JUNE 2003

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San Diego: Scenic Setting for Outstanding Meeting

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AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

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Comments

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ASBMB President Urges VA Renew Commitment To Merit Review

The following is a letter to Nelda P. Wray, Chief Research and Development Officer of the Department of Veterans Affairs. For more on this topic see page 18.

Dear Dr. Wray,

I am writing as President of the American Society for Biochemistry and Molecular Biology (ASBMB) to express my concerns about the decision you made in early April not to fund a number of basic research grants. Ordinarily, this would not be an issue about which I would write, as grant applications are frequently declined for funding after undergoing peer review. However, the VA investigators involved had been notified verbally the previous fall by individuals in the Medical Research Service that the grants would, in fact, be funded.

The aspect of the matter that we at ASBMB find most disturbing is that the long-standing principle of peer review seems to have been ignored or marginalized in the decision to rescind these funding commitments. The early April notices to the investigators in question stated that the grant applications were not good enough to fund, despite the fact that the VA peer review system had judged them to be fundable. This "defunding" decision is nothing less than an assault on the principle of peer review that, whatever its faults, has been determined to be the best way to decide what research should be funded, particularly when public money is involved. We do not view it as an appropriate exercise of administrative authority to override the peer review system and choose **not** to fund grants that this system has recommended for funding, particularly in research areas outside the administrator's expertise.

It appears that a new review model was developed to review the grant applications in question and that, under this model, they were deemed unfundable. However, it is not apparent how this model has been analyzed or evaluated for its ability to predict outcomes and so its efficacy is widely suspect in the medical research community. For example, what publications would be considered high quality under your model? The *Journal of Biological Chemistry* (*JBC*) is consistently ranked by the Institute for Scientific Information with one of the highest impact factors as measured by the number of citations in the literature. Is the *JBC* on your list of acceptable publications? I mention this not from parochial concern about whether the *JBC* is on your list or not but rather to make the point that using publication in specific journals as a measure of the quality of a VA research proposal, or a researcher, is inherently inappropriate.

It is laudable that you have concerns about the quality of the VA peer review system but these concerns should be addressed by ensuring that excellent researchers with appropriate expertise constitute the review panels in the first place. The proper constitution of the review panels will then result in high quality proposals being funded and the VA Merit Review system being recognized as effective and fair.

Finally, the issue of the appropriateness of basic research in the VA system seems to be called into question by your actions in this matter. The grants adversely affected by your decision seem to be mostly basic in nature. Is there no place in your vision of the VA for basic research that focuses on underlying, broad health issues not necessarily related to specific diseases? The grants you have chosen **not** to fund deal with basic research and, in our opinion, this kind of "underpinning" research activity should continue to be an integral part of the VA research mission.

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ASBMB

Bleeding Disorder Tied to Defect in Cellular Transport Mechanism

Defects in a cargo receptor that shuttles proteins from one place to another within the cell lie at the root of a rare bleeding disorder.

That was the finding of an international research team led by ASBMB member David Ginsburg, Professor, Departments of Internal Medicine and Human Genetics in the University of Michigan's Life Sciences Institute, and a Howard Hughes Medical Institute Investigator. The team examined the genes of 19 patients from 12 families with a rare bleeding disorder called Combined Deficiency of Factor V and Factor VIII (F5F8D). An article in the June 2003 issue of *Nature Genetics*, reported that the group concluded that the bleeding disorder is not due to a problem within these two clotting factors; it is a problem of transporting the factors inside the cell.

Dr. David Ginsburg

Dr. Ginsburg said they used genetic analysis of the diseased families to find the problem. "That's the power of genetics," he said. "We can learn some fundamental things about biology by looking at the genes of these families with a rare disease."

Factor V and Factor VIII are just two of the many proteins that participate in a complex cascade of chemical reactions that lead to blood clotting. Various forms of abnormal bleeding and clotting have been tied to problems in many of these blood factors, but this disorder simultaneously involves two factors.

Earlier work on the disorder had identified a genetic mutation that causes defects in a protein called LMAN1, which apparently prevented a cell from secreting Factor V and Factor VIII. But about 30% of the F5F8D patients had normal levels of LMAN1, so this mutation alone couldn't account for all of the disease. The F5F8D patients in this study were all normal for LMAN1.

What the researchers found is that a mutation in a second gene, called MCFD2, can result in the same disease state. (MCFD2 is short for multiple coagulation factor deficiency 2.) The team identified seven distinct mutations in the MCFD2 gene which appeared in nine of the 12 families studied.

The researchers propose that these two proteins, LMAN1 and MCFD2, bind together to form a transporter which is specifically tailored to carry the two blood clotting factors from the cell's endoplasmic reticulum to the Golgi body. A mutation in the gene that makes either of the two proteins will result in a malformed transporter, and thus the inability to secrete Factor V and Factor VIII.

This work on bleeding disorders may also provide a solution for the opposite problem, clotting disorders. A drug that targeted the MCFD2 protein could reduce both Factor V and Factor VIII, lowering the risk of unwanted blood coagulation. Dr. Ginsburg said such a drug might be an attractive alternative to the oral anticoagulants, such as coumadin, because it would not affect other clotting factors. His lab is currently pursuing MCFD2 as a therapeutic target, and the U-M technology transfer office has applied for a patent.

There are still three families in the study who have the bleeding disorder, but weren't found to have mutations in either the LMAN1 or MCFD2 genes.

> ***"That's the power of genetics. We can learn some fundamental things about biology by looking at the genes of these families with a rare disease."***
>
> **— Dr. David Ginsburg**

"It's possible that we just missed it in the genetic screen, but it's also possible that there is a third gene involved," Dr. Ginsburg said.

Dr. Ginsburg's co-author on this work and others involving Factor VIII and LMAN1 is ASBMB member Randal Kaufman, a University of Michigan Biological Chemistry Professor and also an HHMI Investigator.

Columbia University Professors Receive International Award for Research

Two Columbia University researchers and ASBMB members, Dr. Richard Axel and Dr. Wayne A. Hendrickson, will receive the 2003 Gairdner International Award in recognition of their contributions that have led to the advancement of health care. The 44th annual award honors achievements in neuroscience and immunology.

"We congratulate Doctors Axel and Hendrickson on receiving this wonderful award that recognizes their remarkable achievements," said Dr. Gerald Fischbach, Executive Vice President for Health and Biomedical Sciences and Dean of the Faculty of Medicine at Columbia University. "Both scientists have opened new areas of research with innovative methodologies and have made revolutionary discoveries about molecular interactions in the immune system and in the brain."

Dr. Axel, University Professor in the Department of Biochemistry and Molecular Biophysics at Columbia University College of Physicians & Surgeons (P&S) and a Howard Hughes Medical Institute Investigator, is being recognized with Dr. Linda B. Buck, a former fellow of Dr. Axel's at P&S. Dr. Buck now is a full member of the Fred Hutchinson Cancer Research Center Basic Sciences Division. Dr. Axel and Dr. Buck have combined molecular genetics and neurobiology to address the problem of olfactory sensory perception. They have defined the genes involved in odor recognition and the neural circuits engaged in odor discrimination. Their discoveries provide new insight into how smell, the evocative sense, is represented in the brain.

Dr. Hendrickson, University Professor in the Department of Biochemistry and Molecular Biophysics at P&S and an Investigator of the Howard Hughes Medical Institute, is one of the world's preeminent structural biologists. He developed a method to speed the determination of atomic structures for biological molecules from the X-ray diffraction of crystals. Dr. Hendrickson's research team determined the structure of a key molecule that the AIDS virus uses to attach onto a human immune cell during infection, opening a new approach to the design of HIV antiviral drugs.

Other 2003 award recipients include Dr. Seiji Ogawa, Director of Ogawa Laboratories for Brain Function Research, Hamano Life Science Research Foundation, Tokyo, for his seminal work in functional magnetic resonance imaging (fMRI), a non-invasive method for imaging areas of the brain. This method has produced a technological revolution in cognitive neuroscience and is being explored in such clinical domains as aging and presurgical mapping.

Also to receive a Gairdner International Award is Dr. Ralph M. Steinman, Henry G. Kunkel Professor and Senior Physician, Rockefeller University, New York. Dr. Steinman's research addresses the fundamental mechanisms of immunity and the interface of several disease states with the immune system. This includes studies aimed at developing vaccines and immune-based therapies for tumors, infections and autoimmune diseases. Dr. Steinman discovered dendritic cells that are critical sentinels of the immune system differentiating between self and non-self, controlling responses from immune silencing (tolerance) to resistance (immunity).

The Gairdner Award winners will accept their awards, each $30,000 Canadian, at a gala dinner in Toronto on October 23. Also that month, the Canadian Institutes of Health Research and Gairdner Foundation will mount a national program of public lectures by Gairdner Award winners and a public symposium.

About the Gairdner Foundation

Established in 1957 by Toronto businessman James Gairdner, the Gairdner Foundation (www.gairdner.org) first recognized achievement in medical science in 1959. Over the past 44 years, the awards have grown to be one of the most prestigious international awards in medical research. Of the past 264 international awardees, in a variety of disciplines from genetic research to cancer therapy, 59 have gone on to win a Nobel Prize.

Diabetes in the Elderly Linked to Fewer Cellular 'Power Plants'

"By staying active, the elderly might well be able to maintain mitochondrial content and head off such health problems," according to ASBMB member Gerald Shulman, Professor of Medicine and Cellular and Molecular Physiology, Yale University School of Medicine and a Howard Hughes Medical Institute Investigator.

Elderly people may develop insulin resistance — one of the major risk factors for diabetes — because "power plants" in their muscle cells decline or fail with age, according to the findings of HHMI researchers at Yale University School of Medicine.

In studies of young and elderly people, the researchers found that older people had lower levels of metabolic activity in their mitochondria, the "factories" that provide power to cells. The findings suggest that reduced mitochondrial activity underlies insulin resistance, which is a major contributor to type 2 diabetes in the elderly.

In another recent study the researchers also found that physical activity can enhance the number of mitochondria in muscle by activation of a key enzyme called AMP kinase. "This is yet another reason for seniors to maintain an active lifestyle," said the study's senior author, Dr. Shulman. He and his colleagues reported their findings in the May 16 issue of the journal *Science*.

According to Dr. Shulman, pinpointing the cause of type 2 diabetes in the elderly would help solve a major health problem. "Approximately one in four individuals over the age of 60 has type 2 diabetes, which is a remarkable statistic," he said. "And, if you add impaired glucose tolerance, you're talking about 40% of the population."

The estimated economic burden of diabetes in United States is about $100 billion per year, a substantial proportion of which is due to diabetes in the elderly, according to the researchers.

At the biochemical level, the hormone insulin promotes the transfer of glucose in the blood into cells for energy production and storage. Mitochondria within the cells convert glucose and fatty acids into energy via oxidation.

According to Dr. Shulman, previous studies in his laboratory had shown that insulin resistance in muscle and liver tissue can result from accumulation of fat and fatty acid metabolites.

"We hypothesized that there were two routes to this type of fat accumulation," he said. "One is that the fat cells might release more fatty acids to be delivered to muscles and/or defects in mitochondrial oxidation might then lead to the accumulation of these fatty acids."

To trace the cause of insulin resistance in the elderly, the researchers compared glucose and fatty acid metabolism in matched groups of older and younger people. "One possibility is that as people age, they are less active and put on weight, and those factors are contributing to insulin resistance and diabetes," Dr. Shulman said. "So a key aspect of this study is that our older and younger samples of people were matched for fat mass, lean body mass and physical activity habits." The sample groups consisted of 16 elderly volunteers, aged 61 to 84 years, and 13 younger volunteers, aged 18 to 39.

In initial metabolic tests of the effectiveness of insulin in the two groups, Dr. Shulman and his colleagues found significantly higher insulin resistance in the elderly subjects. They traced the insulin resistance to muscle tissue, using a non-radioactive "heavy" tracer isotope and techniques to measure insulin resistance.

The researchers next turned to nuclear magnetic resonance spectroscopy (NMR), to zero in on muscle cells to determine whether they were accumulating fat. In NMR spectroscopy, harmless magnetic fields and radio frequency pulses are used to detect and quantify signals characteristic of specific molecules. The NMR studies revealed that the elderly subjects showed much higher fat accumulation in their muscle cells.

"This finding is important because studies in our lab and others have shown that the amount of lipid inside the muscle cell is a very good predictor of insulin resistance," reported Dr. Shulman.

Studies of the fat tissue in the elderly subjects showed that the fat cells were not releasing the extra fat that was accumulating in muscle. Thus, reasoned the researchers, the fatty molecules in the muscle cells might be accumulating due to defects in the cells' fat-burning mitochondria.

Using NMR to follow chemicals labeled with non-radioactive tracer isotopes, the researchers could specifically measure the metabolism of fat in functioning mitochondria within the subjects' muscle cells. Those studies revealed that, indeed, mitochondrial activity was reduced by about 40% in the cells of the elderly subjects, com-

continued on next page

Anthrax Genome Decoded

The complete genetic blueprint of *Bacillus anthracis*—the microbe that gained notoriety during the 2001 anthrax mail attacks—is now known. A formidable bioterrorist threat and the cause of potentially fatal inhalational anthrax, *B. anthracis* differs very little from the common soil bacterium that is its near relative, the scientists discovered. Those genetic differences are enough to give *B. anthracis* its disease-causing properties and may also give scientists valuable clues to its vulnerabilities.

The team of researchers supported by the National Institute of Allergy and Infectious Diseases (NIAID) and other federal agencies was led by ASBMB member Dr. Claire M. Fraser, and Dr. Timothy Read, at The Institute of Genomic Research in Rockville, Maryland. The complete sequence of the 5.2 million base pairs of the DNA in *B. anthracis*' single chromosome was published in the May 1 issue of *Nature*.

"The pace of microbial genomics research continues to be rapid; *B. anthracis* is just the latest of dozens of important human pathogens to be sequenced," noted NIAID Director Anthony S. Fauci. "As ever more precise details emerge about the genetic make-up of these organisms, our ability to design effective drugs and vaccines against the diseases they cause is greatly improved," he adds. To date, NIAID has supported sequencing efforts for more than 30 medically important microbes, many of which cause infectious diseases or are potential bioterror agents.

Dr. Read and his colleagues compared an isolate of the Ames strain of *B. anthracis* with two closely related *Bacillus* bacteria. "There is remarkably little difference among these genomes," he said. "In the 5,000 or more genes we analyzed, we found only 150 or so significant differences."

He and his coworkers found a number of genes encoding proteins that B. anthracis may need to enter its host's cells. These could provide targets for drugs designed against the organism, says Dr. Read.

Unlike its near relatives, *B. anthracis* possesses genes that give it the ability to thrive on protein-rich matter such as the decaying animal bodies it frequently grows on, the scientists discovered. Their analysis also found that *B. anthracis* has an enhanced capacity to scavenge iron, which it may use to survive in its host.

Dr. Claire M. Fraser

Using techniques of comparative genomics, the investigators gleaned several clues about the possible evolutionary pathway taken by *B. anthracis* ancestors. The similarities between certain *B. anthracis* genes and those of microbes that infect insects, for example, suggest that a recent ancestor of *B. anthracis* may have infected insects. Of note is a similarity between one gene of *Yersinia pestis*, which causes plague in mammals and can also infect insects, and a gene in *B. anthracis*, which infects only mammals.

NIAID supported the anthrax sequencing through the pathogen functional genomics resource center at TIGR. This initiative, launched by NIAID in 2001, trains researchers in the latest techniques in functional genomics. It also serves as a reagent repository. The center's resources are available to the scientific community through online and other services. Besides NIAID, support for the anthrax sequencing effort came from the United States Office of Naval Research, the Department of Energy and the United Kingdom's Defense Sciences Technology Laboratory.

NIAID is a component of the National Institutes of Health (NIH), which is an agency of the Department of Health and Human Services. NIAID supports basic and applied research to prevent, diagnose, and treat infectious and immune-mediated illnesses, including HIV/AIDS and other sexually transmitted diseases, illness from potential agents of bioterrorism, tuberculosis, malaria, autoimmune disorders, asthma and allergies.

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continued from previous page

pared with the young.

Dr. Shulman theorizes that if the same mitochondrial defects occur in the insulin-producing cells of the pancreas, the progression from insulin resistance to diabetes will be complete.

He said that before researchers can develop new clinical treatments to enhance mitochondrial function and thus help prevent diabetes, they must understand a great deal more about mitochondria. More basic research is needed to understand whether the number or individual activity of mitochondria are reduced in the elderly, as well as the role of mutations or other factors in such age-related reductions, he said.

"However, an encouraging note in this study is that — since we've shown that exercise leads to more mitochondria by activation of AMP kinase — by staying active, the elderly might well be able to maintain mitochondrial content and head off such health problems," concluded Dr. Shulman. To test that possibility, the researchers also plan studies to compare mitochondrial activity in active and sedentary elderly people.

Growing Human Skin In Laboratory Can Prematurely Age Cells

Children who receive laboratory-expanded sheets of their own skin to cover severe burns are saved from certain death, but their new skin can have the cellular age of an 80 year old, according to a study at Duke University Medical Center.

The process of growing small patches of human skin into larger sheets, called tissue engineering, makes cells divide so many times that the skin becomes prematurely aged at a cellular level. The dangers of prematurely aged skin are that it will not regenerate for the duration of the child's life, and its wound-healing capacity could be severely compromised, said ASBMB member Dr. Christopher Counter, a cancer biologist in the Duke Comprehensive Cancer Center.

"Although tissue engineering is a life-saving technique... the skin could ultimately lose its regenerative capacity over a period of decades."

—Dr. Christopher Counter

Results of his study were published in the April 19, 2003, issue of the British medical journal, *The Lancet*.

"Although tissue engineering is a life-saving technique, our work suggests that the skin could ultimately lose its regenerative capacity over a period of decades," said Dr. Counter. "Conversely, we might unwittingly select cells that have a mutation and keep dividing uncontrollably in the patient, which is a hallmark of cancer." To date, tissue engineering has saved more than 700 patients who had burns covering more than 75% of their bodies, and, he points out, so far most of these grafts are fine.

To determine the cellular age of expanded skin grafts, Dr. Counter's team analyzed samples from four burn victims years after they received "cultured" skin grown in the laboratory. Culturing the skin involves taking small patches of undamaged skin from the patient and placing them in a large dish, where the skin cells divide and multiply to form a sheet.

The cultured sheets of skin are then placed over the patient's burned tissue. Within days, the skin sheets permanently engraft, attaching to the healing connective tissue in the wound bed. Because the skin is autologous, or derived from the patient, there is no chance of rejection. Such a process is used when there is not enough of the patients' unburned skin to cover expansive, third degree burns.

Dr. Counter said that years after the engraftment, the skin continues to look normal. But a closer analysis of cultured skin showed extensive changes in the chromosomes of skin cells.

Specifically, he and co-investigators Dr. William Press and Dr. Carolyn Compton found that cultured skin cells had much shorter chromosomal tips than did normal skin cells. Chromosomes are the strands of DNA in each cell that carry its genetic code, and the end of a chromosome is its "telomere." Every time a cell divides, its chromosomal telomeres become shorter until they are so short that the cell receives a signal to commit suicide.

The exponential cell division that skin patches undergo during the expansion process caused telomeres to become excessively short, analogous to the skin of an 80 year old. This aging process is what he speculates might curtail the lifespan of the skin.

Dr. Counter said evidence of this phe-

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.

Len Edelstein
University of Medicine and Dentistry of New Jersey and Rutgers University

Sung-Hae Lee Kang
University of Florida, Gainesville

June Oshiro
Rutgers University

Anurag Varsheny*
Yale University School of Medicine

Hongyan Zhong
University of Texas, Houston

** Previous associate member who met the requirements for a free one-year membership.*

nomenon is strong, both from human and animal studies. Certain skin diseases such as dyskeratosis congenita cause telomeres to become excessively short, resulting in skin defects and reduced wound-healing capacity, he added.

Dr. Christopher Counter

"In fact in every organism ever tested, ranging from yeast to mice to humans, extensive loss of telomeric DNA has the same consequence: a reduction in the proliferative capacity of the cells," he noted.

Dr. Counter and his team speculate that briefly adding an enzyme, called telomerase, during the laboratory expansion process might elongate telomeres enough that they would sustain their regenerative capacity. Telomerase is produced by highly proliferative cells, such as adult stem cells, in order to prolong their lifespan. Yet telomerase produced by the wrong cells in the body can unnaturally extend the cell's life and hence promote the growth of cancer. In fact, recent studies have shown that telomerase is found in 85% of all cancers.

Using telomerase briefly and at the right timeframe during skin growth might allow telomeres to be appropriately long without stimulating the over-growth that is characteristic in all cancer, said Dr. Counter. "Not only does our data have relevance to the burn victims, but also is a red flag that other tissues engineered in the lab may run into the same problem."

Charles J. Sherr Awarded Prize for Cancer Research

Charles J. Sherr, a Howard Hughes Medical Institute (HHMI) Investigator based at St. Jude Children's Research Hospital in Memphis, Tennessee, has been awarded the Kirk A. Landon-AACR Prize for Basic Research. The prize includes an unrestricted cash award of $200,000 and the recipient presents a scientific lecture at the AACR Annual Meeting.

Dr. Sherr, an ASBMB member and Herrick Foundation Chair, Department of Genetics and Tumor Cell Biology at St. Jude Children's Research Hospital, is being honored for his significant contributions to the understanding of mechanisms of cell growth control and neoplastic transformation, particularly as they relate to the mammalian cell division cycle. His seminal research ultimately led to the discoveries of two major tumor suppressive pathways that, when mutated, result in human cancer. His work offers the promise of new therapies designed to make cells more sensitive to the many conventional forms of anti-cancer therapy that act by damaging the DNA of tumor cells.

Dr. Charles Sherr

Said Dr. Sherr, "I was surprised and excited to receive this year's Landon-AACR Prize for Basic Science. In essence, this award acknowledges the important contributions of the many postdoctoral fellows, students, and collaborators who have contributed to discoveries in our laboratory. Anyone who has followed my science knows that I share this prize (and much more) with my closest colleague, Dr. Martine F. Roussel."

The Landon/AACR Prizes in Cancer Research were launched in 2002 to promote and reward seminal contributions to the understanding of cancer through basic and translational cancer research. The prizes are designed to bring heightened public attention to landmark achievements in the continuing effort to prevent and cure cancer.

The Kirk A. and Dorothy P. Landon Foundation was created through a bequest from Mrs. Landon who willed that her estate be committed to medical research, especially on cancer and cancer-related diseases.

Letter continued ...

continued from page 2

In summary, it is our hope that the VA will reconsider funding the grants that have been rescinded and that a peer review model be used to assess VA research grant applications in a transparent process that will allow researchers to know what criteria they must meet. We would also be pleased to work with you to develop ways to improve the VA peer review system. Many of our members are experienced NIH study section members and are very familiar with how such a system can function effectively.

Please let us know how we can be of assistance in addressing these problems.

Sincerely,
Bettie Sue Masters, President, ASBMB

Leading Researchers Highlight

A galaxy of award winning scientists were among the many outstanding speakers who discussed the findings of their latest research at ASBMB's Annual Meeting, April 11-15, in San Diego.

Ion Channels was the topic for Roderick MacKinnon, Howard Hughes Medical Institute Investigator and Professor, Laboratory of Molecular Neurobiology and Biophysics, Rockefeller University, and recipient of the 2003 Fritz Lipmann Lectureship, whose keynote lecture opened the Annual Meeting.

Ion channels is a topic which Dr. MacKinnon is eminently qualified to address. In 1998, through the use of X-ray crystallography his laboratory established the structure of the potassium ion channel. This led to his receiving the 1999 Albert Lasker Basic Medical Research Award.

Annual Meeting

Better Understanding Ion Channels

Dr. MacKinnon's research addressed the atomic basis of electrical signaling in living cells. Initially his laboratory used mutational and electrophysiological analyses to show that potassium channels are tetramers of identical subunits and that a specific segment of amino acids—which he and his colleagues called the potassium channel signature sequence—is conserved in all potassium channels throughout nature and forms the selectivity filter. Having reached the limits of information that his initial techniques could provide, he next went on to address the mechanisms of ion selectivity and conduction at the atomic level through X-ray crystallography of potassium and chloride ion channels.

His laboratory has determined the structures of the two known valence selective ion channels, potassium and chloride channels. In their first major breakthrough they showed that potassium channels feature an "inverted teepee-shaped" pore that protrudes through the cell membrane and forms a pore that holds multiple potassium ions during their transmembrane passage. Through the use of monoclonal antibody fragment mediated crystallization they have advanced the resolution to provide an atomic description of potassium coordination in breathtaking detail. The selectivity filter, comprised of the signature sequence amino acids defined in Dr. MacKinnon's laboratory, creates a unique sequence of cages that delicately hold potassium ions via carbonyl oxygen atoms, much in the same manner that water molecules hold potassium in the hydrated state.

Roderick MacKinnon, Howard Hughes Medical Institute Investigator and Professor, Laboratory of Molecular Neurobiology and Biophysics, Rockefeller University, opened the Annual Meeting with the 2003 Fritz Lipmann Lecture.

Recently, he and his colleagues determined the structure of a chloride ion channel. "Nature uses a fundamentally different architecture to conduct the anion chloride as compared to the cation potassium, but it is clear that within the very different architectures similar physical principles—helix dipoles, backbone atoms, partial charges, multiple ions—are used. It is very beautiful."

Discovery Of Proteins Necessary For HIV Release Suggests Possible New Therapeutic Targets

Dr. Wesley Sundquist, Professor of Biochemistry at the University of Utah, discussed his work in elucidating how HIV is manufactured and assembled in the cell.

The raison d'etre of a virus such as HIV is to turn a host cell into a factory that churns out virus copies and releases them to infect other cells. Dr. Sundquist's research has focused on discovering the mechanisms underlying this manufacturing process.

By identifying and characterizing the structures of specific cellular proteins that are crucial to assembling HIV, Dr. Sundquist is providing potential new targets for future anti-HIV drugs. For example, he and his colleagues were the first to show that a protein called TSG101 is required for HIV release. HIV needs TSG101 in order to escape from its host cell in a process termed budding. Dr. Sundquist's team has also

Michael Gresser (at right), Vice President, Research, Amgen Corporation, presents the ASBMB-Amgen Award to Wesley Sundquist, Professor of Biochemistry at the University of Utah. The Award recognized Dr. Sundquist for his significant achievements in the application of biochemistry and molecular biology to the understanding of disease. In his lecture, Dr. Sundquist discussed his work in elucidating how HIV is manufactured and assembled in the cell.

Filled meeting rooms and attentive audiences were the order of the day at ASBMB's Annual Meeting.

Meeting Photos by Nicoli Productions, Escondido, California

Thomas Steitz, Eugene Higgins Professor and HHMI Investigator, Department of Molecular Biophysics and Biochemistry at Yale University delivered a plenary lecture entitled "The Structural Basis of DNA Makes DNA Makes RNA Makes Protein."

determined the structure of the part of TSG101 to which HIV binds. Finding ways to alter this structure or otherwise block its binding to HIV theoretically would prevent budding and slow or halt the infection.

Dr. Sundquist is the 2003 recipient of the ASBMB-Amgen Award. Among the research strengths for which he has been lauded is his use of a wide palette of experimental techniques to determine the structures of key components in HIV assembly. By incorporating nuclear magnetic resonance imaging, cryogenic electron microscopy, genetic analysis, and other technologies into his lab, he has produced compelling findings that have made him a leader in the field of HIV research and structural biology.

Robert Bittman, Distinguished Professor of Chemistry and Biochemistry at Queens College and the Graduate School of the City University of New York, delivered the Avanti Award in Lipids Lecture. He was presented with the Award by Walter Shaw (left), President, Avanti Polar Lipids, Inc.

Perhaps even more significant, he not only produces vivid descriptions of important molecular structures but also uses his findings to predict the potential effects of manipulating these molecules. Having identified the three-dimensional structures of two proteins, Matrix and Capsid, which are key components of the HIV assembly line, Dr. Sundquist and his colleagues now aim to understand exactly how these proteins help assemble the virus. Their studies will guide the development of drugs that target those proteins.

Creating 'Unnatural Analogs' Produces Better Understanding, Weapons in Fight Against Cancer, Viruses and Other Disease

Ceramide, a naturally occurring sphingosine-based lipid, is generated in response to various cellular stresses, including chemotherapy and radiation. That is good, since it works to induce cell death. The problem is that the cells' enzymes quickly learn to recognize ceramide. In their efforts to change the apoptosis-inducing substance, cells add a sugar molecule to the ceramide, turning it into a cell-growth enhancer, not a cancer cell suppressor, or they remove a long chain from ceramide and thereby make it less effective.

Robert Bittman, Distinguished Professor of Chemistry and Biochemistry at Queens College and the Graduate School of the City University of New York, one of organic chemistry's most distinguished scientists, described his current work using chemical synthesis to create unnatural analogs of naturally occurring compounds. Having defined which components of the compounds do what, Dr. Bitmann, a recipient of the 2003 Avanti Award in Lipids, and colleagues were able to create compounds that better achieve desired objectives. By taking out one atom in ceramide and putting in another, for example, they created ceramide-like compounds that more effectively destroy cancer cells in cell cultures while escaping recognition by enzymes that would normally metabolize and wipe out normal ceramide.

Lipid rafts are transient, specialized microdomains in biological membranes that contain cholesterol and various sphingolipids. They are called rafts because the lipids float on top of a tube containing different densities. Many scientists believe lipid rafts are the platforms by which various viruses, including HIV, gain entry into the cells. The viruses may simply be looking for sphingolipids, but the effect can be devastating to the host. Are rafts required in general for viral binding to cell membranes? Knowing the answer to this question would greatly affect the approach taken by scientists in the development of various drugs.

Former ASBMB President Judith Klinman (left) and current President Bettie Sue Masters congratulate Catherine Drennan, Assistant Professor, Chemistry Department, Massachusetts Institute of Technology, on her receipt of the Schering-Plough Scientific Achievement Award. At right is Rob Ralston of Schering-Plough subsidiary Canji, Inc., who presented the Award.

Schering-Plough Scientific Achievement Award recipient Catherine Drennan (left) with her mother, Mildred Luschinsky, who came from Newton, Massachusetts to see her daughter get the Award.

Dr. Bittman and his co-workers recently analyzed the lipids required in the cell entry of two alphaviruses called Semliki Forest virus and Sindbis virus (both carried by mosquitoes but not dangerous to humans). They then created another unnatural compound by synthesizing analogs of a phospholipid called sphingomyelin. Because of their different structure, these new, unnatural compounds do not form rafts. The scientists found that the alphaviruses were able to bind to the cell without rafts, indicating that some viruses fuse with cell membranes that do not contain rafts.

Anti-tumor ether lipids are among the newest experimental anticancer agents and have two strengths. First, because they are unnatural compounds, they are highly resistant to the normal metabolic reactions that degrade most naturally occurring molecules in cells.

Second, they differ from conventional cancer chemotherapeutic agents because they do not interact directly with the cell's DNA, which means they do not give rise to mutations themselves. Instead, they block the growth of different types of cancer cells by a variety of mechanisms that involve interactions with proteins in cell membranes and with intracellular proteins in signaling pathways.

By synthesizing analogs of antitumor ether lipids and studying the mechanisms by which they promote cancer cell death, Dr. Bittman and his co-workers have found that the most promising compound in the antitumor ether lipid family, ET-18-0CH3, kills cancer cells by causing a protein called cytochome c to leak out of the mitochondria. Since mitochondria are the power houses of the cell, this leakage causes the cell itself to die. But, again, there is a price to pay. The naturally occurring ET-18-0CH3 has hemolytic properties so that patients can develop thrombosis. By creating an unnatural compound, changing the structure to put a sugar in the place of another atom, Dr. Bittman's team has made a compound that does not have hemolytic properties but retains its antitumor properties. He is now trying to understand the way the anti-tumor ether lipid interacts with various proteins in the cell.

New Markers for Alzheimer's Found

Those attending an EB 2003 American Physiological Society session, heard how Swiss researchers, all ASBMB members, discovered several new markers that, grouped together, correctly diagnosed Alzheimer's disease in nine out of ten patients studied, using only a very small amount of cerebrospinal fluid. Ten healthy control patients also were all correctly identified.

Dr. Odile Carrette, a postdoctoral fellow in the laboratory of Dr. Denis Hochstrasser, working under the supervision of Dr Jean-Charles Sanchez, Geneva University Hospital, said the discovery of the markers was made possible with a new Surface Enhanced Laser Desorption Ionization (SELDI) technology recently developed by Ciphergen Biosystems.

The SELDI technology is based on the development of specific protein chip surfaces that enable capture, purification, analysis and processing of proteins in complex biological mixtures. The Swiss researchers used the protein chip surfaces to look for proteins with specific biochemical properties in cerebrospinal fluid from 10 Alzheimer's patients and 10 healthy controls. Protein surfaces used were: the hydrophobic surface which retains protein with hydrophobic groupings, the WCX2 which retains protein with anionic grouping at the surface, and the IMAC surface which chooses proteins with some affinity for a divalent ion such as the copper ion.

Once retained on the protein's surface and co-crystallized with an energy-absorbing molecule, the proteins were desorbed and ionized under the pulse of a nitrogen laser, then accelerated through a voltage field and analyzed on a detector. In such conditions, the proteins fly according to their mass and ionic charge. The result is expressed as a spectrum where each different peak corresponds to a protein. The relative intensity of each peak found in all

ASBMB Council Members Vern Schramm, Program Committee Co-Chair (at left) and Treasurer Kenneth Neet were among those attending plenary lecture by Dr. Thomas Hunter, whose topic was "Protein Phosphorylation and Intracellular Signaling Networks in the Postgenomic Era."

ASBMB Minority Affairs Committee member Dr. Juliette Bell, of Fayetteville, N.C., State University, spoke at a symposium on "Diversifying the Profession: Who? What? Where? and How?"

FASEB Excellence in Science Award Lecture was delivered by former ASBMB Council member Joan Steitz. Her topic was "Pre-mRNA Splicing: The Tie that Binds."

the spectra was analyzed to determine which proteins were significantly different between the two groups being compared.

Dr. Carrette says the fact that the individual markers considered separately had only weak diagnostic abilities confirms the complexity of the pathology of Alzheimer's and the need for diagnostic tests that can consider several parameters simultaneously.

Enzyme Phosphatases Play Role in Diseases from the Plague to Cancer and Muscle Myopathies

A large family of enzymes called protein tyrosine phosphatases, or PTPases for short, play important roles in cellular signaling within and between cells. By removing phosphates from proteins, PTPases change how proteins function and respond to environmental signals like growth factors, neuronal firing, even the presence of an invading bacteria or pathogen.

The 2003 William C. Rose Award Lecturer, Dr. Jack E. Dixon, Professor in the Department of Pharmacology, Cellular and Molecular Medicine, and Dean of Scientific Affairs at the University of California, San Diego, is the scientist who first identified the role PTPases played in the plague or "Black Death." His lecture described his current research using functional genomics to define the roles of bacterial virulence factors in animal and plant pathogenesis, and outlined the role the phosphatases play in the plague and other bacterial pathogenesis as well as in the development of cancer and muscle myopathy.

When Dr. Dixon, a former President of ASBMB, first began his research on *Yersinia*, the genus of bacteria responsible for the plague, scientists did not believe any bacteria contained any proteins phosphorylated on tyrosine. Dr. Dixon found that *Yersinia* actually harbors the most active PTPase ever described, and that the presence of PTPase in the bacteria was what allowed it to cause such a virulent disease. He demonstrated that the *Yersinia* PTPase can enter a macrophage and inhibit the cellular processes essential for antigen presentation, thus disarming the body's immune response to the pathogen. This discovery brought him widespread recognition in the scientific community, and he says it also stimulated his laboratory's interest in understanding how other proteins in the *Yersinia* family functioned.

In related research, building on his work on the regulatory paradigm for the PTPases in general, his laboratory was able to identify and determine the function of a tumor suppressor gene, PTEN. PTEN catalyzes the removal of phosphate, beginning a cascade of cellular events that signal cells to survive, not to destroy themselves through apoptosis. Surviving cells begin multiplying and can become cancerous. This helpful gene is noticeably absent in many human cancers, and Dr. Dixon's explanation of the function of PTEN provided the first clear rationale for why its loss plays a key role in oncogenesis, radically altering scientists' thinking about this tumor suppressor gene.

The discovery that the tumor suppressor gene PTEN was a phosphatase promoted a search for other protein phosphatases that might be involved with disease processes. Dr. Dixon's laboratory recently found a protein phosphatase known as myotubularin, which removes a specific phosphate from the cells. Mutations in the

William C. Rose Award Lecturer Jack E. Dixon (left) receives the Award from M. J. Coon, Professor in the Department of Biological Chemistry, University of Michigan Health Center.

One trainer, two ASBMB Award recipients. Dr.Thomas C. Bruice (center), one of the fathers of Bio-Organic Chemistry was, at different times, graduate student advisor to William C. Rose Award Lecturer Jack E. Dixon (left) and ASBMB-Merck Award Lecturer Stephen Benkovic (right). Said Dr. Dixon, "My guess is that is is pretty rare to have a single reseach director train two people who got ASBMB awards in a single year."

Paul Craig, Associate Professor, Rochester Institute of Technology, discussed the new ASBMB Digital Library, BioMoleculesAlive.com.

myotubularin gene cause a muscle myopathy known as X-linked myotubular myopathy. Dr. Dixon's discovery of the novel function of myotubularin suggests that the underlying cause of this disease involves an aberration in phosphoinositide metabolism.

Protacs: New 'Chemical Genetic' Tool Forces Cells to Target, Destroy Harmful Proteins in Those Cells

When 'rogue' proteins begin wreaking havoc within cells, the result is diseases such as cancer, heart disease, and inflammatory diseases like rheumatoid arthritis. Scientists at Yale University and the Howard Hughes Medical Institute at California Institute of Technology have created a new technology to push the out-of-control protein into closer proximity of the cell's natural protein degradatory machinery.

"We hijack the cell's protein degradatory machine for our purposes," says Yale's Craig Crews, Associate Professor in the Department of Molecular, Cellular and Developmental Biology, "and induce the destruction of the protein whether the cells want it degraded or not." He and Cal Tech collaborator Dr. Raymon Deshaies believe the technology has enormous therapeutic and screening potential.

Dr. Crews presented the first evidence that the new technology, called Protacs for Proteolysis Targeting Chimera, works as hoped within intact cells. Earlier studies at Yale and Cal Tech had demonstrated Protacs' success in targeting and destroying proteins in a cell-free assay.

The Protacs system, developed by Dr. Crews in collaboration with Dr. Deshaies, is a carefully constructed chimeric compound. It uses components of the ubiquination pathway, a naturally-occurring pathway of enzymes and ligases that degrade cellular proteins as required for normal maintenance of cellular function. By adding given proteins to specific types of ubiquitin-protein ligases, the team was able to target these proteins for destruction.

In the study reported at Experimental Biology 2003, Dr. Crews first introduced a green fluorescent protein fused with a small molecule receptor into cells grown in a petri dish. Simply adding a Protacs molecule to the cell culture, the green fluorescent protein fusion protein was induced in order to be degraded. This was possible because the Protacs molecule is a dumbbell-shaped compound. On one end, a chemical binds to the green fluorescent protein fusion protein. On the other end a different chemical binds to a ubiquitin ligases.

By binding both target protein and the ubiquitin-mediated protein degradation machinery, Protacs recruit proteins for their untimely demise. In the case of the proof-of-concept experiment performed by Dr. Crews' laboratory, the protein degradation was readily observed as the green fluorescent protein degraded and the cells lost fluorescence within an hour.

Graduate student Jay Schneekloth (left) worked with Dr. Craig Crews (right) to develop a tool that forces cells to target and destroy harmful proteins.

Dr. Crews says these results suggest that Protacs has enormous potential as a therapeutic tool to degrade or destroy the proteins causing problems, in the same way that genetic therapy attempts to change or stop the function of a particular protein by altering the DNA encoding that protein.

With the development of a library of Protacs compounds, Protacs also could be used to perform large-scale chemical genetic screens of protein loss of function.

Howard K. Schachman Public Service Award Honors Ruth Kirschstein

Ruth Kirschstein, Senior Advisor to the NIH Director, was presented with ASBMB's Howard K. Schachman Public Service Award at a special symposium in her honor at the San Diego meeting.

Dr. Kirschstein is the second recipient of the award, and was recognized for her decades of service at the National Institutes of Health, her 20 years of leadership of the National Institute of General Medical Sciences, her two terms as Acting NIH Director, and her staunch support of education and training in biomedical research, especially for those populations long underrepresented in the field.

Dr. Ruth Kirschstein

In presenting the award, Public Affairs Advisory Committee Chairman William R. Brinkley, stated, "This year the HKS Award goes to one who is known, loved and admired by everyone in the biomedical science community. In fact, a few people are so well known that you only need to say their first name, i.e., Madonna, Jackie, Elvis, and everyone recognizes them immediately. The same is true for our awardee. If I mention the name 'Dr. Ruth' (in the context of NIH!), you immediately recognize a most distinguished and beloved leader by the name of Dr. Ruth Kirschstein, who has always been there for our members, whenever she is needed!"

Standing ovation from audience accompanied presentation of Howard K. Schachman Public Service Award to Dr. Ruth Kirschstein.

"Public service in support of researchers at all career levels has filled my entire working life with great joy and I hope to continue such service for many years to come," Dr. Kirschstein wrote to former ASBMB President Robert Wells, who presided at the symposium held in her honor at the Annual Meeting in San Diego.

The award this year was an early-19th century brass student microscope manufactured in Britain, photo (above). The microscope, still in excellent working order, screws into the top of a wooden accessory case which contains two additional lenses and two original specimen slides made of ivory. As a federal official, Dr. Kirschstein is unable to accept the award personally. However, she is donating it to the National Library of Medicine where it will become part of the permanent museum collection there.

The Schachman Public Service Award was founded in 2001, and the first recipient was former Congressman John Edward Porter. The award is named after the Society's longtime Public Affairs Committee Chairman, Howard K. Schachman, to honor his 12 years of service in that role.

John Scott Elected Fellow of Royal Society

Professor John Scott, Senior Scientist and Director of Academic Development at Vollum Institute, Oregon Health & Science University, and Associate Investigator of the Howard Hughes Medical Institute was among 42 new Fellows and 6 Foreign Members from the fields of science, engineering and technology elected by the Royal Society on May 15.

Dr. Scott has pioneered the analysis of anchoring and scaffolding proteins that play a critical role in organizing the process of cellular signal transduction. His work has been instrumental in defining a family of A-kinase anchoring proteins, termed AKAPs, that function to target the cAMP-dependent protein kinase and other signaling enzymes to specific subcellular locations. An elegant combination of molecular and physiological approaches have been used to define the mechanisms by which AKAPs interact with their targets, and to identify cellular activities that depend on AKAP function, such as the modulation of various ion channels, insulin secretion from ßislet cells, cytoskeletal reorganization and specific transcription events. Professor Scott's work has markedly altered the way we think about signal transduction pathways.

Fellows are elected for their contributions to science, both in fundamental research resulting in greater understanding, and also in leading and directing scientific and technological progress in industry and research establishments. A maximum of 42 new Fellows, who must be citizens or residents of Commonwealth countries or Ireland, may be elected annually.

Molecular Pharmacology Pioneer Honored

Dr. Palmer Taylor, Sandra and Monroe Trout Professor and Chair of the Department of Pharmacology at the University of California, San Diego received the 2003 Torald Sollmann Award at the opening ceremony of the American Society for Pharmacology and Experimental Therapeutics meeting, part of EB 2003 in San Diego. The award was established by Wyeth-Ayerst Research to commemorate Dr. Sollman's pioneering work in the fields of pharmacological investigation and education. Dr. Taylor received the award in recognition of his innovative and extraordinary scientific accomplishments and dedication to the field of pharmacology over three decades.

Both an ASBMB and ASPET member, Dr. Taylor is one of the pioneers of molecular pharmacology, with his work on the structural and functional properties of acetylcholinesterase and the nicotinic acetylcholine receptor. He was one of the first to introduce physiochemical methods and natural toxins as a means to deduce ligand binding site topology in receptors, and he fully embraced the power of molecular biology to examine pharmacological targets long before this became generally recognized.

Dr. Taylor has been a long-standing contributor to Goodman and Gilman's Pharmacological Basis of Therapeutics and Principles of Drug Action, serves on several editorial boards and is on the founding board of Molecular Interventions. In expanding and ensuring vitality in the Department of Pharmacology at UCSD, which he chaired for the past 14 years, he and his colleagues have established a Superfund Center on environmental stressors and gene expression, and a Pharmacogenomics Center oriented to targets of drug action.

More recently he led the development of a School of Pharmacy and Pharmaceutical Sciences at UCSD, the second in the University of California system and the only public pharmacy school in southern California. He is a past President of the American Society for Pharmacology and Experimental Therapeutics.

XIX International Congress of Biochemistry & Molecular Biology Cancelled

Due to the most recent outbreak of SARS in the Toronto area, the 2003 Congress Executive and Steering Committees have concluded that it is in the best interest of all delegates, exhibitors, sponsors and partners that the IUBMB Congress scheduled for July 20-24 be cancelled.

The Congress Secretariat will return all registration fees paid in full.

It is each individual's responsibility to cancel his or her hotel reservation. Please contact the Housing Bureau directly at housing@torcvb.com or by fax at (416) 203-8477.

If you are registered for a Satellite meeting, please contact the relevant organizer directly.

All registered exhibitors will be refunded their booth fees, in full. (This does not apply to those who cancelled prior to the cancellation of the Congress). Exhibitors should contact all official suppliers from whom services have been ordered to cancel all previous arrangements.

Air Canada is currently allowing a change of date of travel (to December 31) for $75 plus any fare differential per flight. Other airlines have similar policies. Should the WHO reinstate a travel alert for Toronto, we expect Air Canada will allow one change free of charge. We hope you will be able to use these tickets to attend another meeting or take a vacation in Southern Ontario.

By Peter Farnham, ASBMB Public Affairs Officer

Controversy Erupts Over New VA Research

Dr. Nelda Wray became Chief Research and Development Officer at the Department of Veterans Affairs in January 2003. Among other accomplishments—medical degree from Baylor, Masters of Public Health from the University of Texas, board certification in both internal and pulmonary medicine, first woman to be named Professor of Medicine in Baylor's Department of Medicine—she is also a nationally recognized expert in outcomes research.

However, it is unlikely that her illustrious background prepared her for the outcomes of a controversial decision she made shortly after taking her post as head of research at the Department of Veterans Affairs in January 2003. Among the outcomes: enraged VA researchers, growing congressional annoyance, and negative press, including a tough editorial in *The Scientist* that uses phrases like "breach of integrity", "lack of due process," and "damage to ongoing research" to describe the decision.

In a fax sent to 18 VA researchers on April 1, Dr. Wray informed them that the combination of their priority scores and "productivity" precluded funding their proposals. "Future submissions," Dr. Wray informed the researchers, "should attempt to have improvement in both the overall scientific merit of the proposal and in productivity."

A routine rejection of a proposal, one might say; most researchers have received such a notification at some point in their careers. However, little was routine about these particular rejections, and the decision has ignited something of a firestorm with the tight-knit VA research community.

First, the scientists in question had already received prior verbal notification that their grant proposals would be funded. The notifications came by phone from program officers in the VA medical research service the preceding fall—months prior to Dr. Wray's April fax, and at least one month prior to her taking office. In an April 2 explanatory e-mail to the VA research community, Dr. Wray claimed that "invalid information" had been sent to VA researchers, and that no one in any position of authority was authorized to inform researchers that their grants had been funded.

However, VA researcher Dr. Ron Bach, an ASBMB member at the VA Medical Center in Minneapolis, told *ASBMB Today* that verbal notifications of successful grant applications were commonplace in the past, and had always been considered reliable information on which researchers could act. The phone calls were made to give researchers as much time as possible to hire staff and begin to organize their laboratories. Most of the 18 researchers in question acted upon the phone calls they received.

Why were these particular grants singled out for "defunding" from those chosen for funding from the fall 2002 round of VA research grant applications? According to the VA website, "Today's VA research, leading tomorrow's healthcare" is the new VA research and development vision statement. The slogan spells out an approach that spends less VA research money on basic research and more on translational, or outcomes-based research—that is, research directly related to patient care.

Consistent with this message, Dr. Wray said in February that her goals for VA research were to expand clinical research, expand translational research; and strengthen programs to measure the quality of VA research and interventions. She wants to "rapidly translate the knowledge we develop into clinical practice." *ASBMB Today* was told that the grants in question were considered too unrelated to clinical practice.

However, the VA's major advocacy group in the research community—Friends of VA—notes that 70 percent of VA research dollars are already spent on clinical research. The VA research budget for 2003 is $400 million; thus, the VA will spend about $280 million on translational research this year. The question must be asked: does Dr. Wray believe there is no place for a substantial fundamental research program at VA?

There are those who think so. The 18 grants in question were almost all basic in nature. For example, Dr. Bach's grant focuses on new procedures that may predict an individual's risks of thrombosis. He notes, "thrombosis is the major cause of morbidity and mortality in the VA patient population. Thrombotic events in the form of heart attack, stroke, and pulmonary embolism are responsible for one death every 33 seconds in the United States. Since thrombosis is hard to predict, most of those potentially lethal events occur unexpect-

Chief's 'Defunding' of Research Grants

edly. Consequently, the victims of thrombosis almost never receive the appropriate anticoagulant therapy until after the fact. The economic consequence of this epidemic of vascular occlusion exceeds the combined costs of HIV/AIDS and cancer….I do not know what plans Dr. Wray has for the money that she withheld, but I seriously doubt that it will be spent on anything with a greater potential for improving the healthcare of our veterans."

Merit review is how the vast majority of grant funding decisions are made at VA. In the fall 2002 round of grant proposals—the round from which all 18 rescinded grants came—grants to be funded had to receive a priority score of 25 or better. All 18 grants received at least this score; Dr. Bach's thrombosis grant, described above, received a priority score of 18.4 (as at NIH, a lower score is better).

However, Dr. Wray has implemented a new system to measure the merit of VA research proposals that counts priority score as only one of a set of three factors. In addition to the priority score, Dr. Wray also looks at "the productivity of the investigator as measured by other federal funding and manuscripts in leading journals over the prior 5 years, and the importance of the research area," according to her April 2 e-mail.

Dr. Wray expanded on these factors in a second e-mail to the VA research community, dated April 4. "We developed mathematical models" for the three productivity factors (priority score, number of publications in the last five years, and other federal funding). "We did two different sets of models varying the weight given to the components and varying whether we did or did not include in the Model the academic rank of the investigator. We also factored in credit for publications in the leading clinical and scientific journals" (Interestingly, the issue of "the importance of the research area" was dropped as a factor in this second e-mail).

Unfortunately, no one outside Dr. Wray's immediate staff has seen this model or has explained its components to the research community. No one knows, for example, what are considered "leading clinical and scientific journals." The Institute for Scientific Information consistently ranks the *Journal of Biological Chemistry* as having one of the highest impact factors among scientific publications. Since the list of "leading journals" has not been made public, no one knows if the *JBC* is on Dr. Wray's list.

Likewise, a VA researcher's number of publications is also a factor in productivity measurement, according to Dr. Wray. However, this can also be a tenuous measurement. "Salami slicing" is the term for publishing a series of mediocre papers (that could have been published as one excellent paper) over months or years in order to increase the number of publications on one's CV. Thus, the *quality* of the publications, as well as the quantity, should probably be considered. It is not clear that quality of publications counts in the new model.

In addition, Dr. Mindy Aisen, Dr. Wray's newly-appointed deputy, has made clear to all prospective grant applicants that "Dr. Wray will, of course, make all final decisions." For grants at the margins, the director making the final decision is clearly the appropriate way to resolve their status. Further, few would argue with the proposition that Dr. Wray can and should have the authority to determine the priorities and emphasis of her research program.

However, up to now, most would also agree that funding decisions made before the director came on board should not be overridden, no matter what after-the-fact funding "model" has been developed to justify the decision.

Might Dr. Wray have avoided this entire controversy if her new approach were applied in a prospective manner, rather than revisiting funding decisions that had already been made by a merit review system that has worked quite well over the years? "Exactly," said one VA researcher involved in the flap.

As of this writing, several of the 18 grants at issue have been reinstated, and the other scientists have been promised bridge funding to tide them over until their grants can be resubmitted. We have also been told that the model used to retroactively defund the 18 grants in the fall 2002 round has been junked for use in the spring 2003 round, and all grants that receive a fundable peer review score in this round will be funded.

Still, 15 scientists with fundamental research grants totaling in the tens of millions of dollars are left wondering when—or if—their work will ever again enjoy a home at the VA.

by John D. Thompson, Editor

Imperial College London Seeks to Raise Venture Fund

BioScience Managers Limited (BML), a specialist bioscience fund manager, and Imperial College London (ICL), one of the world's leading science-based universities, have announced a joint initiative to raise a new venture capital fund focused on early stage medical and life science companies. The BML Ventures Imperial Fund, with a target size of 50 million pounds ($81 million U.S.), will make investments in 12-15 start-up and early-stage companies in the healthcare sector.

The fund will have exclusive preferential access to opportunities emerging from ICL in the medical and life sciences sectors, and anticipates that approximately 50% of its funds will be invested in young companies built upon Imperial College science, including research from one of the largest medical schools in Europe. The remainder will be invested in similar opportunities, predominantly in the UK.

BML and Imperial College believe there is significant need in the UK for venture funds that bridge the gap between early-stage entrepreneurial activities and the types of investment opportunity in which traditional, mainstream venture capital firms are engaged. The BML Ventures Imperial Fund will aim to close this development gap which currently leaves newly formed science, technology and healthcare companies struggling to raise funds.

In announcing the new venture, Sir Richard Sykes, Rector of Imperial College London, stated, "Imperial College was founded with the express aim of supporting science that is applicable to industry and we continue to nurture that enterprise culture. Researchers want to see their discoveries out in the world making a difference. The launch of this new fund is an exciting and timely way for some of our very best science with high growth potential to make that difference."

JGI, Diversa Corp. to Conduct Large-Scale Microbial Sequencing

The Department of Energy's Joint Genome Institute (JGI) and Diversa Corporation have announced a collaboration to discover and sequence novel microbial genomes found in a diverse range of unique habitats. Diversa will use its proprietary technologies to extract DNA from environmental samples and make gene libraries, while JGI will perform DNA sequencing. All DNA sequence data from the collaboration will be provided to Diversa and deposited in GenBank within six months of the completion of sequencing to allow public access by scientists around the world.

"The microbial world is the next genomic frontier," said JGI Director Eddy Rubin. "The human genome has been sequenced, and now we're ready to tackle the larger and more complex challenge of sequencing microbial diversity."

"We believe the scientific, environmental, and commercial benefits from this project will be considerable," Dr. Rubin continued, "and we're pleased to be working with Diversa, a company that has clearly demonstrated leadership in legally and efficiently accessing the vast microbial diversity present in the environment."

"There are more genes in a handful of soil than in the entire human genome," said ASBMB member Jay M. Short, President and Chief Executive Officer of Diversa. "At Diversa, we are committed to developing products from the rich genomic resource of uncultured microbes living in nearly every environment on earth. We believe that our sequencing collaboration with JGI will contribute greatly to our understanding and utilization of microbial genes."

Diversa and JGI will sequence DNA from microbes living in environments such as deep-sea thermal vents, insect endosymbionts, soil from nuclear weapons manufacturing sites, and water collected by rainforest epiphytes such as bromeliads that grow on giant trees. Diversa pioneered proprietary, genomics-based methods for discovering unexplored microbial diversity and recently received a patent for sequencing of mixed populations of microbial DNA directly from the environment, which is more efficient and effective than individually culturing and identifying microbes in the laboratory. Diversa estimates that its gene libraries currently contain the complete genomes of over three million unique microorganisms, comprising a vast resource of genetic material, which far exceeds the estimated 10,000 microorganisms that have been described in the scientific literature.

Ariad Licenses Key Protein Signaling Pathway

Ariad Pharmaceuticals has signed its second license deal for the NFκB patents, which covers a heavily researched protein signaling pathway believed to be a key to cancer, osteoporosis, and inflammatory diseases. Reagent maker DiscoveRx signed up for a nonexclusive worldwide license of rights under the patent, which is held by Whitehead Institute of Biomedical Research, Harvard University, and Massachusetts Institute of Technology, and licensed by Ariad, a Cambridge, Massachusetts biotech company.

The NFκB patents, which contains hundreds of claims associated with cellular processes that are the subject of thousands of research projects at the bench, created a stir last summer among academics who feared Ariad would exact royalties and license fees. The company said at the time that it would not invoke the patent against noncommercial researchers and has so far lived up to its promise.

Ariad's deal with DiscoveRx gives the Fremont, Calif. drug discovery technology firm the right to sell NFκB assays to biotechs and pharmaceutical companies, which must negotiate their own research and development licenses with Ariad. Sales to academics and nonprofit institutions are exempt from the independent license agreement.

"We specifically indicated that for not-for-profits, universities and the like, licenses are not needed," Ariad Chairman and CEO Harvey Berger said, in announcing the DiscoveRx agreement. "We entirely encourage noncommercial use without a license."

When the patent was granted last June, Ariad filed a suit against Eli Lilly, claiming that two of that company's products infringed Ariad's rights. The products—Evista, an osteoporosis medication, and Xigris—a treatment for severe sepsis, operate along the NFκB signaling pathway. The lawsuit is currently proceeding in a federal court in Massachusetts.

Pfizer Closing Research Centers; 500 Jobs May Be Lost

Pfizer is closing four Chicago-area laboratory facilities, a biotech unit in South San Francisco, a French research center, and is eliminating Michigan research jobs in cost-cutting moves meant to make the most of the company's $57 billion purchase of Pharmacia.

Pfizer officials declined to say how many jobs were going in the rollup, which will shutter 3 of 25 major research facilities over the next 18 months. However, it is reported that the layoffs could add up to one of the biggest mass firings in a year of belt-tightening that has hit research staffs hard. Illinois state labor officials received a notice from Pfizer that indicated at least 500 jobs could be lost in an action scheduled for June 16 at Pharmacia's Downers Grove operation alone. Pfizer filed the report in compliance with a federal law requiring large employers to give notice of mass layoffs in excess of 500 workers, but the company did not say how many jobs would be cut. Illinois officials have sent a letter asking Pfizer to provide the number to be laid off.

By 2005, Pfizer expects to save $2.5 billion from cuts in the wake of the company's merger with Pharmacia, which closed April 16.

The Changing Face of Bioinformatics

Not long ago bioinformatics was being touted as the "next thing," and market research firms were predicting a potential annual market at anywhere from $2 billion to $40 billion. Bioinformatics, the information technology infrastructure, databases, and software for the life science market, was seen as the key to speedier identification and validation of drug targets and reducing time-to-market for new drugs. This promise has not yet been fully realized and the initial estimates may never be achieved, according to *Drug Discovery Today*.

"Does this mean that bioinformatics is dead?" asked that publication recently. "Certainly not," was its answer.

While bioinformatics is necessary for biotechnology research and does provide important benefits, the number of stand-alone companies that will survive based solely on selling bioinformatics software or licensing databases for drug discovery may be limited. *Drug Discovery Today* noted that many bioinformatics companies have morphed, at least partially, into drug research companies. Instead of just licensing bioinformatics data or tools, some have added internal research capability and now use their own data and tools to identify drug targets. Celera, Incyte, and Variagenics have all diversified in this manner.

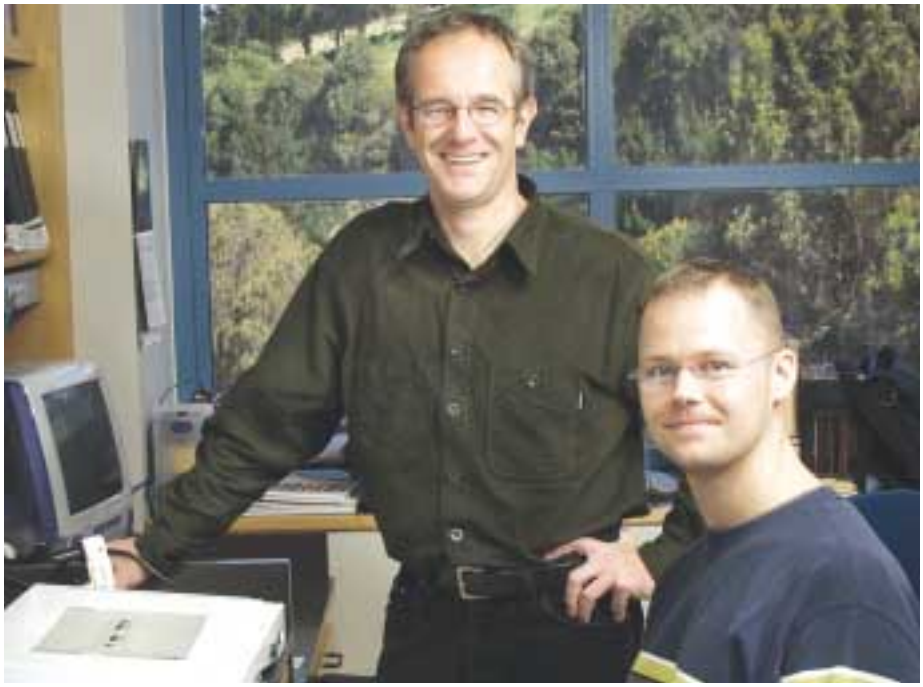
Gladstone Researchers Find Method to Study Hidden HIV Reservoirs

Scientists are now one step closer to understanding how HIV hides in cells and rears its ugly head once patients stop taking combination drug therapy, which can suppress viral loads to undetectable levels. The phenomenon reflects the existence of hidden populations of latently infected cells. As a result, patients must remain on therapy for life.

Eradication of these cells could lead to a cure for HIV infection. However, researchers have been hampered by their inability to identify them. Now Gladstone researchers have found a way to identify and study latently infected cells in the laboratory. Their work was published in the April 15 issue of the *European Molecular Biology Organization Journal*.

"The latent pool is considered to be the barrier to eradication," said senior author Eric Verdin, an ASBMB member and Senior Investigator at the Gladstone Institute of Virology and Immunology and University of California, San Francisco Professor of Medicine. "Our work is geared toward finding a way to obliterate this latent pool, which would take us closer to actually finding a cure for AIDS."

Through genetic engineering, the researchers constructed a recombinant HIV strain carrying a green fluorescent protein. Using this marker, they identified a small fraction of infected cells in which the virus was latent. These cells represented less than one percent of the infected population and had eluded purification until this study.



Dr. Eric Verdin (left) and Researcher Dwayne Bisgrove

"Before, the study of latent infection was restricted to the analysis of rare cells circulating in the blood of infected patients. As an experimental model to dissect the molecular basis of latency, these cells were very limiting," Dr. Verdin said. "We now have a laboratory model that we can use to delve deeply into what is going on."

During infection, the HIV genome integrates into the host cell's DNA. Transcription of the viral genome leads to production of virus. The Gladstone researchers found that, in latently infected cells, the HIV genome is integrated into transcriptionally inactive regions of DNA called heterochromatin.

Dr. Verdin and his colleagues are now trying to identify drugs that can activate latent cells and cause them to produce virus. A preliminary screen identified a number of compounds that can reactivate latent HIV in the laboratory.

"Hopefully, we will soon be in a position to test some of these compounds in an animal model infected with a virus related to HIV. This will allow us to determine whether the "flushing" of latent pools is a viable therapeutic approach in HIV infection," said Dr. Verdin.

The Gladstone Institute of Virology and Immunology is one of three research institutes at the J. David Gladstone Institutes, a private nonprofit biomedical research institution affiliated with UCSF.

GlaxoSmithKline to Award $500,000 to HIV/AIDS Researchers

GlaxoSmithKline (GSK) will award $500,000 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.

Applications, which must be submitted by July 31, are now being solicited for 2003 research grants. These 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.

ASBMB members Dr. Irwin Chaiken and Dr. Elias Lolis are past recipients of GSK Drug Discovery and Development Research Grants.

Since the inception of the Drug Discovery and Development Research Grant Program in 2001, GSK has honored nine researchers for their groundbreaking work toward new pharmaceutical strategies to combat the HIV virus. ASBMB members Dr. Irwin Chaiken and Dr. Elias Lolis are past recipients of GSK Drug Discovery and Development Research Grants.

The research grant carries 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.

An Expert Review Board composed of acknowledged leaders in the field of HIV/AIDS will independently judge and choose the grant recipients. Although GSK will have access to the applications, including proposals, it will not be involved in the selection of recipients.

The research proposals will be considered according to potential importance to the field and health in general, originality, appropriateness of the methodology and scope of the project, and the researchers' ability to conduct the proposed research.

Research grant recipients will be announced in September 2003 at the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in Chicago. The grants will be paid November 1.

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.

Frederick Rickles Appointed FASEB Executive Director

Frederick R. Rickles, M.D., FACP has accepted the position of Executive Director of FASEB. The acceptance by Dr. Rickles of President Steven L. Teitelbaum's offer is the culmination of many months of diligent effort on behalf of the Executive Director Search Committee (Drs. Nick Pace, Mary Lou King, David Williams, Haig Kazazian, Dick Allison, Scott Hunt, Robert Wells and ex-officio members S. L. Teitelbaum and R. R. Rich with staff participation by Ms. Maureen Murphy).

Dr. Frederick Rickles

Dr. Rickles has a rich background of administrative, clinical, and research accomplishments in his academic positions. In 1999, he moved to George Washington University where he has served in administrative and academic functions and was Attending Physician, 1993-1998 at the Center for Disease Control and Emory Clinic in Atlanta, and in 1978-1993 at the University of Connecticut School of Medicine. He received his M.D. degree in 1967 from the University of Illinois College of Medicine in Chicago. His research interests are in the area of hematology. Dr. Rickles will join FASEB this month.

Calendar of Scientific Meetings

JUNE 2003

AAPS Conference on Advances in Pharmaceutical Processing

June 19-20 • Parsippany, New Jersey
Contact: AAPS Meetings Department
Ph: 703-243-2800; Fx: 703-243-9532; Email: meetings@aaps.org
Website: http://www.aapspharmaceutica.com/meetings

4th International Symposium on Hormonal Carcinogenesis

June 21-25 • Palau de la Musica, Valencia, Spain
Contact: Tandria Price/Dr. Jonathan J. Li
University of Kansas Medical Center
Ph: 913-588-4744; Fx: 913-588-4740; Email: tprice@kumc.edu
Website: http://www.kumc.edu/hormonecancers.

ECM IV: Bone Tissue Engineering

June 30-July 2 • Davos, Switzerland
Contact: R. Geoff Richards, Dr. Sci. M.Sc. biol.
Programme Leader AO Research Institute,
Bioperformance of Materials & Devices
email: geoff.richards@ao-asif.ch; Ph: ++41 (0) 81 4142 397
http://www.aofoundation.org/events/ao/ecm/ECMIV/index.shtml

JULY 2003

FEBS 2003 Meeting on Signal Transduction

July 4-8 • Brussels
Contact: V. Wouters; Ph: 32 2 7795959; Fx: 32 2 7795960
Email: febs@iceo.be; Website: http://www.febs-signal.be

AUGUST 2003

First Gordon Research Conference on Cellular Osmoregulation: Sensors, Transducers and Regulators

August 15–20 • Roger Williams University, Bristol, RI
Contacts: Janet M. Wood (jwood@uoguelph.ca) and Karlheinz Altendorf (altendorf@biologie.Uni-Osnabrueck.de)
Website: http://www.grc.uri.edu/programs/2003/cellosmo.htm
Application: http://www.grc.org/scripts/dbml.exe?Template=/Application/apply1.dbm

Sixth International Symposium on Mass Spectrometry in the Health and Life Sciences: Molecular and Cellular Proteomics

August 24-28 • Fairmont Hotel, San Francisco
Contact: Marilyn Schwartz; Ph: 415-476-4893
Email: sfms@itsa.ucsf.edu
Website: http://donatello.ucsf.edu/symposium

Biology of Molecular Chaperones
Mechanisms and Regulation of Chaperones

August 30–September 4 • Tomar, Portugal
Contacts: Dr. Josip Hendekovic or Caroline Walford
Ph: + 33 388 76 71 35; Fx: + 33 388 36 69 87
Website: http://www.esf.org/esf_euresco
Please quote 2003-15 in any correspondence

16th International Mass Spectrometry Society Conference

August 31–September 5 • Edinburgh, Scotland, United Kingdom
Contact: John Monaghan; Email: johnmonaghan@ed.ac.uk
Website: http://www.imsc-edinburgh2003.com

SEPTEMBER 2003

NMR in Molecular Biology
EuroConference on Structural Genomics: From Gene to Structure as viewed by NMR

September 5–10 • Obernai (near Strasbourg), France
Contact: Dr. Josip Hendekovic or Anne-Sophie Gablin
Ph: + 33 388 76 71 35; Fx: + 33 388 36 69 87
Website: http://www.esf.org/esf_euresco
Please quote 2003-14 in any correspondence

Sixth Conference on Protein Expression in Animal Cells

September 7–11 • Mont-Tremblant, QC, Canada
Contact: Marc Aucoin, Technical Officer
Biotechnology Research Institute; Email: 6thPEACe@nrc.ca
Website: http://www.bri.nrc.ca/6thPEACe

American Society for Bone and Mineral Research (ASBMR) 25th Annual Meeting and Anniversary Celebration

September 19-23 • Minneapolis, Minnesota, U.S.A.
Late-Breaking Abstract Submission Deadline is July 15, 2003.
Ph: 202-367-1161; Email: asbmr@dc.sba.com; www.asbmr.org

Third International Conference on the Pathobiology of Proteoglycans

September 20 - 25 • Parma, Italy
Contacts: Roberto Perris, Chair and Ariane De Agostini, Co-chair
Clinique de Stérilité de d'Endocrinologie gynécologique,
Hôpital Cantonal Universitaire de Genève
Ph: 41-22 / 382.43.46; Fx: 41-22 / 347.59.79
Email: Ariane.Deagostini@medecine.unige.ch
Website: http://www.assb.biol.unipr.it/PG2003

OCTOBER 2003

OARSI's 2003 World Congress on Osteoarthritis

October 12-15 • Palais am Funkturm, Berlin
Contact: OARSI Headquarters; Ph: 202-367-1177; Fx: 202-367-2177
Email: oarsi@oarsi.org; Website: www.oarsi.org

AAPS Workshop on Method Validation and Measurement of Biomarkers in Nonclinical and Clinical Samples in Drug Development

Cosponsored with Clinical Ligand Assay Society
October 24-25 • Salt Lake City, Utah
Contact: AAPS Meetings Department
Ph: 703-243-2800; Fx: 703-243-9532; Email: meetings@aaps.org
Website: http://www.aapspharmaceutica.com/meetings

AAPS Annual Meeting and Exposition

October 26-30 • Salt Lake City, Utah
Contact: AAPS Meetings Department
Ph: 703-243-2800; Fx: 703-243-9532; Email: meetings@aaps.org
Website: http://www.aapspharmaceutica.com/meetings

Cytokines, Signalling & Diseases

Oct. 26-30 • Cairns, Australia
Event Host: International Society for Interferon and Cytokine Research; Website: http://www.cytokines2003.conf.au/

FEBRUARY 2004

The 1st Gordon Research Conference on The Biology of 14-3-3 Proteins

February 22-27 • Ventura, California
Chairs: Haian Fu & David Klein, Vice-Chair: Alastair Aitken
email: hfu@emory.edu
Website: http://www.grc.org/programs/2004/14-3-3.htm

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

AUGUST 2004

12th International Conference on Second Messengers and Phospoproteins

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

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

2-7 July 2005 • 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.

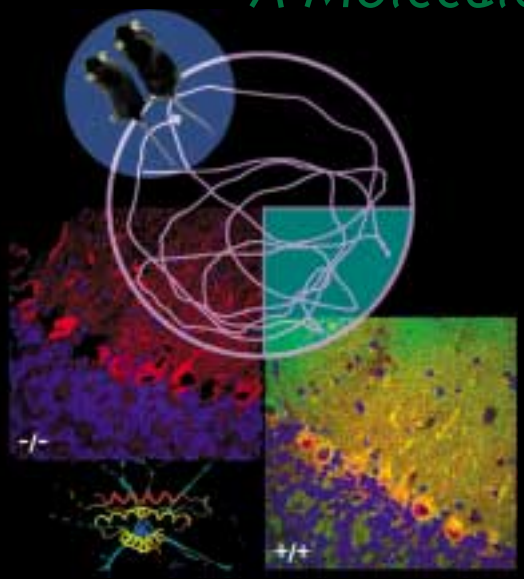
The Society is asking department chairs to provide ASBMB with the names and addresses of each new Ph.D. recipient from their institutions. Upon receipt of this information, we will write the new Ph.D.s to congratulate them on their accomplishment and offer the free one-year membership in ASBMB. Names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

Organized by:

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

Award Lectures

ASBMB-Merck Award
ASBMB-Avanti Award in Lipids
ASBMB-Amgen Award
William C. Rose Award
Herbert A. Sober Lectureship
Schering-Plough Research Institute Award
Howard K. Schachman Public Service Award
Herbert Tabor/Journal of Biological Chemistry *Lectureship*

For further information:

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9650 Rockville Pike
Bethesda, MD 20814
Tel: 301-634-7145
Fax: 301-634-7126
Email: asbmb@asbmb.faseb.org
http://www.asbmb.org/meetings

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

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

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

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

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

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

Meeting VII: Protein Modifications and Degradation
Organizer: William J. Lennarz, *SUNY at Stony Brook*

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

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

Meeting X: The Future of Education in the Molecular Life Sciences
Organizer: J. Ellis Bell, *Univ. of Richmond*