001

Abstracts submitted to ASBMB Satellite Meeting topic categories will be displayed Friday and Saturday, the 19th and 20th in the Sheraton New Orleans from 8:00 AM - 5:00 PM. Posters presented in the Satellite Meetings will not be presented within the Experimental Biology 2002 Meeting, April 20 - 24, 2002.

For information contact: ASBMB Meeting Office, 9650 Rockville Pike, Bethesda, MD 20814  
Tel: 301-530-7145; Fax: 301-571-1824; www.asbmb.org

(\*denotes Chairperson)

# Mass Spectrometry Symposium Provides Broad Overview of Field

By Michael A. Baldwin, Ph.D.

**T**he Fifth Annual Symposium on Mass Spectrometry in the Health and Life Sciences was the first to concentrate on a specific theme, in this case molecular and cellular proteomics.

Although proteomics has become a fashionable buzz-word, there is considerable uncertainty as to what it actually means. One outcome of this symposium was a concerted effort to actually define the field of proteomics.

There is an emerging consensus that proteomics deals with the identification of multiple proteins that are linked through their cellular actions. It is not necessarily the study of an entire proteome but it must involve more than a single protein.

In addition to identifying proteins, it involves defining their levels of expression in different tissues in normal and abnormal states, e.g. during disease. It is also necessary to characterize their posttranslational modifications and their binding partners. Because the organizers selected many presenters, as much for their ability to speak on diverse aspects of protein structure and function as for any expertise in mass spectrometry, the meeting gave a broad overview of this field.

The first plenary lecture by David Eisenberg set the tone, as he was quick to deny any specialist knowledge of mass spectrometry. Nevertheless he gave a fascinating analysis of the factors that determine aspects of protein

behavior, with the example of domain swapping, and how proteins could be classified on the basis of their propensities for such behavior. He made the point that the whole of life depends on the interaction of proteins, and that much of the information concerning these interactions was already in databases. Thus, developing tools to mine protein databases would identify many interacting proteins and the cellular functions of the interactions.

Other plenary lecturers continuing the theme of protein interactions were Ray Deshaies and Tony Pawson.

Pawson's lecture, which concluded the symposium, was a tour de force that described the complex mechanisms by which cells convert external signals into intracellular responses through the signaling properties of protein-tyrosine kinases.

Deshaies talked about charting the "protein complexome" by mass spectrometry. This presentation was essentially that of a cell biologist, but the proteins interacting with various components of the cell-cycle machinery were identified through a collaboration with John Yates at the Scripps Institute, using multi-dimensional chromatography interfaced to ion trap mass spectrometry through electrospray ionization (ESI).

This technique described as multi-dimensional protein identification technology (MudPIT) has produced impressive results on the MS and MS/MS analysis of yeast proteins with minimal prior separation, identifying more than 1400 proteins in a single run.

Julio Celis of the Danish Cancer Society described very demanding, longterm studies on the proteins involved in bladder cancer and reviewed proteomic strategies to identify pre-invasive and invasive carcinomas from biomarkers in urine and biopsy samples.

Martin Rosenfeld combined humor and scientific prediction in a unique presentation that described the life of a young man, Gene, born in 2010, who throughout his life would be the beneficiary of knowledge derived from genomics. On a more serious note he described how the combination of microbial genetic analysis and combinatorial chemistry was leading to novel classes of antibiotics that would resolve the current concerns over drug-resistance towards existing antibiotics.

## ABOUT THE AUTHOR

Michael Baldwin is Adjunct Professor in the Department of Pharmaceutical Chemistry and Deputy Director of the NIH/NCRR Mass Spectrometry Research Resource at the University of California, San Francisco. The Fifth International Symposium on Mass Spectrometry in the Health and Life Sciences: Molecular and Cellular Proteomics, was held in San Francisco, August 26-30. ASBMB co-sponsored the symposium which served as a launch for the Society's new journal, *Molecular and Cellular Proteomics*.



*In photo above, from left to right, Michael Waterfield, Ph.D., Ludwig Institute of Cancer Research, London; Ralph Bradshaw, Ph.D., University of California, Irvine, who is Editor of MCP; and David Eisenberg, Ph.D., University of California, Los Angeles, are seen enjoying a break during last summer's Mass Spectrometry Symposium. Also enjoying a time out from a busy meeting are Steven Martin, Ph.D., Amgen, Inc.; Jay Smith, and Al Burlingame, Ph.D., University of California, San Francisco, the Deputy Editor of MCP.*



In addition to the 5 plenary lectures, there were 26 other oral presentations and more than 100 posters, covering a wide range of topics. Many continued the themes of general or specific cellular protein interactions, while others were more oriented to technical developments in mass spectrometry. It is impossible to refer to all these here, so only a few will be highlighted.

Sensitivity is clearly of major importance for the analysis of cellular proteins, and Norman Dovichi described his attempts to automate the analysis of proteins separated from a single cell by free solution electrophoresis, with detection by fluorescence and mass spectrometry, as a key component in the "single

cell proteome project". He showed that at this stage mass spectrometry requires further optimization to be competitive with fluorescence, although the information potentially available from mass spectrometry is much greater.

Sensitivity and high throughput for protein identification were themes echoed by many authors, particularly combined with the peptide sequencing capabilities of tandem mass spectrometry. Until recently electrospray ionization was virtually the only method compatible with high sensitivity tandem mass spectrometry, but data from new alternative methods for MS/MS analysis of peptides ionized by MALDI were presented by several authors, using ion traps (Brian Chait), quadrupole- $\alpha$ TOF's (Ruedi Aebersold, Ole Jensen) and the new TOF/TOF technology (Marvin Vestal, Lan Huang).

Jensen also described new developments aimed at increasing the sensitivity for electron capture dissociation of large ions, including small proteins. High sensitivity is dependent upon efficient sample introduction, and microfluidic developments based on chip technology were described by Jianjun Li from the laboratory of Pierre Thibault.

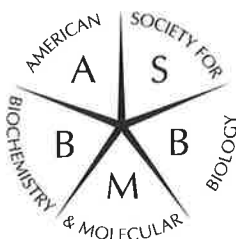
Protein quantization continues to be a major challenge for mass spectrometry and Ruedi Aebersold described enhancements to his ICAT methodology. Approaches to monitoring the folding of proteins were reviewed by David Smith using H/D exchange, and Alain van Dorsselaer described the role of mass spectrometry to monitor non-covalent interactions of proteins.

Although certain classes of proteins continue to be very challenging for mass spectrometry, Julian Whitelegge demonstrated that by using non-polar solvents in ESI-MS, proteomic studies on membrane proteins could be highly successful.

Phosphoproteins are also well known to be problematical for mass spectrometry, but as phosphorylation is probably the most important modification for protein regulation, not surprisingly several authors described strategies for analyzing phosphoproteins and phosphopeptides. Susan Chen highlighted the scale of this challenge, describing the use of multiple techniques for the analysis of just a single protein having a large number of potential phosphorylation sites.

In summary, this symposium combined a broad overview of current proteomic research with many detailed insights into specific aspects of the field.

*Continued on page 20.*



## ASBMB Annual Meeting

In Conjunction with Experimental Biology 2002  
April 20-24, 2002 • New Orleans, Louisiana

Organized by the ASBMB Program Committee  
Chairs: Ralph A. Bradshaw, UC, Irvine and  
Joan W. Conaway, Stowers Inst. for Med. Res., Kansas City, MO

### ASBMB OPENING LECTURE

The Eukaryotic Gene Transcription Machinery  
Roger Kornberg, *Stanford Univ.*

### AWARD LECTURES

ASBMB-Merck Award: Roger Kornberg and Robert Roeder  
ASBMB-Amgen Award: Joseph Heitman,  
ASBMB-Avanti Award in Lipids: Christian R.H. Raetz

ASBMB-Schering-Plough Research Institute Award:  
John D. York  
Herbert A. Sober Lectureship: Jack D. Griffith  
William C. Rose Award: Gordon Hammes.

### THEME I: Cellular Control

#### Plenary Lecturers

Lipid Rafts in Membrane Trafficking  
Kai Simons, *Max Planck Inst., Dresden*

Apoptosis Mechanisms: A Genomics Perspective  
John Reed, *Burnham Inst.*

Title TBD  
Brian U. Druker, *Oregon Hlth. Sci. Univ.*

#### Symposia

##### **Role of Mitochondria in Apoptosis**

\*Douglas Green, Craig B. Thompson, Richard J. Youle

##### **Cell Cycle M-phase Control**

\*J. Wade Harper, Don W. Cleveland, Orna Cohen-Fix,  
Steve Elledge

##### **Control of Cholesterol Homeostasis (In memory of Konrad Bloch)**

\*Dennis Vance, Michael Brown, Howard Goldfine,  
Joseph Goldstein

##### **Combinatorial Signaling Satellite Highlight Symposium**

\*Sarah J. Parsons, John T. Parsons, Stevan Hubbard,  
Margaret A. Shupnik

##### **Endoplasmic Reticulum Stress Response**

\*Randal J. Kaufman, Kazutoshi Mori, Dave Ron

### THEME II: Gene Regulation

#### Plenary Lectures

Multiprotein Complexes that Regulate Transcription by  
Modifying Chromatin  
Jerry L. Workman, *HHMI, Penn State Univ.*

Protein Sorting at the ER Membrane  
Arthur E. Johnson, *Texas A&M University Health Sci.  
Ctr.*

#### Symposia

##### **Signaling to the Nucleus and Beyond**

\*Barbara J. Graves, Eric Olson, Carol Privés

##### **Shuttling To and From the Nucleus**

\*Douglass J. Forbes, Michael F. Rexach, Mary S. Moore

##### **Chromatin Remodeling Machines**

\*Sharon Y.R. Dent, Brad Cairns, Craig L. Peterson

##### **Protein Trafficking at Membranes**

\*Robert E. Jensen, Rosemary Stuart, Colin Robinson,  
Steven M. Theg

### THEME III: Proteomics

#### Plenary Lectures

Issues in the Inference of Protein Function Using  
Bioinformatics Approaches  
Patricia C. Babbitt, *UCSF*

#### Symposia

##### **Protein Machines**

\*Jyoti Choudhary

##### **Protein Dynamics & Function**

\*Arthur G. Palmer, III, A. Joshua Wand,  
Ann E. McDermott

##### **Chemically Reactive Probes for Proteomics and Drug Discovery**

\*James A. Wells, Matt Bogyo, Ruedi Aebersold

##### **Evolution of Function in $(\beta/\alpha)_8$ -Barrels**

\*John A. Gerlt, Frank Raushel, Reinhard Sterner

## FOCUS GROUP SESSIONS

### Regulation of Development and Immunity by

#### Glycoconjugates

Organized by the ASBMB Glycobiology Focus Group

\*John Lowe, Carlos B. Hirschberg

### Lipid Traffic and Enzymology in Membrane

#### Assembly

Organized by the ASBMB Lipids and Membranes Focus Group

\*Dennis R. Voelker, Masahiro Nishijima

### Animal Models for the Study of Metabolic Processes

Organized by the ASBMB Metabolic Regulation Focus Group

\*Richard W. Hanson, Domenico Accili,  
Mulchand S. Patel

### Enzyme Structure, Function and Mechanism

Organized by the ASBMB Enzyme Structure, Function and Mechanism Focus Group

\*Vern Schramm, JoAnne Stubbe, Daniel Herschlag

## EDUCATION AND PROFESSIONAL DEVELOPMENT SYMPOSIA AND ACTIVITIES

### Teaching Biochemistry I — New Methods

\*J. Ellis Bell, \*Christopher E. Rohlman, Jan Serie,  
Fred Rudolph

### Teaching Biochemistry II — New Content

\*J. Ellis Bell, \*Christopher E. Rohlman, Suzanne  
O'Handley, Jonathan Smith, John Boyle

### Careers in the Biotechnology and Pharmaceutical Industries

\*A. Stephen Dahms, David Jensen

### Digital Libraries and Publishing in the Electronic Age

\*Marion O'Leary, Yolanda George, Robert D. Simoni,  
Scott Cooper, Paul A. Craig

### Workshop: How to get students actively involved in learning, even if you have 150 of them in the class.

\*Harold B. White, III, Richard Felder, Rebecca Brent

### Women in Science

\*Esther Sabban, \*Judith G. Voet, Donna J. Nelson  
Mildred Cohn, Virginia A. Zakian, J. Scott Long

### Women Scientists' Mentoring Session/Reception

\*Adele J. Wolfson, Diane Jones, Marilee Benore Parsons

### Sixth Annual Undergraduate Research Achievement Award Poster Competition (Sponsored by the *Biochemical Journal*)

\*Phillip A. Ortiz, Christopher Rohlman

### ASBMB Graduate/Postdoctoral Travel Award Symposium - April 20, 2002

### EB Teaching Poster Sessions

### Travel Awards Available for Undergraduates, Graduates, Post-doctoral fellows, Undergraduate Faculty

## MINORITY AFFAIRS SYMPOSIUM

### Under Representation of Minorities in Science: Can the Leaks in the Pipeline be Fixed?

\*Philip A. Ortiz. Empire State Col., and Thomas D. Landefeld, California State Univ. - Dominguez Hills

### EB Minority Symposium, Poster Session and Reception

## SPECIAL SESSIONS

### ASBMB/ABRF Symposium: What's Real In All These Microarray Data: Learning To Trust Your Intuition While Using Sound Statistical Methods

\*Ronald L. Niece, Brian Yandell, Stephen M. Schwartz, Alan Attie

### ASBMB Public Affairs Session: Presentation of the Schachman Public Service Award to Hon. John Porter, former Member of Congress (1980-2000) and Chairman (1995-2000) of the House Appropriations Subcommittee on Labor, HHS, Education, and Related Agencies. Mr. Porter will also deliver a lecture.

### New Directions and Funding Opportunities at NSF

\*Terry S. Woodin, Maryanna P. Henkart, Jean Chin

## CLOSING SYMPOSIUM - Wednesday, April 24 - 2:00 - 4:15 PM

### Proteomics and Drug Discovery - Sponsored by the NIGMS, NIH in Celebration of its 40th Anniversary

\*Richard A. Ikeda, Marvin Cassman, Marc C. Mumby, Wayne A. Hendrickson, Edward Maggio

### Abstract Deadline - November 7, 2001

For information contact: ASBMB Meeting Office, 9650 Rockville Pike, Bethesda, MD 20814

Tel: 301-530-7145; Fax: 301-571-1824; [www.asbmb.org](http://www.asbmb.org)

(\*denotes Chairperson)

# Congressional Caucus Hears Case for Tissue Engineering

**W**e're in the midst of a biological renaissance," said Allen Russell, Ph.D., in opening his address at the October meeting of the Congressional Biomedical Research Caucus.

Dr. Russell, the Director of the Pittsburgh Tissue Engineering Initiative of the University of Pittsburgh, in opening a briefing for members of Congress and their staffs on "Separating the Hype and Hope of Cellular Therapy and Tissue Engineering." Joining him in the briefing was Peter Johnson, M.D., CEO of Tissue Informatics, Inc., and President of the Tissue Engineering Society, International. The focus of their presentation was tissue engineering using adult stem cells as a supplement, or alternative, to the use of embryonic stem cells.

The U.S., they said, possesses all the necessary resources to become the world leader in tissue engineering research and technology development, an emerging field of biomedicine that has the potential to grow into an industry with a projected income in excess of \$80 billion, and revolutionize healthcare treatment.

Jointly, Drs. Johnson and Russell argued the case for developing a coordinated federal strategy, beginning with a comprehensive review of tissue engineering and the broader field of regenerative medicine, and increased funding for fundamental research.

That biological renaissance to which Dr. Russell referred is epitomized by the effective collaboration of several distinct disciplines—bioengineering, cell biology, chemical engineering, genomics, mathematical science, mechanical engineering, and molecular biology—in the development of regenerative medicine techniques for the development of new tissues. Among these techniques are:

- Artificial organs for the replacement of tissue function.
- Biohybrid organs, functional restoration with synthetic and cellular components.
- Cellular therapies for the repair of tissue and muscle.
- Chemical therapies—gene therapy, growth factor delivery, insertion of scaffolds—that induce a specific tissue response.
- Tissue engineering, the combination of temporary scaffolds with cellular components.

The promise of tissue engineering, said Dr. Russell, is that researchers will no longer be dependent on any one source of cells. Referring to the concerns of some about the ethics of using embryonic stem cells, he emphasized, "Tissue engineering, does not depend on embryonic stem cell research."

"Religious leaders," added Dr. Johnson, "need to understand that tissue engineering doesn't depend on stem cell development."

Tissue engineering research, he said, has the potential to improve the health and quality of life for the millions who suffer from diabetes, heart disease, and injuries that require orthopedic and reconstructive procedures, while at the same reducing healthcare costs.

As an example of the potential benefits, Dr. Russell noted that skin tissue was shipped to New York and Washington, DC, to treat those wounded in the September 11 terrorist attacks. Treatment with skin tissue, he said, could also be a potent factor in improving the physical condition of the military and treating the wounds of combatants in America's 21<sup>st</sup> Century War. In this respect, Dr. Johnson noted, "Tissue is the lifeblood of reconstructive surgery."

At present, tissue engineering is a small sub-set of the biotechnology industry, but according to Dr. Russell its growth rate is expected to exceed 50% a year throughout this decade. However, to realize the potential of tissue engineering, both he and Dr. Johnson, emphasized the need to overcome a series of challenges, including the ever-present need for funding of research and the development of technology.

Dr. Johnson, stressed the need for more funding of fundamental research, noting the findings of a study by the World Technology (WTEC) Division of the International Technology Research Institute, which was sponsored by the Defense Advanced Research Projects Agency, Food and Drug Administration, National Air and Space Administration, National Institute of Science and Technology, and the National Institutes of Health.

"A critical conclusion of this study," he stated, "is that funding in the United States has been more for applied than fundamental research."

The interim final report of that study states, "Until recently, most of the funding for to support activities in

*Continued on page 20.*

# Are You Giving Money to Undermine Medical Research?

*We thank Alice Ra'anan and Gary Kline, of the American Physiological Society, for providing the following guidance on charitable giving.*

**A**re you giving money to undermine medical research? If you make an unrestricted donation to the Combined Federal Campaign (CFC) or your local United Way, you might be inadvertently donating to groups working to promote animal rights or oppose the use of animals in research.

The CFC (for federal employees) and the United Way are umbrella organizations that funnel donations to philanthropic causes. Any nonprofit organization can apply for inclusion. What is striking if you visit the website of the CFC or your local United Way is the wide range of causes represented, and the fact that some of them represent diametrically opposing approaches to controversial issues. With respect to medical research, some of the organizations raise funds to support research on various diseases, while others work actively to oppose any use of animals in research.

When you give to a United Way or CFC campaign, you have the option to designate specific charities to receive your donations. If you do not designate recipients, your donation will be divided among all the participating organizations based upon the proportion of designated funds they receive from other givers. This means that you have no control over where your money goes, and you may well be giving to both sides.

It can be difficult to draw the line between organizations that promote legitimate concern for animal welfare and groups that strive to undermine research and other endeavors involving animals.

As a general rule, it is always good to know something about a charity before giving to it, especially since many charities have similar sounding names.

Websites are a convenient way to get such information. The Combined Federal Fund provides a list with links to participating charities at [www.opm.gov/cfc/](http://www.opm.gov/cfc/). Similar links should also be available from the web site of your local United Way.

To find your local United Way's website, go to the search page at [www.unitedway.org/uwsearch/](http://www.unitedway.org/uwsearch/). Then search under "field of service" using the category "humane concerns - animals" to get a list of the charities


eligible to receive United Way funds in your area. To get a sense of what an organization is doing, review not only its mission statement, but also its newsletter, action alerts, and issue briefs.

Below is a selection of the animal-related charities listed as part of the 2001 Combined Federal Campaign National List:

- Animal Legal Defense Fund ([www.ALDF.org](http://www.ALDF.org))
- Animal Protection Institute ([www.api4animals.org](http://www.api4animals.org))
- Animal Welfare Institute ([www.animalwelfare.com](http://www.animalwelfare.com))
- Doris Day Animal Foundation ([www.ddal.org/ddaf](http://www.ddal.org/ddaf))
- Humane Society of the United States ([www.hsus.org](http://www.hsus.org))
- In Defense of Animals ([www.idausa.org](http://www.idausa.org))
- New England Anti-Vivisection Society ([www.neavs.org](http://www.neavs.org))
- People for the Ethical Treatment of Animals ([www.peta-online.org](http://www.peta-online.org))
- Physicians Committee for Responsible Medicine ([www.pcrm.org](http://www.pcrm.org))
- United Animal Nations ([www.uan.org](http://www.uan.org))

A good example of the pitfalls of giving undesignated funds is People for the Ethical Treatment of Animals (PETA). PETA is included within the CFC even though it condones attacks on research labs and businesses that use animals and is seeking to undermine the fundraising efforts of charities that support animal research.

PETA's "do not give" list contains more than 80 medical research and patient assistance organizations including the Red Cross, March of Dimes, American Cancer Society, St. Jude Children's Research Hospital, Elizabeth Glaser Pediatric AIDS Foundation, Shriners Hospitals for Crippled Children and the Susan G. Komen Breast Cancer Foundation. PETA's list is posted online at [www.peta.org/mall/cc/ccchartest.html](http://www.peta.org/mall/cc/ccchartest.html)

The obvious solution is to designate the charities of your choice when you give! 

# Duke Biochemistry Department Head to Receive Avanti Award

**C**hristian R. H. Raetz, Chair of the Department of Biochemistry at Duke University Medical Center, has been selected to receive the 2002 Avanti Award at the Society's Annual Meeting, April 20-24 in New Orleans. The Award, which recognizes outstanding research contributions in the area of Lipids, consists of a plaque, a stipend, and transportation and expenses to present a lecture at the Meeting.

The Avanti Award alternates between the ASBMB and the Biophysical Society and previous recipients are Robert Bell, Ching-Hsien Huang, Lewis C. Cantley,



Dr. Christian R. H. Raetz

Richard M. Epand, Edward A. Dennis, and Ronald N. McElhaney.

Dr. Raetz was nominated by William Dowhan, Ph.D., Professor and John S. Dunn Chair at the Department of Biochemistry and Molecular Biology, University of Texas-Houston Medical School, who said of him:

“Chris has had an impressive career as a leader in the evolution of modern lipid biology, as a mentor of graduate students and postdoctoral fellows, as vice president of research in a major pharmaceutical company, and now as an academician and departmental chairman. The single most important factor in his prolific contribution to lipid biology has been his ability to

effectively utilize chemistry, biochemistry, molecular genetics, and genomics to solve biological problems.”

“A critical aspect of his contributions to the lipid field has been his willingness to freely distribute cell lines, mutants and reagents and to collaborate with numerous individuals,” noted Dr. Dowhan. “This has not only benefited many in the lipid field but has rapidly disseminated the information he acquired.”

Dr. Raetz received his undergraduate training in chemistry at Yale University and his M.D. and Ph.D. from Harvard Medical School. Early in his career with Dr. Eugene Kennedy, he carried out important studies on the characterization of enzymes of phospholipid metabolism in *Escherichia coli*. During his postdoctoral training at NIH in Herbert Tabor's laboratory, Dr. Raetz first applied a filter paper assay technique to large scale screening of bacterial mutants in phospholipid metabolism. These studies led to the isolation of many of the first mutants in these pathways and made possible the cloning of the respective genes, overproduction of gene products, and purification of these gene products by his laboratory and many others in the field. These mutants not only verified and defined the pathways of lipid metabolism *in vivo*, but led to unraveling of the pathway for the biosynthesis of Lipid A.

He also successfully applied this technique to somatic cells that allowed his and several other laboratories to identify genes of, and make mutants in, eukaryotic cell lipid metabolism. These again were seminal contributions to the lipid field. His filter assay technique is still generally used today and represents a classical method applied in a new way to reveal fundamental knowledge in the area of lipid research.


## Major Accomplishments

Dr. Raetz's research in phospholipid biochemistry is distinguished by its originality, extraordinary quality and inter-disciplinary character. His contributions fall into three areas:

1. The development of methods for mutant isolation and functional analysis of phospholipid pathways.
2. The discovery of new pathways for phospholipid assembly, especially the biosynthesis of outer membrane lipids in Gram-negative bacteria.



3. The discovery of new anti-bacterial agents that target outer membrane lipids.

 The awardee devised the first high throughput screening assays for detecting defined mutants in lipid biosynthetic enzymes by using bacterial colony replicas immobilized on filters. He then carried out the first in-depth analysis of the genetics of membrane phospholipid synthesis in *E. coli*. He identified several key genes that proved the biological relevance of earlier biochemical studies by Dr. Kennedy. Next, Dr. Raetz adapted his mutant isolation procedures to animal cells, based on his discovery of their remarkable ability to form macroscopic colonies on paper or polyester filters. He isolated the first phosphatidylcholine and ether lipid deficient mutants of Chinese hamster cells, and


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**“Dr. Raetz is the internationally recognized leader in the field of Lipid A biosynthesis.”**

***Science magazine 1996***

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discovered a new function for plasmalogen phospholipids as anti-oxidants.


 Dr. Raetz's most original work was enabled by his discovery of novel glucosamine-based phospholipids in his phosphatidylglycerol deficient mutants of *E. coli*. These substances are precursors of Lipid A (endotoxin), which makes up the outer surface of the outer membrane of Gram-negative bacteria and is a potent activator of innate immunity via the receptor TLR4. Dr. Raetz elucidated the 10 key reactions of Lipid A biosynthesis in *E. coli*, and identified the genes encoding the enzymes.

Using genetics, he proved that his pathway is essential for *E. coli* growth, culminating in the 1996 report of new antibiotics that inhibit the second enzyme of the pathway. An accompanying editorial in *Science* described Dr. Raetz as “the internationally recognized leader in the field of Lipid A biosynthesis.”

He and his collaborators also identified the first well-defined endotoxin antagonists among precursors of *E. coli* Lipid A, and reported the first x-ray structure of an acyltransferase. Recently, his work has revealed the existence of additional enzymes responsible for regulated covalent modifications of Lipid A that are critical for bacterial pathogenesis, and has provided insights into the mechanism of bacterial Lipid secretion.

The awardee's most recent work has focused on growth conditions that induce modifications in Lipid A.

Many of these changes are related to host response to environment and appear to play a role in virulence and pathogenesis. He is pursuing such questions as:

- How is the assembled lipopolysaccharide molecule translocated from its site of synthesis inside the cell to its final location at the outer surface of the outer membrane?
- What do the subtle differences in structure that exist between species mean to function?
- Why are these molecules toxic in animal systems? 

#### ***A BIT OF HISTORY:***

### ***The NIH Anaerobic Lab***

Oxygen lability, the constant change or instability of materials under study, has long been known to pose difficulties in microbiology and biochemistry research. Enzymes, electron carriers, and metabolic intermediates can be rapidly lost in the presence of air, and many bacteria are severely inhibited or even killed by exposure to air. This has made the study of anaerobic mutants particularly challenging, as many of the well-established techniques for use with aerobes cannot be adapted for use with anaerobes.

Manipulation can be carried out in conventional anaerobic glove boxes equipped with remote control devices. However, experimental operations become extremely difficult, if not impossible, when multistep procedures using filtration, chromatography, electrophoresis techniques, or massive instrumentation such as spectrophotometry, centrifugation, or refrigeration are necessary.

To facilitate anaerobic experiments under conditions allowing greater versatility in the use of standard laboratory techniques, the anaerobic laboratory chamber was developed in the early 1960s. This gas-tight chamber covers approximately 1,400 cubic feet (40 cubic meters) enclosed by a gas-tight partition. By displacing most of the air with N<sub>2</sub> gas, and then removing the remaining oxygen by combining it with hydrogen, reducing oxygen tensions of less than 100 ppm can be maintained.

To find out more about the anaerobic laboratory chamber, contact at NIH either Theresa Stadtman, 301-496-3002, or Earl Stadtman, 301-496-4096.

# ASBMB Submits Comments on OMB Final Data Quality Guidelines

**I**n a short letter dated October 29, Regulatory Burden Subcommittee chairman Howard K. Schachman submitted comments to the Office of Management and Budget commenting on the interim final Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Dissemination by Federal Agencies. The final guidelines were published September 28, 2001, with certain sections still open for comment through the end of October.

The statutory basis of these guidelines is found in an amendment accepted last year to the Treasury, Postal Service and General Government appropriations bill for FY 2001. The amendment was offered by Rep. Jo Ann Emerson (R-MO), a member of the House Appropriations Committee. The amendment directed OMB to issue by September 30, 2001, government-wide guidelines that “provide policy and procedural guidance to Federal agencies for ensuring and maximizing the quality, objectivity, utility, and integrity of information (including statistical information) disseminated by Federal agencies.”

The amendment also required that each federal agency issue its own guidelines for data quality within one year of the publication of OMB’s guidelines, that “administrative mechanisms” be established to allow “affected persons” to seek and obtain correction of information maintained and disseminated by the agency that does not comply with the [agency] guidelines, and that the agencies report periodically to the OMB director on the number and nature of any “complaints” received by the agency regarding the accuracy of information provided by the agency and finally, how such complaints were handled. OMB’s proposed guidelines are the agency’s attempt to comply with this congressional directive.

OMB published an initial set of draft guidelines in late June, and ASBMB commented on them on August 13. OMB’s final guidelines went a long way toward meeting ASBMB’s concerns, but in his October 29 letter to OMB official Brooke Dickson, Dr. Schachman noted that his subcommittee continues to have concerns about the “substantial reproducibility” language in the final published version.

“Our objections to [the substantial reproducibility] language,” Dr. Schachman noted, “boil down to the concern that the [substantial reproducibility] standard in the guidelines is inherently subjective, and will likely create more difficulty for agencies rather than less.”

Dr. Schachman noted the subcommittee’s support for, and endorsement of, the comments of the Council on Government Relations (COGR), an organization representing large research universities. COGR’s proposed solution was that “the administration should direct agencies to rely on peer review for all information in the scientific and research context, proposed for dissemination by the agencies.’ This allows peer review—the ultimate arbiter of truth and objectivity in scientific literature—to serve as an effective barrier to the sort of problems and that could result from agency reliance on a less adequate measure of objectivity.”

ASBMB’s comments on the data quality guidelines can be found on the Society website at [www.asbmb.org](http://www.asbmb.org). Simply type “data quality” in the search box on the home page; ASBMB’s August 13 letter and several background articles are highlighted. The August 13 letter also contains a link to the OMB guidelines. ☺

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## Research!America Receives Grant to Promote Health Research

Research!America (R!A) has received a 3-year, \$5.5 million grant to build national support for disease prevention and public health research.

According to William Roper, M.D., M.P.H., Chair of R!A’s Prevention Research Initiative, “Ninety percent of this nation’s healthcare budget is devoted to treating the late stages of disease, but less than one percent is spent on disease prevention research. This campaign will help close the gap that exists in funding for health prevention, health promotion, and public health research.”

R!A President Mary Woolley added, “This grant will allow Research!America to bring a greater number of highly targeted, tested and effective messages to the public and opinion leaders regarding the vital importance of the benefits of prevention, health promotion, and public health research.”


R!A is a non-profit, non-partisan organization that seeks to make medical and health research a higher national priority. Its membership represents more than 400 academic institutions, independent research laboratories, teaching hospitals, private industries, professional societies (including ASBMB), voluntary health agencies and philanthropies. ☺

# NIGMS 'Glue Grant' Finances Cell Movement Study

**C**ell movement is an essential process that underlies health and disease. Yet despite many years of intensive study, a good understanding of the mechanics of this important phenomenon has remained out of biologists' grasp.


In an effort to "glue" together large groups of scientists to tackle such pressing problems confronting biomedical scientists today, the National Institute of General Medical Sciences (NIGMS) has provided an \$8 million "glue grant" (for the first year of funding) to a consortium of scientists who will work to unlock the mysteries of cell movement. NIGMS anticipates spending a projected total of \$38 million on the project over the course of 5 years.

The Cell Migration Consortium project brings together a large group of scientists from leading academic medical centers across the country. Leading the project are two scientists from the University of Virginia School of Medicine, Dr. Alan F. "Rick" Horwitz and Dr. J. Thomas Parsons.

 Understanding the mechanism of how cell migration occurs is critical to our understanding of diseases like cancer, arthritis and osteoporosis, as well as wound repair, embryonic development, and tissue engineering," said Dr. Horwitz, Professor of Cell Biology at U.Va. and

the project's principal investigator. "For example, most people who have cancer don't die from primary tumors but from tumor spread—that's a migration problem. And a significant number of congenital brain defects are migration problems."

One of the Consortium's goals is to generate new understanding about the basic mechanisms involved in cell migration. A key part of the plan is to generate new and sophisticated imaging strategies to visualize the fundamental signaling pathways that regulate cell migration—technologies that are sorely needed by the scientific community currently investigating cell movement. Another objective of the Consortium is to catalyze the translation of new discoveries in cell migration to the development of novel therapeutic drugs and treatments.


The Consortium will consist of biologists, chemists, biophysicists, optical physicists, mathematicians, computer scientists, geneticists, and engineers. Using state-of-the-art Internet and interactive video technologies, Consortium researchers will share and discuss data as it is collected, Parsons explained. A Consortium website ([www.cellmigration.org](http://www.cellmigration.org)) will be accessible to scientists everywhere. 

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## Protein Structure Initiative Adds New Members


**T**he National Institute of General Medical Sciences (NIGMS) has welcomed two new members to its Protein Structure Initiative (PSI), expanding the Institute's support in the area of structural genomics research. Seven teams of scientists received awards for research centers in September 2000, and annual NIGMS funding for the initiative exceeds \$40 million.

The two new awards, totaling \$8.8 million for the first year of funding, have been made to:

 The University of Wisconsin, Madison, where John L. Markley, Ph.D., an ASBMB member, is the principal investigator, will receive \$4.4 million for the first of four years of funding provided to the Center for Eukaryotic Structural Genomics to develop high-throughput methods

for protein production, characterization and structure determination from *Arabidopsis thaliana*, a plant that is frequently used in laboratory research and that has many genes in common with humans and animals.

The University of Washington will receive \$4.4 million for the first of 4 years of funding provided to the Structural Genomics of Pathogenic Protozoa Consortium to develop new methods and technologies for obtaining protein structures from protozoans, many species of which cause deadly diseases such as sleeping sickness, malaria, and Chagas' disease.

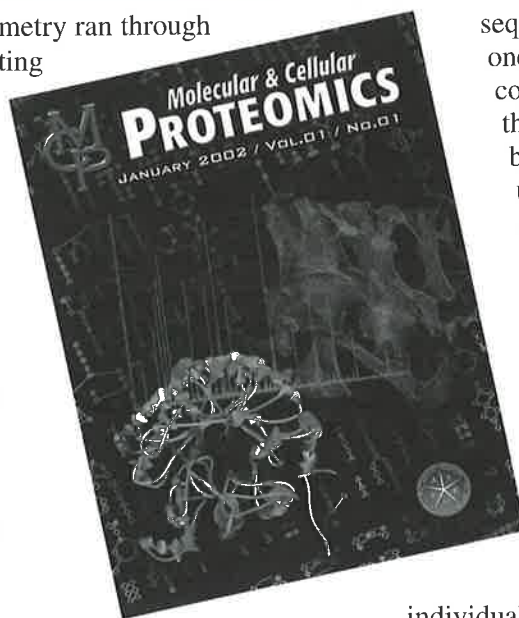
For more information on the NIGMS Protein Structure Initiative in structural genomics, go to the NIGMS website at [www.nigms.nih.gov/funding/psi.html](http://www.nigms.nih.gov/funding/psi.html). 

## Mass Spectrometry . . . from page 11

Inevitably the theme of mass spectrometry ran through many of the presentations, but the meeting gave a very realistic appreciation of all of the components required for successful proteomics research, mass spectrometry being only one contributor.

The limitations of current mass spectrometric methods were emphasized as least as much as their strengths. Where proteomic research is going is hard to say, although a very upbeat presentation from N. Leigh Anderson of Large Scale Biology Corporation suggested it is going to be carried out on a factory scale in the near future.

Inevitably proteomic research will follow multiple paths and, in contrast to genomic



sequencing, it is impossible to envisage one or two government-sponsored or corporate research entities taking over the field. The number of questions to be answered in proteomics is almost uncountable and the methods of approaching them so diverse as to be impossible to bring together in one organization.

For the foreseeable future, proteomics is a wide open, fascinating and challenging field that requires inspired input from a large community of scientists. Symposia such as this help to show the way ahead, but the ingenuity of

individuals will ensure that this field moves forward in directions of which we have not even dreamt. ❁

## Tissue Engineering . . . from page 14

tissue engineering in the United States has been in support of commercial development, leading to large amounts of applied research but lesser amounts of fundamental research. In Japan and Europe, the tissue engineering field is being largely driven by government funding, allowing researchers to perform more basic and potentially more broad, intellectual property-generating, research.”

### A Major Challenge

The WTEC report also noted, “regulatory issues present a major challenge to the worldwide development of the tissue engineering industry,” and Dr. Johnson called on the U.S. to be a leader in the development of regulatory standards.

“If we are not leaders in the attempt to harmonize standards,” he warned, “we may find that we have standards that are not compatible with the rest of the world.” ❁

## Satellite . . . from page 8

direct the cell to do conflicting things, such as to grow vs. to differentiate or undergo programmed cell death. Signaling pathways emanating from single receptor classes, like tyrosine kinase receptors, G protein-coupled receptors, cytokine receptors, etc., have been elucidated. But the challenge facing us today is to learn how a cell integrates all the different extracellular signals it receives to respond in a specific and singular way.”

To initiate studies to answer these questions, investigators have begun examining how different signaling pathways that emanate from two distinct receptor classes network within the cell to elicit a cooperative or antagonistic response. The Combinatorial Signaling Satellite Meeting will focus on several examples of such mixed signals, including integration of extracellular matrix-induced signals (adhesion and migration) with growth factor-induced signals, and cross-talk between G-protein induced, steroid receptor-induced, or cytokine receptor-induced signals and tyrosine kinase receptor-induced pathways.

“The studies that will be discussed,” said Dr. Parsons, “begin to address such issues as strength of signal and complexity of signals vs. response. They are novel and ground-breaking and are likely to represent the forefront of many such investigations that are yet to come.” ❁

# Members in the News

## ASBMB Members Elected to Institute of Medicine

Eight ASBMB members were among 25 FASEB Society members in a group of 60 scientists and public-health officials recently elected to the Institute of Medicine (IOM). ASBMB They were:

Joan S. Brugge, Professor, Department of Cell Biology, Harvard Medical School.

Robert W. Mahley, M.D., President, J. David Gladstone Institutes, and Professor of Pathology and Medicine, University of California, San Francisco.

Edward R.B. McCabe, M.D., Professor and Executive Chair, Department of Pediatrics, and Director, Child Health Research Center, School of Medicine, University of California, Los Angeles.

Douglas A. Melton, Investigator, Howard Hughes Medical Institute, and Thomas Dudley Cabot Professor in the Natural Sciences, and Professor of Molecular and Cellular Biology, Harvard University.

Edward E. Penhoet, Professor of Health Policy and Administration, and of Molecular and Cell Biology, and Dean, School of Public Health, University of California, Berkeley.

Gregory A. Petsko, Professor of Biochemistry and Chemistry, and Director, Rosenstiel Basic Medical Sciences Research Center, Brandeis University, Waltham, Massachusetts.

Stephen J. Weiss, M.D., Professor of Internal Medicine and Oncology, Medical School, University of Michigan.

## FASEB EXCELLENCE IN SCIENCE LECTURE AND AWARD 2003

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For Call for Nomination and information contact:

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or visit the FASEB web site: <http://www.faseb.org>

**DEADLINE FOR NOMINATIONS IS MARCH 1, 2002**

# Members in the News

## Bone Disease Researcher Joins Pitt Cancer Institute

David Roodman, M.D., Ph.D., an internationally renowned researcher in multiple myeloma and bone marrow culture techniques, has joined the University of Pittsburgh Cancer Institute (UPCI) as Director of the Multiple Myeloma Center. He was also appointed Professor of Medicine, Division of Hematology/Oncology in the university's School of Medicine, and Director, Center for Bone Biology. At UPCI, Dr. Roodman will focus on the investigation of multiple myeloma, a cancer



Dr. David Roodman

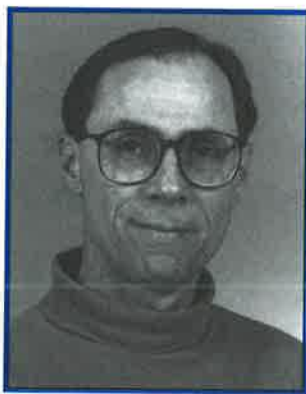
of the plasma cells which play a vital role in the body's immune defenses.

Most patients with multiple myeloma die within three to five years of diagnosis. In addition to a low survival rate, multiple myeloma has a devastating impact on the patient's quality of life, because it causes bones to weaken and erode causing pain and possible fractures.

As well as multiple myeloma, Dr. Roodman's research will focus on Paget's disease of the bone which affects some two million Americans. Current treatment for this and multiple myeloma addresses the symptoms only. Dr. Roodman will be working to identify the root causes of both diseases. ☼

## ASBMB Member Named MacArthur Foundation Fellow

Norman R. Pace, Ph.D., of the University of Colorado at Boulder has been named a fellow of the John D. and Catherine T. MacArthur Foundation. He was honored for "revolutionizing our conception of the range and diversity of microbial life."



Norman Pace, Ph.D.

Dr. Pace was one of the 23 recipients of the foundation's 2001 MacArthur Fellowships.

Each fellow receives \$500,000, paid out over five years with "no strings attached," although the foundation hopes recipients will use the awards to support their work.

The awards recognize and encourage individual creativity in a number of fields, including the performing arts, law, community development, astrobiology, and papyrology.

Candidates for the fellowships are nominated by a group of anonymous "nominators" selected for their ability to identify exceptionally creative people. Nominees can number several hundred at first, but an anonymous 12-member selection committee makes final recommendations to the foundation's Board of Directors, which typically chooses 20 to 30 fellows. ☼

## JBC Board Member's Award Is 'First' for Japanese Science

Professor Naoyuki Taniguchi, M.D., Ph.D., this year became the first Japanese researcher to receive the International Glycoconjugate Award (IGO).

Dr. Taniguchi, whose award was presented during Glyco XVI in the Netherlands, was also scheduled to receive the title and diploma of Docteurs Honoris Causae from the Université Henri Poincaré in Paris this October.

Professor Taniguchi, Chair of the Department of Biochemistry at Osaka University Medical School, serves as a member of the *Journal of Biochemistry* (Tokyo) and the *JBC* editorial boards, and will be the Secretary General of the IUBMB Congress in 2006 in Kyoto. ☼

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# Calendar of Scientific Meetings

## **American Society for Cell Biology 41st Annual Meeting**

December 8-12, 2001 • Washington, DC

Ph: 301-347-9300; Fx: 301-347-9310; Email: [ascbinfo@ascb.org](mailto:ascbinfo@ascb.org); Website: [www.ascb.org](http://www.ascb.org)

## **Glycogenomics: Impact of Genomics and Informatics in Glycobiology Biochemical Society Joint Meeting with the Physiological Society**

December 17-19, 2001 • University of York, UK

Contact: Meetings Office, Biochemical Society

Ph: +44 (0)20 7580 5530; Fx: +44 (0)20 7637 7626; Email: [meetings@biochemistryorg](mailto:meetings@biochemistryorg)

Website: [www.biochemistryorg/meetings/](http://www.biochemistryorg/meetings/)

## **Oxygen Club of California 2002 World Congress, IXth Annual Meeting**

Co-sponsored by the Society for Free Radical Research International (SFRRRI) and with the Linus Pauling Institute (LPI).

March 6-9, 2002 • Parker's Doubletree Resort, Santa Barbara, California

Contact: Enrique Cadenas; Ph: 323-442-1418; Fx: 323-224-7473; Email: [cadenas@hsc.usc.edu](mailto:cadenas@hsc.usc.edu)

Website: [www.oxyclubcalifornia.org](http://www.oxyclubcalifornia.org)

## **Biomaterials—The Next Frontiers: Biomedical, Bioelectronic, Biomineralization, Bioanalytical**

March 12-13, 2002 • Trabant University Center, University of Delaware

Contact: Kathleen Werrell; Ph: 302-831-4863; email: [enggoutreach@udel.edu](mailto:enggoutreach@udel.edu)

## **Proteomics—The New Frontiers**

March 14-15, 2002 • Trabant University Center, University of Delaware

Contact: Kathleen Werrell; Ph: 302-831-4863; email: [enggoutreach@udel.edu](mailto:enggoutreach@udel.edu)

## **ASBMB Satellite Meetings:**

**I - Transcriptional Regulatory Mechanisms**

**II - Combinatorial Signaling**

**III - Scientific and Technical Challenges in the Human Proteome**

April 19-20, 2002 • New Orleans, Louisiana

Contact: Kelly Gull; Ph: 301-530-7145; Fx: 301-571-1824; Email: [kgull@asbmb.faseb.org](mailto:kgull@asbmb.faseb.org)

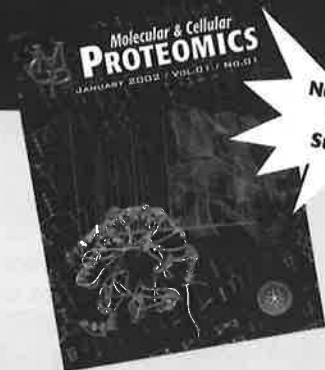
Website: [www.asbmb.org](http://www.asbmb.org)

## **American Society for Biochemistry and Molecular Biology Annual Meeting in Conjunction with EB2002**

April 20-24, 2002 • New Orleans, Louisiana

Contact: EB2002 Meetings Office; Ph: 301-530-7010; Fx: 301-530-7014; Email: [eb@faseb.org](mailto:eb@faseb.org)

Website: [faseb.org/meetings/eb2002](http://faseb.org/meetings/eb2002)



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- In addition to manuscripts describing research advances in proteomics, articles concerning technological advances will also be accepted. In addition, MCP will publish large data sets as either appendices to regular manuscripts or as stand alone contributions. The latter must include a summary, not to exceed two printed pages, describing the germane points and importance of the information. The data sets themselves (either as appendices or as separate articles) will appear only in the on-line version. A letter of intent describing the extent and format of this supplemental material must precede submission of the manuscript.
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