JUNE 2004

www.asbmb.org

ASBMB Today

Constituent Society of FASEB

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

ALSO IN THIS ISSUE

Shortage of Scientists Likely Here

Page 4

For Complex Proteomic Problems

Ask about our integrated packages with substantial savings!

- PhosphoExploration™ – Phosphorylation site mapping and phosphospecific antibody production
- Complex mixture separation and protein ID
- Protein sequencing and antibody production

Contact us for expert technical support and quantity discounts.

**Peptide sequencing at no extra charge w/ affinity purified Abs and peptides purified to >90%!*

Visit us at ASBMB BOSTON Booth 524

www.21stcenturybio.com

P 508.303.8222 Toll-free: 877.217.8238 F 508.303.8333 E info@21stcenturybio.com

www.asbmb.org

ASBMB Today

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

JUNE 2004,
Volume 3, Issue 3

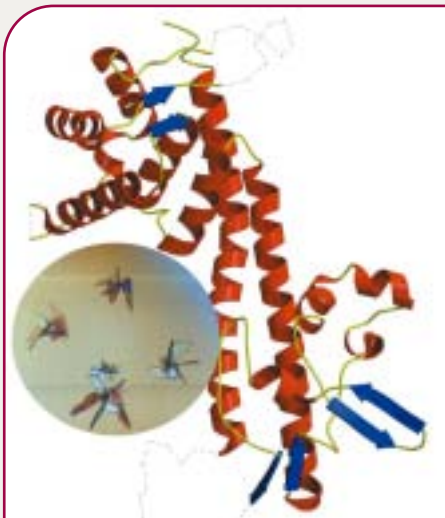
features

ON THE COVER:

18

departments

13



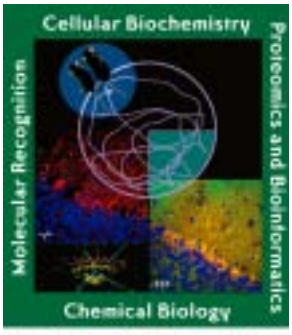
ASBMB Today
is a monthly publication
of The American Society for
Biochemistry and Molecular Biology

Comments

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

John D. Thompson
Editor, *ASBMB Today*
9650 Rockville Pike
Bethesda, MD 20814-3996
Phone: 301-634-7145; Fax: 301-634-7126
E-mail: jthompson@asbmb.org

Symposium on Publishing Issues Scheduled for Annual Meeting



What are the qualities in a journal that would lead one to recommend to a junior colleague that they publish in it? What are the scientific community's unmet needs that would warrant significant change in current publishing models? How well served is the public by the existence of differing models for publication of scientific literature? What should (or will) the scientific publishing world look like in ten years' time?

These are among the many questions and issues associated with the changing world of scientific publishing that will be considered at a symposium scheduled for the ASBMB's upcoming annual meeting in Boston, Massachusetts. The symposium, sponsored by the ASBMB Public Affairs Advisory Committee, is called "Where Should Scientists Publish: The Future of Scientific Communication."

This symposium will be held in Room 306, Hynes Convention Center, on Tuesday, June 15, 2004, 12:15 –2:15 p.m. It will be moderated by Dr. Ralph Bradshaw, University of California at Irvine, and editor of ASBMB's journal, *Molecular and Cellular Proteomics*.

The program will consist of 15-minute talks by three speakers, followed by a panel discussion involving these speakers and four additional discussants. Time will be available at the end of the symposium for questions from the audience.

The speakers are:

Dr. Pat Brown, Stanford University.

Dr. Michael Mabe, Director of Academic Relations, Reed-Elsevier.

Dr. Robert Simoni, Stanford University, and Deputy Editor of *The Journal of Biological Chemistry*.

The panelists are:

Mr. Rudy Baum, Editor, *Chemical and Engineering News*.

Dr. Catherine Drennan, Massachusetts Institute of Technology.

Dr. Martin Frank, Executive Director, American Physiological Society.

Dr. John Inglis, Cold Spring Harbor Press.

Dr. Michael Keller, Librarian, Stanford University.

The committee's intent in arranging the symposium is to provide a forum where many of the issues associated with scientific publishing can be discussed by leading proponents of various current approaches, as well as most of the major stakeholder groups. The committee has worked hard to obtain speakers and discussants that fill this bill. Thus, advocates of open access; commercial, academic and society publishers; and faculty members, librarians, and the press, are all represented.

The Public Affairs Advisory Committee hopes you will plan to attend this lively, timely, and provocative discussion.

If It's Proteomics; You Should Be Reading *MCP*

If you are working with proteomics, *Molecular & Cellular Proteomics (MCP)* is must reading for you. In the three short years since ASBMB introduced this journal, *MCP* has become a highly respected information resource for clinicians and researchers worldwide. Just consider this April's special issue, a first for *MCP*, on Cancer Proteomics.

Papers in that issue included: HUPO Initiatives Relevant to Clinical Proteomics; Clinical Infrastructures to Support Proteomic Studies of Tissue and Fluids in Breast Cancer; The Human Plasma Proteome: A Nonredundant List Developed by Combination of Four Separate Sources; and How Industry Is Approaching the Search for New Diagnostic Markers and Biomarkers.

"The application of proteomic technologies to the study of clinically relevant cancer samples, in a well-defined clinical and pathological framework, is becoming widespread worldwide, and *Molecular & Cellular Proteomics* has taken the lead by providing a unique forum for these activities," says Julio E. Celis, Guest Editor and Chair, Clinical Proteomics Advisory Committee. "This special issue gives a flavor of some relevant developments in the rapidly emerging field of cancer proteomics, and emphasizes the need for creating integrated research environments in order to accelerate the translation of basic discoveries into the clinical practice."

While the typical issue of *MCP* will not be dedicated solely to one topic, Dr. Celis noted that additional clinical proteomic issues are being planned in order to cover other important diseases. "Among the themes in planning for future special issues," he said, "are Cardiovascular Diseases and Neurological Issues, and Signal Transduction."

MCP is available free to ASBMB members online and the print copy is available by subscription. For more information email asbmb@asbmb.org, or go to www.mcponline.org/subscriptions.

by Peter Farnham, CAE, ASBMB Public Affairs Officer

Shortage of Scientists Here Likely as

The United States remains the world's leading producer of and a net exporter of high-technology products and ranks among the global leaders in research and development (R&D) spending. That's the good news. The bad news is that ongoing economic and workforce changes make the outlook for the future uncertain.

So says *Science and Engineering (S&E) Indicators 2004*, a biennial report of the National Science Board to the President. The National Science Board oversees the activities of the National Science Foundation.

"The United States is in a long-distance race to retain its essential global advantage in S&E human resources and sustain our world leadership in science and technology," said NSB Chair Warren M. Washington. "For many years we have benefited from minimal competition in the global S&E labor market, but attractive and competitive alternatives are now expanding around the world. We must develop more fully our native talent."

Among the most disturbing findings of the report is that the United States is producing too few American scientists and engineers to fill its ever-increasing need for such specialists.

A May 5 story in the *New York Times* noted that the NSB report said that the recruitment problem "grows out of the nation's economic success and the rising demand for employees trained in science and engineering. For decades, such jobs have grown faster than overall employment. They went to 3.8 percent of civilian jobs from 2.6 percent between 1983 and 2002. Unchecked, the trends in technical employment will leave a dearth of scientists to meet the rising demand . . . the number of United States citizens qualified for science and engineering jobs could remain level."

The shortage of U.S.-born scientists and engineers is not new; this concern has been raised repeatedly since at least the 1980s. However, for the past 20 years our country has been able to make up for shortages of American scientists and engineers by encouraging the immigration of thousands of foreign-born scientists and engineers to make up the shortfall. Unfortunately, the report notes, the nation may soon be unable to rely on foreign citizens to fill the gap, either because of limits to their entry or because of intense foreign competition for those skills.

Record levels of foreign-born scientists and engineers have helped make possible rising U.S. employment in science and engineering in the past several decades. The report highlights U.S. Census data from 2000 showing about 17 percent of those with bachelor's degrees, 29 percent with master's degrees, and 38 percent with doctorates employed in science and engineering are foreign-born.

On the other hand, the number of high-skill-related visas issued to students, exchange visitors and others has declined significantly since 2001. These numbers reflect both a drop in applications and higher U.S. State Department refusal rates. Visas granted to students, exchange visitors, and highly skilled foreigners dropped from

Science Abroad Improves, Says Report

787,000 in 2001 to 625,000 last year. Visa applications have dropped as well.

In addition, a number of countries, particularly in Asia and Europe, are becoming more prominent in technology development because of their large, ongoing investments in S&E education and R&D. This trend is also revealed by a growing number of journal articles from East Asia, which suggests an accompanying increase in basic R&D in these nations. While NSB data show that U.S.-based authors continue to produce the largest share of scientific journal articles, article output has flattened since 1992.

Inevitably, this trend has attracted the attention of our nation's politicians. Senate Democratic Leader Tom Daschle (D-SD) noted at a recent American Association of Advancement of Science meeting in Washington, DC:

"According to a recent study, America's rate of scientific discovery is lagging behind that of European countries. The number of scientific papers published by American researchers declined last year, and has been flat for the past several years. In contrast, every country in Europe has increased its rate of discovery. In the last two decades of the 20th century, France, Germany, and the United Kingdom doubled their production of doctorates in science and engineering. Japan doubled its production of science and engineering doctorates in just one of those decades. If this stagnation is allowed to continue, it will have profound implications for every aspect of American society. If we are to remain the land of the future, we must reaffirm the partnership that created America's dominant position within the world of science."

Daschle characterized this trend as "disturbing," and perhaps it is. But let's take a look at the implications. First, these trends are the logical outcome of a major aspect of American policy in recent decades. While we have been able to fill our needs for scientists and engineers through recruiting foreign talent, tens of thousands of students have been trained here and have returned to their homelands. These scientists, who have benefited by some of the world's best training, return home and begin to practice science there instead of the U.S., and thus inevitably begin to improve the science infrastructure in their own countries. What we are seeing is therefore perfectly natural and a logical outcome of U.S. policy in this area.

For the past 20 years our country has been able to make up for shortages of American scientists and engineers by encouraging the immigration of thousands of foreign-born scientists and engineers.

Like most complex occurances on the global level, there are a number of implications to consider. First, it is obvious that the U.S. position as the world's science colossus would begin to slip as other countries' science infrastructure improves. Second, this will probably cause some dislocations in the short term as world-class work begins to occur overseas with increasing frequency. Third, this is not necessarily bad. Improved science infrastructure around the globe will inevitably (if over the long haul) improve the economies of other nations around the world, reducing the economic gap between the world's rich and poor nations, with the accompanying benefit of greater global stability.

Still, American students continued lack of interest in science and engineering is a disturbing trend that, if allowed to continue, will inevitably affect our own economy. The trend toward fewer students in scientific and engineering fields can only be exacerbated by the recent analysis of the American Association for the Advancement of Science, which noted that in 2004, 21 of 22 federal science agency budgets declined in real terms. Thus, improved science funding, easing of visa restrictions for foreign students, and more attention to basic science education in our schools, would seem to be in order.

The NSB report can be read on the National Science Foundation website at: http://www.nsf.gov/sbe/srs/seind04/

ASBMB Supports Changes in Visa Regulations

ASBMB announced its support for changes in visa regulations on May 10, signing onto a statement issued by the American Association for the Advancement of Science (AAAS). The "Statement and Recommendations on Visa Problems Harming America's Scientific, Economic, and Security Interests" makes six recommendations to address problems that have developed over the past two years.

The problems the statement mentions include: repetitive security checks and an inefficient visa renewal process, both of which cause lengthy visa issuance delays; a lack of transparency and priority processing in the visa system; inconsistent treatment of visa applications; repetitive processing of visa applications for those with proven track records; and a poorly designed fee collection mechanism proposed under a recently-implemented student and visitor tracking program.

To address visa issuance delays, the statement recommends that the validity of security clearances for international students, scholars and scientists be extended from the current one-year time period to the duration of their course of study or academic appointment. In addition, visa delays could be diminished or eliminated by allowing visitors who leave the country to attend a conference or on family business to begin the process of revalidating their visas before leaving the United States. Such a change would also allow them to continue their studies and work uninterrupted.

Concerning a lack of transparency in the system, visa applicants should be allowed to inquire about the status of their applications, and those pending for more than 30 days should be given a higher priority for processing, thus helping to ensure that applications do not get "buried at the bottom of the pile."

Regarding inconsistent treatment of applications, consular staff should be better trained, and protocols for more rigorous review should be clearly established. These changes could greatly enhance security while simultaneously reducing the number of applications submitted for more rigorous review, thereby alleviating potential delays.

To address repetitive processing of visa applications, visa reciprocity agreements between the United States and

countries such as China and Russia that send a lot of students and scientists to the U.S. should be revised to extend the duration of visas each country grants, thereby reducing the number of times that visiting international students, scholars, and scientists must renew their visas.

Regarding the proposed fee payment system, that would allow for a variety of simple payment methods that are quick, safe, and secure, including payment after the individual arrives in the United States.

The statement tries to strike a balance between the need for greater security in the post-9/11 environment, and the concern that foreign students and scholars are beginning to go elsewhere to learn or practice science. While the United States is still the world's science and engineering colossus, trends are emerging that indicate problems in this area in the future (see the accompanying article, *Shortage of Scientists Here Likely as Science Abroad Improves, Says New Report*).

As the statement notes, "there is increasing evidence that visa-related problems are discouraging and preventing the best and brightest international students, scholars, and scientists from studying and working in the United States, as well as attending academic and scientific conferences here and abroad. If action is not taken soon to improve the visa system, the misperception that the United States does not welcome international students, scholars, and scientists will grow, and they may not make our nation their destination of choice now and in the future. The damage to our nation's higher education and scientific enterprises, economy, and national security would be irreparable. The United States cannot hope to maintain its present scientific and economic leadership position if it becomes isolated from the rest of the world."

While acknowledging that the Federal government has responded to some of the concerns noted above, the statement indicates that "serious problems remain." In addition to the recommendations noted above, the statement calls for additional funding and staffing at the State and Homeland Security departments.

The entire statement is posted under what's new on the ASBMB website at www.asbmb.org

HIGHEST QUALITY

INOSITIDES

LOWEST PRICES

^{14}C **^{3}H**

Catalog	Product Description	Quantity	ARC
ART 1298	12-Deoxyphorbol 13-phenyl acetate [20-^{3}H]	5 μCi	$999
ART 222	Glycerophoshoinositol [myo-inositol-2-^{3}H]	5 μCi	$999
ART-473	Glycerophoshoinositol [myo-inositol-2-^{3}H] 4,5 bisphosphate	5 μCi	$1199
ART-472	Glycerophoshoinositol [myo-inositol-2-^{3}H] 4 phosphate	5 μCi	$1199
ARC-232	Inositol, myo, [^{14}C(U)]	5 μCi	$479
ART-261	Inositol, myo, [1,2-^{3}H(N)]	1mCi	$729
ART-116	Inositol, myo, [2-^{3}H(N)]	1mCi	$649
ART-171	Inositol-1-phosphate, D-[inositol-2-^{3}H] (1-IP)	5 μCi	$299
ARC-233	Inositol-1-phosphate, D-[inositol-2-^{14}C(U)]	5 μCi	$299
ART-268	Inositol-3-phosphate, D-[inositol-2-^{3}H]	5 μCi	$359
ARCD-166	D-myo-Inositol 1-phosphate dipotassium salt, “Cold”	1 mg	$179
ART-264	Inositol, scyallo, [2-^{3}H(N)]	250 μCi	$749
ART-872	Inositol 1,3,4,5 tetrakisphosphate D-[inositol-1-^{3}H(N)]	5 μCi	$629
ARCD-108	Inositol, myo D-1,4,5 triphosphate, “Cold”	1 mg	$209
ARCD-109	Inositol, myo L-1,4,5 triphosphate, “Cold”	1 mg	$199
ART-270	Inositol, 1,4,5-triphosphate, D-[inositol-2-^{3}H(N)] (1,4,5-IP3)	5 μCi	$579
ART-487	Phorbol-12,13-diacetate, [20-^{3}H(N)]	50 μCi	$309
ART-485	Phorbol-12,13-dibutyrate, [20-^{3}H(N)]	50 μCi	$299
ART-486	Phorbol-12-myristate-13-acetate [20-^{3}H(N)]	50 μCi	$319
ART-184	Phosphatidylinositol, L-α-[myo-inositol-2-^{3}H(N)] PI [^{3}H]	10 μCi	$599
ART-183	Phosphatidylinositol 4,5-biphosphate [myo-inositol-2-^{3}H(N)] PIP_2[^{3}H]	5 μCi	$559
ARCD-131	Phosphatidylinositol 4,5-biphosphate (PIP_2), “Cold”	1 mg	$209
ARE-100	Phosphatidylinositol specific phospholipase C (PI-PLC)	5 units	$339
ART-185	Phosphatidylinositol 4-phosphate, [myo-inositol-2-^{3}H]	5 μCi	$649
ART-1297	Prostatin [20-^{3}H] [dPAC]	50μCi	$999

CALL OR FAX TOLL FREE FOR OUR NEW 2004 CATALOG
COMPLETE SATISFACTION OR 100% MONEY BACK GUARANTEED

American Radiolabeled Chemicals, Inc.

101 ARC Drive, St. Louis, MO 63146-3502
Telephone: 314-991-4545 Toll Free: 800-331-6661 Web: http://www.arc-inc.com
Fax: 314-991-4692 Toll Free Fax: 800-999-9925 E-mail: arcinc@arc-inc.com

By Peter Farnham, CAE, ASBMB Public Affairs Officer

NIH Releases Conflict of

A panel on conflict of interest issues at NIH released a report on May 6 recommending a number of new conflict of interest policies involving NIH employees. "The Report of the NIH Blue Ribbon Panel on Conflict of Interest Policies" was produced in just 66 days—a near record for such a report—indicating the urgency with which NIH Director Elias Zerhouni viewed the matter.

Although a number of specific allegations had been raised against certain NIH employees, the panel did not investigate or review individual cases. Rather, it merely noting that "relatively few NIH employees engage in consulting agreements with biotechnology or pharmaceutical companies"—currently only about 120 of NIH's 17,500 employees.

However, the report also indicates that "a substantial number of NIH employees are involved in outside activities with professional societies and with academic and research institutions," including teaching, speaking, or writing. NIH scientists are also recognized for outstanding scientific achievements, leadership, or public service and sometimes receive awards. The report characterized these activities as "essential" for NIH scientists, "because they are part of the tradition of science and provide evidence of the value and significance of the NIH research community to the larger scientific community."

The report also noted considerable confusion at NIH about existing conflict of interest policies, brought about by what it termed "an extremely complex set of rules" that are widely misunderstood "by some of the very people to whom they are intended to apply, thereby creating uncertainty as to allowable behavior and adversely affecting morale." The panel urged speedy adoption of its 18 recommendations.

Among the recommendations is a requirement that "NIH senior management and NIH extramural employees who are responsible for program funding decisions and recommendations, and professional staff managing grants and contracts and application review, should not engage in consulting activities with pharmaceutical or biotechnology companies or in paid consulting for academia," including speaking for compensation at an industry site.

It also "reaffirms current federal law" that intramural scientists conducting research with human subjects should not have any financial interest in or relationship with any company whose interests could be affected by their research or clinical trial.

The report also makes specific recommendations on outside earnings for NIH employees involved in administration or conduct of NIH research programs—for example, "The total amount earned annually from compensated consulting with industry or academia should not exceed an amount equal to 50 percent of the employee's annual salary, and no one source should account for an amount exceeding 25 percent of annual salary." In addition, employees should not receive compensation in the form of stock options or other forms of equities for their services or spend more than 400 hours per year on these activities (writing excepted).

The panel also proposed a number of changes in reporting and public disclosure requirements, and called for increased supervisory training. It also recommended that consideration be given to raising the compensation level for senior NIH staff to make employment at NIH more competitive with the private sector.

The report also recommends that "NIH intramural scientists should continue to be allowed to engage in compensated speaking, teaching, and writing for professional societies and for academic and research institutions as an outside activity providing that all ethics review and approval requirements are met."

The *Los Angeles Times* ignited the initial public controversy over this topic last December with a lengthy expose of the financial relationships that exist between certain senior NIH officials and private industry. This article provoked at least one congressional investigation that is still on-going, as well as a round of painful congressional hearings with yet more scheduled. Dr. Zerhouni and NIH continue to enjoy broad bipartisan support on Capitol


Report of the
National Institutes of Health
Blue Ribbon Panel on Conflict of Interest Policies
A Working Group of the Advisory Committee to the Director
National Institutes of Health
DRAFT: May 3, 2004

Interest Recommendations

Hill, particularly in the Senate, but the hearings were an embarrassment and Dr. Zerhouni obviously got the message that Congress wanted him to move quickly.

Dr. Zerhouni announced establishment of the panel on January 22, and charged it with reviewing existing laws, regulations, policies, and procedures regarding financial conflict interest of NIH staff, including consulting arrangements, stock ownership, speaking engagements and receipt of awards, as well as financial reporting requirements (including public disclosure).

The report has been generally well-received, with the Association of American Medical Colleges noting in a statement that:

"These recommendations would help create a robust, credible, and more transparent system to monitor potential financial conflicts of interests…their speedy adoption will help sustain and strengthen the public's essential trust in the NIH's intramural research programs, and more broadly in the extramural biomedical science enterprise."

The 109-page report can be read online at: http://www.nih.gov/about/ethics_COI_panelreport.htm.

Computers Combat Disease:

New Modeling Grants Target Epidemics, Bioterror

A new initiative harnesses our nation's computing skill to enhance our ability to respond to disease epidemics and bioterrorism. The initiative, called MIDAS, will develop powerful computer modeling techniques to analyze and respond to infectious disease outbreaks, whether they occur naturally, such as SARS, or are released intentionally in a bioterrorist attack. MIDAS (an acronym for Models of Infectious Disease Agent Study) is sponsored by the National Institute of General Medical Sciences (NIGMS), a part of the National Institutes of Health (NIH) that has a strong interest in bioinformatics and computational biology.

NIGMS recently awarded the first four grants in this new initiative, totaling more than $28 million over five years. Three of these grants will support the creation of mathematical models to study various aspects of infectious disease epidemics and community responses. These research grants together total $9.5 million over five years (averaging more than $640,000 per grant for the first year). A fourth award, totaling $18.8 million over five years ($3 million for the first year), funds researchers to develop a central database to organize information from the other three groups. It also supports the development of user-friendly computer modeling tools for the broader scientific community, policy makers and public health officials to use to simulate epidemics and response strategies.

"MIDAS will play a key role in the NIH biodefense plan," said Elias A. Zerhouni, M.D., NIH director. "The computer models created through this initiative will help us determine the best strategies to detect, control and prevent the spread of disease."

MIDAS will bring together interdisciplinary teams of scientists with expertise ranging from mathematics and computer science to epidemiology, genetics, and public health. The network of MIDAS scientists will be guided by a steering committee of investigators with broad expertise in modeling, infectious diseases and public health. This committee will establish policies for the network, set standards for data management, evaluate progress and provide a forum for the exchange of ideas within and beyond the MIDAS network.

"MIDAS is designed not only to help prepare us for infectious disease crises, but also to be an active part of the response," said Jeremy M. Berg, Ph.D., NIGMS director. "In the case of a national medical emergency, MIDAS scientists can redirect their work to help government officials quickly determine the best way to deal with the epidemic."

"The modeling tools will also advance our ability to study complex systems with many interacting parts, which is essential to truly understand biological processes," he added.

The awards have been made to:

A collaboration of scientists at the Johns Hopkins Bloomberg School of Public Health (lead), the Brookings Institution, the National Aeronautics and Space Administration, the University of Maryland and Imperial College (London). This research group will create highly visual, user-friendly computational analyses of disease outbreaks. These models will use historic and modern data about epidemics and incorporate factors such as disease incubation period, transmission rate, weather patterns, peoples' individual susceptibility and social networks. The researchers will then introduce and evaluate the effectiveness of containment methods like vaccination, contact tracing and quarantine. They will initially focus on smallpox, dengue fever and West Nile virus, then will apply their model to study other infectious agents. (Donald Burke, M.D., principal investigator)

A group of scientists at Los Alamos National Laboratory. This research group will explore the effects of social networks in hypothetical urban areas (population 1.5 million) on the spread and possible containment of multiple, interacting disease-causing organisms. The scientists will model how social contacts might change in response to an outbreak or to intervention strategies. They will modify the social networks and populations to simulate epidemics in a variety of hypothetical cities. (Stephen Eubank, Ph.D., principal investigator)

A research team at Emory University. This research group will model a disease outbreak in hypothetical American communities (population sizes 2,000 to 48,000) to find the best method(s) of controlling the epidemic. The researchers will examine the effectiveness of policies including surveillance and containment, vaccination, medical treatment and the closing of key institutions. They will adapt their model for smallpox, SARS, pandemic influenza and other possible bioterrorism agents or naturally occurring diseases. They will also investigate how certain microorganisms cause disease within individual people and then spread through a population. (Ira Longini, Ph.D., principal investigator)

An informatics group spearheaded by Research Triangle Institute International. This team includes members with diverse expertise from SAS Institute, Inc., IBM and Duke and Emory universities. The group will provide the scientific community, policy makers and medical personnel with a wide array of computational and analytic tools and data sources tailor-made to model emerging infectious diseases and public health responses. (Diane Wagener, Ph.D., principal investigator)

More information about MIDAS and other NIGMS-supported efforts to model infectious diseases is available at http://www.nigms.nih.gov/research/midas.html.

NIGMS supports basic biomedical research that lays the foundation for advances in disease diagnosis, treatment and prevention. For NIGMS news releases, science education booklets and other materials, visit www.nigms.nih.gov. NIGMS is part of the National Institutes of Health, U.S. Department of Health and Human Services.

Presence of Gene Mutation Tightly Linked to Drug Effectiveness in Lung Cancer

Mutation of a gene involved in non-small cell lung cancer (NSCLC) increases the likelihood that the drug gefitinib (Iressa™) will show a beneficial response, researchers at the Dana-Farber Cancer Institute, the National Cancer Institute (NCI) and two other institutions announced in the online version of *Science*, May 6, 2004. Previously, gefitinib had been shown to cause tumor regression in certain patients, but researchers had not been able to predict which patients would be responsive to the drug. With this discovery, doctors will be able to select those lung cancer patients who could most benefit from gefitinib and may identify additional patients with other types of cancer who may respond to similar treatments.

The mutation discovered was in the epidermal growth factor receptor (EGFR), a gene that codes for an enzyme in the tyrosine kinase family of proteins. Tyrosine kinases are a class of enzymes involved in cellular signaling that have been shown to undergo mutations in various cancers. Inhibition of this type of enzyme has recently been a focus for scientists, but gefitinib had not been as effective as some had expected based on earlier clinical trials conducted in Japan.

The gene mutations identified in this study cause the kinase to be overactive. The sensitivity to gefitinib in both patients entered into a clinical trial and to tumor cells grown in a lab was shown to be highly correlated with the presence of tumors that contained these EGFR mutations. While this type of drug sensitivity was shown earlier for the drug imatinib (Gleevec), which is most effective against certain leukemias and gastrointestinal stromal tumors that possess specific genetic mutations, this is the first demonstration of a targeted therapy in a common adult malignancy.

"One of the more striking results we found in this study was the difference in response between Japanese and American patients, which raises the question of genetic variation in different ethnic, cultural, and geographic groups to this particular drug," said Dr. Bruce E. Johnson of the Dana-Farber Cancer Institute, who led the Lung Cancer Biology Section at NCI before leaving for Dana-Farber.

To conduct the study, researchers examined 58 lung cancer tumors from Japan (Nagoya City University Hospital) and 61 tumors from the United States (Harvard Medical School). They also examined additional tumors from U.S. patients who had demonstrated a response to gefitinib. The presence of EGFR mutations and the best clinical response to gefitinib therapy occurred most frequently in women, non-smokers, and in patients with a lung cancer called adenocarcinoma.

Gene mutations were seen in 26 percent of Japanese NSCLC cancer patients vs. only 2 percent of American patients. Japanese women with adenocarcinoma showed the highest percentage of EGFR mutations (57 percent) and also showed the best clinical response to gefitinib. Lung cancer is the leading cause of cancer death in the United States and worldwide for both men and women.

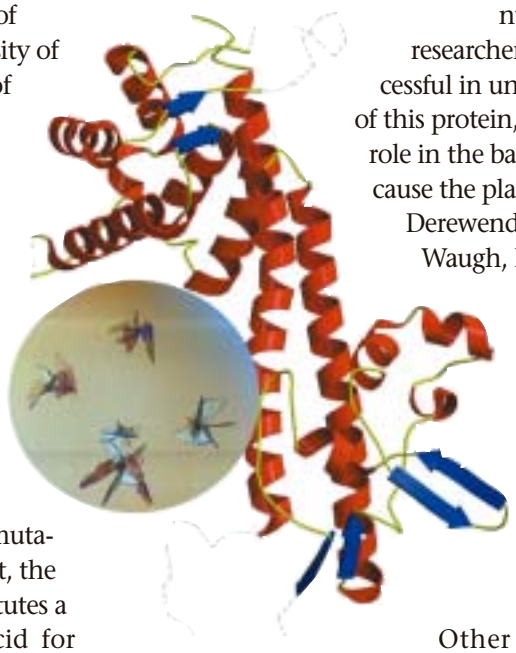
"This is another example of successfully exploiting our ever-increasing understanding of the genetic aberrations of cancer," said Andrew C. von Eschenbach, Director, NCI. "Understanding how to maximize the benefits of anti-EGFR treatments should improve the outcome for many patients with lung cancer. In addition, the larger percentage of EGFR mutations in patients from Japan compared to the United States is striking and raises many unanswered questions, suggesting new avenues for basic research, as well as new considerations in the design of clinical trials."

'Crystal Engineering' Helps Scientists Solve 3-D Protein Structures

Research Aids Drug Design; Sheds Light on Plague and Other Diseases

A new technique for engineering protein crystals is helping scientists figure out the three-dimensional structures of some important biological molecules, including a key plague protein whose structure has eluded researchers until now. The technique, developed with support from the National Institute of General Medical Sciences (NIGMS) of the National Institutes of Health (NIH), promises to help pharmaceutical companies develop more effective drugs to treat various diseases by tailor-making molecules to "fit" a protein's shape.

In the cover article of the April 2004 issue of *Structure*, University of Virginia School of Medicine researcher Dr. Zygmunt Derewenda, described how his group was able to coax certain proteins to crystallize by carefully altering their surfaces using "targeted mutagenesis." In effect, the technique substitutes a small amino acid for certain large ones. This effectively shrinks bulky groups of atoms on protein surfaces that might otherwise prevent the proteins from crystallizing.



"In order to determine a high-resolution structure of a protein, we need to study it in its crystal form," Dr. Derewenda explained. "Yet many proteins do not crystallize easily, or even at all, with current laboratory techniques. Using our approach, we can make some of these proteins more amenable to crystallization without seriously affecting their overall structure or function."

Already, the crystal engineering technique has helped solve the structures of some particularly stubborn proteins, including the so-called *V antigen* of *Yersinia pestis*, the bacterium that causes the plague. Despite numerous attempts, researchers had been unsuccessful in unlocking the secrets of this protein, which plays a key role in the bacterium's ability to cause the plague. Working with Derewenda's group, David S. Waugh, Ph.D., of the NIH's National Cancer Institute in Frederick, Md., was able to crystallize the protein and then determine its structure by X-ray diffraction.

Other large biological molecules whose structures were recently solved thanks to the new technique include a protein complex containing ubiquitin, which is involved in a wide range of cellular processes.

The technique was also used by a team at Merck Research Laboratories to yield a much more accurate structure of a potential anticancer drug target called insulin-like growth factor-1 receptor.

Development of the technique was made possible by funding from NIGMS' Protein Structure Initiative, a 10-year project launched in 2000 that is aimed at dramatically reducing the time and cost of solving protein structures.

Photo Courtesy of Dr. Urszula Derewenda

ASBMB Welcomes New Ph.D.s

ASBMB extends its congratulations to these individuals who recently received their Ph.D. degrees. In recognition of their achievement, ASBMB is presenting them with a free one-year membership in the Society. The new Ph.D.s are listed below with the institution from which they received their degree.

Dan Chen
University of California, San Diego

Dony Maiguel
University of Maryland, Baltimore

Shawn Sweeney
University of Texas, A&M University

Misty J. Ward
University of Arkansas

Katharine H. Wrighton
Kings College, University of London

Redox Signaling in Biology and Medicine

A Special ASBMB-Sponsored Symposium

Kiawah Island, South Carolina October 21-24

Organizers: **Roy J. Soberman**, *Harvard Medical School and Massachusetts General Hospital*
Larry Marnett, *Vanderbilt University*

Living in an environment rich in oxygen has given all organisms on earth the benefit of a flexible energy source; and, as all students of biochemistry know, eukaryotes have the ability to convert the redox properties of oxygen into energy.

It has become increasingly clear that the biological benefits and consequences of oxidation-reduction are far more complex than was appreciated even five years ago. Mammals, in particular, have evolved the ability to sense and use oxidation-reduction. We are continually balancing this use of oxygen as a source of energy against the byproducts of these beneficial processes, the generation of oxygen radicals leading to cellular damage, death, and disease.

These radicals come from a variety of sources including mitochondrial disruption, the activation of cellular NADPH oxidases, and the metabolism of xenobiotics. These processes and other forms of oxidative stress can lead to lipid peroxidation, protein damage, and mutations in DNA. Not only have mammals evolved a highly flexible system to sense changes in oxygen tension and the cellular redox state, but we have evolved the ability to use these changes to transmit information in cells. Furthermore, the systems that use redox-based signaling to transmit biological information are highly organized, and form a signaling universe, different, but equally as intricate as the signaling pathways that employ the reversible addition of phosphates to impart information.

Because of the increasing breadth and impact of redox signaling on diverse areas of biology, ASBMB has decided to bring together investigators from differing, but overlapping areas of research for a small, focused meeting October 21-24 at Kiawah Island, South Carolina. We are fortunate to have a range of outstanding speakers participating. Our Plenary Speaker will be Dr. Stephen L. McKnight of the University of Texas, who will discuss the regulation of mammalian clock genes, which are regulated by the ratio of NAD/NADH.

The cell nucleus is the ultimate site in which information must be delivered in an organized manner to allow transcription of genes. How redox changes are interpreted at the level of transcription and in the nucleus is the focus of one of four major sessions at this meeting. "**Interpreting Redox and Oxygen Changes in the Cell Nucleus**" will be chaired by Dr. William Kaelin of the Dana Farber Cancer Center and will focus on questions in this area.

All organisms, and mammals in particular, have evolved a number of transcription factors that employ different molecular mechanisms to directly sense changes in cellular oxidation-reduction states and oxygen tension. Recognition of HIF-1a by the Von Hipple-Lindau protein is linked to enzymatic hydroxylation of conserved prolyl residues in HIF-1a by members of the EGLN family of proteins. This results in the oxygen-dependent degradation of HIF-1a. Clock genes are regulated by the ratios of NADH/NAD. Finally, the development of mitochondrial permeability and damage can be sensed indirectly by a remarkably interesting protein Apoptosis-Inducing Factor (AIF) that has differing functions in the mitochondria and nucleus. This subject will be addressed by Dr. Susan Ackerman of the Jackson Labs.

How do cells use oxidation-reduction to transmit informa-

Continued on page 17

Transcriptional Regulation by Chromatin and RNA Polymerase II

A Special ASBMB-Sponsored Symposium

Organizer: **Ali Shilatifard**, *St. Louis University School of Medicine*

Developmental processes are regulated by differential gene expression, controlled principally at the level of transcription of messenger RNA (mRNA). Synthesis of mRNA in eukaryotic organisms is a highly orchestrated and harmonious process whose perturbation results in developmental complications. During the past few years, transcription and chromatin biology has become one inseparable field. RNA polymerase II and the basal transcriptional machinery play essential roles in modification and remodeling of chromatin. Chromatin and its posttranslational modifications play a pivotal role in the regulation of gene expression. Importantly, this field has now entered a post-genomic era defining global gene expression analyses. There is a rapid growth in this area, with many investigators trying to define the molecular mechanisms of gene expression control by chromatin and RNA polymerase II.

Due to the expansion in the breadth and impact of the regulation of gene expression in cellular development and pathogenesis of human diseases, ASBMB is bringing together investigators from different, but overlapping, areas of research for a small, focused meeting entitled **Transcriptional Regulation by Chromatin and RNA polymerase II,** October 29 to November 1 at Granlibakken Resort at Lake Tahoe, Tahoe City, California, organized by Dr. Ali Shilatifard, Saint Louis University Medical Center and Saint Louis University Cancer Center.

There are invited speakers, but most talks will be chosen from the submitted abstracts. Thus, there is ample opportunity for both oral and poster presentations. Invited speakers include Drs. Joan and Ronald Conaway of the Stowers Institute, who will deliver the plenary lecture. Other symposium speakers include Shelley Berger, Jacques Côté, Dale Dorsett, Barbara Graves, Tony Kouzarides, Robert Roeder, Ramin Shiekhattar, Kevin Struhl, and Jerry Workman.

The plenary lecture, **Ubiquitin Ligases and Transcriptional Regulation,** by the Conways will describe recent work from their laboratory on the role of transcription factor modification by ubiquitination and regulation of gene expression by RNA polymerase II.

Defining how changes in chromosomes and chromatin alter transcription and development will be the focus of the first session, **Chromosome, Chromatin and Transcription,** to be chaired by Dr. Dale Dorsett, Saint Louis University School of Medicine. Dr. Barbara Graves, Huntsman Cancer Institute, will chair the second session, **Transcription Machinery, From Structure to Function,** which will focus on the role played by transcription factor structures in the biology of gene expression. The third session, **Posttranslational Modifications of the Transcription Machinery,** will be chaired by Dr. Shelley Berger of the Wistar Institute, and will bring together recent studies on the role of histone and transcription factor modifications and the regulation of mRNA synthesis.

The fourth and the fifth sessions, **Transcriptional Initiation, Elongation and Termination,** will be chaired by Dr. Robert Roeder, Rockefeller University, and Dr. Shilatifard. These two sessions will concentrate on recent studies defining the diverse biological roles of basal transcriptional initiation factors, co-activators, and elongation factors in cellular differentiation and development. Dr. Tony Kouzarides, University of Cambridge, will chair the sixth session, **Transcriptional Regulatory Complexes,** which will explore the role of many macromolecular complexes implicated in transcriptional regulation.

Meeting Organizer Ali Shilatifard

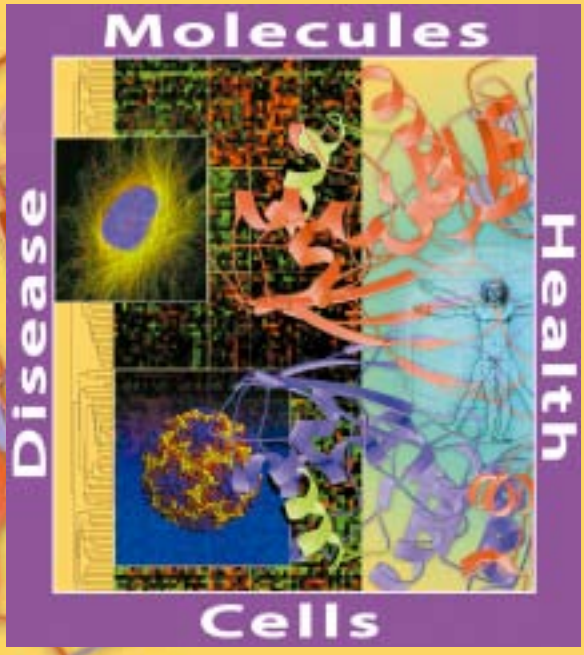
The final session, **Genomic/Proteomic Approaches in Transcription,** will be chaired by Dr. Ramin Shiekhattar of the Wistar Institute, and will reflect on post-genomic global gene expression studies defining many aspects of transcriptional regulation.

For more information and to register email asbmb@asbmb.org, A large portion of the oral presentations will be selected from the submitted abstracts. Status (talk/poster) of abstracts will be posted on the ASBMB website, www.asbmb.org, by September.

All registrations and abstracts MUST be submitted by the abstract deadline, August 1. Due to space limitation (about 200 participants) we anticipate an oversubscription for this meeting. Late registration may be accepted after the abstract deadline if the meeting is not over-subscribed. In the event of over-subscription, we will make every effort to make sure that as many as possible of the research groups who wish to participate are represented.

See you at Granlibakken this fall.

See You Next Year in San Diego!



2005 ASBMB Annual Meeting

Held in conjunction with EB 2005

April 2-6, 2005

San Diego, CA

Meeting Organizers

Dennis R. Voelker, National Jewish Medical Research Center

Cecile Rochette-Egly, IGBMC, Strasbourg

and the 2005 ASBMB Program Planning Committee

Symposia Themes

Dynamics of Protein—Protein Interactions (Bumping in the Night)
Chair: Ben Margolis, HHMI, University of Michigan

DNA Replication and Associated Processes/Recombination/Repair
Chair: Charles S. McHenry, University of Colorado Health Sciences Center

Coordinate Regulation of Transcription
Chair: Cecile Rochette-Egly, IGBMC, Strasbourg

Interactions and Functions of Glycoconjugates
Chair: Mark A. Lehrman, University of Texas Southern Medical Center

Specificity in Signaling Networks
Chair: Alex Toker, Beth Israel Deaconess Medical Center

Minority Affairs Committee Symposia
Chair: Phil Ortiz, Empire State College

Biochemistry and Molecular Biology of Lipids
Chair: Charles O. Rock, St. Jude Children's Research Hospital

Organelle Biogenesis and Dynamics
Co-Chairs: Carla Koehler, UCLA and Danny Schnell, University of Massachusetts, Amherst

Proteolysis and Disease
Chair: Charles Craik, University of California, San Francisco

Catalysis: Structure, Function, and Evolution
Chair: John Gerlt, University of Illinois, Urbana-Champaign

Metabolic Regulatory Circuits
Chair: M. Daniel Lane, Johns Hopkins University School of Medicine

Genomes and Proteomes
Chair: Andrew Link, Vanderbilt University

Experimental Biology 2005

www.asbmb.org/meetings

ASBMB American Society for Biochemistry and Molecular Biology

Redox Signaling continued ...

Continued from page 14

tion from the surface of the cell to engage specific signaling pathways? This is a complex question, but two molecules that are used are hydrogen peroxide (H_2O_2) and are Nitric Oxide (NO). These molecules can reversibly oxidize, or react with sulfhydryl groups, with the resulting changes engaging signaling pathways and modifying cell functions. Two sessions will focus on the molecular basis of how cells regulate the use of H_2O_2 and NO to transmit information.

We are fortunate to have Dr. Michael Marletta from Berkeley and Dr. Linda Roman from University of Texas San Antonio, to participate in the session "**Signaling by Nitric Oxide**" chaired by Dr. Bettie Sue Masters, the current President of ASBMB.

The mechanisms by which cells use redox based signaling will be further addressed in a second signaling session "**Signaling by H_2O_2 and Sulfhydryl Bonds**" chaired by Roy Soberman of Harvard Medical School. Topics ranging from signaling networks of H_2O_2 (Dr. Soo Gue Rhee of the NIH) to the role of redox signaling in controlling aspects of the immune response (Dr. Peter Cresswell, Yale; Dr. M. Amin Arnaout, Harvard; and Dr. David Hildeman, University of Cincinnati) will be discussed.

Finally, the session entitled "**The Cellular Consequences of Redox Signaling**" chaired by Dr. Larry Marnett of Vanderbilt University, will address the consequences of redox signaling and oxygen radicals in cells. This section will emphasize not only the biological importance of cellular damage, but state-of-the art approaches to identifying the post-translation modification of proteins and DNA secondary to oxidative damage, including lipid peroxidation.

Obesity

It May Be How You're Wired

New studies by Howard Hughes Medical Institute researchers at show that the appetite-regulating hormone leptin causes rewiring of neurons in areas of the brain that regulate feeding behavior.

The discovery is another important clue about how leptin exerts its effects on the brain to cause decreased food intake and increased energy expenditure, said the researchers. The research also suggests that natural variability in the "wiring diagrams" of the neural feeding circuits of individuals may influence whether a person will be obese or lean.

The research team, which was led by HHMI Investigator Jeffrey M. Friedman at Rockefeller University and Tamas L. Horvath at Yale University School of Medicine, published its findings in the April 2, 2004, issue of the journal *Science*.

Dr. Friedman and his colleagues discovered leptin in 1994. They also showed that it is produced by fat tissue and secreted into the bloodstream, where it travels to the brain and other tissues, causing fat loss and decreased appetite. In the brain, leptin affects food intake by acting on distinct classes of neurons in the hypothalamus that express the leptin receptor.

Leptin decreases feeding and fat deposition by acting on two classes of neurons. Leptin suppresses the activity of neuropeptide Y (NPY) neurons and it enhances the activity of proopiomelanocortin (POMC) neurons. Conversely, the absence of leptin increases feeding and fat deposition by exciting NPY neurons and suppressing the activity of POMC neurons.

While the action of these two types of neurons had been inferred, said Friedman, there had been no direct studies exploring the specific mechanism by which leptin affected the neurons.

Jeffrey M. Friedman

"There are a number of theoretical ways in which a molecule such as leptin might modulate the activity of neurons," said Dr. Friedman. "And I'm sure it's the case that leptin can act in many different ways. But what we have discovered is a particularly striking modality of action that wasn't what we initially would have suspected was the likeliest."

The major problem in studying in detail the action of leptin on NPY and POMC neurons was in distinguishing the two classes of neurons, according to Dr. Friedman. "If you just look at a region of the brain, you can't tell one neuron from the next," he said. "And in this case, you had in one brain region neurons theorized to stimulate appetite right next to those believed to inhibit appetite."

The solution, he said, was to genetically engineer mice to have NPY and POMC neurons that each expressed a distinctive version of a green fluorescent protein. These fluorescent proteins literally lighted the way for the scientists to perform detailed studies of the action of leptin on the two neuronal types.

The researchers generated both normal mice and those deficient in leptin production — called ob/ob mice — containing the fluorescently labeled neurons. They then compared the neurons in the two strains of mice.

One of the co-lead authors in the *Science* paper — Aaron G. Roseberry in Friedman's laboratory — compared the electrophysiological properties of the two types of neurons, in both normal and ob/ob mice. These studies revealed the relative activity of the two types of neurons in the two mouse strains.

Another co-lead author — Shirly Pinto in Friedman's laboratory — worked with Horvath to perform comparative microscopy studies of the labeled neurons in the two strains of mice. These studies revealed the relative numbers of excitatory and inhibitory neuronal connections in the two types of mice.

Both sets of studies revealed that leptin acted directly to rewire the neuronal feeding circuitry itself in the brains of mice, specifically suppressing NPY neurons and exciting POMC neurons.

The researchers also found that administering leptin to the leptin-deficient ob/ob mice produced changes in neuronal connections—and their elec-

"If we knew that the basic circuitry that controls feeding is wired differently in different people, it might change public perception of the causes of obesity," said HHMI investigator Jeffrey M. Friedman.

trical activity—to mimic those of normal mice. The neuronal changes preceded the behavioral changes in the ob/ob mice. This is significant, according to Dr. Friedman, because it suggests a cause-and-effect relationship between the rewiring and feeding behavior.

Furthermore, when the researchers tested the effects of ghrelin, another appetite-stimulating peptide, on the two types of neurons in normal animals, they also observed a decrease in excitatory connections to POMC neurons. "Taken together, the findings with leptin and ghrelin suggests that the findings of this rewiring are general," he added. "Overall, these findings begin to suggest that the wiring diagram of the feeding circuit is highly dynamic, and they lead us to at least ask to what extent is the wiring diagram of these neural circuits different in obese people relative to lean people.

"If we knew that the basic circuitry that controls feeding is wired differently in different people, it might change public perception of the causes of obesity," said Dr. Friedman. "Some people might have a more potent drive to eat and to weigh more than do others. And it might mean that conscious factors can't fully explain how a person eats."

Such findings might also contribute in time to a broader understanding of why administering leptin can reduce weight in some obese people and animals, but not in others. The variable response to leptin suggests that some individuals are obese because they are leptin resistant. Advances about how leptin works in the brain could contribute to a better understanding of leptin resistance and obesity, and may ultimately lead to new ways to combat obesity, explained Dr. Friedman.

Gene Linked to Brain Development

With the identification of the gene responsible for a newly recognized type of mental retardation, researchers at Beth Israel Deaconess Medical Center (BIDMC) have also discovered what appears to be the key target in the evolution of the frontal lobes of the brain's cerebral cortex. The findings, reported in the March 26, 2004, issue of the *journal Science*, offer a key insight into the complex puzzle of human brain development—and the evolution of human behavior.

"The cerebral cortex is the part of the brain that distinguishes humans from other species," explains the study's senior author Christopher A. Walsh, a Howard Hughes Medical Institute investigator in the Neurogenetics Division at BIDMC and Bullard Professor of Neurology at Harvard Medical School. "And the frontal lobes are the part of the cortex that govern social function, cognition, language, and problem-solving. Patients with damage to the frontal lobes exhibit changes in behavior, and frontal lobotomies were once performed to alter aggressive behavior."

Bilateral frontoparietal polymicrogyria (BFPP), a recessive genetic disorder characterized by mental retardation, gait difficulty, language impairment and seizures, results in severely abnormal architecture of the brain's frontal lobes, as well as milder involvement of parietal and posterior parts of the cerebral cortex.

In this new study, lead author Xianhua Piao and colleagues used magnetic resonance imaging (MRI) to identify BFPP patients, and then used linkage analysis, homozygosity mapping, and candidate gene analysis to identify the BFPP gene as GPR56, located on an area of chromosome 16.

"We showed that mutations in GPR56, which encodes an orphan G protein-coupled receptor (GPCR), were responsible for BFPP," explained Dr. Piao. GPR56 is expressed in the neural stem cells produced in the cerebral cortex, and plays an especially important role in the frontal portions of the cortex.

Walsh's laboratory uses gene mapping to identify genes that disrupt the normal development of the brain's cerebral cortex, thereby helping to define the clinical syndromes of certain human developmental disorders and develop diagnostic tests for at-risk individuals. These new findings, he says, suggest that GPR56 may have been a key target in the evolution of the cerebral cortex.

"The frontal lobes of the human brain are the most highly developed part relative to other animals and it has long been thought that the evolution of the frontal lobes parallels the development of human communication and civilization," Dr. Walsh added. "Being able to access the complete sequence of the human genome has allowed us to identify increasing numbers of genes that are required for cortical development. Although these genes cause mental retardation, by studying the biological function of their gene products we also gain insight into the normal development and function of the human brain."

Fulbright Offers Lecturing/Research Grants in 140 Nations

This past year some 800 U. S. faculty and professionals taught or conducted research in over 140 countries as Fulbright Scholars. Their grants enabled them to expand their professional interests, enrich their teaching, and advance their scholarship.

Grantees come from all areas of the humanities, social sciences, and natural and physical sciences, as well as from applied fields such as business, journalism, and law. Grants are awarded to faculty of all academic ranks, including adjunct and emeritus.

Opportunities are available not only for college and university faculty and administrators but also for professionals from business and government, as well as artists, journalists, scientists, lawyers, independent scholars, and many others.

Traditional Fulbright awards are available from two months to an academic year or longer. A short-term grants program, the Fulbright Senior Specialists Program, offers two- to six-week grants in a variety of disciplines and fields.

While foreign language skills are needed in some countries, most Fulbright lecturing assignments are in English. Some 80 percent of the awards are for lecturing.

Application deadlines for 2005-2006 awards are:

August 1, 2004 for Fulbright traditional lecturing and research grants worldwide.

November 1, 2004 for the summer German Studies Seminar and for spring/summer seminars in Germany, Korea, and Japan for academic and international education administrators.

For more information and to register and apply online go to www.cies.org.

Resilience Through Improvisation

Our cells are resourceful when it comes to copying DNA, even when the DNA is damaged.

Billions of cells divide every day in our bodies to replace those that wear out. To be able to do so, their DNA must be copied. A new Weizmann Institute study shows that the molecules in charge of the task of copying DNA (DNA polymerases) are able to improvise in order to achieve this crucially important goal. This new insight into DNA replication and repair could assist in the diagnosis and treatment of diseases in which DNA damage is involved, such as cancer. The findings appeared in the December 9, 2003, issue of *Proceedings of the National Academy of Sciences*. (http://www.pnas.org/cgi/content/full/100/25/14760).

DNA polymerases travel along the DNA, producing new "printouts" each time the cell divides. This genetic information is passed on in our bodies and from generation to generation. However, problems begin when the DNA is damaged due to factors such as cigarette smoke, radiation, and certain reactions in the body. Though our body possesses special enzymes that fix DNA, some damage escapes their notice–and DNA polymerases must deal with it.

ASBMB member Zvi Livneh, Professor in the Department of Biological Chemistry, at the Weizman Institute, and postdoctoral student Ayelet Maor-Shoshani cut a DNA strand from an *E. coli* plasmid and inserted material similar to that which composes crude oil. As expected, the regular DNA polymerase stopped working when it reached the foreign material. However, a specialized DNA polymerase jumped in to rescue the stalled replication process, and continued the copying, inserting nonexistent genetic components into the "printout" when it encountered the foreign material. This can be compared to people who may forget a few words in a song but make up new ones so they can continue to sing along.

In other cases, the specialized DNA polymerase skipped over the foreign material or deleted it and thus was able to continue its work as usual. "This shows the remarkable capability of a cell to reproduce," reported Dr. Livneh. "And it makes one hope that even if extreme types of chemicals are accidentally introduced into our DNA, the body will be able to manage."

Still, when DNA polymerase improvises a tune, mutations may occur in the new cells' DNA. If too many mutations occur, this increases the risk of disease, primarily cancer. Obviously, the best situation would have been to minimize exposure to DNA damage in the first place, or to repair the damage in an error-free manner. However, in most cases, there are damages that need to be dealt with also with less ideal ways, like killing the cell, or causing a mutation. Cells have a difficult choice to make, However, Dr. Livneh says, since that the body cannot feasibly let all cells with damaged DNA die, for there are too many of them. "Only if the DNA contains a very high level of damage will the cell's machinery give up and let the cell die," he explained. "We do not yet fully understand the making of the decision to kill a cell or continue replication and cause a mutation. However, once this issue is clarified, we might have chance to harness the knowledge to help fighting diseases like cancer."

Disorderliness in Some Proteins Lets Them Interact With Diverse Molecules

Discovery of the sequence of events in the binding of p27 to a protein complex is a model for explaining how 30% to 40 % of the body's proteins exploit their flexibility in order to do different tasks in the cell

Investigators at St. Jude Children's Research Hospital have demonstrated for the first time that—contrary to the long-held belief among scientists that proteins must maintain a highly ordered structure in order to perform an assigned task—many proteins actually exploit disorderliness in their structure to perform a variety of different jobs. The findings of this research appear in the current, online issue of *Nature Structural and Molecular Biology*. The St. Jude finding explains how many of the body's proteins can adapt their structures to the needs of the moment, binding to different molecules depending on the job at hand.

"The potential importance of disorder in the function of some proteins has been discussed by researchers for several years," said Richard W. Kriwacki, Associate Member of the St. Jude Department of Structural Biology and senior author of the report. "But until now no one had actually demonstrated how such flexibility allows a protein to interact with different molecules. We've taken a big step in understanding the subtle details of a critical biochemical process in the life of the cell."

Previously, other researchers suggested that 30% to 40% of the body's proteins do not rely on a rigid structure to interact with target molecules. In the current study, the St. Jude team verified that idea by showing how a protein called p27 uses two flexible arms to help it bind to a protein complex called Cdk2-cyclin A. This interaction is important because Cdk2-cyclin A is one of the so-called "master timekeepers" of cell division. These timekeepers trigger sequential events leading to the production of new daughter cells. By binding to Cdk2-cyclin A and blocking its activity, p27 disrupts this sequence and prevents the cell from dividing. The importance of p27's role in regulating cell division is highlighted by findings showing that loss of p27 function is a key contributing factor in several types of cancer.

The researchers demonstrated that the p27 protein resembles a relatively rigid helical (twisted) rod with a wobbly piece of spaghetti hanging off each end. One of the wobbly arms binds to cyclin A, while the other arm binds to Cdk2.

When p27 is by itself in a solution, the arms are loose and disordered. But when p27 encounters Cdk2-cyclin A, one of its arms binds to cyclin A by folding into a rigid shape. After the first arm binds, the center rod settles across the entire Cdk2-cyclin A complex. Finally, the second arm also folds into a rigid shape onto the Cdk2 part of the complex. In this way, proteins such as p27 act as molecular 'staples' that fasten onto their targets.

> ***"We've taken a big step in understanding the subtle details of a critical biochemical process in the life of the cell."***
>
> **—Richard W. Kriwacki,**

"The very act of binding to the Cdk2-cyclin A complex makes the loose, disordered arms of p27 fold up and become rigid," Dr. Kriwacki explained.

The researchers also discovered how proteins like p27 can identify and bind to complexes with different types of Cdk and cyclin, such as Cdk4-cyclin D—an ability that is critical for them to correctly identify which complexes they are supposed to regulate.

"We discovered that all Cdk molecules look pretty much alike to p27," Dr. Kriwacki said. "But a certain part of each type of cyclin is unique. The first flexible arm of p27 recognizes only certain types of cyclin, based on that unique part of the molecule. The first arm binds to this part of the cyclin, and the rest of the p27 follows along."

Using nuclear magnetic resonance spectrometry, which combines radio wave emissions and a powerful magnetic field to determine the structure of proteins suspended in solutions, the team determined the shape of p27 when it was unbound. In order to study the interaction between p27 and Cdk2-cyclin A, researchers in the St. Jude Hartwell Center for Bioinformatics and Biotechnology used a technique called surface plasma resonance. This technique measures the changes in the reflection of light off p27 before and after it binds to Cdk2-cyclin A.

Lack of Specific Brain Protein Causes Marked Deficits in Learning, Memory

A protein involved in the release of neurotransmitters in the brain is essential to learning and memory in mice, researchers at the University of Texas Southwestern Medical Center at Dallas have found.

A study published in *Neuron*, April 8, 2004, offers the first evidence that lack of this protein—known as RIM1 alpha—causes profound deficits in the learning process. The discovery is a major step in understanding the molecular events that underlie learning and memory – complex processes that can be impaired in human neuropsychiatric disorders such as Alzheimer's disease, mental retardation and schizophrenia.

"We found that when you delete this molecule, the mice essentially become incredibly stupid," said Thomas Südhof, Director of both the Center for Basic Neuroscience and the C. Vincent Prothro Center for Research in Basic Neuroscience at UT Southwestern and co-author of the paper.

Researchers hope that further study of the protein's role in learning and memory will lead to potential treatments for some neuropsychiatric disorders.

"This is the first indication that these proteins could be good targets for treatment of specific brain disorders," said Craig Powell, Assistant Professor of Psychiatry and Neurology at UT Southwestern and the study's lead author.

The researchers compared behaviors of normal mice to those of three sets of genetically altered mice—each of which was missing a specific protein involved in releasing neurotransmitters. The mice lacking the RIM1 alpha protein, unlike the others, lacked the ability to learn the location of an escape platform in a pool of water despite repeated attempts over several days.

Dr. Eric Nestler, chairman of psychiatry at UT Southwestern and senior author of the study, said another notable finding was that, while the other two sets of genetically altered mice displayed some of the same cellular abnormalities as the RIM1 alpha mice, these other mice exhibited no behavioral deficits.

"The brain was able to compensate for the loss of these other two proteins, but it was not able to compensate for the lack of RIM1 alpha," Dr. Nestler said. "That tells us that RIM1 alpha is involved in so many important functions that, when it is missing, gross changes in behavior occur."

Proteins involved in the release of neurotransmitters are known as presynaptic proteins. In the past, postsynaptic proteins, as opposed to presynaptic proteins, were shown to play an active role in learning and memory. Postsynaptic proteins receive the neurotransmitters released by presynaptic proteins.

Swiss Computing Center Opens

A new computing center that will provide life scientists with access to high-performance hardware and a software consulting service has been established by the Swiss Institute of Bioinformatics, the Universities of Lausanne, Geneva, and Basel, l'Ecole Polytechnique Fédérale de Lausanne, and the Ludwig Institute for Cancer Research in Lausanne, in collaboration with Intel Corporation and Hewlett-Packard (HP).

Inaugurated this past April, the Lausanne-based Vital-IT center is equipped with two HP clusters of 32 production and 8 development servers, based on Intel's Itanium 2 processor. These kinds of clusters allow life scientists to run complicated software 10 to 50 times faster, thereby opening new research avenues, says Christos Ouzounis at the European Bioinformatics Institute. "You can think of problems that you could not think of otherwise if you had a limited computational capacity," he told The Scientist.

The impact of the new computing power may soon be felt not only by scientists directly associated with Vital-IT, but by researchers worldwide who use the services available through the Swiss Institute of Bioinformatics, such as proteomics tools on the ExPASy (Expert Protein Analysis System) servers.

The Vital-IT center also employs four information technology specialists who have access to the full technological know-how of Intel and HP. According to the center's director, Victor Jongeneel, a major aim is to develop software for the life sciences that is more robust and that performs better than the current programs, which are often written by people who are not professional programmers.

The new software will run on the Itanium 2 architecture, which is particularly suited for large-scale computational problems.

by John D. Thompson, Editor

Protein-centric Drug Development and Functional Glycomics

Researchers are beginning to see a potential for breakthrough in healthcare through glycomics.

"The rapid evolution of glycomics as a natural extension of proteomics provides a better understanding of glycoproteins, glycosylation process, and its role in the protein function," according to Frost & Sullivan Industry Analyst Giridhar Rao. "This in turn facilitates the development of novel biodrugs."

The rapid progress of glycomics in the biopharmaceutical industry is evident from the existence of approximately half a dozen drugs, in which manipulation of carbohydrates and proteins provides advanced drug properties. For example, Epogen—a glycotherapeutic drug—contains two additional carbohydrate groups that can extend circulatory half-life and magnify efficiencies.

Active research on glycosyltransferases to understand the role of carbohydrate interactions in a cancerous cell is also likely to provide further opportunities for application of glycomics. One such prospect lies in the development of protein serum-based cancer diagnostics.

Glycoprotein therapeutics is the fastest growing segment in the biopharmaceuticals industry with an annual growth rate of 24 percent, which is expected to accelerate further, according to Frost & Sullivan. However, maintaining adequate manufacturing capacity is a critical challenge.

"With around 100 protein-based drugs that are in late-stages of human clinical trials, few are likely to hit the market in the coming years," says Rao. "Hence, raising the demand for production capacity at least by four times more than the existing capacity. This may be essential to maintain the demand-supply equilibrium."

This creates an urgent need for alternate manufacturing media such as transgenic plants and animals, besides the mammalian and microbial and fungal cell culture systems.

Where Now Novartis?

With Novartis having been foiled in its bid to acquire Aventis, by the French government's outspoken aversion to the very thought of a Swiss firm taking over one of France's pharmaceutical titans, industry observers are wondering what will be the next move for Daniel Vasella, Novartis' hard-charging leader. Many of those observers are also skeptical of the wisdom of France's preference for Sanofi-Synthelabo as opposed to Novartis.

Novartis, after all, has the edge on distribution to doctors in the U.S., the world's biggest pharmaceutical market, and has a record of getting more of its research than either Aventis or Sanofi. In addition, a quarter of its sales come from products less than five years old, with 11 of them approved by the FDA in the past four years. As a result, 40 percent of Sanofi's sales are in products that face patent expiration as early as 2006 compared to just 17% of Novartis products.

Could Novartis be looking next door in Basel, where Vasella's firm has already acquired nearly a one-third stake in Roche. The two firms, after all, have very compatible marketing strategies. Novartis focuses on general practitioners while Roche targets specialists. The fly in that ointment, however, is in the form of Roche's two founding families. They have a controlling share in the company plus an agreement preventing its sale until 2009. Can Novartis wait that long, and is there any incentive for a well-performing Roche to a well-performing Roche to take on a partner whose shares have been languishing for the past seven years.

Biotech Moving Slowly in Europe

A recent report on the European Commission's Life Sciences and Biotechnology Strategy pointed to slow and partial implementation of EU legislation by some member states as a major obstacle to the development in the life sciences and biotechnology.

The report, released in April, faults the member states for inaction that is hampering the biotech industry's development, discouraging innovators and the potential investors whose finance is so desperately needed. One problem cited in the report concerns proposed legislation for the protection of biotechnological inventions. The commission says that the failure of eight member states to implement such legislation "leaves companies engaged in innovative biotechnology research uncertain as to whether they are fully entitled to the commercial fruits of their work."

Institute for Systems Biology, Pacific Northwest National Laboratory Announce Collaboration

The Institute for Systems Biology (ISB) and the Pacific Northwest National Laboratory (PNNL) have formed a Joint Program in Systems Biology which is expected to focus on expanding and strengthening the technical capabilities of each organization in systems biology and related areas.

"PNNL brings to the world of biology enormous technical and computational capabilities, which are fundamental to our ability to transform biology and medicine," said ISB President Leroy Hood, in announcing the agreement. "We are excited about this partnership as it provides a unique opportunity to leverage these capabilities in a way that will further our efforts in studying and applying systems biology and ultimately lead to predictive and preventive medicine."

The program's goals include building the infrastructure to solve complex biological problems faster, refining the technological and computational abilities to measure and predict complex cell, and to strengthen existing collaborative research and development projects in systems biology.

Those current collaborations include "computational approaches to predicting protein structure," said H. Steven Wiley, Director of the Biomolecular Systems Initiative at PNNL, which manages the NIH Proteomics

European Space Project Eyes Commercial Research

The European Space Agency (ESA) is seeking to gain more revenue from scientific research in outer space. increasing efforts to encourage life science companies to use the International Space Station and other ESA facilities for zero-gravity research, according to ESA officials.

Maurizio Belingheri, who directs ESA's commercial projects, recently told *The Scientist* that the agency would like to see 30% of its research to be conducted by life science companies. He said the agency would be retaining agents to contact such firms and encourage them to submit research proposals to ESA. The agency last year opened bidding from life science–focused firms interested in being the agency's primary commercial agent for attracting research in the fields of health, biotechnology, food, and nutrition, and hopes to name its commercial agent by June.

Firm To Set Up Nanomanufacturing Plant

Luna Innovations of Blacksburg, Virginia., has announced plans to establish a nanomanufacturing facility in Danville. The plant will produce buckyball materials for medical diagnostics and other military and commercial applications. This technology was developed in part with a 2001 award from the National Institute of Standards and Technology's (NIST) Advanced Technology Program (ATP). The ATP grant helped to accelerate the development process for new nanomaterial-based medical reagents.

The Danville plant, sited in the city's old tobacco warehouse district, will produce Trimetaspheres, soccer ball-shaped molecules made of a carbon exterior which encloses three metal atoms. Trimetaspheres, a discovery made at Virginia Tech and exclusively licensed to Luna Innovations, are expected to have a major impact as a contrast agent for magnetic resonance imaging (MRI). The molecules reportedly provide enhanced MRI images at least 25 times better than currently marketed contrast agents. In addition to improving imaging and enabling smaller, less expensive MRI machines, Trimetaspheres can be modified chemically to make them soluble and to attach specific molecules that seek out cancer cells, or other targeted cells.

The company also plans to manufacture empty cage buckyballs and nanocomposite thin films. Commercial applications for these materials include both consumer and military products with possible uses in vehicle parts, stain resistant textiles, ship hull coatings and fuel cells.

HHMI Seeks up to 50 New Scientists

The Howard Hughes Medical Institute (HHMI) is seeking as many as 50 new scientists in the field of biomedical research through a national competition announced today.

The Institute is looking for candidates from the full range of biological and biomedical inquiry who demonstrate exceptional promise early in their careers as independent researchers. Nearly 200 universities, medical schools, and research institutes have been invited to nominate their best scientists for the competition. Between 30 and 50 scientists will be chosen to join the Institute in 2005.

"HHMI places a high value on innovation and our distinctive approach to supporting biomedical research frees our scientists to use their creativity to extend the boundaries of scientific knowledge," said Thomas R. Cech, President of the 50-year-old philanthropy.

He said the competition represents a commitment by the Institute to invest as much as $350 million in additional support for biomedical research over the next seven years. HHMI's annual research budget now stands at nearly $500 million a year.

Currently, the Institute employs 318 scientists who head Hughes laboratories at 66 universities, medical schools, and research institutes through long-term research collaboration agreements. These scientists and their research groups study fundamental biological questions, including the causes of many human diseases such as Alzheimer's, diabetes, and AIDS.

Mark Your Calendar

ASBMB Annual Meeting in Conjunction with EB2005

April 2 – 6, 2005, in San Diego

$250,000 in Grants for HIV/AIDS Research

GlaxoSmithKline (GSK) will award $250,000 in grants for innovative HIV/AIDS drug research in recognition of the need to produce new alternatives and hope in the fight against the HIV/AIDS pandemic. Since the inception of the program in 2001, GSK has awarded $1.25 million and honored 14 researchers for their groundbreaking work toward new pharmaceutical strategies to combat the HIV virus.

Applications are now being solicited for 2004 research grants and must be submitted by July 31. For detailed information about the GSK Drug Discovery and Development Research Grant Program, as well as an application, call 1-888-527-6935 or visit www.dddresearchgrant.com.

The one-time research grants range from $25,000 to $150,000 and are intended to further the development of inventive treatments for HIV/AIDS, including therapies aimed at treating infection, prophylactic vaccines, or microbicides designed to prevent transmission of the virus.

The grants carry no obligation to the recipient's organization for licensure, patenting, or transfer of confidential information, although GSK may discuss the possibility of future collaboration with some applicants.

Research grant recipients will be announced in October 2004 at the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Washington, D.C. The grants will be paid December 1, 2004.

Career Opportunities

RESEARCH ASSISTANT PROFESSOR

Department of Medicine/ Gastroenterology, Tulane University

Research Assistant Professor in the Department of Medicine/Gastroenterology to study the molecular basis of gastrointestinal cancer. Job responsibilities include establishing a productive research project, overseeing graduate students and postdoctoral fellows, some lab administration duties and teaching undergraduate/graduate courses at the Department of Medicine. Requires: M.D. or Ph.D. degree in Cell Biology or related field and minimum of three years research experience in biochemistry, molecular and cellular biology. Essential requirements include scientific writing skills and completion of a postdoctoral fellowship in molecular or cancer biology. Send resumes to Robert Coffey, M.D., Department of Medicine, Gastrointestinal Division, Vanderbilt University, 4140 MRB III, Nashville, TN. 37232-8355.

MOLECULAR SYSTEMS BIOLOGY

TENURE TRACK POSITION IN MASS SPECTROMETRY OR CHEMICAL BIOLOGY

Center for Advanced Research in Biotechnology (CARB)

Applications are invited for a tenure-track faculty position at the level of Assistant, Associate, or full Professor. The successful applicant will be expected to develop a rigorous, externally funded research program using modern mass spectrometry or chemical approaches to study and manipulate biological processes at the molecular level. A competitive startup package will be provided.

CARB is developing an integrated program in molecular systems biology, to include components in chemical biology, mass spectrometry, structural biology, bioinformatics, experimental and computational biophysics, and systems modeling. Six new faculty hires are anticipated over the next two years, and a new research building equipped with state-of-the-art facilities is under construction and will open in 2005. We are particularly interested in applicants who are seeking a highly collaborative research environment.

A research center of the University of Maryland Biotechnology Institute and the National Institute of Standards and Technology, CARB has strong existing programs in areas that include macromolecular crystallography, high-resolution NMR spectroscopy, and experimental and computational molecular biophysics. See www.carb.nist.gov for further information.

Applications should include a curriculum vitae, a statement of research plans, and three letters of reference, sent to Chair, Faculty Search Committee (Position # 300491), Center for Advanced Research in Biotechnology, 9600 Gudelsky Drive, Rockville, MD 20850. Review of applications will begin on 7/1/04 and will continue until a suitable candidate is selected.

The University of Maryland Biotechnology Institute is an Equal Opportunity/Affirmative Action Employer. Women, minorities, veterans, and candidates with disabilities are encouraged to apply.

FACULTY POSITION

DIVISION OF CLINICAL NUTRITION & DIETETICS PROGRAM

School of Health Related Professions, The University of Alabama at Birmingham

Applications are invited for a full-time, regular, twelve-month faculty position, in the Division of Clinical Nutrition & Dietetics Program, Department of Nutrition Sciences, School of Health Related Professions, The University of Alabama at Birmingham. Salary, academic rank, and tenure status will be commensurate with qualifications and experience. Responsibilities include participation in teaching, scholarly activities, and service. A masters degree in Nutrition or a masters degree in Exercise Physiology and at least 2 years experience is required. Current registration with the Commission on Dietetic Registration and licensure with the Alabama Board of Examiners for Dietetic/Nutrition Practice required. To apply, submit your curriculum vitae to:

Sarah L. Morgan, MD, RD, Chair,
Search Committee
For Instructor Faculty Position
1714 9th Avenue South
Birmingham, Alabama 35294-1270
205-934-3235

UAB is an Equal Opportunity/Affirmative Action Employer

Calendar of Scientific Meetings

JULY 2004

International Conference on Genomics, Proteomics and Bioinformatics for Medicine

July 14-19 • 2004 Moscow, Russia
Fx: +7 (095) 245-0857
http://www.ibmh.msk.su/gpbm2004/english.htm

4th ANNUAL CONFERENCE OF FOCIS (Federation of Clinical Immunology Societies)

July 18-23 • Montréal, Canada
Early Registration: April 30, 2004
Website: www.immuno2004.org

AUGUST 2004

12th International Conference on Second Messengers and Phospoproteins

August 3–7 • Montreal, Canada
Contact: smp2004@eventsintl.com
Website: http://www.secondmessengers2004.ca

FASEB Conference: Transcriptional Regulation During Cell Growth, Differentiation, and Development

August 14–19 • Saxtons River, Vermont
Co-organizers: Barbara Graves and John Tamkun
Go to http://src.faseb.org to fill out online application.
Student travel awards available.

Macromolecular Organization & Cell Function

August 15–20 • Queen's College, Oxford, UK
Ph: 401-783-4011; Email: grc@grc.org
Website: http://www.grc.uri.edu/programs/2004/macromol.htm

EuroScience Open Forum 2004: Highlighting Science, Technology & Innovation in Europe

August 25–28 • Stockholm
Contact: Gabriella Norlin, Project Leader
Phone: +46 8 546 44 154; Fax: +46 8 546 44 155
Email: gabriella.norlin@esof2004.org
Postal address: Swedish Research Council
SE-103 78 Stockholm, Sweden

International Congress on Biocatalysis 2004

August 29–September 1 • University of Technology, Hamburg, Germany
Contact: Gerlinde Loebkens; FON +49-40-76618012
FAX +49-40-76618018; e-mail: loebkens@tutech.de
Website: www.biocat2004.de

8th International Symposium on the Maillard Reaction

August 28–September 1 • Charleston, South Carolina
For detailed information about the meeting, including abstract submission, a call for papers and deadlines.
Website: http://Maillard.chem.sc.edu
Email: Maillard@mail.chem.sc.edu

5th Meeting on Methods in Protein Structure Analysis

August 29-September 2 • University of Washington, Seattle
Ph: 206-706-8118; Email: mpsa2004@u.washington.edu
Website: http://depts.washington.edu/biowww/mpsa2004/

SEPTEMBER 2004

Relaxin 2004: Fourth International Conference on Relaxin and Related Peptides

September 5-10 • Grand Teton National Park, Jackson Hole, WY
This conference will present recent advances on the chemistry, physiology, and pharmacology of relaxin, related peptides, and their receptors.
Email: relaxin-2004@ad.uiuc.edu
Website: http://www.life.uiuc.edu/relaxin2004/

Stem Cell Biology: Development and Plasticity

September 16-19 • Scheman Continuing Education Building Iowa State University, Ames, Iowa.
Abstracts due July 16, 2004; Registration deadline: August 16, 2004
Student Travel Grant Applications due July 16, 2004
Contact: Growth Factor and Signal Transduction Conferences Symposium Office
Ph: 515-294-7978; Fx: 515-294-2244; Email: gfst@iastate.edu
Website: http://www.bb.iastate.edu/-gfstlhomepg.htmi

Cellular and Molecular Basis of Regeneration EuroConference on the Molecular Pathways Leading to Regeneration

September 18–23 • San Feliu de Guixols, Spain
Contact: European Science Foundation, EURESCO Office
Ph: +33(0)3 88 76 71 35; Fx: +33 (0)3 88 36 69 87
Email: euresco@esf.org; Website: http://www.esf.org/euresco

OCTOBER 2004

Cytokines in Cancer and Immunity: Joint Conference of ICS and ISICR

October 21-25 • San Juan, Puerto Rico
An exceptional meeting bringing together leading investigators in cytokine biology, cancer and immunology.
Keynote speakers: Michael Karin and Tak Mak.
Abstract deadline: June 11, 2004
Email: info@cytokines2004.org; Fax: 706 228-4685
Website: www.cytokines2004.org

An ASBMB Sponsored Symposium:
Redox Signaling in Biology and Disease

October 21 – 24 • Kiawah Island, South Carolina
Organized by Larry Marnett, Vanderbilt U. and Roy J. Soberman, Harvard Med. School
Plenary Lecture: Regulation of Mammalian Clock Genes
Steven L. McKnight, U. of Texas, Southwestern Medical Center
Contact: Joan Geiling, Ph: 301-634-7145; Fax: 301-634-7126
Email: asbmb@asbmb.org; Website: www.asbmb.org

An ASBMB Sponsored Symposium:
Transcriptional Regulation by Chromatin and RNA Polymerase II

October 29 - November 1 • Granlibakken, Lake Tahoe, California
Organized by Ali Shilatifard, St. Louis U. School of Med.
Keynote Speakers: Joan Conaway and Ronald Conaway
Contact: Joan Geiling, Ph: 301-634-7145; Fax: 301-634-7126
Email: asbmb@asbmb.org; Website: www.asbmb.org

NOVEMBER 2004

4th International Congress on Autoimmunity

November 3–7 • Budapest, Hungary
Deadline for Receipt of Abstracts: June 20, 2004
Contact: 4th International Congress on Autoimmunity Kenes International—Global Congress Organisers and Association Management Services,17 Rue du Cendrier, PO Box 1726, CH-1211 Geneva 1, SWITZERLAND
Ph: +41 22 908 0488; Fx: +41 22 732 2850
Email: autoim04@kenes.com
Website: www.kenes.com/autoim2004

American Association of Pharmaceutical Scientists AAPS Annual Meeting and Exposition

November 7-11 • Baltimore, Maryland
Ph: 703 243 2800; Fx: 703 243 9650
Website: www.aapspharmaceutica.com/meetings/futuremeetings/

Second National Meeting of the American Society for Matrix Biology

Nov 10–13 • San Diego, California
Contact: ASMB, 2019 Galisteo Street, Building I-1, Santa Fe, NM 87505; Ph: 505 989-4735; email: cindi@sciencemanagers.com
Website: http://www.asmb.net

DECEMBER 2004

American Society for Cell Biology, 44th Annual Meeting

December 4-8 • Washington, DC
Ph: 301-347-9300; Fx: 301-347-9310
Website: http://www.ascb.org/

Department Heads Take Note:

ASBMB Offers Free Membership to New Ph.D.s

ASBMB is now offering a free one-year Associate membership to all students who have, within the past year, earned a Ph.D. degree in the molecular life sciences or related areas.

ASBMB implemented this program as a way to recognize the significant accomplishment of earning the Ph.D., and to provide new Ph.D.s with something tangible and of economic value. Membership in ASBMB brings with it a free subscription to the online versions of the *Journal of Biological Chemistry* and *Molecular and Cellular Proteomics,* as well as subscriptions to *The Scientist* and the Society's magazine, *ASBMB Today*, discounts on other publications, and a host of other benefits.

The Society is asking department chairs to provide ASBMB with the names and addresses of each new Ph.D. recipient from their institutions. Upon receipt of this information, we will write the new Ph.D.s to congratulate them on their accomplishment and offer the free one-year membership in ASBMB. Names and addresses of the new Ph.D.s should be sent to:

Kathie Cullins
Membership and Subscriptions Manager
American Society for Biochemistry
& Molecular Biology
9650 Rockville Pike
Bethesda, MD 20814
Email: asbmb@asbmb.faseb.org

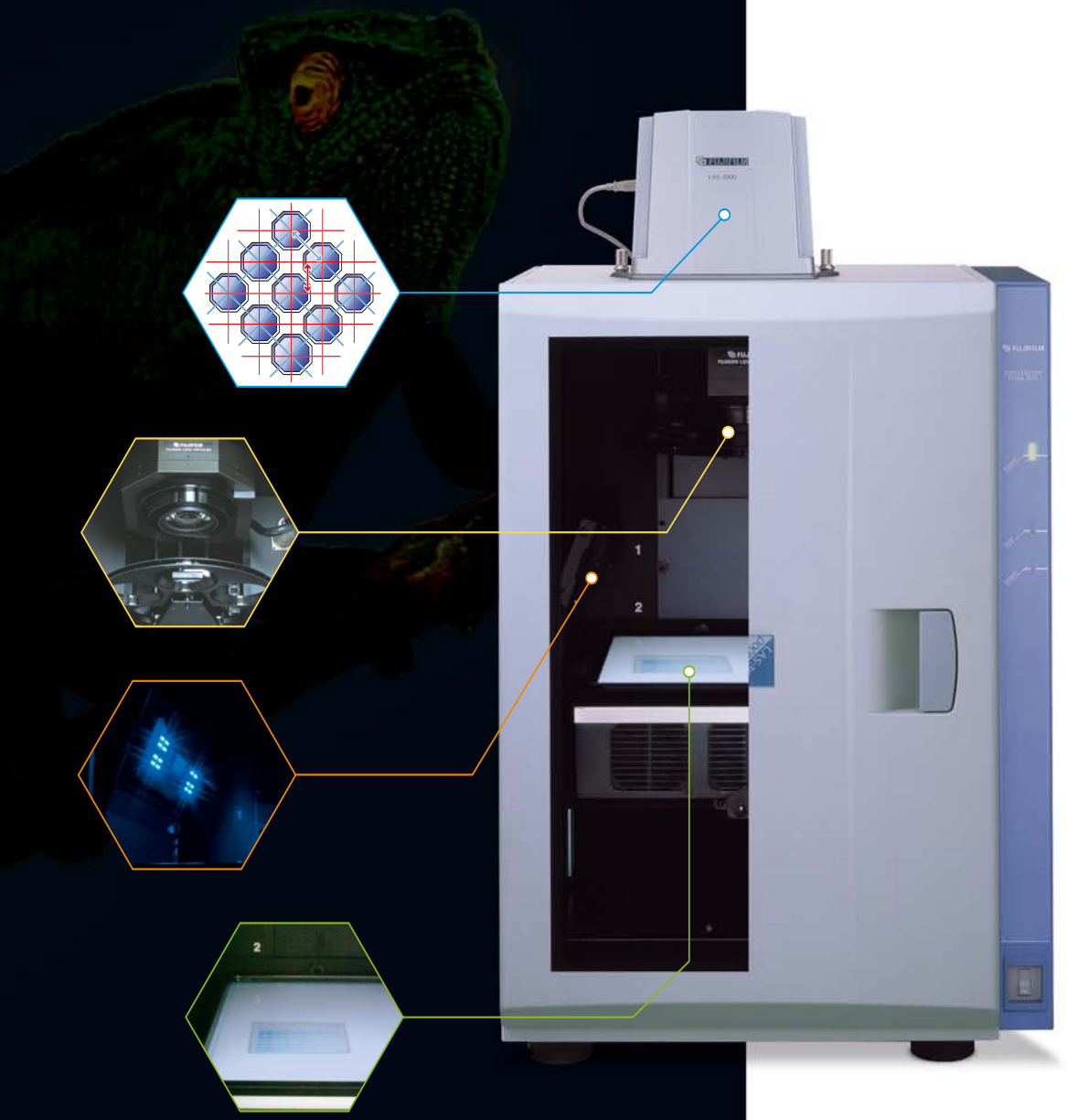
This is an ongoing project; please advise us whenever a student in your department earns the Ph.D., so that we can make this free membership offer to him or her.

FUJIFILM
I&I – Imaging & Information

Science Systems
Luminescence - Fluorescence - Digitization

Introducing Fujifilm's new LAS-3000 Imaging System.

SUPER CCD TECHNOLOGY LETS YOU SEE THE UNEXPECTED.



- Super CCD imaging chip
- High-sensitivity FUJINON camera lens
  5-position filter wheel
- Blue epi-illuminator
  White light epi-illuminator
- White light transilluminator
  UV transilluminator

As a complete system, the LAS-3000 can be used for Chemiluminescence, Fluorescence, UV visualization and Digitization.

APPLICATION VERSATILITY

The LAS-3000 with Super CCD is ideal for a variety of applications including Western blots, stained gels and membranes, 1-D gels, 2-D gels, microtiter plate-based assays (in conjunction with the Fresnel lens tray) and applications in genomics/proteomics.

FEATURES

- 5-position electric turret makes filter selection convenient and fast
- 4 levels of function supported by unique software result in enhanced sensitivity
- 4 optional light sources allow flexibility of applications
- Software control of illumination, filter wheel and focusing

Japan Tel: +81-3-3406-2201
Fax: +81-3-3406-2158
http://home.fujifilm.com/products/science/index.html
Email: sginfo@tokyo.fujifilm.co.jp

Europe Tel: +49-211-5089-174
Fax: +49-211-5089-139
http://www.fujifilm.de
E-mail: mkaling@fujifilmeurope.de

U.S.A. Tel: +1-203-324-2000 ext. 6112
(1-800-431-1850 ext. 6112 in the U.S.A.) Fax: +1-203-351-4713
http://www.fujimed.com
E-mail: SSG@fujimed.com

Booth 223 & 225