FEBRUARY2004

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AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

ALSO IN THIS ISSUE

2004: A Difficult Year for Biomedical Research

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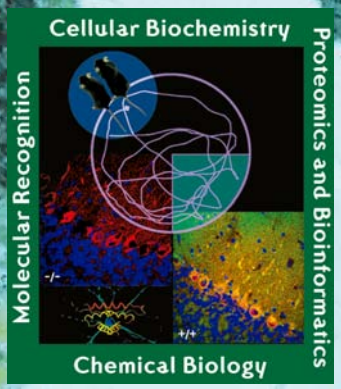

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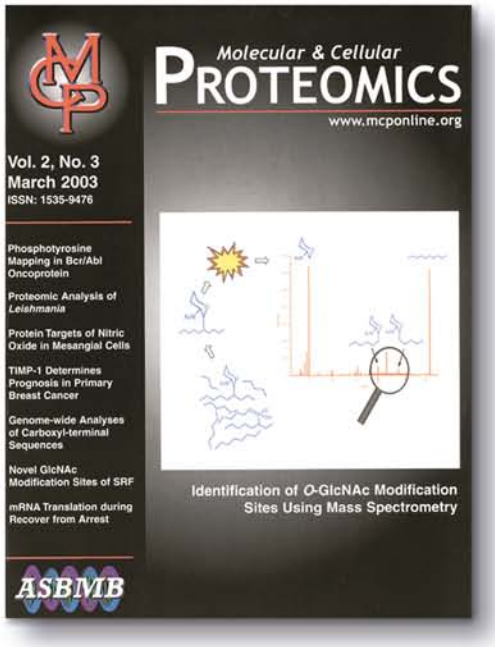

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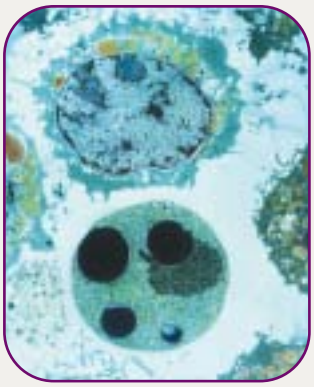
features



ON THE COVER:
Colored transmission electron micrograph (TEM) of a section through a human myeloid white blood cell (leukocyte, lower center) during apoptosis. The apoptotic cell no longer has typical protuberances from its cell surface and its nucleus (black) is breaking down.

Credit: Dr Gopal Murti / Photo Researchers, Inc.

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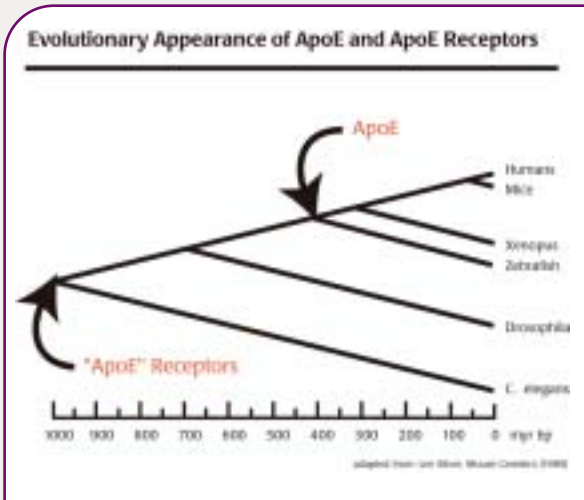

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departments

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Comments

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John Whitehead Named

Philanthropist John Whitehead has been selected as the 2004 recipient of the Howard K. Schachman Public Service Award. The annual award "recognizes an individual who best demonstrates dedication to public service in support of biomedical science." Past recipients of the award, instituted in 2002, are Honorable John Edward Porter and Ruth L. Kirschstein.

ASBMB President Bettie Sue Masters informed Mr. Whitehead, the founder of the Campaign for Medical Research (CMR), of his selection in early December, noting that "we are cognizant of your many contributions to the advancement of biomedical research through your diligent and constant efforts to maintain the awareness level of the U.S. Congress with respect to the funding of the National Institutes of Health. No one has been more generous with their time and resources than you."

"I am speechless," Mr. Whitehead declared upon learning the news of his selection. "John Porter and Ruth Kirschstein are really giants for their contributions, each in their own way, to the medical research enterprise. I am deeply honored and humbled to be recognized along with them by ASBMB."

In an interview with *ASBMB Today*, Mr. Whitehead noted, "I have been interested in biology for as long as I can remember. In college I majored in biology and chemistry and I went on to study biochemistry in graduate school for several years. During my working career, I ran several biotech, analytical chemistry, and multi-disciplinary R&D organizations. I also served (and continue to serve) on several biotech boards. During the 1970s and early 80s, I was very involved with my father in organizing the Whitehead Institute."

Schachman Award recipient John Whitehead

Mr. Whitehead joined the Research!America Board in 1992 and began to pay attention to the Washington politics of medical research funding. At this time he noted, "U.S. spending on basic biology research had fallen well below the minimum investment required to be an important contributor to our country's economic future."

By the mid-1990s, the idea of doubling the NIH budget began to take hold, "but there was no clear legislative

2004 Schachman Award Recipient

strategy to make it happen. In late 1997, with the help and advice of a lot of people in Washington, we decided to form a lobbying group to promote a unified strategy for the NIH doubling. Accordingly, in early 1998, the Campaign for Medical Research was born." Over the next five years, Whitehead's and CMR's tireless efforts made enormous contributions to completing the doubling of the NIH.

With the achievement of that goal, "Our challenge now," Whitehead said, "is to maintain the gains and momentum we achieved."

This will not be easy. President Bush proposed a 2 percent increase for NIH in 2004, and Congress was set to approve no more than a 3.7 percent increase for NIH in late January. The President is expected to propose only a 2 percent increase for NIH for FY 2005.

Whitehead continues to be involved in biomedical research advocacy and urges the community to do the same. First, he noted that many of the Congressional champions who enabled the NIH doubling have retired, with the exception of Senators Arlen Specter (R-PA) and Tom Harkin (D-IA). He says that the community needs to cultivate "a new generation of champions."

"We also need to make sure the importance of the NIH is reflected in the campaign platforms of the Presidential candidates in 2004.

He continued, "The science community needs to get comfortable with the idea of speaking out in easy-to-understand words on the importance of the research enterprise—to lay people, to the media, and to the folks in Washington. Power, money and connections are important, but our elected officials need votes to stay in office. When constituents speak clearly, frequently and in numbers, the politicians listen!

"Finally, the advocacy and public outreach efforts of the science community need to be joined with those of the major disease groups. Molecules and test tubes are interesting, but nothing matches the emotional appeal of a disease survivor or the ravaged family of a patient who has succumbed to disease."

As for Whitehead's own intentions for the future, "I hope to continue to play a constructive role in the medical research advocacy community. We are working, now, to broaden the leadership of the Campaign for Medical Research, so that it has an institutional life and agenda that can be sustained beyond the efforts any one person or small group of people. Further, I hope to explore ways in which we can constructively broaden our NIH advocacy efforts to coordinate effectively with the larger science community."

The Schachman Award is named after Howard K. Schachman, who served as Chairman of ASBMB's Public Affairs Advisory Committee for more than 10 years, as well as in a variety of other public capacities in addition to his responsibilities as teacher and researcher at the University of California, Berkeley. The award consists of a keepsake, as well as a stipend or charitable contribution of $5,000. In addition, the recipient is invited to deliver a lecture at the ASBMB annual meeting.

by Peter Farnham, CAE, ASBMB Pulic Affairs Officer

Happy New Year—Not;

The great American philosopher Yogi Berra once observed, "You gotta be careful when you make predictions—especially about the future." Yogi's always sage advice notwithstanding, here is one prediction we can make: 2004 will be a difficult year for biomedical research in a variety of ways, from funding, to policy issues involving the National Institutes of Health, to the upcoming elections. In some cases, trouble looms not only from Washington, D.C., but also at the state and international levels.

Funding

The Federal budget is, as usual, in a state of chaos. Fiscal Year 2004 began on October 1, 2003, and Congress left town for the holidays in December with seven appropriations bills uncompleted. These bills had been rolled into a gigantic omnibus appropriations bill which the House passed on December 8. But it was not until January 22 that the Senate finally approved this bill. The bill contains $328 billion in discretionary spending and $820 billion overall.

For NIH, the conference report includes $27.983 billion, an increase of $1 billion (3.7 percent) over FY 2003. However, the conference report also includes a 0.59 percent across-the-board cut, which reduces the NIH budget to $27.818 billion. This amount will be reduced further by the transfer of $150 million from the NIH for the Global HIV/AIDS fund, as well as a 2.2 percent departmental evaluation transfer "tap." These various demands on the NIH budget reduce the effective increase from $1 billion to about $736 million, about 2.8 percent over the program level for FY 2003.

For 2005, the President is expected to propose a 2.5 percent increase for NIH, about $695 million. This is slightly better than the biomedical community had been expecting—a flat 2 percent. Unfortunately, rough calculations indicate that an increase this parsimonious will mean about 1,000 fewer new and competing renewal grants being funded in 2005 than in the previous year.

Trapped in the same omnibus bill as NIH funding was funding for the National Science Foundation, which fared a bit better than NIH. The agency was slated for a $300 million increase to about $5.61 billion. Factoring in the across-the-board cut of $33 million, the agency will get about $5.58 billion this year. This increase represents a rare occasion when the agency gets a larger percentage increase (about 5.6 percent) than NIH. So far, we have been unable to learn what the administration intends to ask for NSF for 2005. However, the administration plans to hold discretionary spending increases to about 3 percent overall; thus, NSF can probably expect an increase in the 2 - 2.5 percent range.

Stem Cells/Cloning

For the past two years, human stem cell research opponents and advocates have fought to a draw in Congress. Opponents have been able to pass a human stem cell research ban in the House, but advocates hold enough votes in the Senate to forestall passage of such a ban. The issue will very likely come up again in Congress this year, with similar results expected.

In some ways this continuing stalemate is unfortunate, because no one in Congress supports reproductive cloning, that is, cloning to produce a human infant, and there is widespread fear that irresponsible fanatics will attempt to clone a human child. Indeed, a cult called the Raelians—which believes human life began from clones planted here by aliens—claims it has already done so. A bill narrowly targeted at human reproductive cloning would pass with little if any opposition. The problem is that many opponents of reproductive cloning also oppose therapeutic cloning, that is, somatic cell nuclear transfer (SCNT), and are pushing for a ban on this type of cloning as well.

2004 will be a difficult year for biomedical research, from funding, to policy issues involving the National Institutes of Health, to the upcoming elections.

While stalemate continues in Washington, there are growing efforts to advance the anti-stem cell agenda in

2004 Outlook Tough at Best

state legislatures around the country. In 2003, 29 state legislatures considered stem cell legislation. Unfortunately, most of the bills introduced would have banned SCNT as part of a general ban on reproductive cloning—such a ban is now in effect in four states—and we can expect these efforts to continue in 2004.

However, the news is not all bad. California passed a bill specifically allowing SCNT research to continue while banning reproductive cloning, and last December New Jersey followed suit, becoming the second state to allow SCNT research. Also, ASBMB, and President Bettie Sue Masters in particular, played an integral part in defeating anti-SCNT legislation in Texas last fall. To build upon these successes, the ASBMB public affairs officer is working on a state legislative affairs initiative; which should soon have some capacity to mobilize our greatest asset—you, our members—to support research issues when they threaten to become politicized in the capitals of states receiving the greatest amount of federal research funding.

SCNT research is also under fire at the international level. This past fall ASBMB was involved in an effort to head off a proposed UN treaty, supported by the United States, that would ban SCNT research worldwide. Enough outcry was raised that a vote on the treaty was put off until fall 2004; however, biomedical researchers have a lot of work to do before then to convince the United States to change its position.

NIH's Woes Continue

The Congress, having completed doubling the NIH budget in 2003, is now exercising its oversight role with vigor, and the House Energy and Commerce Committee has launched a whole host of investigations. The latest is focused on conflicts of interest involving senior NIH staff who have financial relationships with pharmaceutical companies and yet are allegedly overseeing clinical trials involving drugs produced by these same companies. This allegation surfaced in a December 8 article in the Los Angeles Times that named specific senior NIH officials as being involved in such situations. The Energy and Commerce Committee has demanded detailed information, and Senator Arlen Specter (R-PA) held a hearing on the issue at the end of January (we will report on this hearing in the March issue of *ASBMB Today*).

This flap is only the latest in a string of congressional inquiries about how NIH has been conducting its business since the doubling. For a look at these inquiries, visit the House Energy and Commerce Committee website at http://energycommerce.house.gov/, and click on "letters" (all committee investigational letters are posted by month). Letters focusing on NIH were sent in March, June, July, November, and December.

Oh, Yeah—the Election

Finally, Senator Specter, our greatest champion in Congress, is facing primary opposition this spring. Rep. Pat Toomey (R-PA) has launched a campaign to unseat Specter as the Republican nominee. While Specter is probably not in too much trouble, Toomey is running a spirited campaign and is even trying to use Specter's unwavering support for NIH against him. Last summer Toomey attempted to delete funding for seven NIH grants that dealt with gender and sexual behavior. Toomey's efforts failed, but not by much. Since then, a second, more determined effort has been launched by the Traditional Values Coalition, which has identified over 200 NIH grants that the Coalition considers inappropriate subjects for research.

This flap is only the latest in a string of congressional inquiries about how NIH has been conducting its business since doubling the NIH budget in 2003.

So, as we enter 2004, we are facing an election year, the country is at war, budget deficits are expected to approach $450 billion next year, and the sea of red ink is expected to persist for at least the next five years. Given these facts about the overall situation, it is a wonder that NIH and biomedical research are doing as well as they are.

NIH Revises Rules on Conflicts of Interest

In the first week of the new year, the National Institutes of Health finalized changes to financial conflict of interest regulations for outside experts participating in peer review of research grants and research and development contracts. The new rules raise the financial threshold for such conflicts from $5,000 to $10,000 per year, and attempt to clarify distinctions between "real" and "apparent" conflicts. The new financial threshold of $10,000 is the same as in other federal regulations

House and Senate subcommittees, meanwhile, are planning hearings to review allegations, first reported in the *Los Angeles Times* on December 7, 2003, that senior NIH officials secretly received millions of dollars in consulting contracts from pharmaceutical and biomedical companies that had dealings with the agency. Three days later, Dr. Zerhouni announced the creation of a "blue ribbon panel" to review how NIH addresses outside consulting activity "in order to identify systemic solutions for improvement."

The rules published in the *Federal Register* on January 5 apply to outside experts participating in scientific review groups. The final regulations were scheduled to go into effect February 4.

The term "finances" includes all sources of income, including fees, honoraria, and stock holdings. "These provisions are intended to allow for routine sharing and exchange of scientific information as a result of invitations to speak at seminars, scientific consultations, and similar events that would not automatically be considered a conflict of interest for the reviewer," according to the Federal Register.

The new rules state that a "real" conflict exists when the financial threshold is met, when the reviewer acknowledges the presence of an interest that would likely bias his or her review, or when the official managing the review determines the reviewer has such an interest. An "apparent" conflict occurs when the financial threshold for a "real" conflict has not been met but other personal interests exist that would "cause a reasonable person to question the reviewer's impartiality." Under certain conditions, the NIH director can make a determination allowing a "real" or "apparently" conflicted peer reviewer to participate.

Representatives Billy Tauzin (R-La.), chairman of the House Energy and Commerce Committee, and James Greenwood (R-Pa.), chairman of the Subcommittee on Oversight and Investigations, plan to hold hearings on NIH's consulting practices. The hearings were expected to begin as early as January 22.

Honey Bee Genome Assembled

The National Human Genome Research Institute (NHGRI), has announced that the first draft version of the honey bee genome sequence has been deposited into free public databases.

The sequence of the honey bee, *Apis mellifera*, was assembled by a team led by Richard Gibbs, Director of the Human Genome Sequencing Center at Baylor College of Medicine in Houston. The honey bee genome is about one-tenth the size of the human genome, containing about 300 million DNA base pairs.

Researchers have deposited the initial assembly, which is based on six-fold sequence coverage of the honey bee genome, into the NIH-run, public database, GenBank (www.ncbi.nih.gov/Genbank). In turn, Genbank will distribute the sequence data to the European Molecular Biology Laboratory's Nucleotide Sequence Database, EMBL-Bank (www.ebi.ac.uk/embl/index.html), and the DNA Data Bank of Japan, DDBJ (www.ddbj.nig.ac.jp).

Sequencing of the honey bee genome began in early 2003. NHGRI provided about $6.9 million in funding for the project and the U.S. Department of Agriculture contributed $750,000.

its importance in agriculture, the honey bee serves as a model organism for studying human health issues including immunity, allergic reaction, antibiotic resistance, development, mental health, longevity and diseases of the X chromosome. Biologists also are interested in the honey bee's social instincts and behavioral traits. In addition, researchers want to compare the honey bee's genome with the genomes of other organisms to find genes and regulatory regions within DNA. Scientists are particularly interested in comparing the honey bee's genome with the previously sequenced insect genomes, such as the fruit fly and mosquito, as well as with DNA sequences from Africanized bee strains that have invaded many areas of the southern U.S.

Arteries Clog Earlier in People With Lupus

People with the autoimmune disease lupus may develop carotid atherosclerosis (the buildup of fatty deposits in the arteries) at an accelerated rate and independently of many risk factors normally associated with cardiovascular disease, according to a new study supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a part of the National Institutes of Health. The work was reported in the December 18 issue of the *New England Journal of Medicine*.

The study, carried out by Mary J. Roman, M.D., at Weill Medical College of Cornell University, Jane E. Salmon, M.D., at the Hospital for Special Surgery, New York, and their colleagues examined 197 people with lupus and the same number of matched controls. Risk factors for cardiovascular disease, including family history of heart disease, cholesterol levels, smoking and hypertension, were similar in both groups, but atherosclerosis, as evidenced by carotid ultrasound, was more prevalent in lupus patients. The scientists also found that people with lupus who had the disease longer, had more damage from the disease, and had used less of the immunosuppressive drug cyclophosphamide to treat it were more likely to develop fatty deposits in their arteries.

"Although we've known for some time that there is an association between lupus and premature heart attacks," said NIAMS Director Stephen I. Katz, M.D., Ph.D. "until now we haven't understood well the reasons. This study gives us a basis to pursue intervention strategies for reducing cardiovascular risks."

Calcium Channels Control

"If drugs could be developed that would open the channel, it might lead to relaxation and opening of the arteries," says HHMI investigator and ASBMB member Kevin Campbell, Professor, University of Iowa College of Medicine.

Researchers have discovered that a specific type of calcium channel, a pore-like protein that nestles in the cell membrane and controls the flow of calcium into the cell, regulates the relaxation of coronary arteries.

The studies found that mice engineered to lack these calcium channels had constricted coronary arteries and had fibrous tissue in their hearts, which was evident when the animals' hearts reacted to chronic blood restriction. The researchers hypothesize that drugs targeting this calcium channel might one day be used to treat cardiovascular disease by opening arteries.

The findings of the group led by Dr. Campbell were published in the November 21, 2003, issue of the journal Science. He and his colleagues at the University of Iowa collaborated with researchers from the Veterans Administration Medical Center in Iowa City, Loyola University Medical Center, and the University of Texas Southwestern Medical Center.

The calcium channel under study is triggered by voltage differences across the cell membrane that cause it to open, allowing calcium to flow into the cell. The operation of calcium channels is crucial to a wide array of physiological functions, including transmission of nerve impulses, muscle contraction and activation of genes. Although one type of calcium channel, called the L-type, had been shown to control muscle contraction, the action of the other type, called the T-type, remained largely unknown, according to Dr. Campbell. The L-channel opens in response to large voltage differences across the cell membrane, while the T-channel responds to a weaker "depolarization," he said.

Dr. Campbell and his colleagues first became interested in exploring the T-channel because research by other scientists hinted that it might be involved in the fusion of muscle cells, or myoblasts, to one another during the development and repair of muscles. Campbell's laboratory concentrates on muscular dystrophies, and the scientists reasoned that better understanding of the muscle-formation machinery would aid that effort. To study the T-channels, the researchers created a knockout mouse lacking one type of T-channel, called the α1H channel.

"Although our main interest was initially to look at how the myoblasts would function and fuse, we found that myoblasts looked completely normal in these animals," said Dr. Campbell. "We then realized that another type of channel, the α1G, could upregulate to compensate for

Lawsuit Calls on FDA to Regulate GloFish

The first genetically modified (GM) pets being sold in the U.S., fluorescent red zebrafish called GloFish, are the focus of a lawsuit filed last month against the Food and Drug Administration (FDA) by environmental and food safety groups seeking federal regulation of the animals. The suit was filed by a coalition led by the Center for Food Safety in Washington, DC.

GloFish is the commercial name for genetically modified zebrafish, which are found only in India's Ganges River in India, and are normally striped black and grey. They are commonly used for research purposes in labs, and also in home aquariums. Scientists at the National University of Singapore engineered the fish, to detect water pollution, with the gene for red fluorescent protein obtained from sea anemones and coral. The gene is injected into embryos before they hatch.

The Center claims that GloFish sets a precedent for genetically engineered animals, and according its legal director, Joseph Mendelson, runs counter to the position of the National Academy of Sciences and other scientific review boards.

The FDA, which has jurisdiction over the commercial development of genetically modified animals, stated last December that there was no reason to regulate zebra fish, because they are not used for food purposes and consequently pose no threat to the food supply.

Coronary Artery Relaxation

the loss." However, when the scientists studied the structure of the various muscle tissues, they found a striking accumulation of fibrous tissue in heart muscle.

"We believed that this fibrosis was probably not due directly to the cardiac muscle abnormality, because we knew that a T-channel was not present in adult ventricular muscle," he added. "So, it must have been caused by another abnormality, maybe in the blood vessels."

When visual studies were performed of the coronary arteries of the mice and their contractility measured, the arteries were found to be irregularly shaped and constricted, although the vessels contracted normally. Such aberrations would have starved the heart of blood, inducing fibrosis, said Dr. Campbell.

To test the ability of the coronary arteries of the knockout mice to relax, researchers administered drugs that in wild-type mice caused arterial dilation. These drugs, however, produced no such effect in the knockout mice.

"So, this impaired relaxation strongly suggested that this channel was involved in arterial relaxation, which was a surprise because calcium channels had been implicated in contraction, but not in relaxation," reported Dr. Campbell. This was supported when the researchers administered nickel, which blocks T-channels, to wild-type mice and the dilation of their arteries was decreased.

Previous research had shown that an entirely different channel, a potassium channel, plays a key role in regulating muscle relaxation. Dr. Campbell and his colleagues theorized that calcium ions flowing through T-channels might somehow "fine-tune" potassium channels.

Findings from two of their experiments supported this idea, he says. A drug that opens potassium channels caused arterial dilation in both wild-type and T-channel knockout mice. Also, when they isolated the potassium channel, they found it to be physically associated with the T-channel.

Many puzzles remain concerning how the T-channel functions in coronary artery relaxation. One arises from the scientists' finding that an artery-relaxing drug, called sodium nitroprusside, produced some arterial relaxation in the knockout mice. This drug releases the artery-relaxing chemical nitric oxide, leading the scientists to believe that only nitric-oxide-mediated relaxation is defective in the knockout mice.

A better understanding of T-channels function could lead to new treatments for cardiovascular disease, said Dr. Campbell. "Our current findings indicate that blocking this channel causes coronary artery constriction, which is clearly something you don't want to do in treating heart disease. However, if drugs could be developed that would open the channel, it might lead to relaxation and opening of the arteries. There are currently a number of treatments for opening blood vessels, but it's possible that understanding this process could lead to new approaches to causing vasorelaxation."

Genomics Providing Clues to

Genomics is providing clues to how herpes simplex virus (HSV) manages to lie dormant inside infected neurons. The virus alters the way host genes are expressed, researchers report.

HSV can persist inside infected people indefinitely. From the initial site of infection, usually the skin or mucosal epithelia, the virus invades the sensory nerve endings and takes up permanent residence in the host's neurons. There it lies dormant, with occasional periods of reactivation when the virus replicates, shedding infectious virus from the oral or genital tracts and often producing its trademark cold sores.

Comparing ganglia latently infected with the virus and mock-infected ganglia, researchers found that there were significant changes in gene expression.

"HSV latency is the most clinically vexing part of herpes infections," said Don Coen, Professor of Biological Chemistry and Molecular Pharmacology at Harvard Medical School and an ASBMB member. "Finding out how it does this would shed light, not only on the virus but on the nervous system."

He and his colleagues studied mouse trigeminal ganglia, the sensory ganglia that innervate the various portions of the face, including the surface of the eye and the lip—a popular model because they are relatively large in size.

The researchers examined the patterns of gene expression in the ganglia using a microarray containing 2556 selected mouse genes, just under a tenth of all those estimated in the mouse genome. Comparing ganglia latently infected with the virus and mock-infected ganglia, they found that there were significant changes in gene expression between the two states.

What's more, using in situ hybridization, the researchers showed that at least some of the changed genes were expressed in neurons only, discounting the possibility that the changes were due to other cell types present in the ganglia. "We've convinced ourselves that some of them are truly expressed in neurons," said Dr. Coen in an interview with *BioMedNet News*.

This is a key point, according to Richard Thompson, Associate Professor of Molecular Genetics at the University of Cincinnati Medical Center. There is a persistent immune response occurring in latently infected ganglia, he says, and various types of immune cells, including T cells and B cells, remain resident in latent ganglia.

The study, published in *The Journal of Virology*, is the first to show that the pattern of gene expression in host neurons is altered by latent HSV infection, noted Dr. Thompson. Previous studies have concentrated on changes in expression of the viral genes.

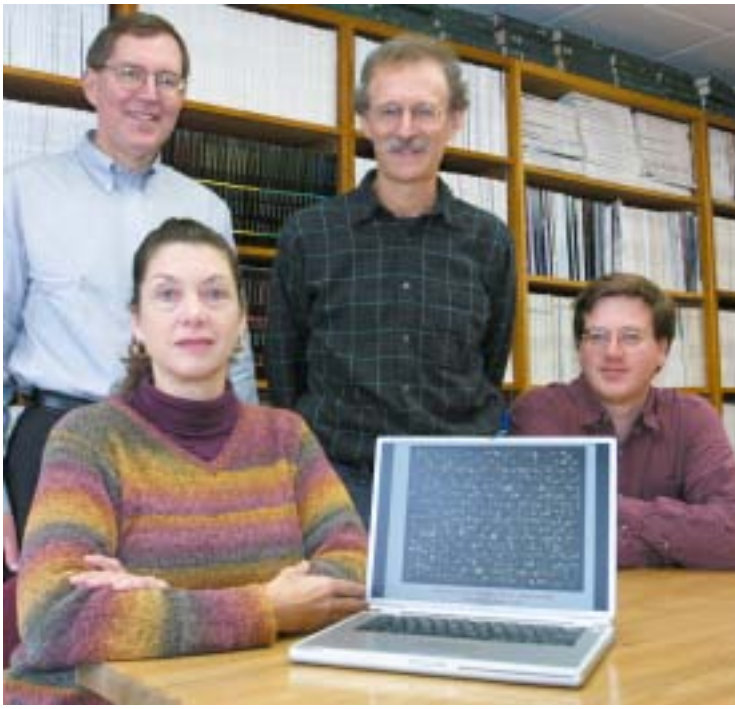
"Of the genes highlighted by the study, several are involved in regulating the expression of other genes–an interesting finding," says Dr. Coen. "We think of latency operationally as being a question of regulation of gene expression. So obviously our attention is drawn to genes known to be involved in gene expression."

Certain of the genes whose expression increased encode proteins, such as homeodomain interacting protein kinase, involved in transcriptional repression. Conceivably, they could contribute to the shutdown of expression of viral productive-cycle genes during latency. Others, such as muscarinic cholinergic receptor 1, are connected to signaling pathways that have been reported to either promote or inhibit reactivation of virus from latency. Still others, such as certain voltage gated potassium channels, affect neuronal excitability, raise the possibility that latent HSV can affect neuronal physiology and even sensation. There are previous studies in mice and humans that are consistent with this possibility.

The group has come up with some ideas to explain what's going on. One hypothesis Dr. Coen suggests is that the presence of the viral DNA, or the viral genes being expressed in the neuron, leads to alterations in the expression of particular genes in those neurons. For example, the major gene products expressed by HSV during latency, the latency-associated transcripts, which contribute to the repression of viral productive cycle genes, could conceivably contribute to the up-regulation of neuronal genes. Another possibility is that the response is more indirect, for instance through increased immune activity and the immune system having effects on the neuronal gene expression. For example, latency is associated with persistent expression of cytokines such as gamma interferon that are known to alter host gene expression. The increased expression of the cytokine-induced transcription factor, Stat 1, observed in the study is consistent with this kind of mechanism. To try to distinguish between these two possibilities, efforts are underway to measure the presence of viral DNA and the expression of relevant genes in single neurons using PCR-based methods.

How HSV Works

The team has a long list of other questions, including how changes in host gene expression affect the virus, and whether they contribute to the virus' ability to remain latent or to be better prepared for reactivation. Certain hypotheses can be tested by knocking out or over-expressing specific host genes in latently infected ganglia. "We have a lot of work in front of us," Dr. Coen predicted.



Four of the authors from Harvard Medical School are seen around a laptop showing an image of a hybridized microarray. From left to right are Don Coen, David Knipe, Fritz Roth, and Martha Kramer.

Report Finds States Ill-Prepared for Bioterror Attack

States are not much better prepared now to deal with public health emergencies than they were before the September 11 terrorist attacks, according to a report, Ready or Not? Protecting The Public's Health in the Age Of Bioterrorism, released in late December by the Trust for America's Health, a nonpartisan, nonprofit organization funded in part by The Pew Charitable Trusts.

The report examined each state's bioterror preparedness in three areas: funding (including state budgets for public health programs); public health infrastructures (such as laboratories and communications capabilities); and indicators that show how new bioterror funding has impacted public health systems.

California, Florida, Maryland and Tennessee achieved the highest rankings by meeting seven of 10 preparedness indicators. Arkansas, Kentucky, Mississippi, New Mexico and Wisconsin scored the worst, meeting just two of the indicators. Seventy percent of states met between three and five indicators, the report said.

"With bioterrorism, chemical terrorism, SARS (Severe Acute Respiratory Syndrome) and West Nile virus representing only a handful of today's health threats, state and local health agencies are being pushed and pulled beyond their limits," Lowell Weicker, the Trust's board president and a former Connecticut governor and U.S. senator, said in a prepared statement. "We need to ensure public health preparedness remains a top national priority and doesn't get caught up in red tape."

All 50 states have initial bioterrorism plans approved by the federal Centers for Disease Control, but coordination and implementation of these plans is not as far along as it first appeared to be, the report said.

For example, 26 states failed to spend 90 percent of their allotted federal bioterror funds in fiscal 2002, based on a fall 2003 survey by the National Association of State and Territorial Health Officials (ASTHO). Congress provided the U.S. Centers for Disease Control and Prevention $940 million in fiscal 2002 and $870 million in fiscal 2003 to support state and local public health readiness. Since it was a new source of money, the report said, many states had first to develop spending plans for the funds, which are now in place for future allocations.

"Individual states are certainly going to have some questions and concerns about how they have been evaluated on some of these indicators," George Hardy, Executive Director of ASTHO told Stateline.org, an internet website that reports on state news. "We are totally supportive of the bottom line findings that progress has been made, considerably more needs to be made and that the sustained commitment (by the federal government) is required."

Another shortcoming cited in the report is that 39 states did not make state-specific information about the SARS outbreak available to the general public and health professionals.

It also said 48 states do not have enough staff to receive and distribute medication and supplies from the Strategic National Stockpile.

And 37 states said they do not have a completed plan for dealing with the emergence of a new, lethal strain of influenza.

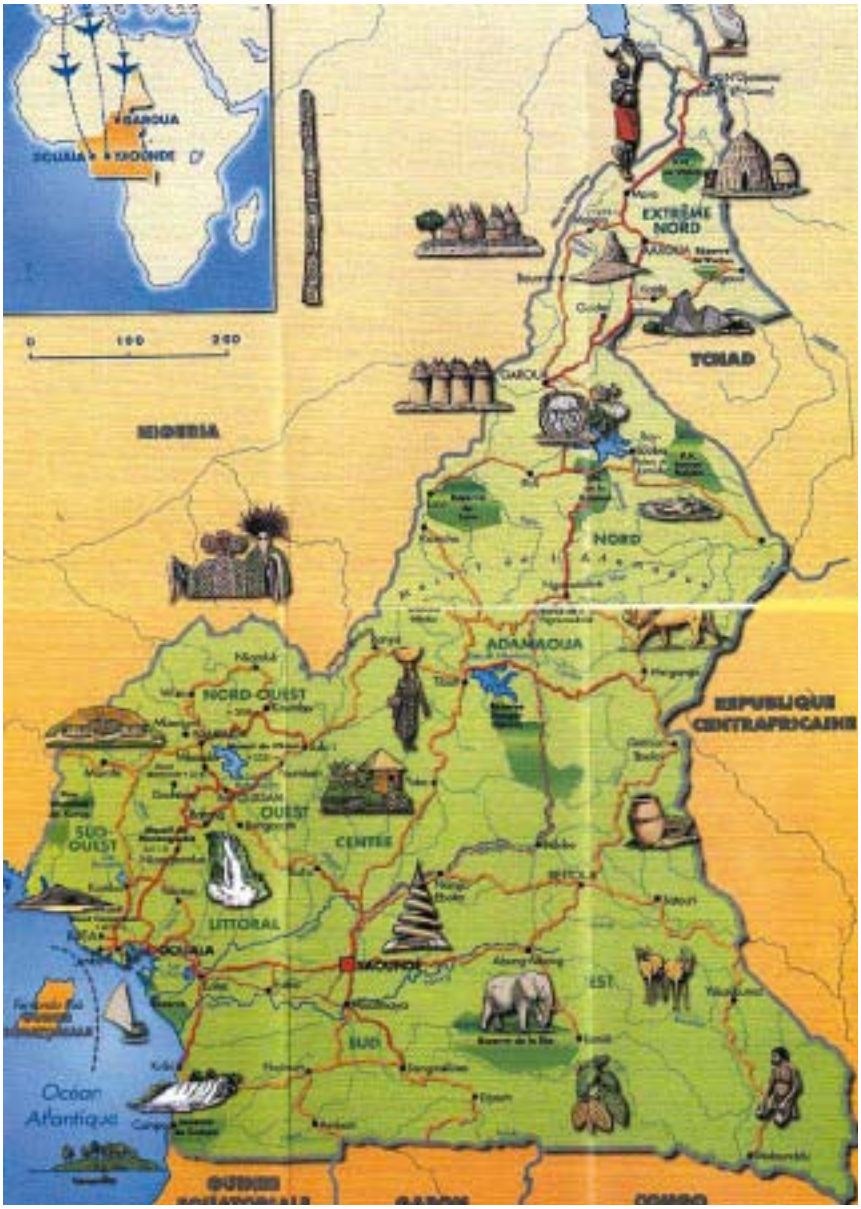
The report attributed low readiness scores in part to state budget cuts in public health that occurred in 32 states.

"Clearly states have cut spending in public health . . . and we hate to see that, but I think that what you'll hear from governors' offices and legislators is that there were cuts in every agency in state government," Hardy told Stateline.org. In most cases, he said, public health wasn't singled out.

A Visit to Africa

The FASBMB Congress in Yaounde, Cameroon, and the University of Buea

By Ralph A. Bradshaw,
Professor, Department of Physiology & Biophysics, University of California Irvine



While most Americans were feasting on turkey and cranberry sauce, or something like it, in celebration of Thanksgiving Day, we were indulging in ndole, folon and various other Cameroonian delicacies, occasioned by the 4th International Congress of the Federation of African Societies of Biochemistry and Molecular Biology (FASBMB).

Held in Yaounde, the capital city of Cameroon, from November 25-28, it brought together a few overseas visitors (we were the only Americans), a sampling of

The author with His Excellency, the Minister of Higher Education, Professor Maurice Tchuente (center) and Professor Vincent P. K. Titanji, Deputy Vice-Chancellor of the University of Buea and President of the FASBMB (right).

African biochemists from Cairo to Cape Town and an enthusiastic delegation of Cameroonian scientists. The meeting took place in the quite impressive Palais du Congress, which is situated on a prominent hill near the center of the city and thus affording excellent views of Yaounde and its surroundings, and was opened by His Excellency, the Minister of Higher Education, Professor Maurice Tchuente. His enthusiasm was infectious and was quite representative of the warm hospitality and camaraderie we experienced with all of the delegates and the Congress supporting staff. It was also inspiring to meet such a clearly dedicated member of the government, who has managed, in only a relatively short time (he had been in office a little more than one year), to have had an important impact on higher education in Cameroon.

The 4th FASBMB Congress was hosted by the Cameroon Society of Biochemistry and Molecular Biology (SOCAB) and was organized in collaboration with the International Union of Biochemistry and Molecular Biology (IUBMB), who provided substantial support. In addition to a short opening address by Professor Angelo Azzi, University of Bern, the representative of the IUBMB, Professor Karel Wirtz of the University of Utrecht brought greetings from the Federation of European Biochemical Societies (FEBS), another supporter, and I spoke on behalf of the U.S. National Committee for Biochemistry and . Molecular Biology and the ASBMB.

The locale of the meeting reflected the present President of the FASBMB, Professor Vincent IP. K. Titanji, Deputy Vice-Chancellor of the University of Buea and a world expert on parasitic diseases, who served as convener of the Congress. In organizing this Congress, Professor Titanji and his colleagues chose the theme "Biochemistry and Molecular Biology for the Development of Africa" and the pragmatic tone of many of the presentations, that strongly focused on HIV/AIDS and parasitic diseases, such as malaria and river blindness, reflected the reality of African science: the appropriate necessity of applying limited resources to the solution of real (and devastating) problems. However, there was also a clear recognition that the empowerment of today's approaches to biology, rooted in

The author with Professor Karel Wirtz (center), who represented FEBS, and Professor Angelo Azzi (right), who represented the IUBMB.

genomics, proteomics, and bioinformatics, will also pay dividends in helping the developing countries of Africa in alleviating the staggering burdens of disease and hunger. Indeed, following three days of scientific sessions, there were workshops on bioinformatics, education (the teaching of biochemistry and molecular biology in Africa) and drug design, as well as a pre-meeting workshop on bioinformatics held at the Biotechnology Center of the University of Yaounde 1. Conducted by teams of local and international scientists, they presented excellent opportunities for African scientists to get together and discuss issues and problems that they face mutually on an otherwise enormously diverse continent.

One of the highlights of the meeting, and one for which there was substantial agreement that it captured the sense of what is now African science, and what it can become, was a short after-dinner presentation by Professor Peter Ndumbe, Dean of the Medical School at the University of Yaounde 1. Delivered with a delightful mixture of sincerity and mirth, he left all with a glimpse, not only of what has been accomplished, but what can be—through education, commitment and hard work. A little help from outside Africa should not, however, be discouraged. It was very evident during the Congress what relatively modest collaborations (and financial support), particular from the Sweden and the U.S., have done. It would not be an exaggeration to say that a good bit more is needed.

The second half of our trip required us to leave the rolling inland hills of Yaounde and drive northwest for three hours, through the port of Douala, the largest city in Cameroon, and on for another hour to the coastal town of Limbe. Just beyond Douala, one crosses into the Anglophone (or English speaking part) leaving behind the larger Francophone (French-speaking part) that arose after World War I when the former German colony of Kamerun was divided between the victorious French and English powers. Although now a single independent nation (since 1960), these lingual distinctions remain, and Cameroon is indeed a bilingual nation, similar to Canada. Limbe is only a few kilometers from the Nigerian border and is situated at the base of Mount Cameroon, a decidedly active volcano. (We visited a lava flow that occurred only a couple of years ago that cut the road to Nigeria and almost reached the sea.) Just a short half hour drive inland from Limbe and pretty much straight up the side of Mount Cameroon lies the small town of Buea, which still retains architectural vestiges of its German and then British occupations, when it was

Below: The author with Professor Titanji (left) and Professor Roland Ndip (center), the Head of the Biology Dept., University of Buea.

Penny Bradshaw enjoying a break in the program with Karel Wirtz.

a capital city. It is also the site of the University of Buea, situated in a lovely campus that is only 10 years old.

My visit to the University of Buea was arranged by Professor Titanji and was hosted by Professor Roland Ndip, the head of the Biology Department (See Fig 3). Following a tour of the campus a research seminar and visits to several laboratories, we were treated to an informal and quite lively dinner with faculty and students (they were most curious to hear about the new Governor of California!). The research activities of the department are also heavily orientated to parasitology and the identification of antigens for the preparation of effective vaccines, a goal that has largely eluded scientists to date. I was particularly struck by the enthusiasm of the group (the seminar was presented on Saturday afternoon to a room full of scientists—not something that would likely occur in the U.S.) and the sophistication of both their research and their knowledge. The department is clearly growing in size (they have several hundred students including 12 doctoral students) and new building activity was evident.

As might be expected, there was not an oversupply of large instruments and these scientists clearly have need of more resources. Professor Titanji actively collaborates with laboratories in the U.S. and Sweden, and these arrangements have certainly been invaluable in the development of his team's projects. More such interactions would certainly be beneficent for all the workers at Buea.

Our Cameroonian sojourn was certainly a pleasant and informative experience. At the moment it is certainly not a tourist center, but therein is also much of its charm. It will grow and be discovered I'm sure and that would undoubtedly help its development. I hope it can do this and also remain unspoiled.

Esmond Emerson Snell, Noted Biochemist and Vitamin Researcher

Esmond Emerson Snell, a leading biochemist and vitamin researcher at the University of California, Berkeley, who discovered several B vitamins, including folic acid, in the mid-1900s, died December 9, 2003, in Boulder, Colorado. Dr. Snell, who was 89, died of prostate cancer and congestive heart failure, according to his family.

Dr. Snell, an ASBMB member (emeritus), was a nutritional biochemist whose work on vitamins and the chemistry of their actions was recognized internationally. His research was considered by many to be on a par with that of other scientists who received Nobel Prizes in the 1930s and 1940s for their discovery of vitamins A, C, K, B2 (riboflavin) and biotin.

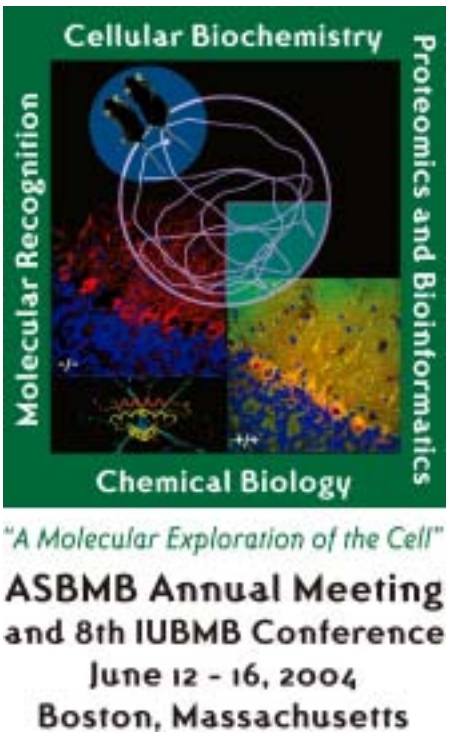
"He was nominated several times for the Nobel Prize, and should have received one" for his work on the coenzyme form of vitamin B6, called pyridoxal phosphate, said Jack Kirsch, Professor of Polecular and Cell biology and of chemistry at the University of California, Berkeley.

Lester Reed, a long-time friend and colleague and Professor Emeritus of Biochemistry at the University of Texas at Austin, agreed. "I consider him to be one of the top biochemists in the world from the 1940s on," he said. "He led the way in using bacteria to study metabolic processes, and that work was some of the best biochemistry and microbiology ever."

"Snell was a giant in biochemistry," concurred colleague Howard Schachman, Professor of the Graduate School in UC Berkeley's Department of Molecular and Cell Biology.

Stanford's Ronald Davis to Deliver Herbert A. Sober Lecture

The Herbert A. Sober Lectureship recognizes outstanding contributions to biochemical and molecular biological research, with particular emphasis on development of methods and techniques to aid in research. The Lectureship provides a plaque, stipend, and transportation and expenses to present a lecture at the ASBMB Annual Meeting. Recent recipients have included Jack D. Griffith in 2002, Roberta F. Colman, Howard K. Schachman, Y.C. Lee, Charles R. Cantor, Thomas D. Tullius and Roger Y. Tsien. This year's recipient, Ronald W. Davis, Professor in the Department of Biochemistry, Stanford University School of Medicine, will deliver the lecture at the 2004 ASBMB Annual Meeting at 4:45 – 5:45 p.m., Tuesday, June 15.



"Dr. Davis is a world leader in biotechnology and the development and application of recombinant DNA methodology to biological systems," wrote Suzanne Pfeffer, Chair, Department of Biochemistry, Stanford University School of Medicine, in her letter of nomination for the awardee. "His lab was instrumental in the development of phage lambda vectors, which are now the most common method for the primary cloning of cDNA molecules using *E. coli*. This includes the creation of expression-cloning systems using the vector, lambda gtll. Dr. Davis and his colleagues also developed many of the currently used yeast vectors and helped to develop yeast as a host for recombinant DNA. In addition, with Dr. Gilbert Chu, he established a new means of resolving chromosome-sized DNA molecules, a method termed contour-clamped homogeneous electric field electrophoresis."

He is currently developing new technology for constructing genetic maps and for high throughput DNA sequencing. His current focus is on whole genome analysis, and his technological contributions have led to the completion of sequences for large portions of the genomes of yeast, *E. coli*, human, Plasmodium falciparum, Chlamydia, and Arabidopsis.

Dr. Davis is also renowned as a lecturer.

"Even 20 years ago," wrote Jasper Rine, Professor of Genetics at the University of California,. Berkeley, "Ron's lectures were highpoints in the academic year among the students and postdocs of the Stanford Biochemistry department. Many postdocs would

Ronald W. Davis, who will deliver the Herbert A. Sober Lecture.

sneak in and sit in the back to listen to Ron's amazing ability to turn the arcane dimensions of lambdology into a spellbinding tale of molecular logic and precision. In more recent years, with his ever-expanding technological vision, I find Ron's lectures to be penetrating looks into the future of what science will be like for all of us. He is simply a superb choice for this lectureship."

"I was a postdoctoral fellow in Dr. Davis' lab," recalled HHMI Investigator Steven J. Elledge in his letter supporting the awardee's nomination, "and I can attest to his many contributions to technological advancement in the biological sciences based on firsthand knowledge. Ron was the first person to make bacteriophage lambda work as a recombinant DNA vector.

"He figured out the sequence of the EcoRI restriction enzyme and was the first to use it in lambda to make recombinant molecules and libraries. The vectors he developed were used worldwide to stimulate recombinant DNA research. His lab invented the

Continued on next page

At the ASBMB Annual Meeting: Grant Writing for Success

Grant writing and an understanding of the peer review process are essential ingredients to success in the competition for funding of research, and both topics will be addressed at the ASBMB Annual Meeting, June 12-16 in Boston.

The FASEB Career Resources and MARC Program Office in association with the National Institutes of Health will offer a three-part grant seminar workshop in the Career Resources Center/Placement Service at IUBMB/ASBMB 2004. Dr. Anthony M. Coelho, Jr., Review Policy Officer at NIH, will chair the workshops. IUBMB/ASBMB 2004 registration is required to participate in these seminars. You can register online at www.asbmb.org.

Advance seating reservation is also required. For seating reservation forms, visit https://ns2.faseb.org/careerutilities/bmbnih04.pdf.

Peer Review of NIH Grants - Part I

This workshop is focused on providing information on how to understand the peer review process, which is essential to competing successfully for funding. The workshops also provide an overview of how scientific peer review is carried out at NIH.

Grant Writing for Success - Part II

This workshop provides an introduction to factors that contribute to applications that succeed in obtaining research funding. This presentation is focused on the fundamental principles of successful grant writing, the most common reasons that grant applications fail, how to make an application "reviewer friendly," how to meet the needs of the reviewers and the funding agency, how to avoid the need for resubmission and tips and strategies for resubmitting, including what should and what should not be done if resubmission becomes necessary.

NIH Mock Study Section - Part III

This workshop will provide participants with an overview of the working dynamics of peer review at NIH. Those attending will get to see the peer review process in action.

Handouts and resource materials for each seminar workshop will be provided for the participants who make advance seating reservations. The deadline date to make advance reservations is Tuesday, June 1.

For further information on the MARC Travel Awards and NIH workshops, contact Lisa Dennison or Jacquelyn Roberts at the FASEB Career Resources and MARC Program Office, 9650 Rockville Pike, Bethesda, MD 20814-3998; Phone: 301-634-7930; Email: marc@faseb.org.

Davis continued ...

Continued from previous page

immunological screening of expression libraries through development of the lambda gt11 system."

"Dr. Davis' lab is credited with being the first to isolate centromeres and origins of replication from the budding yeast *S. cerevisiae*. The significance of these contributions cannot be underestimated. Virtually every lab working on yeast, and there are thousands, utilize vectors based on these discoveries to carryout their research with great dispatch.

"Once these elements were elucidated, Ron was one of the first proponents of using them and the newly discovered telomeric DNA to make libraries of human DNA in yeast artificial chromosomes, YACS. This was one of the first steps to the orderly assembly of human chromosomal DNA and was one of the key developments that ultimately spurred on the human genome project."

"In many ways," wrote Dr. Elledge, Ron Davis is an inventor, pure and simple. He has focused his creativity towards pressing technological problems that at the time held up progress in biological research. He is not one known for a major discovery in a single field such as cloning an important gene. His efforts have always been aimed at the very fabric of scientific research, attacking the fundamental issues of how research in general is carried out. His discoveries cut across disciplines to make many fields accelerate their discoveries simultaneously. Thus, his work has had a much greater significant impact on biology as a whole than individual discoveries within a given field. In my opinion, his technological contributions to biology and their overall impact on biological research have been truly spectacular."

Upsetting the Balance: Lipoprotein

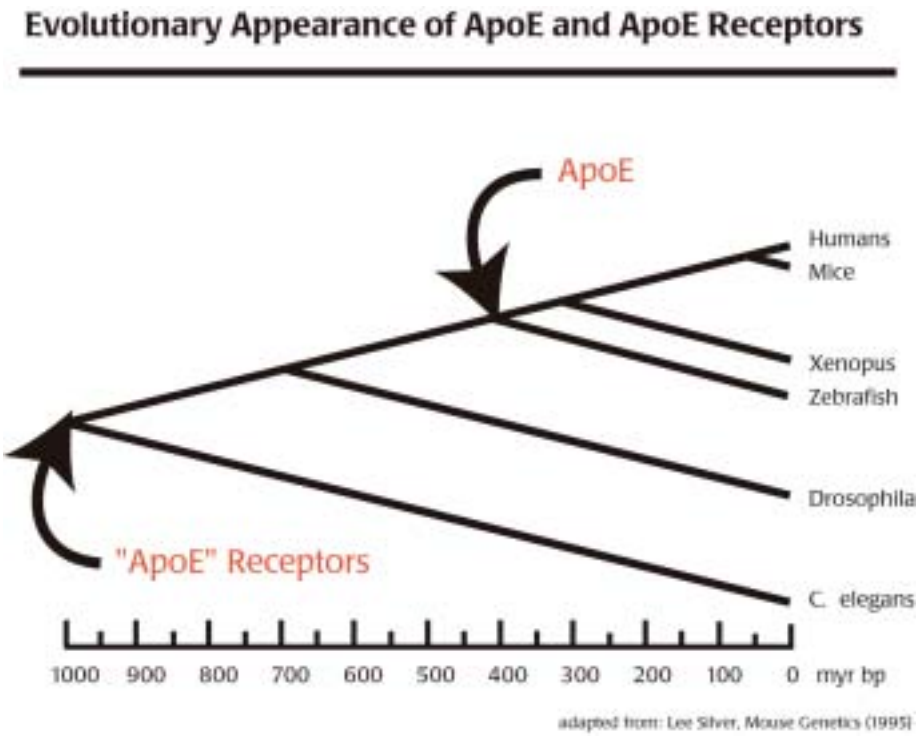
An imbalance between two roles of lipoprotein receptors—cholesterol transport and neuronal signaling in the central nervous system (CNS)—may help explain the link between apolipoprotein E4 (ApoE4) and Alzheimer's disease, according to some neuroscientists.

ApoE4 predisposes carriers to late-onset Alzheimer's disease, explains ASBMB member Joachim Herz, Professor of Biophysics and Molecular Genetics at the University of Texas Southwestern Medical Center. "What we were wondering was whether the receptors that ApoE binds to might also be involved," he said.

The receptors that ApoE binds appear in primitive multi-cellular organisms, like the nematode worm. "These receptors must have had completely different functions, because they are already present in the worm in virtually the modern form, and there was no ApoE around at that time," said Dr. Herz.

ApoE arose during mammalian evolution, and may have evolved to fit a pre-existing receptor. "We think that the primordial roles of these receptors are important in tissue organization and transmitting signals between cells in various tissues, for instance in the vascular walls, or in the CNS where it is regulating the development of the neocortex and the cortical layering," he explained. "Our hypothesis is that apolipoprotein E, because it evolved onto a pre-existing receptor system, might actually interfere with these original functions, for instance, in regulating neuronal migration, or, as we are now showing, in regulating synaptic neurotransmission itself."

Dr. Herz's team examined the three different apolipoprotein E isoforms, ApoE2, -E3 and -E4. They found that the rare E2 isoform binds very poorly to the receptors because it is missing a positive charge in the region that interacts with the receptors. In the same region, ApoE4 has one more positive charge than the more-common E3 and two more positive charges than E2, so ApoE4 can bind very well to the receptors and the cell surface. Also, the lipoprotein particles around which ApoE4 assembles tend to be larger than the ApoE3 particles.



The above shows on an evolutionary time scale the appearance of the receptors and the appearance of ApoE. Dr. Herz believes that this demonstrates that ApoE apparently evolved on top of a pre-existing receptor system that served its requirements for mediating cholesterol transport (i.e., Endocytosis capability).

"All in all, this makes ApoE4, in our minds, a better competitor for ligand binding to the receptors than E3 or E2, and it will be interfering more with the primordial function of the receptor," was the conclusion of Dr. Herz.

The enhanced binding of ApoE4 to these receptors would then 'dampen' their primordial physiological function, and, he surmised," Instead of having a receptor system that is active at 100 percent, the system might only be active at 80 percent or 9o percent. And by dampening a pro-survival, pro-neuronal function, you might actually gain the modifier effect that you see in late-onset Alzheimer's."

Dr. Herz and his colleagues found a ligand called reelin that is present in the CNS and binds to two apolipoprotein receptors, ApoER2 and the VLDL receptor. Reelin regulates neuronal migration and positioning in the brain during embryonic development, but is also expressed in the adult brain.

"This molecule very potently enhances synaptic transmission, and the strengthening of synaptic contacts between neurons, which is commonly thought to be one of the processes which is underlying memory and the maintenance of synapses," said Dr. Herz. Since the synaptic loss is closely associated with Alzheimer's disease and dementia, he believes that the interference of this process by ApoE4 might be involved in late-onset Alzheimer's disease.

In addition, he suspects that the lipoprotein receptors will turn out to

Receptors in the CNS

have other ligands as well. "There are seven members of this gene family of receptors and all of them are expressed on neurons at some point during development, either throughout the brain or in specialized subsets," he noted. "We have identified a specific ligand, reelin for two of them, which means that the others most likely will have functional ligands about which we simply do not know."

His goal is to identify these ligands. "We have a very strong lead on one of them," said Dr. Herz. "We are using mutants in which we have made very specific mutations in the receptors, which allows us to assess their role in the synapse. And from that we now have much more detailed information of how in the synapse ApoE receptors function in modulating neurotransmission."

Dr. Herz and colleagues research on the various aspects of ApoE receptor function has been reviewed in, among others, *Neuron*, March, 2001; *Nature Review*, Volume 1, October 2000; and *Annu. Rev. Biochem*. 2002.

NIH Director Defends Study Process

HIH Director Elias Zerhouni last month announced that he would defend dozens of AIDS, sexual behavior and addiction studies challenged by conservative critics as a waste of taxpayers' money. The Director made his decision following a review by NIH staff of some 190 studies that had been criticized by the Traditional Values Coalition, a conservative advocacy group.

In explaining his decision, Dr. Zerhouni told *USA TODAY,* "When you look at the impact of sexually transmitted diseases—you're talking about HIV/AIDS and many others that affect millions of people and their reproductive lives."

NIH officials said the Director's letter would be sent to members of the Senate Committee on Health Education, Labor and Pensions and the House Energy and Commerce Committee. The response is the latest salvo in a controversy that began last summer, when the House narrowly rejected an amendment by Rep. Pat Toomey, R-Penn., that would have blocked $1.5 million in funding for five studies examining sexual behavior.

by John D. Thompson, Editor

Biotech: Where the Jobs Are

While a shrinking workforce has been the story for most industries in the past few years, one industry—biotechnology—has been bucking that trend since the beginning of the twenty-first century. According to a U.S. Department of Commerce report released late last year, from 2000 through 2002 the biotech industry had a higher rate of job growth—12 percent—than any industry in the nation.

As for the future, that looks good too. According to the Commerce Department, "Biotechnology will be essential to national long-term economic growth and leadership. From job creation to revenue generation, strength in biotech will be a core building block of America's national competitiveness in the twenty-first century."

The analysis and findings in the report are largely based on data collected from a survey of more than 3,000 firms engaged in biotechnology-related activities. The findings include the following:

Firms engaged in biotechnology activities range from small, dedicated biotechnology companies that are R&D-intensive and operate primarily on venture capital, grants, initial public offerings (IPOs) and collaborative agreements, to large diversified companies that have greater in-house resources and well-established production and distribution systems.

Larger firms account for the majority of net sales and operating income of businesses with biotech activities, although 90 percent (917 firms) of survey respondents had 500 or fewer employees. Only 19 firms (2 percent) reported more than 15,000 employees, while 600 (58 percent) had fewer than 50.

Survey respondents that are engaged in biotechnology research, development, and applications reported that in 2001 they had more than 1.1 million employees, total annual net sales of about $567 billion, operating income of $100.5 billion, capital expenditures of $29.5 billion, and R&D expenditures of $ 41.6 billion.

For 90 percent of firms, biotech-related business lines accounted for more than 75 percent of total net sales, employment, and operating income. These companies generally are smaller firms with fewer than 500 employees. For all respondents, biotechnology accounted for almost 40 percent of total R&D expenditures.

International markets accounted for at least 16 percent of firms biotechnology-related net sales or $8 billion in revenues in 2001. The leading foreign market was Europe which accounted for 56 percent of export revenues followed by the Asia/Pacific region with 24 percent.

Patent data underscore the dynamic and rapidly evolving nature of biotechnology. In the last quarter of 2002, companies reported 33,131 pending applications for biotechnology products or processes, compared with 23,992 current patents. That roster of patents pending represented, according to *The Scientist,* a potential increase of 50 percent in the value of the firms intellectual property holdings.

Despite that rosy prospect, the industry as a whole has yet to be a big money maker, according Ernst & Young reports which indicate that the typical firm spends some three to four times as much on research as it generates in revenue.

As for job creation, the industry still employs relatively few scientists. The Commerce Department estimates that 34,000 scientists work for biotech companies, with the vast majority of these jobs located in just six states.

Still, the growth in biotech jobs offers increased options to those in the academic world. at a time when traditional academic opportunities appear in shorter supply. The NSF and other sources have indicated that tenure track positions are not keeping up with demand, with the result that many Ph.D. graduates are looking to careers in industry.

The U.S. Department of Commerce report, October 2003, is available at http://www.technology.gov/reports/Biotechnology/CD120a_0310.pdf

Stockholm Seeking

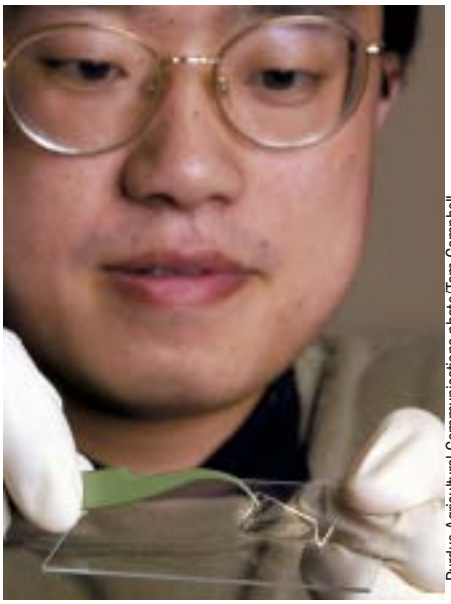
Stockholm, one of Europe's major centers of biomedical research, is now seeking a spot on that continent's biotech map. A group composed of AstraZeneca, one of the world's major pharmaceutical companies, the city of Stockholm, and Sweden's Karolinska Institute plans to invest $650,000 annually over five years to support biomedical research and to promote regional investments.

The new group, the Stockholm BioRegion, will focus on supporting revenue-generating operations, marketing the area, and seeking ways to encourage young people to study natural sciences. Uppsala, north of Stock-

Engineers Develop Quick, Inexpensive Method to Prototype Microchips

Purdue University researchers have developed a new method to quickly and inexpensively create microfluidic chips, analytic devices with potential applications in food safety, biosecurity, clinical diagnostics, pharmaceuticals and other industries.

Microfluidics is a branch of nanotechnology that involves manipulating minute quantities of liquids, typically in a chip device approximately the size of a postage stamp. Microchips have traditionally been made through a lengthy and expensive process called photolithography, which uses X-rays or ultraviolet light to form a pattern on a glass or silicon wafer that is then etched by washing the wafer with a variety of solvents. The key to controlling the shape and size of the patterns on the wafer is the production of a template, which can take weeks to develop.



Purdue Agricultural Communications photo/Tom Campbell

Purdue University graduate student Tom Huang assembles a new microfluidic chip by placing a thin layer of a flexible polymer on a glass microscope slide. The new method of producing these chips saves time and money and uses materials easily acquired by any research laboratory.

Michael Ladisch, Distinguished Professor of Agricultural and Biological Engineering and Biomedical Engineering, and his team have developed an alternative method that uses materials easily acquired by any research laboratory, including glass microscope slides, tweezers, thin glass fibers such as those found in glass wall insulation, and a flexible polymer called PDMS that is available from most scientific supply companies.

The new chip assembly method involves placing a fine fiber - approximately one-tenth the width of a human hair - on a glass slide and covering it with a small square of the polymer PDMS. The polymer flexes slightly over the fiber, creating a small channel on either side of the fiber, much the same way that a sheet of plastic wrap placed on top of a pencil would bend, making two channels running the pencil's length.

In their proof-of-concept paper, published in the November 2003 issue of the *American Institute of Chemical Engineers Journal*, the team showed that coating the fibers with materials that attract different types of molecules allowed them to separate specific proteins from a mixed solution. By manipulating the fiber's properties, scientists can identify or separate various types of molecules, such as proteins or antibodies, from solutions pumped through the chip. Depending on the properties of the fiber, liquids placed at one end of the channel move through the device by "wicking" along the fiber, or by being pulled through by with a weak vacuum at the opposite end of the channel. This ability translates into numerous potential applications, such as the ability to diagnose diseases or detect foodborne pathogens and biological agents.

"These kinds of chips are essential from a security perspective," said Bob Armstrong, senior research fellow at the National Defense University, one of the organizations that funded this research.

Place on Biotech Map

holm, has a similar organization, Uppsala Bio, and the two bodies have announced that they will work toward integration during 2004, and should not be viewed as competitors.

According to Barbro Berg, head of Innovation and Development at the Stockholm Economic Development Agency, the BioRegion's activities, told *The Scientist* that the main focus of the project is to support moneymaking applications. "The project aims at strengthening the commercialization of research, not research in itself," he said.The investments around Norra Station will create 1000 new job opportunities and 2000 new residences.

Australian Society for Medical Research Honors Former FASEB President

Former FASEB President Mary J.C. Hendrix, President and Scientific Director, Children's Memorial Institute for Education and Research, Northwestern University Feinberg School of Medicine, has been selected to be the national lecturer of the Australian Society for Medical Research (ASMR) during that organization's Medical Research Week this coming June, when she will be awarded the ASMR Medal.

ASMR Medical Research Week seeks to raise awareness of the benefits of medical research. Nobel Laureate Peter Doherty was the inaugural ASMR Medalist. His lecture tour in 1998 is regarded as a critical element in the push to double funding for Australia's National Health and Medical Research Council. Other ASMR national lecturers include Professor Ralph Bradshaw, also a Past-President of FASEB; Dame Bridget Ogilvie, Past-CEO of the Wellcome Trust; Professor Alan Bernstein, President of the Canadian Institutes of Health Research; Professor Lee Rosenberg, previously Chairman of the Funding First Organization and Chief Scientific Officer of Bristol Myers Squibb; and Professor Terry Dwyer, Director of the Menzies Institute for Population Health Research at the University of Tasmania.

In writing Dr. Hendrix, an ASBMB member, to inform her of her selection, ASMR President Andrew Sinclair stated:

"We keenly look forward to your participation in ASMR Medical Research Week in what will be a key year for the future of the Australian medical research community. In 1998, funding for medical research in Australia received a significant boost, with a doubling of NHMRC support over a five-year period. This injection of support is coming to an end and over the next year the ASMR Board of Directors will be advocating to the highest levels of Federal Government to ensure that funding for medical research is further increased to a level commensurate with other OECD countries. In Australia, 2004 is a federal election year and we want a commitment (from both major parties) to increased funding for health and medical research. Key to this outcome is a process of benchmarking Australian research performance and output, which is currently underway in Australia. If you are able to accept our invitation we would like you to consider focusing your lecture tour on the issue of benchmarking and developing a government framework for research."

The lecture tour covers Brisbane, Adelaide, Sydney, Canberra, Melbourne, and Perth. In Canberra, Dr. Hendrix is to deliver a nationally televised address at the National Press Club.

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.

Jason L. Burkhead*
Oregon Health and Science University

Yi Cao
Kansas State University

Rebecca J. Fairclough*
Oxford University

Christopher C. Marohnic
University of South Florida

Luminita Pojoga
Clemson University

Anita M. Preininger
Vanderbilt University

Shine S. Tu
Jolla Institute of Allergy and Immunology

** Candidates with an asterisk were previous Associate members who met the requirements for a free one-year membership.*

Career Opportunities

POST-DOCTORAL RESEARCH FELLOW (Job 4096)

A position is available at the Puget Sound Blood Center in Seattle, WA in the laboratory of Dr. Jonathan Drachman to study megakaryocyte development and thrombopoiesis. Projects will focus on signal transduction in hematopoietic cells and genetic studies of inherited platelet disorders. Candidates must have a Ph.D. or M.D. degree, a background in hematopoiesis, genetics, or signal transduction, and a valid Visa permitting work in the United States. Experience with tissue culture, molecular biology techniques, and protein analysis is desirable. Salary is in accordance with NIH postdoctoral pay scale. Qualified applicants should send their curriculum vitae and the names of three references to: Human Resources, Puget Sound Blood Center, 921 Terry Avenue, Seattle, WA 98104-1256, or email to HumanResources@psbc.org.

NATIONAL UNIVERSITY OF SINGAPORE

The National University of Singapore invites applications for a faculty appointment as Head of the Department of Biochemistry.

The Department of Biochemistry has 25 full-time academic staff and 10 adjunct staff. It has teaching commitments to medical, dental and science students and an active postgraduate research programme. It has a strong reputation in the broad research areas of molecular toxicology, molecular medicine, neurobiology, bioinformatics and structural biology, with special emphasis on research in venoms and toxins, gene cloning and expression, therapeutic gene transfer, ion channels, cell signaling, liposomes, ubiquitination, protein structure, proteomics, antioxidant and free radical biochemistry, nitric oxide, and neurodegenerative disease (further details at http://www.med.nus.edu.sg/bioweb/). The Department has excellent facilities for research in biochemistry and molecular and cell biology. The candidate should be an outstanding scholar who will be able to provide strong leadership in research and teaching. The candidate should have an excellent track record and international recognition in any area of research in biochemistry. Administrative experience would be an added advantage. Research support and laboratory facilities are available. Remuneration will be commensurate with the candidate's qualifications and experience. Leave and medical benefits will be provided.

Interested parties should submit their applications, supported by a c.v. and names of at least six referees to: Dean, Faculty of Medicine, National University of Singapore, Clinical Research Centre, Block MD 11, 10 Medical Drive, Singapore 117597. Fax:+65-6778-5743. Email: medleemk@nus.edu.sg . Closing Date: 15th April 2004

NATIONAL CANCER INSTITUTE

Postdoctoral fellowship

One 3-5 year Postdoctoral fellowship position is immediately available in the Department of Health and Human Services (DHHS), National Institutes of Health (NIH), National Cancer Institute's Laboratory of Molecular Immunoregulation operating in Frederick, Maryland. Candidate (M.D. or Ph.D. required) will have training in most aspects of molecular biology and biochemistry with a working knowledge of DNA repair, DNA methylation and gene transcription. Candidate is expected to provide leadership and independence in cancer cell apoptosis models. Good English writing and speaking skills are preferred. Interested candidates should submit their CV and three letters of reference to:

Dr. William Farrar
Principal Investigator
Molecular Immunoregulation Lab
Bldg. 560, Room 31-68
Frederick, MD 21702-1201
Phone: 301-846-1503
Fax: 301-846-7042
Email: farrar@ncifcrf.gov

DHHS and NIH are Equal Opportunity Employers

TULANE UNIVERSITY HEALTH SCIENCES CENTER

Training in Lung Molecular and Cellular Pathology

Three Post Doctoral positions are available to train in the basic mechanisms of lung disease, focusing on lung cell and molecular biology. Trainees in the program, using emerging technologies and new approaches, will acquire the skills necessary to design and conduct basic research in the pathobiology of fibrogenic, obstructive or neoplastic pulmonary diseases. The postdoctoral fellows will spend a minimum of two years in research training, supported by an NIH-level stipend.

Qualified applicants must present evidence of an earned M.D. or Ph.D degree and be a U.S. citizen, non-citizen national of the U.S., or must have been lawfully admitted for permanent residence. Successful applicants can start immediately. We emphasize that our Training Program is highly committed to increasing the representation of minority groups in scientific research.

Interested parties should include a curriculum vitae and introductory letter with any application sent to: Ms. Odette Marquez, Department of Pathology, Tulane University Health Sciences Center, 1430 Tulane Ave., New Orleans, LA 70118, Email: omarque@Tulane.edu, Phone (504) 588-5225.

Calendar of Scientific Meetings

MARCH 2004

Oxygen Club of California 2004 Congress

Co-sponsored by the Linus Pauling Institute and the Society of Free Radical Research International
March 10–13 • Santa Barbara, California
Contacts: Enrique Cadenas (cadenas@usc.edu); Lester Packer (packer@usc.edu); Website: http://www.oxyclubcalifornia.org

APRIL 2004

7th International Conference on Plasma Membrane Redox Systems and their Role in Biological Stress and Disease

April 14-17 • Asilomar State Park and Conference Center, Pacific Grove, California
Website: http://redox.cfs.purdue.edu

Experimental Biology 2004

April 17–21 • Washington, DC
Deadline for Submission of Abstracts: November 12, 2003
Website: http://www.faseb.org/meetings/eb2004/

Xth International Symposium on Amyloid and Amyloidosis

April 18-22 • Tours, France
A transdisciplinary meeting that will address basic as well as clinical aspects of this field
Deadline for Receipt of Abstracts: December 15th, 2003
Abstracts must be submitted in English and only via the web via http://www.colloquium.fr/isaa2004 where you will find all the necessary information for submission.
COLLOQUIUM-ISAA2004, 12 rue de la Croix-Faubin 75557 PARIS cedex 11 (France); Ph: +33 (0)1 44 64 15 15
Fx: +33 (0)1 44 64 15 16; email: isaa@colloquium.fr

MAY 2004

FEBS Lecture Course on Cellular Signaling & 4th Dubrovnik Signaling Conference

May 21-27 • Dubrovnik, Croatia
Application Deadline: March 1, 2004
The FEBS Lecture Course on Cellular Signaling and 4th Dubrovnik Signaling Conference are meeting jointly so that students who participate at the FEBS Lecture Course will also be able to attend all seminars and will have special tutorial sessions organized for their education.
TOPICS: Signaling cascades, Protein kinases and phosphatases, Cell compartmentalization and signaling, Receptor endocytosis and trafficking, Structural biology, GTPase signaling and diseases, Molecular targets for cancer therapy, Proteomics, Diabetes and Cardiovascular diseases
website: http://www.icst.irb.hr

Gene Transcription in Yeast EuroConference

May 29–June 3 • 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

JUNE 2004

American Society for Biochemistry and Molecular Biology Annual Meeting and 8th IUBMB Conference

June 12–16 • Boston, Massachusetts
Contact: Kelly Gull; Ph: 301-634-7145; Fx: 301-634-7126
Email: kgull@asbmb.faseb.org; Website: www.asbmb.org/meetings

JULY 2004

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

July 18-23 • Montréal, Canada
Abstract submission: January 23, 2004
Travel Award applications (FOCIS): January 23, 2004
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

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

SEPTEMBER 2004

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

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/

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/

JULY 2005

30th FEBS Congress — 9th IUBMB Conference, 2005 The Protein World; Proteins and Peptides: Structure, Function and Organization; Science is Fun: A Conference for Your Creativity

July 2–5 • Budapest, Hungary
Contact: Ms. Franciska Morlin, Chemol Travel Congress Dept. H-1366 Budapest, P.O.Box 28, Hungary
Ph:+36-1-266-7032, Fx: +36-1-266-7033
Email: incoming@chemoltravel.hu; www.febs-iubmb-2005.com

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.

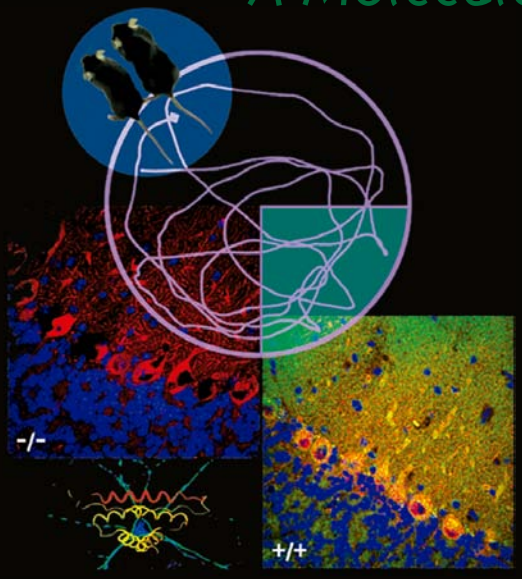
The Society is asking department chairs to provide ASBMB with the names and addresses of each new Ph.D. recipient from their institutions. Upon receipt of this information, we will write the new Ph.D.s to congratulate them on their accomplishment and offer the free one-year membership in ASBMB. Names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

IUBMB/ASBMB 2004

"A Molecular Exploration of the Cell"



June 12 – 16

Boston, MA

American Society for Biochemistry and Molecular Biology Annual Meeting and 8th IUBMB Conference

Proteomics and Bioinformatics ■ Chemical Biology ■ Molecular Recognition ■ Cellular Biochemistry

Opening Lecture

First Annual Herbert Tabor/Journal of Biological Chemistry *Lectureship*
Robert J. Lefkowitz, *HHMI, Duke University Medical Center*

Organized by:

John D. Scott, HHMI, *Vollum Institute;* Alexandra C. Newton, *UCSD;* Julio Celis, *Danish Cancer Society*, and the 2004 ASBMB Program Planning Committee

Cellular Organization and Dynamics
Organizer: Harald A. Stenmark, *Norwegian Rad. Hosp.*

Genomics, Proteomics and Bioinformatics
Organizers: Charlie Boone, *Univ. of Toronto* and Michael Snyder, *Yale Univ.*

Integration of Signaling Mechanisms
Organizer: Kjetil Tasken, *Univ. of Oslo, Norway*

Molecular and Cellular Biology of Lipids
Organizer: Dennis Vance, *Univ. of Alberta*

Molecular Recognition and Catalysis
Organizer: Jack E. Dixon, *UCSD*

Protein Modifications and Turnover
Organizer: William J. Lennarz, *SUNY at Stony Brook*

Protein Structure, Catalysis and Dynamics
Organizer: Susan Taylor, *UCSD*

Regulation of Gene Expression and Chromosome Transactions
Organizer: Joan W. Conaway, *Stowers Inst. for Med. Res.*

Signaling Pathways in Disease
Organizers: Alexandra Newton, *UCSD* and John D. Scott, *HHMI, Vollum Inst.*

The Future of Education and Professional Development in the Molecular Life Sciences
Organizer: J. Ellis Bell, *Univ. of Richmond*

For further information:

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Bethesda, MD 20814
Tel: 301-634-7145
Fax: 301-634-7126
Email: asbmb@asbmb.faseb.org
http://www.asbmb.org

www.faseb.org/meetings/asbmb04

Abstract Deadline: February 11, 2004