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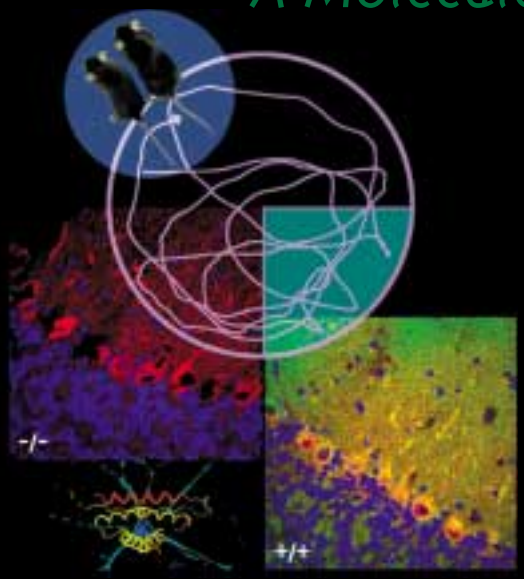

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Meeting I: Molecular Recognition and Catalysis
Organizer: Jack E. Dixon, *UCSD*

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
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Meeting IX: Signaling Pathways in Disease
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Meeting X: The Future of Education in the Molecular Life Sciences
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ASBMB Today

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

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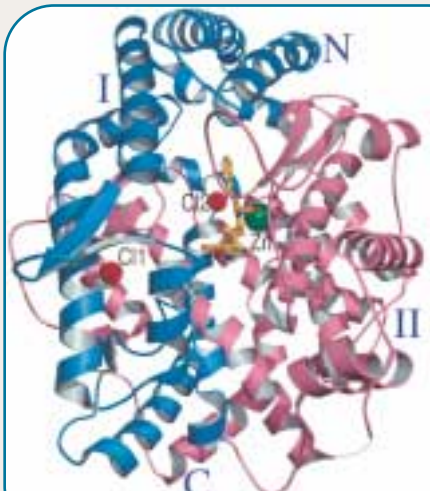

departments

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New Era Begins for

When the July issue of the Journal of Lipid Research (JLR) rolls off the presses this month it will open a new era for that publication. The transfer of ownership from Lipid Research, Inc. (LRI) to ASBMB became effective this month, and the JLR's issue will be the first published since ASBMB agreed to manage the publication of the Journal.

Edward A. Dennis, Editor-in-Chief, and Joseph L. Witztum, Deputy Editor-in-Chief, who began their service July 1, expressed their enthusiasm in a joint statement stating, "We are very excited about the opportunities and challenges that editing the JLR raises for the future of lipid research."

Dr. Dennis, who is Professor and Chair of the Department of Chemistry and Biochemistry, University of California, San Diego, said:

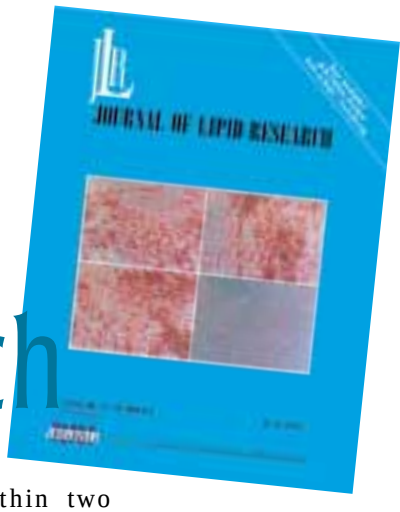
"The JLR has been the premier journal for lipid biochemistry for almost half a century and I am both honored and excited to be asked to help shape its future during this critical transition to being part of the ASBMB family. This includes a responsibility to help shape and define the relationship of the JLR to the JBC which will soon celebrate a full century of publishing. Many of the earliest seminal papers published in the JBC were on a variety of aspects of lipid metabolism and biochemistry and JLR has played a critical role in publication of the best work on lipid metabolism and its relationship to disease. Joe and I will strive to evolve and expand the influence of this important journal in all areas of lipids from basic science to clinical implications.

"I like to think of the living universe as being composed of four kinds of molecules, namely nucleic acids, proteins, carbohydrates, and lipids, but biochemistry and molecular biology is integrative. We don't view the JLR as a specialty journal, but rather as one that focuses on all aspects of biochemistry, metabolism, and disease that touch in some way on lipids or membranes."

Dr. Witztum, a Professor in the Department of Medicine at the University of California, San Diego, stated: "There is currently a virtual explosion of interest in the role of lipids in both basic research in cell biology and in clinical medicine. Lipids not only play a central role in providing structural integrity for cells but serve as key intracellular signaling molecules. Disturbances in lipid metabolism effect basic cellular homeostasis and on the clinical level are responsible not only for rare diseases such as lipid storage and neurological diseases, but alterations in levels and composition in plasma play key pathogenic roles in the most common diseases affecting humans, including atherosclerosis and diabetes.

"We hope that the new JLR will be a home to all investigators interested in lipid metabolism in all of its varied aspects and we will provide rapid and expert review to investigators with online publication following acceptance. The next few years should see the development of lipidomics to match the growth in genomics and proteomics currently ongoing, and we the editors hope to make the JLR the leading journal to further study of this vital area of research."

Following are excerpts from the editorial in the July issue of the Journal of Lipid Research:



Journal of Lipid Research

At the end of the twentieth century, we saw a revolution in "genomics" that is having profound effects on basic science and clinical medicine today. Currently we are in the middle of another revolution, namely "proteomics," the extension of genomics to attempt to identify, characterize, and quantify the primary products of the genes (identified in the human genome project) and understand their interactions, We predict that the next revolution in biomedical science will be in "metabolomics," the extension of proteomics to identify, characterize, and quantify all of the metabolic products of the protein synthetic machinery in our cells. A large portion of those metabolic products are lipids, and we predict a parallel revolution leading to an emerging new field of "lipidomics."

We are very excited about the opportunities and challenges that editing the JLR raises for the future of lipid research. The JLR has traditionally been recognized as the premier journal in which to present state-of-the-art manuscripts on traditional aspects of lipid metabolism. While we hope to continue and even expand the strong and distinguished traditions established by previous Editors, we also hope to dramatically advance the breadth, depth of coverage, and integration of the exciting advances occurring in the lipid, membrane, lipoprotein, signaling, and atherogenesis fields. We hope to broaden coverage to include the "genomics, proteomics, and metabolomics" of lipid and lipoprotein metabolism, including both basic and clinical aspects. We especially wish to encourage manuscripts dealing with state-of-the-art studies of those aspects that directly impact the arterial wall, leading to atherogenesis, Our understanding of the etiology of atherosclerosis has exploded recently, and we wish to make the JLR a premier journal in which authors can present relevant work on the lipidomics of atherogenesis as well as all other basic aspects of lipids. Your active participation as an author, reviewer, and reader will be vital to helping us achieve these goals.

A major goal of the new JLR will be to provide fair, rapid, and expert review for all manuscripts. Consistent with the general policies for ASBMB, Associate Editors will now have full responsibility for their assigned manuscripts. Specifically, they will select at least two reviewers for each of their manuscripts (relying frequently on our Editorial Board), collect reviews, make the final decision on the manuscript, and correspond directly with the authors regarding the decision. Associate Editors may also serve as one of the reviewers. Thus the importance and influence of the Associate Editors will be greatly enhanced under this new Editorial policy. All reviews of manuscripts will be Web-based, and correspondence with the members of the Editorial Board and other outside expert reviewers will be handled electronically by the Associate Editors.

The Associate Editors will also serve as key advisers to the Editor in developing Editorial policy and directives. All submissions, reviews, decision letters, and correspondence will be handled electronically to minimize review time and time to publication. Once a manuscript is accepted, it will appear as a "Paper in Press" within two weeks of acceptance, consistent with current JLR policy.

The popular Thematic Review series will continue with exciting topics in lipid biology and medicine. In addition, the entire forty-four-plus years of JLR published papers is now available on the Web. We hope you, as a JLR author, reviewer, and reader will participate fully with us to help enlarge the scope and influence of the JLR. Our purpose is to increase the opportunity for authors to communicate their important new observations in the field of lipidomics and thereby to facilitate study of this exciting and expanding discipline.

You may have noticed the logo on the table of contents page regarding ASBMB's Bronze Award from the Society of National Association Publications. Seen above is Public Affairs Officer Peter Farnham, who earned the award for his article "Balance Is the New Refrain" in the October 2002 issue of ASBMB Today.

Kettering Prize Honors V. Craig Jordan for Advances in Cancer Therapy

The General Motors Cancer Research Foundation (GMCRF) has awarded the 2003 Charles F. Kettering Prize to ASBMB member V. Craig Jordan, Ph.D., Diana, Princess of Wales Professor of Cancer Research and Professor of Molecular Pharmacology and Biological Chemistry at the Robert H. Lurie Comprehensive Cancer Center of the Feinberg School of Medicine of Northwestern University. Dr. Jordan's research on the breast cancer drug tamoxifen revolutionized the field of cancer therapy, reportedly contributing to the survival of over 400,000 breast cancer patients.

"This is a superb accolade for my research group," Dr. Jordan said of his team, which has been researching the pharmacology and toxicology of tamoxifen for the past 30 years.

The Kettering Prize is awarded annually for the "most outstanding recent contribution to the diagnosis or treatment of cancer," at the GMCRF Scientific Conference, held at the NIH campus. Dr. Jordan gave a Laureate Lecture at the conference on June 11 recounting the major changes in cancer research that occurred because of his research.

Dr. Jordan's research introduced the concept of targeted treatment in cancer therapy. Tamoxifen negatively affects only cancerous cells in the breast tissue, rather than every cell in the body, as chemotherapy does. In breast cancer, cancerous cells in the breast overproduce an estrogen receptor and grow as they receive more and more estrogen. Tamoxifen can bind to these receptors, blocking estrogen from entering the cells and promoting their proliferation.

Dr. V. Craig Jordan

The first clinical trials were performed on post-menopausal women, who do not produce large quantities of estrogen naturally. The theory was that if tamoxifen acted as an antiestrogen in other parts of the body, it wouldn't matter in women who no longer need estrogen. However, until the 1980s, it was not known what effect an antiestrogen would have on a pre-menopausal woman, who still produces estrogen naturally. It was not known whether the antiestrogen would inhibit estrogen's effects in other areas of the body. Dr. Jordan contributed to clinical trials that found that the women experienced no negative effects from tamoxifen. Why did tamoxifen seem to have an effect in breast tissue, but do nothing with other tissues that also made use of estrogen?

The answer came with Dr. Jordan's next breakthrough in the field of cancer therapy. His team discovered that tamoxifen does actually affect other areas of the body in post-menopausal women, but not in the same way in every place. He termed tamoxifen a selective estrogen or antiestrogen (now called selective estrogen receptor modulator, or SERM) because it could act in opposition to estrogen in some areas but like estrogen in others. While tamoxifen is an antagonist in the breast, it is an agonist in tissues such as the uterus, bones and liver. Both estrogen and tamoxifen preserve bone density and lower cholesterol.

The Northwestern researchers took advantage of the fact that selective estrogen receptor modulators have different effects in different tissues to advance the concept of chemoprevention in large numbers of women. Previously, only women who were at a high risk of developing breast cancer were taking tamoxifen as a preventative therapy. However, Dr. Jordan reasoned that women who were at high risk for other disorders, such as osteoporosis and cardiovascular diseases due to high cholesterol, could also prevent breast cancer while treating the conditions they had. For example raloxifene, a close relative of tamoxifen, is being tested in clinical trials to treat women with osteoporosis. While it preserves bone density as its primary function, it also helps to prevent breast cancer by acting as an antiestrogen in the breast. These data are the basis for the study of tamoxifen and a raloxifene (STAR) trial that seek to improve the chemoprevention of breast cancer.

The success of targeting therapy for cancer with tamoxifen and other SERMs and the philosophy of "killing the cancer and not the patient" has opened the door to current drug discovery in cancer.

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ART-899	Palmitoyl, [9,10-3H] D-erythrosphingosine	50 µCi	$1099
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ARC-376	Phosphatidylcholine-L-α-dipalmitoyl [choline methyl-14C]	10 µCi	$649
ARC-657	Phosphatidylcholine-L-α-dipalmitoyl [dipalmitoyl 1-14C]	10 µCi	$349
ART-284	Phosphatidylcholine-L-α-dipalmitoyl [choline methyl-3H]	250 µCi	$599
ART-532	Phosphatidylcholine-L-α-dipalmitoyl [2-palmitoyl 9,10-3H(N)]	250 µCi	$629
ART-533	Phosphatidylcholine-L-α-1-0 hexadecyl-1-2-arachidonyl [arachidonyl -3H(N)]	10 µCi	$499
ARC-852	Phosphatidylcholine-L-α-1-palmitoyl-2-arachidonyl, [arachidonyl 1-14C]	10 µCi	$699
ARC-853	Phosphatidylcholine,L-α-1-palmitoyl-2-linoleoyl [linoleoyl 1-14C]	10 µCi	$699
ARC-854	Phosphatidylcholine, L-α-1-palmitoyl-2-oleoyl [oleoyl 1-14C]	10 µCi	$469
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ART-481	Sphingomyelin (bovine) [choline methyl-3H]	50 µCi	$679
ART-490	Sphingosine D-erythro [3-3H]	50 µCi	$599
ART-859	Sphingosine D-threo [3-3H]	50 µCi	$719
ART-778	Sphingosine, D-erythro-[3-3H]-1-phosphate	10 µCi	$1199
ARC-1048	Sulphatide [stearoyl 1-14C]	50 µCi	$1299
ARC-1492	N,N,N-Trimethylsphingosine, [N-methyl-14C]	10 µCi	$599
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'Immortalized' Cells Enable Researchers to Grow Human Arteries

In a combination of bioengineering and cancer research, a team of Duke University Medical Center researchers has made the first arteries from non-embryonic tissues in the laboratory, an important step toward growing human arteries outside of the body for use in coronary artery bypass surgery.

The results of the Duke experiments were published June 6 in *EMBO Reports*, the journal of the European Molecular Biology Organization.

Four years ago, Duke researchers led by Laura Niklason, M.D., reported in the journal *Science* on experiments in which they grew pig arteries in a novel "bioreactor" system that mimics the fetal environment, and then successfully implanted these bioengineered arteries back into the pig. Unfortunately, researchers found that human artery cells did not possess enough life cycles to be grown into functional arteries.

The key to overcoming this hurdle was eventually found in a cancer research lab. Every time a cell divides, the ends of its chromosomes, or telomeres, erode until they become so short that the cell receives a signal to stop growing. While at the Massachusetts Institute of Technology, current Duke researcher Dr. Chris Counter, an ASBMB member, had previously cloned the hTERT (human telomerase reverse transcriptase subunit) component of the enzyme telomerase that stops telomeres from shortening, and had shown that expression of hTERT permitted some human cells to continue to divide indefinitely, in effect making them immortal.

Working with Dr. Niklason and Dr. Counter, medical student Andy McKee found that when the hTERT gene was introduced into smooth muscle cells, key components of an artery, the life span of the cells were extended long enough to form arteries in the laboratory.

"After introducing the human cells with hTERT, we found that the resulting cells not only proliferated long beyond their normal lifespan, but retained characteristics of normal smooth muscle cells," Dr. Niklason explained. "Furthermore, using these smooth muscle cells, we were able to engineer mechanically robust human arteries, a crucial step toward creating arteries for bypass patients."

This is the first time arteries have been grown from non-neonatal vascular cells, the researchers said. This achievement is important, they continued, since the goal is to engineer arteries that will resist immunological attack, so they must be grown from cells taken from the actual patients who will ultimately receive the arteries.

To create the arteries, the researchers fashioned a tube from a thin sheet of a biodegradable polymer, which, like a sponge, is 97% air. The treated smooth muscle cells were then impregnated throughout the polymer tube. The bioreactor pulsed a vitamin and nutrient solution through and around the tube, approximating as closely as possible the conditions that would exist in nature.

Once the smooth muscle cells proliferated and filled all the spaces within the dissolving polymer scaffolding, the researchers added endothelial cells, which line the interior of blood vessels, to complete the artery.

"We view the results of this study as the proof-of-principle that this approach will ultimately lead to tissues that can be used in humans," Dr. Niklason said.

According to Dr. Counter, the hTERT component of telomerase was first cloned in 1997, and researchers in the areas of cancer and bioengineering are slowly turning their attention to potential new avenues to exploit the properties of telomeres.

"Telomeres are present in all normal dividing cells and act as a built-in check against unwanted cellular proliferation," he explained. "In this case, telomere shortening worked against us, preventing the cells from dividing long enough to form an artery in the laboratory. So we stole a trick cancer cells use to keep dividing; namely we turned on hTERT to stop telomerase shortening."

The researchers did not detect any signs of unwanted cellular proliferation in their bioengineered arteries, although Dr. Counter did emphasize that before these arteries can be implanted into humans, the researchers must "turn off" hTERT. It is expected that the implanted arteries would then "age" as would native arteries.

Dr. Niklason estimates that it could take up to 10 years before these bioengineered arteries will be routinely implanted in patients with heart disease. Currently, it takes about 12 to 13 weeks to grow an artery strong enough to withstand the blood pressures experienced in humans, so she is exploring new approaches that will create stronger arteries faster. Also, it is still not known how the arteries would react once inside the body.

It is estimated that about 100,000

Continued on next page

Acetylation is Here to Stay

By Lisa Samols

The running joke in any undergraduate biology class is that the answer to every question regarding protein function is "phosphorylation." Not so anymore. Within the past seven years, researchers have multiplied exponentially their understanding of a similar function, acetylation, which may well prove to be as driving a force in biology as phosphorylation.

ASBMB member Eric Verdin, Investigator at the Gladstone Institutes and Professor of Medicine at the University of California, San Francisco, chaired a Novartis Symposium in this past May in London to discuss the progress of research on reversible protein acetylation and the possibilities of the future of the field.

"We might be at the tip of the iceberg, but only time will tell how far it will go," said Dr. Verdin.

Lysine acetylation was discovered in the 1960s in histone proteins, around the same time as phosphorylation. However, technology limited what could be examined in the process of acetylation, both in what happens when proteins become acetylated and what enzymes catalyze the acetylation and deacetylatin reactions. There are no convenient radioactive isotopes to mark acetyl groups and track their movements, as P^{32} does in phosphate groups. Additionally, until recently, it has been difficult to identify and use antibodies to acetyl groups, though antibodies for phosphate groups were discovered and used as markers soon after phosphorylation was first observed.

Since the identification of the first histone acetyltransferase and histone deacetylase in 1996 by the groups of Dr. David Allis at Rockefeller University and Dr. Stuart Schreiber at Harvard University, a growing number of acetyltransferases and deacetylases have been identified, and many proteins besides histones were found to be acetylated. These include tubulin, many transcriptin factors, and a rapidly growing number of other types of proteins. As the number of research papers on acetylation increases exponentially every year, scientists are getting a clearer picture of what acetylation does to a protein.

"The field is exploding because people are realizing that many proteins are regulated via acetylation," said Dr. Verdin.

Thus far, it has been observed that acetylation marks a protein, changing its surface and regulating the activity of the acetylated domain, much like phosphorylation does. Much of the recent work on acetylation has consisted in the identification of the enzymes responsible for acetylation and deacetylatin. Dr. Verdin's laboratory has been involved in the cloning of several human histone deacetylases and in the characterization of their biology.

"Acetylation is here to stay," said Dr. Verdin.

The author of this article, Lisa Samols, just finished her junior year at Columbia University where she is majoring in biology. She is an intern at ASBMB this summer.

Continued from previous page

out of 1.4 million Americans who need small vessel grafts are unable to get them because their own or prosthetic vessels are unsuitable. While polymer vessels can be used when large vessels are required, the smaller ones tend to become clogged with clots.

The research was supported by the American Foundation for Aging Research and the National Cancer Institute.

Loss of Enzyme Cripples Common Fungal Infection

Disrupting a single enzyme in a fungus responsible for a significant percentage of hospital-acquired infections prevents the organism from becoming potentially fatal, found a new study by Howard Hughes Medical Institute researchers at Duke University Medical Center.

The finding identifies a new target for drugs to fight the illness, called candidiasis, said ASBMB member Dr. Joseph Heitman, an HHMI investigator and Director of Duke's Center for Microbial Pathogenesis, who was the recipient of the 2002 ASBMB-Amgen Award. The research was reported in the June 2003 issue of the journal *Eukaryotic Cell*.

The researchers studied the molecular machinery of the fungus *Candida albicans*, which accounts for more than 10% of hospital-acquired infections. The condition is fatal in up to 40% of patients who contract the invasive form of the illness.

C. albicans occurs naturally in the body, where it lives on the surface of the intestines, esophagus and other internal body surfaces. Benign bacteria normally help keep the fungus in check, Dr. Heitman said. Natural immune defenses in the blood of healthy people also prevent the fungus from infecting the bloodstream.

"But sometimes that natural balance gets tipped and the fungus begins growing out of control," Dr. Heitman added. The most familiar results are yeast infections, including vaginitis and thrush, an infection of the oropharynx.

In immunocompromised people—such as patients who have undergone organ transplantation, have late-onset diabetes, or are taking broad-spectrum antibiotics—the result can be more serious. The fungus can invade the bloodstream and progress to full-blown candidiasis.

The researchers suspected that *C. albicans*' switch from a benign to a pathogenic form must require the fungus to sense and respond to changes in its environment. That theory led them to an enzyme called calcineurin, a protein important for mediating stress responses in fungi and plants.

To test the idea that calcineurin is critical for the virulence of *C. albicans*, the researchers infected laboratory mice with either normal *C. albicans* or a mutant strain that lacked calcineurin.

Mice infected with the intact fungus died by the eighth day after infection, the researchers found. In contrast, 27 of 30 mice infected with the mutant strain survived until 30 days later, the team reported.

To understand the underlying cause of the mutant strains' lost virulence, the researchers tested its ability to undergo transitional steps known to be important in candidal pathogenesis—survival at high temperatures, filamentous growth and host cell adherence and invasion—in laboratory cultures.

However, the mutant and normal fungus showed no differences in any of the tested characteristics of infection.

"That calcineurin is essential to fungal virulence was absolutely clear," said Heitman. "But when we asked why, we found that none of the characteristics known to be important in infection could explain it."

Since the main cause of death in mice with candidiasis is acute infection of the kidneys, the researchers studied the kidneys of mice infected with the mutant fungus, finding that they contained many fewer fungal cells than those infected with the normal fungus. Further studies revealed that the mutant fungal cells survived and grew at much lower levels in serum, the soluble component of blood, than normal fungal cells.

"When we grew the cells in test tubes with serum, the mutant fungal cells began gradually disappearing after six hours," said first author of the study Jill Blankenship, also of Duke. "By nine hours the difference between the mutant and wild-type fungus was even more pronounced." After 24 hours, the mutant fungal cells had nearly all died, while the normal cells had increased by more than 14,000-fold.

"The result was a big surprise," Dr. Heitman said. "Nobody had recently studied survival in blood as an important step in fungal pathogenesis. The finding suggests an alternate means of preventing the transformation of *C. albicans* from a benign fungus to a serious disease and could lead to new treatments."

Calcineurin plays a role in the virulence of a second fungal pathogen *Cryptococcus neoformans*, according to the team's earlier work, which suggests that drugs targeting the enzyme may provide broad-spectrum antifungal action, Dr. Heitman added.

Today only a handful of treatments exist for treating such fungal infections, Dr. Heitman said. Of those, one of the most commonly prescribed medications, fluconazole (trade name Diflucan), often fails to completely eliminate the infection. A second alternative developed in 1957, amphotericin B, frequently has serious side effects including fever, chills, muscle aches and kidney toxicity.

A next step in the research, said Heitman, will be to identify the blood component responsible for the mutant fungus' failure to invade the bloodstream.

Cloning Embryos from Cancer Cells

Nuclei removed from mouse brain tumor cells and transplanted into mouse eggs whose own nuclei have been removed, give rise to cloned embryos with normal tissues, even though the mutations causing the cancer are still present. This research, from scientists at St. Jude Children's Research Hospital, appeared in the June 1 issue of *Cancer Research*.

The finding demonstrates that the cancerous state can be reversed by reprogramming the genetic material underlying the cancer, according to ASBMB member James Morgan, Ph.D., Co-Chair of the St. Jude Department of Developmental Neurobiology, and lead author of the study. The findings also indicate that genetic mutations alone are not always sufficient to cause a cell to become cancerous.

Dr. James Morgan

Dr. Tom Curran

"Specifically, it shows that so-called epigenetic factors are key elements in the development and maintenance of tumors," Dr. Morgan said.

Epigenetic factors are those that influence the cell's behavior. Examples include environmental effects and chemical modification.

"The concept of epigenetic factors having a role in cancer is already largely accepted," explained Dr. Morgan. "In fact, it's already known that epigenetic alterations of chromosomes can cause certain rare forms of cancer. And some anti-cancer agents actually target epigenetic changes. But this is the first formal proof of the theory in a living animal."

Unlike mutations, epigenetic modifications of DNA are potentially reversible molecular events that cause changes in gene expression. Some genes that help prevent the development of cancer (e.g., tumor suppressor genes) can be targets of epigenetic factors. The inactivation of such a gene might make the DNA more vulnerable to developing a cancer-causing mutation.

The St. Jude researchers used nuclei from mouse medulloblastoma cells to create the clones. Medulloblastomas are brain tumors that tend to spread to the spinal cord. They account for about 20 percent of childhood brain tumors and most often occur in children under 10 years of age.

The team, led by Dr. Morgan and Department Chair Tom Curran, also an ASBMB member, placed nuclei from medulloblastoma cells into mouse eggs whose own DNA had been removed.

"Since the embryos did not develop tumors, we conclude that the cancerous properties were removed by reprogramming," Dr. Morgan said.

"The use of mouse eggs to reprogram cancer cell DNA represents a new strategy for investigating the molecular basis of cancer," noted Dr. Curran. "By studying this model we hope to identify which epigenetic factors may contribute to this form of brain tumor. In addition, it also gives us a valuable tool for testing new therapies."

UCSD Researchers Demonstrate Protein Role Required for Normal Brain Development

An essential step in understanding how the brain develops and related brain disorders that occur when the movement of neurons is defective, has been announced by researchers at the University of California, San Diego (UCSD) School of Medicine in the July 2003 edition of the journal *Nature Genetics*.

The researchers found that normal brain development requires 14-3-3 epsilon, a member of a protein family universally found in everything from yeast to mammals. In studies with humans and mice, the researchers determined that death or severe brain abnormalities occurred when the protein was defective or missing.

"This is the first demonstration in mammals that 14-3-3 epsilon is essential for brain development," said the paper's senior author, ASBMB member Anthony Wynshaw-Boris, UCSD Associate Professor of Pediatrics and Medicine, UCSD. "We also showed that the gene is always deleted on one chromosome in patients with a rare, but severe brain disorder called Miller-Dieker syndrome (MDS), a form of lissencephaly, which means 'smooth brain'."

In normal brain development, neurons migrate to various areas of the brain. Lissencephaly is a severe developmental defect of the brain caused when neurons born deep within the brain are unable to migrate normally to areas such as the hippocampus and cortex. In addition to smoothness of the brain surface, there is a thickening of the cortex, with four rather than six layers. Children with MDS, in addition to a severely damaged brain from lissencephaly, have characteristic facial features, such as a prominent forehead, short nose, and malformed ears and eyes. Patients with MDS have the severest form of a lissencephaly, which renders individuals with profound mental retardation, increasingly severe epilepsy and early death.

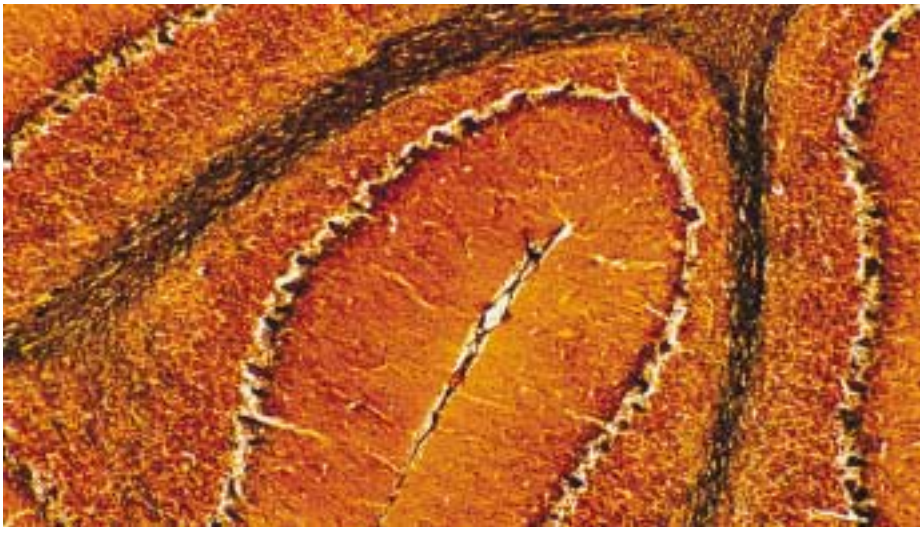
LIS1 (Lissencephaly-1) is a gene that is deleted or mutated on a chromosomal region of chromosome 17 (called 17p13.3) in many children with lissencephaly. LIS1 resides fairly close to the 14-3-3 epsilon gene on this chromosome. Patients with lissencephaly only have deletions of one copy of LIS1, but never 14-3-3 epsilon, while patients with MDS have deletions of both genes on the same chromosome.

One of the genes that directly interacts with LIS1 and is involved in that migration, called NUDEL, was discovered and named by the Wynshaw-Boris team, which published their findings December 20, 2000 in the journal *Neuron*. In new studies with mice lacking 14-3-3 epsilon, the Wynshaw-Boris team determined that 14-3-3 epsilon binds to NUDEL, which may explain its essential role in neuronal migration.

Dr. Wynshaw-Boris explained that NUDEL becomes phosphorylated (combines with phosphoric acid or a phosphorus-containing group) by interaction with another molecular compound called Cdk5/p35. By binding to the phosphorylated form of NUDEL, 14-3-3 epsilon protects NUDEL from losing its phosphorylation through interactions with other molecules, thus stabilizing it for its role in neuronal migration.

"Not only does out study determine a novel function for 14-3-3 epsilon, but it also provides a molecular explanation for why MDS patients have more severe lissencephaly," Dr. Wynshaw-Boris said.

The study was supported by grants from the National Institutes of Neurological Diseases and Stroke, an institutional grant from the Howard Hughes Medical Institute, and UCSD School of Medicine funds.



Determination of ACE Structure Could Lead to New Treatments for Cardiovascular Disease

Scientists at the University of Bath in the UK and South Africa's University of Cape Town Medical School have opened the door to new research in drug therapies for some forms of cardiovascular disease.

Members of the team were, from Bath, ASBMB member K. Ravi Acharya, Professor, and Ramanathan Natesh, Research Officer, Department of Biology and Biochemistry; and from Cape Town, Edward Sturrock, Honorary Lecturer, and Dr. Sylva Schwager, Senior Technician, Division of Medical Biochemistry and Medical Research Council, University of Cape Town Liver Research Centre. Their findings suggest a new approach to drug design based on the structure of angiotensin-converting enzyme, and the team described the first 3D structure of human testicular angiotensin-converting enzyme in the January 30, 2003, issue of *Nature*.

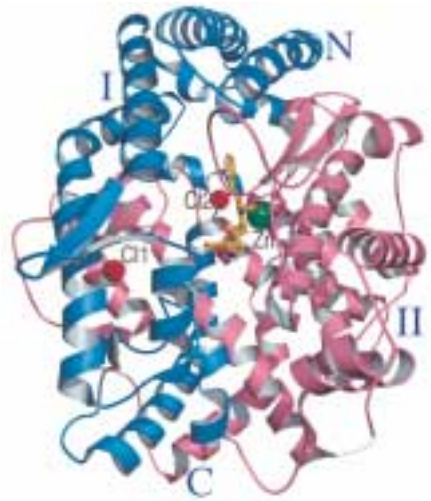
Angiotensin-converting enzyme (ACE) has two forms and two functions in the human body. Somatic ACE exists in most cells and testicular ACE (tACE), which is half the size of somatic ACE, is found only in the testis. Both convert inactive angiotensin I to its active form, angiotensin II, which stimulates blood vessel constrictiontraction. Both forms of ACE also inhibit inactivate bradykinin, which stimulates blood vessel dilation. The result of both actions is to raise blood pressure, which can lead to heart failure, coronary artery disease, and kidney failure—major killers worldwide.

Researchers have taken note of the twofold blood pressure-raisingdual action of ACE in blood pressure regulation, and in the 1970s and 1980s developed drugs that inhibit ACE. However, these inhibitors were designed as substrates for ACE under the assumption that its structure and mechanism were similar to that of carboxypeptidase A, the structure of which had been known for some time. The result is that these inhibitors are not specific to ACE and can cause several side effects. By determining the structure of human testicular ACE, Dr. Acharya and his colleagues hope to stimulate research on the design of second generation ACE inhibitors based on its actual structure.

"My association with Dr. Sturrock has been a collaboration in the true sense of the word—the breakthrough would not have been achieved without his input and vice versa" Dr. Acharya said.

Engineering tACE amenable for structural work in Dr. Sturrock's laboratory was a crucial step for the successful determination of the structure of tACE using X-ray crystallography. The team found that tACE is roughly an ellipsoid in shape, divided into two subdomains

Dr. K. Ravi Acharya



Crystal structure of human testis ACE (Natesh et al., 2003)

by a central groove. The active site is towards the bottom of the groove, and is capped by an N-terminal lid, which prevents large molecules from fitting into the active site. ACE is capable of hydrolyzing only small peptides 25-30 amino acids long. Dr. Acharya and his colleagues used the well known ACE inhibitor lisinopril (known commercially as Prinivil or Zestril) to find help define the active site.

The enzyme is composed of α-helices for the most part, and incorporates a zinc ion and two chloride ions. The functions of the inorganic ions were determined by previous research, and Dr. Acharya's results clarify the understanding of their action. It is known that chloride ions activate tACE, and it was suspected that they interacted with the substrate as well. However, the structure of tACE, as described by Dr. Acharya, places the chloride ions outside the active site. Therefore, it is likely that

Continued on page 13

Will Today's Innovations in Graduate Education

Advanced education faces significant challenges from the impact of changing population demographics, the information technology revolution, the globalization of science, and evolving workforce needs, but lacks key data needed to evaluate educational innovations. That was the assessment of participants in a recent National Science Foundation-hosted Future of Graduate Education Workshop.

The March 19-20 workshop focused on the potential impact of forces changing the future environment of graduate education, the desirable characteristics of graduate education, and how to ensure that such education meets the needs of the nation. Participants included scientists, educators, students, and executives from academia, government, nonprofit organizations and industry.

"Graduate education is evolving right now at an unprecedented rate as student populations change and new methods of learning emerge along with new disciplines," said Joan F. Lorden, Dean in Residence at NSF's Division of Graduate Education and a workshop organizer. "The workshop participants pointed out that graduate education still faces competing pressures and structures that tend to perpetuate the status quo and there is a massive gap in graduate education research."

The workshop participants took note of burgeoning features of graduate education such as on-line learning and mobile student populations and surmised that for-profit colleges and professional master's degrees will also become more prevalent as future generations seek knowledge that will allow them to immediately capitalize upon employment opportunities.

Jennifer Slimowitz, an American Association for the Advancement of Science Fellow with NSF's Division of Graduation Education and the workshop's co-organizer, said, "It's expected that business and industry will seek targeted knowledge to reach specific objectives using international teams comprised of interdisciplinary members . . ."

The basic conclusion drawn from the workshop was that graduate education in the U.S. is in a period of change and likely to look quite different in the next 15-20 years. How to meet these changes is the challenge.

The U.S. graduate education system attracts a growing number of students from the U.S. and abroad, and is critical in building the nation's future intellectual capital in science, math, engineering, and technology. Universities have historically provided the workforce for basic research in part through the employment and training of graduate students and postdoctoral scholars. Graduates supply the workforce for basic and applied R&D in industry and other positions in academia, government, the non-profit sector, and business. The premise of the workshop was that to understand how graduate education will be shaped in the future, it is necessary to understand how changing forces will influence the demands of all stakeholders.

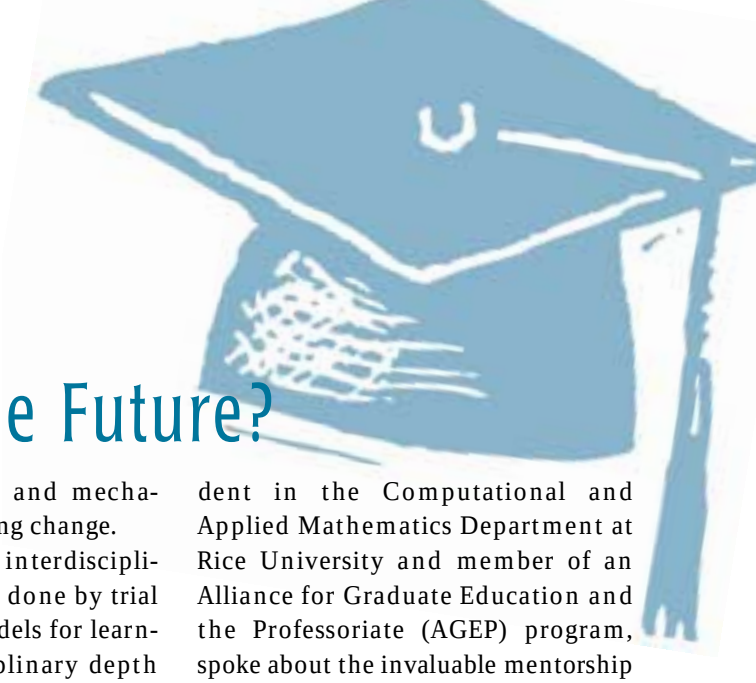
Who will be the students of the future?

The perception of a graduate student as an individual with a bachelor's degree from an high profile school studying full-time for his doctorate needs to be broadened to accurately represent the graduate student of the future, and probably, the graduate student of the present. Speaker Clifford Adelman of the Department of Education projected that students will have bachelor's degrees from a broad range of institutions and will display a high level of mobility from one institution to another.

Questions, however, were raised as to whether the interest of U.S. students in science can be sustained. Economist Richard Freeman of Harvard discussed the difficulty in recruitment of U.S. students into scientific careers that require doctoral education. Long periods of preparation during which relatively low stipends form the basis of support may contribute to flagging enthusiasm for scientific careers. Placed in the context of a variety of other careers for which the preparation time is shorter and more certain, science may look unattractive to students who are U.S. citizens and who are in the position to select from a variety of more lucrative professions.

How will students learn?

Graduate students of the future will seek targeted opportunities for learning instead of traditional degree-oriented programs. This predicts growth in certificate programs and continued development of professional master's degrees, such as those seeded by the Alfred P. Sloan Foundation, that are targeted to specific employment opportunities. Degrees offered on-line



Meet the Challenges of the Future?

and from for-profit institutions will become more prevalent.

Educational partnerships between the corporate, academic, government, and non-profit sectors will play a large role in post-baccalaureate education. This trend will be promoted by the ongoing globalization of science that moves people and ideas across national boundaries.

What will students learn?

Problems that cut across disciplinary boundaries will drive the curriculum in many programs. Programs such as NSF's Integrated Graduate Research and Education Traineeship program and the Interfaces in Science program sponsored by the Burroughs-Wellcome Fund suggest that at least some faculty and students are ready to embrace new approaches that are responsive to the challenges that students will face upon leaving the academy. However, there was seen a need for programs that cut across not only field boundaries but also geographic boundaries to reach students and faculty.

What information is needed?

The workshop concluded with a discussion of what the information participants felt was most needed to effectively shape graduate education. Currently, the absence of a body of research on graduate education hampers future development. Innovations in graduate education that address the changing population of students and the emergence of new methods of learning and new disciplines may yield best practices, but studies are needed to evaluate the outcomes and mechanisms for institutionalizing change.

The development of interdisciplinary curricula is largely done by trial and error. Different models for learning that preserve disciplinary depth and the passion for discovery while allowing students to prepare for a variety of careers in a changing global context warrant systematic investigation. For the doctorate, the definition of a successful outcome needs to be rethought. As new types of programs emerge to meet the demands of the labor market, it is important to define the unique contributions of Ph.D. education and its value to both society and the individual.

The Importance of Community

One theme that ran through the workshop was the importance of community in graduate education. This arose in a variety of contexts and on several different levels. A doctoral student in the Computational and Applied Mathematics Department at Rice University and member of an Alliance for Graduate Education and the Professoriate (AGEP) program, spoke about the invaluable mentorship and camaraderie he found among the AGEP students in his program and credited his success to AGEP. Another told of the intellectual community that includes undergraduates, graduate students, faculty, and teachers from K-12 that was created in their Vertical Integration of Research and Education (VIGRE) mathematics program. He cited the importance of these interactions across levels as one factor that had produced a sharp increase in the number of undergraduate mathematics majors at his school. Similar comments were expressed by other students attending the workshop.

NSF's Directorate of Education and Human Resources published the workshop's summary online at www.ehr.nsf.gov/dge/InnovMTG.htm.

New Treatments ... continued

Continued from page 11

they to play an indirect role in substrate activation. The zinc ion lies in the active site and interacts directly with lisinopril, as indicated by previous research. Dr. Acharya and his colleagues also showed the structure of tACE to be similar to several other proteins, including ACE forms found in other species, as well as other zinc-containing metallopeptidases.

Somatic ACE consists of two parts (called the N- and C- domains), each with a different function, and drugs that are now on the market inhibit both domains. The newly described tACE structure (which is identical to the C-domain structure of somatic ACE) will now serve as a template for the ongoing research in both laboratories which is supported by the Wellcome Trust, a major biomedical charity in the UK. Using a structure-based approach, the design of specific domain-selective ACE inhibitors is expected to produce new drugs that are safer and more effective.

NIH Urges Researchers To Share Mouse Strains

The National Institutes of Health (NIH) is urging scientists to be more open about mouse resources they create with the assistance of NIH grants. While a recently released draft policy, open for public comment until August 1, does not require researchers to share mouse strains with others, it warns that failure to include a plan to do so in future research proposals may lead to their rejection.

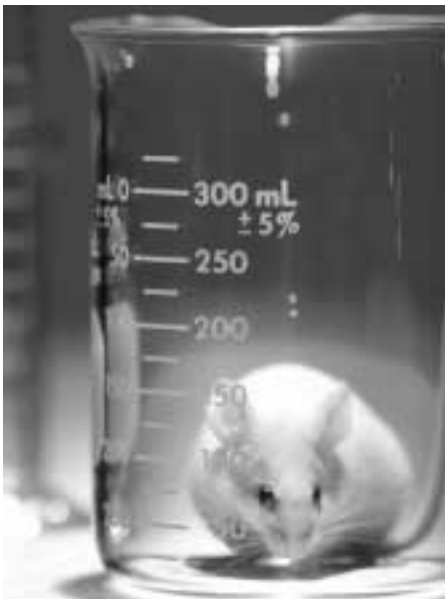
A Frequently Asked Questions and Answers section attached to the draft policy states that while NIH "recognizes that the investigators who generated the mouse resources have a legitimate interest in benefiting from their investment of time and effort. However, unnecessary delay of publication and prolonged exclusive use of the mice are not in the best interests of the research community or the public health."

The draft policy suggests that researchers who want money from the NIH should plan to deposit mice and mouse data with one of two public repositories, Jackson Laboratories in Bar Harbor, Maine, or the Mutant Mouse Regional Resource Centers, a consortium supported by the National Center for Research Resources.

Scientists could choose to respond to requests for genetically modified mice themselves, but considerations of time and money are likely to argue against that. Costs at Jackson Laboratories in some cases can run as high as $200 to $300 per mouse, due to the cost of keeping mice with suppressed immune systems alive, shipping them safely, and ensuring that a steady supply of sterile mice is available.

The facility has been providing mice and mouse data at cost to scientists for decades. Business took off in the past 10 years as genetic modification technology and fast computers made the mouse the animal of choice for researchers.

James Battey, Director of the National Institute on Deafness and Other Communication Disorders, who co-chaired the NIH's drafting process, suggested that researchers add the cost of complying with the new policy into the calculations for grants.



Public Comment Period for Draft NIH Statement on Sharing and Distributing Mouse Resources

The NIH is providing significant support for the development of mice with genetic changes. This resource is being developed to assist the scientific community in furthering its interest in biomedical research. To ensure that these mouse resources are made available to the scientific community in a timely manner, the NIH has developed a draft policy, which can be found at http://www.nih.gov/science/models/mouse/sharing/index.html.

Any modifications to the draft statement will appear at that site after the 60 day public comment period. Institutions, organizations, and individuals are invited to comment on the draft statement and associated documents. Comments must be received no later than August 1, 2003. Please send any comments concerning the NIH Draft Statement via email to sharemymouse@nih.gov or by mail to Share-My-Mouse, NSC, 6001 Executive Blvd, Rm 4263, Bethesda, MD 20892. NIH will consider all comments and make changes to the policy where warranted in both the draft statement and associated documents. This statement was published in the May 28, 2003 NIH Guide announcement.

Leader in Computational Biology is First Director of NIGMS Center

Dr. Eric Jakobsson has, after a two-year search process, been named the first director of the Center for Bioinformatics and Computational Biology at the National Institute of General Medical Sciences.

"I am pleased that Dr. Jakobsson has taken the helm of our newest component," said Judith Greenberg, Acting Director of NIGMS. "His vision and leadership in computational biology will spur growth and innovation in this important field."

"It's very good news that NIH finally got someone to move forward with BISTI [the Biomedical Information Science and Technology Initiative]," said Larry Smarr, founder of the California Institute of Telecommunications and Information Technology, in an interview with The Scientist, "The BISTI report was presented in June 1999, and very few of the recommendations have been acted on. BISTI is the only road map for the future of NIH-sponsored research for telecommunications and information technology."

Implementing BISTI is essential to NIH's development of the information infrastructure to support a national model for biomedical research, said Dr. Smarr, Dr. Jakobsson's former colleague at the National Center for Supercomputing Applications at the University of Illinois.

The NIGMS Center for Bioinformatics and Computational Biology (CBCB) supports research and training in areas that join biology with the computer sciences, engineering, mathematics and physics. Examples include computer modeling of biological networks and dynamic processes; quantitative approaches to cellular, molecular and developmental biology; and the development of databases and other analytical tools. James Cassatt, Director of the NIGMS Division of Cell Biology and Biophysics, has served as CBCB's Acting Director since the center was established in 2001.

Before coming to NIGMS, Jakobsson was a Professor in the Department of Molecular and Integrative Physiology and in the programs in biophysics, neuroscience and bioengineering at the University of Illinois at Urbana-Champaign. Additionally, he was a Professor at the University of Illinois' Beckman Institute and a research scientist at the National Center for Supercomputing Applications.

The NIGMS Center for Bioinformatics and Computational Biology supports research and training in areas that join biology with the computer sciences, engineering, mathematics and physics.

He recently served as Director of the Center for Biophysics and Computational Biology at the University of Illinois at Urbana-Champaign. He also directed and helped establish the bioengineering program there.

Dr. Jakobsson's research focuses on the computational and theoretical study of biological membranes. He is also a leader in the use of computers and other technology in education. Among his achievements is a computer system that enables users with a web browser to simultaneously access several databases that would otherwise be incompatible.

As the new Director of CBCB, Dr. Jakobsson will also assume from Dr. Cassatt leadership of the Biomedical Information Science and Technology Initiative (BISTI). This initiative brings together senior-level representatives of various components of NIH and other Federal agencies interested in the use of computer science to address issues in biology and medicine. BISTI will hold its first symposium, called "Digital Biology: The Emerging Paradigm," on November 6-7, 2003 (www.bisti.nih.gov/2003meeting/).

By Peter Farnham, ASBMB Public Affairs Officer

Peer Review Changes at VA Drawing Senate Attention

In a June 4 letter to Anthony J. Principi, Secretary of Veterans Affairs, Senate Veterans Affairs Chairman Arlen Specter (R-PA) and ranking minority member Bob Graham (D-FL) urged that changes in the VA peer review system be "well justified" and that the VA "proceed deliberately when mapping the future of VA research."

The letter was prompted by strong concern in the scientific community that the VA's Chief Research and Development Officer, Dr. Nelda Wray, has begun to implement changes in the VA peer review system without considering carefully "how proposed research policy changes might affect VA's physician-investigators." The issue has attracted growing attention in the science press in recent months, and the Specter-Graham letter makes clear that the issue has attained sufficient mass to prompt congressional concern.

Dr. Wray took office in January, and in early April cancelled the funding notifications that 18 VA researchers had received the previous fall. In doing so, she said that the cancelled grants were of poor quality and that the researchers were not sufficiently productive. In a separate note a few days later, she argued that there was not enough money available in the VA research budget to fund all the grants that had been approved for funding, and that researchers in the Medical Research Service—an arm of the VA's research and development office—had been improperly notified and provided with incorrect information. The individual responsible for the notification no longer works in the Medical Research Service.

Dr. Wray has proposed a new peer review model to replace the old one at the VA. The new model takes into account a peer review score, but also includes a measure of productivity based on the number of papers published in top journals, and how much funding from other agencies the researcher has.

ASBMB President Bettie Sue Masters wrote to Dr. Wray in early June on these same issues (the letter appeared in last month's issue of ASBMB Today *and is also posted on the Society website). As of this writing, she had not received a reply.*

The senators expressed concern that some of Dr. Wray's proposed changes "have provoked considerable anxiety among VA researchers, and criticism from the general scientific community. VA researchers who are already struggling with new educational and credentialing requirements must now also contend with changing merit review standards, and fears that funding will be diverted from basic research to clinical quality assurance activities."

The senators noted what *ASBMB Today* reported in the June issue, that "Researchers have found several aspects of the newly applied standards troubling, including using the number of weighted publications as a measure of productivity…. publication rates can vary significantly depending on the discipline and the size of the research laboratory. Researchers investigating conditions that affect veterans disproportionately are more likely to publish their findings in specialty journals than in *The New England Journal of Medicine*, but this does not always predict the quality or significance of the publications."

The senators also asked that Secretary Principi provide them with an update on how the new merit standards will be applied during current and future funding cycles to VA researchers' proposals, an explanation of how these criteria were developed and who contributed to their design.

These questions precisely mirror the concerns that have been raised in the scientific community about the changes in the VA's approach to the science it funds since Dr. Wray took office in January. For example, at a meeting on June 12, Dr. Wray described her vision, saying that in the context of VA research, "generating basic information is not science. Translating this information to health care is science." She argued that her office has an obligation to conduct investigations that are of importance to the mission of the VA.

Dr. Wray also said that there seemed to be an entitlement mentality among some VA researchers, and that the peer review system at the VA was not very good. She also noted that while a good peer review score is important, other factors are routinely considered when measuring research quality. "I know of no academic administrator who doesn't measure productivity" of researchers, she noted. "Why shouldn't I?"

The senators observed in their letter to Secretary Principi that "An increased emphasis on productivity may hone some VA research programs, but this should not come at the cost of physician-investigators who have joined VA for the rare opportunity to provide quality care to our nation's veterans while pursuing their research interests. For many VA medical centers, a loss of funding for small basic research programs may translate directly into the loss of scarce medical specialists, with an immediate impact on clinical care."

Ten Lessons From The Texas SCNT Battle

By Peter Farnham, CAE ASBMB Public Affairs Officer

"The nearest run thing you ever saw in your life," was how the Duke of Wellington characterized his victory at Waterloo in June 1815. The battle ended once and for all 20 years of French dominance of the European continent.

Wellington's quotation is applicable in other contexts. Consider the epic battle this spring in the Texas Legislature over a bill to ban somatic cell nuclear transfer (SCNT) in the state.

Texas attracted $918 million in NIH research dollars in 2002, and the Lone Star State is on pace to receive over $1 billion in NIH money in 2003. Obviously, a state law forbidding SCNT would have had been a major blow to medical research in Texas.

But a small group of activists affiliated with two local groups—Texans for the Advancement of Medical Research, and the Texas chapter of the Juvenile Diabetes Research Foundation—managed to halt and then reverse almost certain passage of a bill, HB1175, that would have banned SCNT as "human cloning".

How this feat was accomplished is worth reviewing, and pro-research groups can glean at least 10 lessons from the successful effort.

Do your homework. Supporters of the ban had stolen a march on pro-research advocates, and had made very good progress on getting the bill passed. Since most state legislators are not trained in biomedical science, the one-sided positions of the SCNT opponents won support.

The pro-research advocates had to become quickly familiar with the details of HB1175, and the arguments used by its supporters. They also had to develop arguments that unscientific legislators could understand. All legislators then had to be categorized into those strongly in favor of the bill, those leaning in favor, those who were undecided, those leaning against, and those strongly against. Only then were pro-research advocates able to go to work.

Communicate. Advocates win by keeping everyone informed, and this was made easier by modern communications. Being able to instantly communicate with hundreds of people who then made telephone calls and sent faxes and e-mails to legislators was vital in turning around the almost impossible situation faced by pro-research advocates in early March 2003.

Be vigilant. Advocates must monitor everything in the legislative session. In Texas, people were on-site at the capital every day, monitoring subcommittee and committee deliberations, floor action, and picking up other information. One read through every one of the 150 bills under consideration in the last couple of days of the legislative session, just to make sure that the SCNT ban was not quietly attached to one of them.

Be agile. Advocates must adapt and react quickly to changing circumstances and strategy. Sometimes phone calls, faxes, and emails were needed on a few minutes' notice as bills came up, amendments offered, and deals cut.

Be lucky. Late in the session, a group of Republican legislators tried to reopen the issue of congressional redistricting, which had been settled a couple of years earlier. They saw an opportunity to redraw district boundaries in order to increase the number of seats that would likely become Republican in the 2004 elections.

Texas Democrats, in the minority, knew that they did not have the votes to prevent redistricting, so they adopted a simple tactic—they left the state, thus shutting down the legislature which lacked a quorum. When the Democrats finally returned to the Legislature, there was only enough time left in the session to consider a few critical bills, and the SCNT ban was not among them.

A lucky break? Of course. But, if SCNT supporters had not been working very hard in the weeks prior to the Democratic exodus, HB1175 would surely have been passed. Fortune can work in one's favor, but it helps to be prepared when it appears.

Being able to instantly communicate with hundreds of people was vital in turning around the almost impossible situation.

It ain't over 'til it's over. Like most of Yogi Berra's comments, this one becomes more true the more one thinks about it. Consider the May 28 e-mail to pro-research advocates headed, "THIS IS AN EMERGENCY! CALL CALL CALL CALL CALL. …Bill 2292 being heard on the floor RIGHT THIS VERY MOMENT!!…[Tell your representatives to] vote AGAINST ANY LANGUAGE OFFERED BY NELSON and VOTE FOR LANGUAGE OFFERED BY SHAP-

Continued on page 18

Leader In Biomedical Research To Head Children's' Memorial Research Institute

Cancer biologist Dr. Mary J. C. Hendrix, an ASBMB member and Past President of FASEB, has been named President and Director of Children's Memorial Institute for Education and Research. The institute, the research arm of Children's Memorial Hospital and the Center for Pediatric Research at Northwestern University, conducts basic science, clinical and translational research on diseases and other problems that affect children and their parents.

Dr. Hendrix is currently head of the Department of Anatomy and Cell Biology at the University of Iowa in Iowa City, as well as the Deputy Director of the Holden Comprehensive Cancer Center in the university's Carver College of Medicine. She is planning to move to Chicago in January 2004 along with her interdisciplinary research team.

"After an exhaustive search, we are ecstatic to have found precisely the right person to develop the research institute into a mature scientific enterprise at the forefront of pediatric research," said Patrick M. Magoon, President and CEO of Children's Memorial Medical Center. "Dr. Hendrix brings scientific excellence and visionary leadership to research at Children's Memorial and Northwestern University."

Dr. Mary J. C. Hendrix

Dr. Hendrix, who has published more than 150 scientific papers plus numerous books and book chapters, is expected to be appointed Professor of Pediatrics and Cell Biology at Northwestern University's Feinberg School of Medicine. Children's Memorial Institute for Education and Research is one of 13 interdisciplinary research centers and institutes at the Feinberg School.

"I am extremely pleased to have the opportunity to work with the exceptional people associated with the institute, Children's Memorial Hospital, and Northwestern University," said Hendrix, "and I look forward to the potential good we can accomplish, working together toward the common goal of translating research with enhanced educational programs to benefit children and parents."

Dr. Hendrix is a member of the National Advisory Council for Human Genome Research, and is on the boards of directors of the Public Responsibility in Medicine and Research and the Annenberg Center for Health Sciences at Eisenhower Medical Center. She is also President of the Association of Anatomy, Cell Biology and Neuroscience Chairpersons, and recipient of the 2002-2003 Distinguished Achievement Award by the University of Iowa Committee on the Celebration of Excellence Among Women.

Ten Lessons ... continued

Continued from page 17

LEIGH...." With the note was a list of legislators and their telephone numbers.

The note was successful; three hours later, just before the Legislature adjourned, Bill 2292 passed without an amendment to ban SCNT in Texas.

Don't gloat. Coalitions form, dissolve, and shift every day. The groups you oppose one day may be vital allies the next. Do not burn bridges by public gloating. Be gracious in victory. Uncork the champagne bottles in private, and don't invite the press to your victory parties.

Thank your friends. No political victory is ever won by one person; this particular victory required the efforts of literally hundreds. Make sure each and every one of your allies is personally thanked, and the most important among them publicly recognized.

Get ready to start over. All victories in politics are temporary. When the Texas legislature next reconvenes, we can expect a new effort to ban SCNT. The supporters of a ban will have learned from their experience this year, and will be even harder to defeat. So, be prepared for a continuing series of battles and think long-term.

And above all else, get involved.

Noted Sickle Cell Researcher to Become AACBNC President in 2005

Noted sickle cell disease researcher Dr. Steven R. Goodman of the University of Texas at Dallas has been elected president of the Association of Anatomy, Cell Biology and Neurobiology Chairpersons (AACBNC), a key national organization providing leadership and advocacy in the biomedical sciences. Goodman will become president-elect of the association in January 2004 and president one year later.

Top 25 Institutions Receiving NIH Awards in FY 2002

Listed below in rank by dollar amount are the 25 institutions that received the most NIH awards in FY 2002. For a complete listing of numbers and amounts of training grants, fellowships and other awards for all institutions receiving NIH funding, go to http://grants1.nih.gov/grants/award/trends/rnk02all1to100.htm on the NIH website.

Rank	Organization	All Awards	Research Grants	R&D Contracts
1	Johns Hopkins University	$ 510,005,326	$ 445,344,636	$ 30,188,835
2	University of Pennsylvania	$ 418,546,510	$ 387,193,228	$ 5,015,657
3	University of Washington	$ 405,729,042	$ 364,789,351	$15,872,705
4	University of California, San Francisco	$ 365,365,909	$ 319,767,828	$ 28,084,352
5	Washington University	$ 343,792,077	$ 318,508,574	$ 9,081,524
6	University of Michigan	$ 325,786,206	$ 296,201,913	$ 8,420,376
7	University of California, Los Angeles	$ 317,017,181	$ 291,264,313	$ 10,613,357
8	University of Pittsburgh	$ 308,144,862	$ 287,445,611	$ 10,982,841
9	Science Applications International Corp.	$ 294,152,069	----------	$294,152,069
10	Yale University	$ 289,899,944	$ 264,325,680	$ 5,545,658
11	Duke University	$ 277,393,166	$ 256,215,850	$ 7,532,810
12	Harvard University	$ 273,147,799	$ 248,591,756	$ 508,782
13	Columbia University	$ 269,844,585	$ 250,171,534	$ 4,107,809
14	University of North Carolina, Chapel Hill	$ 264,263,425	$ 223,159,299	$ 25,378,504
15	Baylor College of Medicine	$ 263,540,460	$ 245,689,782	$ 10,234,203
16	Stanford University	$ 247,636,170	$ 223,815,022	$ 5,743,760
17	University of California, San Diego	$ 244,713,718	$ 226,249,960	$ 5,342,582
18	Massachusetts General Hospital	$ 243,612,895	$ 232,063,792	$ 4,995,966
19	University of Wisconsin, Madison	$ 227,807,000	$ 202,356,845	$ 11,001,587
20	University of Minnesota	$ 217,209,642	$ 190,425,016	$ 15,894,596
21	University of Alabama at Birmingham	$ 211,672,387	$ 186,542,547	$ 15,846,376
22	Brigham and Women's Hospital	$ 205,122,985	$ 192,388,091	$ 6,056,882
23	Case Western Reserve University	$ 203,883,400	$ 175,970,262	$ 18,430,647
24	Vanderbilt University	$ 195,248,691	$ 176,939,221	$ 2,529,813
25	Scripps Research Institute	$ 190,777,342	$ 185,665,788	$ 995,597

Calendar of Scientific Meetings

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: http://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

50th Anniversary Gordon Conference on Isotopes in Biological and Chemical Sciences

February 15-20 • Ventura, California
Chair: David N. Silverman, Vice Chair: Charles L. Perrin
Email: silvrmn@ufl.edu
Website: http://www.grc.org/programs/2004/isotopes.htm

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: http://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

2-5 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

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