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Organized by Stephen H. White, UC, Irvine

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Organized by A. Stephen Dahms, California State Univ. System Biotechnology Program

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Over 300 scientists will be selected from the abstracts submitted to ASBMB Topic Categories to make oral presentations. Scientific sessions corresponding to the above themes will be held each day in which speakers from the volunteered abstracts will present. Oral presenters will also present a poster at the meeting.

**Opening Lecture**
*Roderick MacKinnon, The Rockefeller Univ.*

For more information contact:
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ON THE COVER:

10 An Outstanding Success
Attentive audiences filled meeting rooms and the exhibit floor during the ASBMB Annual Meeting and EB2002 sessions.
The April issue of ASBMB Today on page 5 contains a discussion of the proper terminology for cell structures derived from the transfer of nuclei from somatic cells to an unfertilized egg. Because cloning of plant cells is far advanced over that of mammalian cells, you may find some helpful perspectives from the experience with plants.

Forty years ago F. C. Steward at Cornell University cultured bits of tissue from carrot root under sterile conditions. Shaken gently in an ordinary mix of nutrients, the carrot cells replicated endlessly as undifferentiated cells. So far, this was a familiar demonstration. But then Steward gave the cultured cells a certain mix of plant hormones, and the globs magically differentiated into structures that looked for all the world like carrot embryos. These structures subsequently developed into mature carrot plants. This transformation of mature, somatic tissue to the form of embryos was subsequently duplicated with numerous species, became the standard means of culturing orchids inter alia, and provided the ultimate proof of the 19th-century doctrine of totipotentiality.

The embryo-like structures derived from somatic cells of plants are commonly known as embryoids. Although current technologies with mammalian cells fall short of those of plant-cell culture, the term embryoid might offer a useful distinction.

A related comment: it is widely recognized that plants derived from embryoids that have been cultured under conditions of environmental or nutritional stress typically show a wide range of mutations, a phenomenon known as somaclonal variation. One can imagine that the high proportion of clone-derived mammals that show mutations could, as in plants, also be the result of suboptimal conditions of cell culture.
ASBMB Supports Bill To Double NSF Budget

ASBMB announced its support on May 7 for a bill that would authorize the first three years of a plan to double the budget of the National Science Foundation. The bill, introduced by Rep. Nick Smith (R-MI), would authorize 15 percent increases for NSF each year through 2005, and authorizes a $720 million increase in the NSF budget for FY 2003. Smith chairs the House Science Subcommittee on Research, which has oversight authority over the NSF.

Smith noted that “I think tax funded basic research has been a very worthwhile investment. Continuing our support of basic research forms the building blocks for the applied research that keeps our security, health, and economy strong.” He also noted that NSF’s success breeds imitation. “All over the world, nations devote significant portions of their R&D budgets to monitoring the work of agencies like NSF. They have also been moving very rapidly to adopt NSF’s model of peer-reviewed, competitive funding of basic research.”

The 15 percent increases are needed, according to Smith, to allow an increase in the size and duration of NSF grants, and to increase graduate stipends to make it easier for more students to pursue graduate degrees in mathematics and science. ASBMB President Bob Wells singled out these reasons for ASBMB’s support of a doubling of the NSF budget when he testified in favor of the plan on April 16 before the House Appropriations Subcommittee on VA/HUD, which has funding authority over NSF.

Smith noted that 15 percent increases would provide support for new initiatives at NSF such as education, cyber-security, nanotechnology and information technology, and would address the problem of backlogged major research equipment projects that have been waiting for funding.

“The thinking behind this bill is simple—but not simple-minded,” Science Committee Chairman Sherwood Boehlert (R-NY) said. “NSF funds research that is of critical importance to the future of the nation’s economy, to the nation’s security, to the nation’s health and well-being, and to the nation’s students.”

He also noted that “Congress has quite properly committed to doubling the budget of the National Institutes of Health . . . but NIH does not and cannot fund the full range of research activities the nation needs to remain prosperous—and healthy. NSF has the broadest research mission of any federal science agency and the clearest educational mission. It needs the funding that goes with that expansive—and expensive—mandate.”

The bill, H.R.4664, debuted on May 7 at a hastily-arranged press conference in the Science Committee’s main hearing room. Members of the committee attending were ranking Democrat Ralph Hall (TX), Smith, ranking Research Subcommittee Democrat Eddie Bernice Johnson (TX), Committee Vice Chairman Vern Ehlers (R-MI), Connie Morella (R-MD), and Lamar Smith (R-TX). ASBMB President Bob Wells attended the press conference, as did President-elect Bettie Sue Masters. Officials from the Ecological Society of America, Association of American Universities, and American Mathematical Society were also present, in addition to five senior officials from private industry.

Approximately 50 representatives of the science community were present, and most of the organizations represented provided press releases endorsing H.R.4664.

The bill is on the “fast-track” in the House, and cleared the Research Subcommittee within a week of its introduction, and the full committee on May 22. No comparable legislation has been introduced in the Senate, although Senators Kit Bond (R-MO) and Barbara Mikulski (D-MD) have called for a doubling of the NSF budget in a “dear colleague” letter that circulated last year.

There does, however, appear to be a growing consensus in Congress that NSF needs more funding. This has been a long-standing position of the ASBMB and one of its major policy goals.
Foreign Scientists Seen Essential to U.S. Biotechnology

By Stephen Dahms, Ph.D.

The scarcity of skilled technicians is seen by the biotechnology industry in the U.S. and Canada as one of its most serious challenges. The success of this industry is dependent on the quality of its workforce, and the skills and talents of highly-trained people are recognized as one of the most vital and dynamic sources of competitive advantage.

The U.S. biotechnology industry workforce has been growing 14% to 17% annually over the last six years, and is now over 190,000 and conservatively estimated to reach 500,000 by 2012. Despite efforts by the industry to encourage U.S. institutions to increase the production of needed specialists, a continual shortfall in the needed expertise requires access to foreign workers.

Foreign workers with unique skills that are scarce in the U.S. can get permission to stay in the U.S. for up to six years under the H-1B classification, after which they can apply for permanent resident status. There are currently over 600,000 foreign workers in this category across all industries, and they are critical to the success and global competitiveness of this nation. Of these H-1B visa holders, 46% are from India and 10% are from China, followed in descending order by Canada, Philippines, Taiwan, Korea, Japan, U.K., Pakistan, and the Russian Federation.

Our annual national surveys have demonstrated that between 6% and 10% of the biotechnology workforce have H-1B visas. The constant shortfall in specialized technical workers that has been experienced by the biotechnology industry over the past six years has been partially alleviated by access to talented individuals from other nations. However, the industry’s need is sufficient to justify a 25% increase in H-1Bs in 2004.

Biotechnology industry H-1B visa holders are mainly in highly-sought after areas such as analytical chemistry, instrumentation specialization, organic synthesis, product safety and surveillance, clinical research/biostatistics, bio/pharm quality, medicinal chemistry, product scale-up, bioinformatics and applied genomics, computer science, cheminformatics, pharmacokinetics, and pharmacodynamics.

Forty percent of H-1B foreign workers are at the Ph.D. level, 35% MS, 20% BS, and 5% MD. In comparison, the U.S. biotechnology industry technical workforce is estimated to be 19% Ph.D., 17% MS, 50% BS, and 14% combined voc-ed/community college trained. These and other survey data by industry human resource groups clearly show that the H-1B worker skills match the most pressing employment needs of the biotechnology industry. The data demonstrate that maintaining a reasonably-sized H-1B cap is critical to the industry.

Although the national annual H-1B visa cap was raised from 115,000 to 195,000 in the 106th Congress via S. 2045, the cap has already been exceeded. The increased cap remains in effect until 2003 and efforts are underway to ensure that it remains high.

The Third Annual National Survey of H-1B’s in the biotechnology industry found that 80% are from U.S. universities, and 85% of those eventually get Green Cards. Companies now spend, on average, $10,200 in processing fees and legal expenses to obtain each Green Card, an estimated cost to the industry of more than $150 million over the past five years.

In the wake of the 9/11 World Trade Center attack, debate has been focused on more restrictions on foreign students, a development that would have a severe impact upon the competitiveness of the U.S. biotechnology industry. Therefore the National Academy of Sciences is recommending extreme caution in creating new restrictions upon foreign students that will directly impact the number and quality of the U.S. graduate student research pool, which is so critically dependent upon foreign students.

Clearly, the H-1B route provides a temporary solution to shortages in the national and domestic biotechnology labor pools, shortages mirroring the inadequate production of appropriately-trained U.S. nationals by U.S. institutions of higher learning. The reality is that universities have inadequate resources for expanding the training pipeline, particularly in the specialized areas of the research phase of company product development. Efforts should be directed toward influencing greater Congressional and Federal agency attention to these important topics.

The author of this article, A. Stephen Dahms, is Executive Director of the California State University System Biotechnology Program (CSUPERB); Chair of the Workforce Committee, Biotechnology Industry Organization; and a member of the ASBMB Education and Professional Development Committee. Statistical data are from surveys conducted by CSUPERB, as an activity of the Biotechnology Industry Organization’s Workforce Committee; and for Canada, from Statistics Canada.
Bush To Set Up Monitoring System For Foreign Students

A May 10 White House briefing for representatives of the scientific community outlined the Bush Administration’s plans to establish an interagency panel to review the applications of certain foreign graduate students and postdocs seeking visas to study in the U.S.

The panel, called the Interagency Panel on Advanced Science and Security (IPASS), will be established by executive order “as quickly as possible,” according to administration spokesmen from the White House Office of Science and Technology Policy. The panel will be made up of representatives from federal science agencies such as the NIH, the NSF, and the Departments of Defense and Energy (among others) and representatives from various law enforcement and security agencies, such as the FBI.

The goal of IPASS is “to ensure that international students or visiting scholars do not acquire uniquely available and sensitive education and training in U.S. educational institutions or facilities that may be used against us in a terrorist attack,” according to an OSTP staffer who read a written description of the panel.

The panel will review visa applications for foreign graduate students and postdocs who want to study or conduct research in “uniquely available” and “sensitive” areas of study. Uniquely available was defined as a subject of study only available in this country. A student wanting to study general biology here would not be subject to an IPASS review, according to the briefing, because biology is taught at almost any university in the world. A uniquely available course of study could be something as specific as working with a key professor or in a specific department that specialized in a particular scientific area.

An area of study would be considered “sensitive” if it provided knowledge that could be used against the United States in a terrorist attack. A graduate student or postdoc would have to apply to study a field that was both uniquely available and sensitive in order to trigger a review.

The IPASS review process would be another layer of review on top of the layers of review foreign students already undergo when applying to study in this country. The panel would review only those applications that were sent to IPASS as the result of lower level reviews. Among the variables that might trigger review are the background and previous education of the applicant; country of origin; the scientific area of study, training or research involved; and the nature of other work at the university where the student would be studying.

The OSTP staffers conducting the briefing assured that they would oversee the activities of the IPASS to make sure it struck an appropriate balance between the need to conduct science in an open manner, and national security. They also promised to provide the scientific community with “something in writing” as soon as possible.

PAAC Members Press Legislators on NIH, NSF Funding

“Ten percent of the Senate!” That was the pleased summation of a member of the Society’s Public Affairs Advisory Committee (PAAC) at the end of the committee’s recent Capitol Hill Day.

Committee members met with Senator Gordon Smith (R-OR) and visited the offices of John Warner (R-VA), Russ Feingold (D-WI), Ron Wyden (D-OR), Bill Frist (R-TN), Fred Thompson (R-TN), Arlen Specter (R-PA), Mike DeWine (R-OH), George Voinovich (R-OH), and Herb Kohl (D-WI).

The committee’s message on NIH was simple—finish the plan to double the agency’s budget by the end of this year. Every staff member and senator assured us the doubling would be completed on schedule. Just as important, the committee also recommended that in the years after 2003, the NIH budget should continue to increase at a rate of between 7 and 10 percent per year. This will enable NIH to fund current services after 2003, and also allow some new growth.

Unfortunately, the Administration’s plan for the years following FY 2003 is for increases only in the range of 2%. This would mean that by 2007 the NIH budget will, in effect, be precisely where it would have been had the doubling never taken place.

The committee also urged a doubling of the NSF budget, and received some positive feedback. However, many of the staff we visited were not familiar with even basic facts about NSF, such as its size and mission.

The committee members also discussed human cloning and somatic cell nuclear transfer, but the congressional responses were mixed, reflecting the deep divisions on the issue in the Senate. Most of the senators had taken a position on the Brownback bill, and some were actually cosponsors. However, two senators considered “undecided” by most seemed amenable to our arguments.

Visit your representatives and senators when you are in Washington, they need to hear from scientists. Peter Farnham, ASMB’s public affairs officer, will be happy to arrange a visit for you.
NIH Grants Infrastructure Awards For Human Embryonic Stem Cell Research

The National Institutes of Health announced, in late April, the granting of four resource infrastructure enhancement awards for human embryonic stem cell research. The awards are intended to stimulate the use of embryonic stem cells in basic research by providing funds for expansion, testing, quality assurance, and distribution of existing cell lines that meet the President’s criteria for federal funding.

Recipients of the awards are Cell-saurus, an Athens, Georgia subsidiary of BresaGen, Ltd.; ES Cell International Pte. Ltd., of Singapore and Melbourne, Australia; the University of California, San Francisco; and the Wisconsin Alumni Research Foundation of Madison, Wisconsin.

BresaGen is an Australian biotechnology company committed to the discovery and commercial development of innovative biotherapies. During two decades of experience, the company has been involved in reproductive and developmental biology and in the manufacture of recombinant protein pharmaceuticals.

ES Cell International is a regenerative medicine company focusing on developing therapeutic products from human embryonic stem cells. The company was incorporated in Singapore in July 2000. Its corporate headquarters, together with a dedicated research and production facility, are housed within a leading Australian Medical Research Precinct. ES Cell International funds research collaborations with the Monash Institute of Reproduction and Development, Australia; the National University of Singapore; Hadassah Medical Organisation, Israel; and the Hubrecht Laboratory in the Netherlands.

“These awards represent the first major expenditure by the NIH for supporting human embryonic stem cell research,” said Ruth Kirschstein, M.D., Acting NIH Director. “By providing these funds, the NIH is hoping to get these cells into the hands of basic scientists as quickly as possible.”

The four entities are listed on the NIH Human Embryonic Stem Cell Registry, http://escr.nih.gov and have a combined total of 17 stem cell lines that will be available to basic scientists for research. These awards provide a total of approximately $3.5 million over two years. NIH sponsors of the awards include the National Center for Research Resources; National Heart, Lung, and Blood Institute; National Institute of Aging; National Institute of Diabetes and Digestive and Kidney Diseases; and the National Institute of Mental Health. NN

NIBIB Awards Its First Research Grants

The National Institute of Biomedical Imaging and Bioengineering (NIBIB), the newest of the NIH funding institutes, has awarded its first research grants to the following institutions: Yale University School of Medicine, University of California at San Francisco, and Tribofilm Research, Inc. of Raleigh, North Carolina. The National Institute of Neurological Disorders and Stroke will join NIBIB in supporting the Yale University research.

The Yale University project, which will receive $1.4 million in total costs this year, will be headed by James S. Duncan, who is developing magnetic resonance functional and spectroscopic imaging techniques to study and treat neocortical epilepsy. This grant is part of the NIH Bioengineering Research Partnership program which encourages multi-disciplinary teams of biomedical and quantitative scientists to work on biomedical research problems. This is the first such grant to be awarded by the NIBIB.

The University of California at San Francisco Cardiovascular Research Institute will receive $330,000 in total costs this year as the first competing renewal research grant awarded by the NIBIB. The project, headed by Alan S. Verkman, will be developing new optical methods for imaging cellular architecture and dynamics. The first small business innovation research award, $420,000 in total costs for this year, was issued to Tribofilm Research. This project will be headed by Paul M. Vernon to develop new silicone-free, low-friction coatings for syringes. This project is timely due to the increasing interest in developing alternatives to silicone-based lubricants which are typically used in medical devices.

For more information about NIBIB and related funding opportunities, visit http://www.nibib.nih.gov.
Researchers Use Gene Therapy to Destroy HIV Virus

“This could be the smart bomb in our arsenal,” said John Rossi, Chair of the Division of Molecular Biology at the City of Hope Cancer Center and an ASBMB member, in discussing his team’s research into the use of gene therapy to destroy the HIV virus.

Dr. Rossi was quoted by Reuters in a news article about how the virus that causes AIDS can be stopped in its tracks, by using gene therapy to tell infected cells how to prevent the virus from replicating. He is the lead author of a study that appeared in the May issue of Nature Biotechnology showing that small pieces of RNA can prevent HIV from growing in cells.

“This is a new form of target-specific destruction,” Rossi stated, regarding drugs that use molecular technology to block pathways associated with disease.

By analyzing the genetic sequence of HIV, his team found two proteins the virus makes once it enters a cell and starts to replicate. “We can prevent the virus from producing the proteins. It’s like a light with no light switch,” Rossi said. The small pieces of RNA, called siRNA, that get an infected cell to attack HIV can’t be activated in the body because of an overriding mechanism, the researcher said.

In order get the body to make the siRNA, bone marrow would be taken from patients, combined outside of the body with genes that make the siRNA and then reintroduced into the patient’s bone marrow where new cells are continuously generated.

“The body will repopulate with cells that protect against HIV,” Rossi said.

The City of Hope researchers expect to begin testing the gene therapy system in human AIDS patients late this year or early in 2003.

2001-2002 ASBMB Graduation Survey

In early July, the ASBMB Education and Professional Development Committee will mail the fifth annual graduation survey to Biochemistry and Molecular Biology Department Chairpersons. Respondents may either mail the survey to the Society or complete the form online in the Education section of the ASBMB website. The results of this survey will be published in ASBMB Today and placed on the Society’s website.

The data will enable the Committee to more fully serve our members by providing up-to-date demographics and showing trends over time. It also will help the Committee to better identify which institutions offer degrees and at what level. Additionally, the data will be of help to research universities in identifying recruiting areas that they may not have previously identified.

The deadline for return of the survey will be August 1. Please visit the Education section of the ASBMB website to see if your department is currently on our “List of Schools” which offer Biochemistry and Molecular Biology degrees. You may also view a list of the respondents to last year’s survey. Survey results for the past four years are available online. The results for 2000-2001 were published in the May edition of ASBMB Today.

Dutch Firm Joins With NIH to Develop Ebola Vaccine

The U.S. government has joined forces with a tiny Dutch biotechnology company to develop a vaccine against Ebola, the virus that bleeds people to death and which could be a powerful weapon in bioterrorism. Crucell NV will develop the vaccine together with the National Institutes of Health, and could test it on humans within two years and sell it by 2008.

The Ebola virus causes Ebola fever, one of the deadliest diseases known to man and for which there is no cure. Victims’ internal organs literally disintegrate and they die rapidly, bleeding from every orifice. Recent outbreaks of the jungle fever have occurred in Africa, resulting in hundreds of deaths. A major outbreak in a heavily populated area has so far not occurred, but last year’s September 11 attacks and the anthrax attacks in October have raised the specter of deadly viruses like Ebola and smallpox being unleashed in large quantities as weapons of terror.

Crucell said that under the partnership’s terms it had the option to acquire the exclusive right to sell the vaccine once it is made. Logtenberg declined to put a value on potential sales but said Crucell would target travelers, government officials, military personnel and people living in Ebola endemic areas.
Three ASBMB members are among 177 newly elected Fellows of the American Academy of Arts and Sciences. The 2002 class of 177 Fellows and 30 Foreign Honorary Members include a United States Senator and Representative, four college presidents, three Nobel Prize winners, six Pulitzer Prize winners, three MacArthur Fellows and six Guggenheim fellows. Senator Edward M. Kennedy, former Senator Warren Rudman, violinist Itzhak Perlman, Academy Award winner Anjelica Huston, author and physician Oliver Sacks, National Medal of Science for Research on Mental Illness recipient Nancy C. Andreasen, and Nobel Prize winning chemist George Olah are among this year’s new Fellows.

ASBMB members elected Fellows are, in Biochemistry and Molecular Biology, Joan W. Conaway and Ronald C. Conaway of the Stowers Institute, and in Medical Sciences (including Physiology and Pharmacology), Clinical Medicine, and Public Health, Professor Jerold M. Olefsky, University of California, San Diego.

The American Academy of Arts and Sciences was founded in 1780 by John Adams, James Bowdoin, John Hancock and other scholars-patriots “to cultivate every art and science which may tend to advance the interest, honor, dignity, and happiness of a free, independent, and virtuous people.” This year’s new Fellows and Foreign Honorary Members will be welcomed at the annual Induction Ceremony at the Academy’s headquarters in Cambridge, Massachusetts, on October 5.
Two ASBMB members were named by President Bush to receive the National Medal of Science and another member was awarded the National Medal of Technology. These are the nation’s highest awards for lifetime achievement in science and technology. The honorees are to receive the medals at a White House ceremony on June 13.

“Each one of these individuals has helped advance our country’s place as a leader in discovery, creativity and technology,” the President said. “Their contributions have touched all of our lives and will continue to do so.”

ASBMB members chosen to receive the National Medal of Science are:

Mario R. Capecchi, of the University of Utah School of Medicine, who developed new tools that revolutionized the study of mammalian genetics and provided important new models for human genetic diseases. Capecchi was also recently elected a Fellow of the American Association for the Advancement of Science.

Harold Varmus is well-known for his Nobel Prize-winning discovery with J. Michael Bishop, Chancellor of the University of California, San Francisco, that normal human and animal cells contain genes capable of becoming cancer genes, which led to an aggressive and successful search for genetic origins of cancer by the scientific community. Varmus is now President of Memorial Sloan-Kettering Cancer Center in New York City after serving as Director of the National Institutes of Health for six years.

Receiving the National Medal of Technology is Sidney Pestka, Chair of the Department of Molecular Genetics, Microbiology and Immunology at the Robert Wood Johnson Medical School of the University of Medicine and Dentistry of New Jersey. Pestka was honored for his pioneering achievements that led to the first recombinant interferons for the treatment of cancer, leukemia, hepatitis, and multiple sclerosis, and for discoveries in chemistry, biochemistry, genetic engineering, and molecular biology.

“Their contributions to the world around us are enormous. Their ideas have led to major breakthroughs in human health and the tools evolving from their research have put the U.S. in the forefront of many new industries,” NSF Director Rita Colwell said of those honored. “We are proud of these extraordinary people—and grateful for their unceasing inquisitiveness, creativity and dedication to obtain new knowledge for the good of all humankind.”

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 institutes from which they received their degrees.

Marion L. Carroll,
Xavier University

Shih-Ming Huang,
National Defense Medical Center, Taiwan

Isabel D. Markl,
University of Southern California, Keck School of Medicine

Thalia Nittis,
Washington University School of Medicine

Irina Rudik,
University of Pennsylvania

Gurveen S. Saberwal,
Rush Cancer Institute

Jean-Claude Twizere,
Texas A & M University
This year’s Annual Meeting was an unqualified success for all and ASBMB is looking forward to another winner April 11–15 next year in San Diego.

“The Annual Meeting of ASBMB in conjunction with EB was a wonderful success,” said ASBMB President Robert Wells. “Much exciting new science was presented. In addition, numerous opportunities were available for young scientists to present their work and to interact with their contemporaries. The scientific exhibits were numerous, interesting, and informative. We anticipate that the San Diego meeting in ’03 will be even better.”

Said ASBMB Executive Officer Chuck Hancock, “I think the program arranged by Joan Conaway and Ralph Bradshaw was outstanding. There is no doubt the attendees in New Orleans would agree that the meeting was a wonderful success. I am confident that Claudia Kent and Vern Schramm will organize an equally exciting meeting in 2003 in San Diego.”

From the opening day to the final session, the Annual Meeting provided a rich menu of science in lectures, posters, and exhibits. It also included a special highlight, a call to action by former congressman John Porter who received the Howard K. Schachman Award in recognition of his role in getting the NIH budget doubled. Porter spoke of the need for continued increases in NIH funding, and urged scientists to make their voices heard in Washington on this and the need to keep science free from politics. The complete text of his address was published in the May issue of ASBMB Today.

Lecturers at this year’s ASBMB Annual Meeting shared information concerning an array of projects on the forefront of today’s research. Following is a sampling of the topics that were heard and discussed by those who made the trip to New Orleans.

Roger Kornberg, Department of Structural Biology, Stanford University School of Medicine, who shared the ASBMB-Merck Award with Doctor Robert G. Roeder, Biochemistry and Molecular Biology Lab, Rockefeller University, delivered the opening lecture. Kornberg’s topic was The Eukaryotic Gene Transcription Machinery. Following is an abstract provided by Dr. Kornberg:

A complete RNA polymerase II transcription system has been derived from the yeast *Saccharomyces cerevisiae*. Fractionation and sequence analysis identified some 50 required polypeptides, as well as components of chromatin-remodeling (SWI/SNF, RSC), complexes. Among the required polypeptides are 20 that form a Mediator of transcriptional regulation. The structure of yeast RNA polymerase II has been determined at 2.8 Angstroms resolution. The structure comprises 10 polypeptides with a total molecular weight in excess of half a million Daltons. This structure led to a molecular replacement solution for a paused RNA polymerase II elongation complex, containing template DNA and product RNA. The results explain many aspects of transcription, including the formation and maintenance of the transcription bubble, RNA and DNA translocation during transcription elongation, and the extraordinary stability of elongation complexes.

The topic for Doctor Roeder’s lecture was Regulation of Eukaryotic Transcriptions Through Diverse and Complex Transcriptional Machineries. His work in this area has been described as “in a class by itself.” From his discovery of RNA polymerases I, II, and III, to his discoveries of general transcription factors, the first gene-specific activator, and the demonstration of Mediator and other general and cell-type-specific coactivators in human cells, he has been a major leader in a wide range of studies that have in common the quest to understand, in detail and depth, transcription and its regulation in eukaryotes.

**Disrupting the Protective Armor of Bacteria**

The lecture topic for Christian R.H. Raetz, Chair of Biochemistry at Duke University Medical Center and winner of this year’s Avanti Award for Outstanding Lipid Research, was Assembly, Secretion and Function of Gram-negative Endotoxin: a Potent Lipid Activator of Innate Immunity.

So-called Gram-negative bacteria, like the common intestinal bacterium *Escherichia coli* or its much more nasty cousin *Yersinia pestis* (the cause of the plague in the Middle Ages), protect
pressive drugs like cyclosporin A interfere with the cell's ability to recognize foreign matter, enabling the body to accept transplanted organs. He found they accomplish this feat by blocking signals required for the activation of immune system T-lymphocytes that are conserved in yeast and fungal cells, resulting in the identification of the targets of three immunosuppressive drugs (cyclosporin A, FK506, and rapamycin) that have revolutionized transplant medicine.

Dr. Heitman also pioneered the use of yeast to understand fungal pathogenesis. He identified the central role that calcineurin, the target of cyclosporin A, plays in virulence, and studies are now testing novel agents as antifungal drugs.

Joseph Heitman, a Howard Hughes Medical Investigator in the Department of Molecular Genetics and Microbiology and the Center for Microbial Pathogenesis at Duke University Medical Center, and this year's recipient of the ASBMB-Amgen Award, used Baker's yeast for his pioneering studies to elucidate how immunosuppressive drugs like cyclosporin A interfere with the cell's ability to recognize foreign matter, enabling the body to accept transplanted organs. He found they accomplish this feat by blocking signals required for the activation of immune system T-lymphocytes that are conserved in yeast and fungal cells, resulting in the identification of the targets of three immunosuppressive drugs (cyclosporin A, FK506, and rapamycin) that have revolutionized transplant medicine.

Using his model of the pathogenic fungus C. neoformans, Dr. Heitman also pioneered the use of yeast to understand fungal pathogenesis. C. neoformans causes cryptococcosis, one of the most serious global fungal diseases.

As the prevalence of AIDS and other diseases that compromise the immune system continues to grow, there has been a virtual explosion of cryptococcosis worldwide—and a growing threat of drug resistant strains. Dr. Heitman recently discovered unique features of signaling in this pathogen that are proving to be targets for therapeutic intervention. He identified the central role that calcineurin, the target of cyclosporin A, plays in virulence, and studies are now testing novel agents as antifungal drugs.

Although yeast and humans diverged from a common ancestor over a billion years ago, long before the two yeasts studied in the Heitman laboratory did, Dr. Heitman's studies show that "yeasts and human cells, like the original Model-T automobile, are constructed from universal components that are readily interchangeable."

**Yeast as Model-T Cells**

**Ed Marklin and Kelly Gull** were just two of many staff who welcomed visitors to the ASBMB booth and explained the value of membership to nonmembers.

Ed Marklin and Kelly Gull were just two of many staff who welcomed visitors to the ASBMB booth and explained the value of membership to nonmembers.

**Advances in Ability To Visualize DNA Structures**

This year's winner of the Herbert A. Sober Lectureship, Jack D. Griffith, of the Lineberger Comprehensive Cancer Center, University of North Carolina,
Dr. Griffith discovered that telomeres, the complex structure of DNA at the end of chromosomes, didn’t simply end in stubs but in long, rather elegant loops of DNA. Unknown few decades ago, telomeres became a focus of intense research when scientists found that the structures had something to do with how cells age. With each replication of the cells, the next generation of telomeres became shorter and shorter. When they became too short to allow the cells to replicate once more, the cells simply died. The telomere story became even more curious when scientists found that the telomeres of Dolly, the first cloned animal, were born shortened, closer to the length of the sheep from which she was cloned than the little lamb that she was.

Dr. Griffith believes that the loop at the end of the telomere helps protect the chromosome but it shrinks each time the cells replicate, and eventually the telomere begins to fray, causing the cell to die. Other research teams are now looking for drugs that could serve as switches to telomere switching. The body already has one method—a naturally occurring enzyme called telomerase—that can prevent the telomere from shrinking.

Developing drugs that could do the same thing might slow down the progression of degenerative diseases and aging. Cells that stop producing telomerase, stop dying and instead keep growing—as tumor cells. Being able to switch telomere shrinkage on in these cells might prevent the rapid growth of cancer. That, however, would be a careful balancing act, said Dr. Griffith.

Over 100 Genes Linked to Apoptosis

Over 100 human genes have been linked to apoptosis and many more are just waiting to be discovered, according to John C. Reed, Scientific Director of the Burnham Institute, who delivered a plenary lecture on the mechanisms of apoptosis regulation.

That hundred-plus total, he told the scientists in attendance, does not include several proteins already known to be involved in apoptosis as modulators of the core process.

The Burnham Institute Director classified the apoptosis-related genes in six groups. The first group consists of 11 genes for caspases, the ultimate cell executioners according to Dr. Reed, who noted that some caspases are only indirectly involved in apoptosis.

That hundred-plus total, he told the scientists in attendance, does not include several proteins already known to be involved in apoptosis as modulators of the core process.

Differences among caspases are a rich area for pharmaceutical discovery, he says, because studies suggest that interfering with them could provide therapeutic benefit for the many human diseases in which programmed cell death is a factor.

The second group includes caspase recruitment domains (CARDs). At present this group includes 22 genes. CARDs are involved not just in caspase activation, but can also suppress apoptosis, Dr. Reed says.

Apoptosis gene groups 3 and 4 are the death domains (DD) and the death effector domains (DED). To date, researchers have identified 28 DDs and 13 DEDs. Only one human gene, FADD, a homologue of the fruit fly apoptosis genes, grim, reaper, and hid, has been found to contain both the death and the death effector domains.

The fifth group consists of eight genes for BIR domains, which are present in all members of the IAP (Inhibitor of Apoptosis) family.

The sixth group currently lists 24 genes with Bcl-2 homology domains. Bcls are a large and diverse protein category, some of which promote apoptosis and others of which interfere with its development. As Bcl is over-produced in several cancers, Dr. Reed reported that strategies for blocking Bcl-2 are being explored for therapeutic possibilities.

A database of genes linked to apoptosis is under development with funding from NSF, and Dr. Reed expressed the hope that it will eventually include genomes of organisms other than those common to humans.

Death and Dying in Drosophila

At a symposium on the role of mitochondria in apoptosis, Douglas Green, Head of the Division of Cell Immunology, La Jolla Institute of Allergy and Immunology, explained that programmed cell death in fruit flies is unexpectedly different from the
pathway in vertebrates. However, mitochondria, critical to the "incredibly orchestrated process" in vertebrates, may still be involved.

In vertebrates, the Bcl-2 family of proteins controls the integrity of the mitochondrial outer membrane. When the membrane becomes permeable, proteins like cytochrome c and Apaf-1 leak out, activating caspases that carry out cell execution.

"In Drosophila, when we look at what we think is the same pathway, we can test the hypothesis that permeability is central," Dr. Green said. "But the surprise is that it seems not to be. Drosophila has gone down a different route to creating the apoptosis pathway."

To find parallels for the apoptotic pathway in fruit flies, the researchers first looked for homologs of the vertebrate proteins. The fruit fly homolog of Apaf-1 is Apaf-1-related killer (ARK). Using RNA interference (RNAi) to block expression of ARK eliminates apoptotic cell death induced by stress agents, Katja Zimmermann, a postdoctoral fellow in Dr. Green's lab, found.

The results suggest the Apaf-1 homolog is important, Dr. Green explained, but "that's when we hit the surprise." Unlike in vertebrates, there was no evidence of cytochrome c release, and no evidence that the mitochondrial outer membrane was permeable. "Most damming was that, using RNAi, we couldn't find any evidence that cytochrome c was important for ARK or caspases," he reported.

It is known that Bcl-2 prevents permeability of the mitochondrial membrane in human cells, and blocks apoptosis in Drosophila cells. "We have to find out where Bcl-2 is acting," Dr. Green said. "Our first guess is that it will involve the mitochondria in some way, but not through permeability of the membrane."

Apart from illuminating the evolution of the apoptotic pathway, he says, the studies also provide a window on the behavior of Bcl-2, a molecule that is of particular interest to researchers.

Apoptosis has so far been studied only in vertebrates, worms, and flies. "We need to cast a wider net," said Green. "Whenever we've done that, we've learned new things about the behavior of our cells."

**Mouse Experiments Knock Out Dopamine Data**

Neurodegeneration caused by high dopamine levels in mice lacking dopamine transporters (DATs) does not occur in the pre-synaptic dopamine neurons where DATs are missing, says neurobiologist Marc Caron. Instead, it is the post-synaptic spiny neurons that die.

Dr. Caron, James B. Duke Professor of Cell Biology at Duke University, and his colleagues generated lines of mice in which the DAT genes are ablated. They are now trying to characterize the phenotype of the mouse knockouts.

DATs regulate the intensity and duration of dopamine's presence in the synapse by removing it, and are critical for maintaining homeostasis at the dopamine terminal, says Dr. Caron.

Scientists believe DAT is the main target of psychostimulants. But the paradoxical behavioral effects of psychostimulants, which reduce locomotion in the usually hyperactive DAT knockout mice, suggest there are other targets of action. Dr. Caron and his colleagues are "pretty sure" the serotonin system is also involved, for example.

Dr. Caron and his colleagues have been exploring the relationship between high dopamine levels and neurodegeneration in the knockouts. Mice missing DATs have a high mortality rate, particularly before six months of age, and their deaths are associated with symptoms of motor dysfunction, especially dyskinesia.

Analysis of the knockout mouse gait reveals a pattern that is not characteristic of cerebellar ataxia, but more akin to striatal degeneration, he says. But dopamine terminals are not affected in the symptomatic knockouts, and there is no evidence for pre-synaptic neurodegeneration.

Knockouts seem to have about the same number of neurons as normal mice, and the projections from them are also normal, Dr. Caron reports. However, they do exhibit loss of post-synaptic neurons that synthesize and release gamma-aminobutyric acid (GABA).

High levels of extracellular dopamine might lead to over stimulation of signaling events and initiate degeneration, he suggests, adding the researchers have some evidence supporting his theory.

The hypothetical pathway is notably complex. In the simplified version, cyclin-dependent kinase5 expression is induced by chronic, but not acute, cocaine exposure. Cdk5 is upregulated in Alzheimer's disease and in animal models of ischemia and amyotrophitic lateral sclerosis, and it is present in the Lewy bodies of Parkinson's disease.
Undergraduate Poster Competition Draws Outstanding Entries

The 2002 ASBMB Undergraduate Research Achievement Award Poster Competition drew 75 outstanding undergraduates from all over the United States and Canada. The competition was held on Monday, April 22, in the Sheraton New Orleans as part of ASBMB’s Annual Meeting in conjunction with Experimental Biology ’02. The competition was organized by Drs. Phillip A. Ortiz of Empire State College and Christopher E. Rohlman, Albion College. The winning students and the titles of the abstracts are listed on the page at right.

The Biochemical Journal, published by Portland Press, Inc. sponsored the grand prize award at the poster session. The winner of the Biochemical Journal prize, Allyn J. Schoeffler of Louisiana State University, received a certificate and a $500 check presented by Dr. Tony Turner, Chairman of the Editorial Board of the Biochemical Journal.

Many participants were also recipients of an ASBMB Undergraduate Travel Award that covered up to $300 toward travel expenses and complimentary registration for EB ’02. The students reported that they enjoyed the poster session and appreciated meeting other undergraduate students with whom they could network, especially at a large meeting such as EB. The general public was also invited to view the posters.

ASBMB would like to thank the 2002 judges: J. Donald Smith, University of Massachusetts, Dartmouth; Marilee Benore Parsons, University of Michigan at Dearborn; Marguerite W. Coomes, Howard University College of Medicine; Thomas E. Smith, Howard University College of Medicine; Judith G. Voet, Swarthmore College; Donald Voet, University of Pennsylvania; Elizabeth Roberts-Kirchhoff, University of Detroit, Mercy; James Zimmerman, Clemson University; Roberta F. Colman, University of Delaware; Joseph A. Bobich, Texas Christian University; Mary Lou Caspers, University of Detroit, Mercy; Brian Ernsting, University of Evansville; Frieda L. Texter,
Portland Press Grand Prize Winner ($500 & Certificate)

Allyn J. Schoeffler

ASBMB First Prize Winners ($100 & Certificate)

Donnie Berkholz
Probing the Active Site of 3-phosphoglycerate Dehydrogenase: The Role of Acid Base Catalysis and the Local Charge Environment of the Transition State in V Type Regulation by Serine. D. Berkholz, E. Bell. Gustavus Adolphus College, University of Richmond.

Suzanne E. Biehn
Induction of organelle membrane biogenesis by Ca2+-ATPase (SERCA1a) expression. S.E. Biehn, K.J. Czymmek and N.J. Karin. University of Delaware.

Gene L. Bidwell, III

Michelle M. Daniels
Characterization of the 5' and 3' ends of the human choline transporter-like 1 (hCTL1) gene. M.M. Daniels, M. Bakovic. University of Guelph.

Shawn K. Desai

Justin R. DiAngelo

Lavonne Sheresse Hunter
Differential neurotoxic effects of prostaglandins and cyclooxygenase-2 up-regulation in mouse neuronal (HT4) cells. L.S. Hunter, S. Wright and M. E. Figueiredo-Pereira. Hunter College of CUNY.

Jamie E. Rubin

Steven A. Smith

The ASBMB Undergraduate Poster Competition will be held once again at EB’03 in San Diego, April 11 – 15. All registered meeting participants are invited to attend. Please stop by next year’s competition and support undergraduate research. If you are interested in more information, please contact Kelly Gull (kgull@asbmb.faseb.org).
Innovation is the name of the game at Virginia Commonwealth University (VCU). In the 12 years since Dr. Eugene Trani became president of the institution and chairman of the board of directors of the related VCU Health System, VCU has gone from being a "city university" for Richmond to an educational and research fulcrum for the entire state.

"We took three big gambles back in the 1990s," said Dr. Trani. "We set up the Virginia Biotechnology Research Park, we restructured the medical center and set it up as a public authority health system, and we created a new School of Engineering.

"The latter," he pointed out, "is not a Rust Belt school. It's for high-tech manufacturing, computers, and the relationships between life sciences and engineering."

Those gambles have paid off, and VCU's latest innovation promises to add more luster to the school's image. This past fall, VCU opened the Trani Center for Life Sciences and committed to training students for the new fields that have been opened up by the human genome project. A unique mission of VCU's life sciences program is to expose undergraduate students from their first days at the university to faculty members who previously taught only graduate and medical school students. The result, the capstone introductory course Life Sciences 101 (see sidebar), will be graduating its second class of freshmen this spring.

"We bet the farm on life sciences," says Trani, who became president of VCU in 1990. "There's nothing like the VCU life sciences program anywhere in the U.S. It begins with 18-year-olds and prepares them for life sciences in any one of many professions—forensics, biology, public health, the environment."

To underline its commitment to life sciences, VCU named a vice provost for life sciences, one of only two in the United States. He is Thomas F. Huff, Professor of Microbiology and Immunology, who was appointed vice provost in May 2001 after serving in an acting role for a year. "The life sciences," explains Huff, "are key to our entrepreneurial mission. The 21st century will see a life sciences revolution."

VCU Life Sciences brings together the university's top researchers and

VCU Life Sciences:

VCU's Eugene P. and Lois E. Trani Center for Life Sciences houses the Department of Biology, the Center for Environmental Studies, the Center for the Study of Biological Complexity, a satellite lab of the Nucleic Acid Research Facility, the Bioinformatics Computational Core Laboratory Suite and the Office of the Vice Provost for Life Sciences.

The life sciences building features 17 undergraduate instructional laboratories. In addition to general biology and anatomy laboratories, the building offers specialty laboratories for advanced courses including genetics, molecular biology, bioinformatics, ecology, environmental science, botany, physiology and microbiology.

A top-floor greenhouse is a research-grade facility that can be controlled by humidity, temperature and light. The 3,000-square-foot greenhouse supports a pesticide-free room and three environments simultaneously: desert, mild climates much like Central Virginia, and tropical.

An aquatics facility, located in the basement, houses up to 20 research tanks for controlled experiments on both marine and freshwater fish, amphibians and other aquatic organisms.

One in every five undergraduate students majors in the life sciences, and VCU believes that for many students in the post-dot.com world, the VCU Life Sciences curriculum will be the secret of success.

Life sciences is seen as the new intellectual revolution of the 21st century. It is not a single discipline but an interdisciplinary approach to studying the complexities of life, whether a molecule, an organism, a disease or an ecosystem.

VCU Life Sciences is comprehensive in its involvement of all levels of...
logical Complexity that positions VCU at the forefront of universities using discovery science and massively parallel computer assets to define how complex biological systems obey rules that do not apply to their components.

VCU sets a high priority on life sciences public education, as evidenced by its creation of a Mini-Med School, where doctors teach the public about health issues. Recently, VCU joined several other institutions as advisors to a new public television program, “Secrets of the Sequence,” which made its debut nationwide in early April. The 30-minute show, which features three or four topics weekly, is focused on explaining genomic research to lay persons. Dr. Huff sees “Secrets of the Sequence” as "the biggest example of our commitment to life sciences public education. Those eight-minute segments showing scientists and their young assistants working in the lab that appear in the 52 programs will be valuable educational instruments, not only for our faculty members who teach our introductory Life Sciences 101 course, but also for use by teachers in high schools nationwide."

VCU is also an economic engine, with tight ties to local business development efforts. Not only is VCU contributing to the revitalization of blighted areas of Richmond’s downtown Broad Street area, its Virginia Biotechnology Research Park is home to increasing numbers of startup life sciences companies based on technology and research developed in VCU laboratories.

Donald J. Abraham, Chair of VCU’s Department of Medicinal Chemistry and Director of the Institute for Structural Biology and Drug Discovery, is a faculty member from VCU’s academic and medical campuses in an interdisciplinary team to teach all fields of science that explore the complexities of life—whether a molecule, organism, disease or ecosystem. On the team are immunologists, biologists, geneticists, chemists, physician/scientists, ecologists and other researchers. In addition, VCU Life Sciences has partnered with industry and other research universities in the Virginia Bioinformatics Consortium. And it opened a think tank for life sciences faculty researchers called the Center for the Study of Biological Complexity that positions VCU at the forefront of universities using discovery science and massively parallel computer assets to define how complex biological systems obey rules that do not apply to their components.

Educating the Locksmiths

"IF WE ARE TO UNLOCK more of life’s secrets, we must first educate more locksmiths"

—Dr. Eugene P. Trani

students in the study of life sciences, from freshmen to students in the professional programs to Ph.D. candidates. It integrates diverse disciplines from all over the university, including the academic health center as well as arts and humanities. New curricula will focus on the 21st century life sciences job market.

Life Sciences 101, VCU’s unique gateway course, introduces freshmen to the elements of the study of life sciences. Taught by top research, clinical and teaching faculty—including many from VCU’s School of Medicine — this course allows students to understand the entire scope of the life sciences, exploring such areas as cancer, bioinformatics, chemical and structural biology, neuroscience, complex genetics, biotechnology, biomedical engineering and ecology.

Faculty from the School of Engineering, the College of Humanities and Sciences and the schools on VCU’s Medical College of Virginia Campus offer VCU students their expertise in clinical and research experience, from atomic structure and molecular biology to environmental science and artificial organs. In addition, a 342-acre site with a 70-acre lake on the historic James River—the Rice Center for Environmental Life Sciences—is a living laboratory for ecology and environmental studies classes in VCU Life Sciences.

Virginia Commonwealth University’s Trani Center for Life Sciences integrates diverse disciplines from all sections of the university, and is a key factor in the revitalization of downtown Richmond.
good example of how VCU links research and business. VCU located Dr. Dr. Abraham's institute at the research park, which was key to launching a company based on an oxygen-delivery drug developed by him. That company is now part of Colorado-based Allos Therapeutics, Inc., which develops and commercializes innovative small molecule drugs for improving cancer treatments. Allos continues to have research facilities at the research park. Dr. Abraham and his colleague, Dr. Glen E. Kellogg, went on to start eduSoft, LC, which is located in the research park and develops modestly priced, computer-based tools for drug design and molecular biology. "I'm still a professor and always will be," says Dr. Abraham, the scientist/inventor/businessman. "But I just started my third company, an educational software company." The new company is called kSero Corp., which will use the latest brain science and computer technology to create toys and games to accelerate learning in children and adults. It is located at the research park's incubator.

Richard C. Franson, Director of Technology Transfer, is a key figure in VCU's entrepreneurial activity. Dr. Franson works with the university's researchers to transfer their research to the commercial marketplace—securing licenses for VCU and helping the researchers with patents. "What happens in the university is that there are these enormously talented people, and I have to talk to them and tell them that they can do abstracts and consult with pharma, but they have to understand the process," Dr. Franson says. "Academics tell me, 'You're interfering with my job.' They're interested in teaching, research and publishing. It's sometimes difficult for them to understand the commercial aspects."

VCU shares 50 percent of all licensing revenue with the researchers. "Last week I wrote two $25,000 checks to faculty members," Franson says. For the fiscal year that ended June 30, 2001, VCU had 119 invention disclosures, 22 new licenses and licensing revenue of $1 million. But the emphasis on technology transfer to the marketplace is about more than money. "We're not so much interested in making dollars as in promoting scholarship and research," Franson says. "Having top people enables us to harness their power."

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**Bio-Attack Detector to Fight Chlamydia**

Military technology designed to counter biological weapons is being adapted to speed up the detection of chlamydia, a common sexually transmitted infection that is a leading cause of infertility.

Researchers at Britain's Defense Science and Technology Laboratory will receive 4.6 million pounds ($6.6 million) from the government to develop a portable machine to improve the diagnosis and treatment of the illness. Instead of waiting up to two weeks, the new machine will produce screening results in 40 minutes.

The machine rapidly analyzes DNA sequences to detect the presence of biological agents, and will be used to increase the number of patients being screened for the illness and reduce the number of false negative results. Chlamydia is the most common bacterial sexually transmitted infection. It often does not produce any symptoms and many women are unaware they have it. The infection can cause pelvic inflammation and ectopic pregnancy.

Treating the infection and its consequences costs Britain 50 million pounds ($71 million) a year.

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**ASBMB Participates in MIST Network Science Career Days**

In early May, the ASBMB participated in the Minorities in Science and Technology (MIST) Network Science Career Days for middle and high schools in the Greater Washington, DC area.

Some 1500 students, teachers and parents attended the three-day event at the Marvin Center at George Washington University. More than 25 scientific associations, corporations and government agencies staffed tables and booths or conducted workshops for students.

The goal of the event was to stimulate the interest of minority students in science and technology careers and to answer their questions concerning achieving their career goals. An ASBMB representative distributed materials to attendees and answered questions about careers in biochemistry and molecular biology.
The HighWire Press Portal:
“Citation Search:” Type Just Three Numbers to Get Any Article

Early this year, ASBMB News introduced the new “portal” site from Stanford’s HighWire Press, which allows you to search all of Medline plus over 330 journals’ full-text at once—including the JBC, MCP, JLR and BAMBED, of course! This article is fifth in a monthly series highlighting tools or features of this new site for researchers’ sore eyes. The new site is at http://highwire.stanford.edu

One of the most frequent tasks the designers of the new HighWire Portal saw researchers doing was also the most obvious one: looking up an article based on a reference citation. The design of the new HighWire site makes this as fast as it can possibly be: you type three numbers and click.

If you have the publication year, the volume, and the first page for any article in the 4,500 journals covered by Medline and HighWire’s full-text journals (which includes JBC, MCP, JLR, BAMBED and hundreds of others), you can retrieve an article. You don’t even have to type the journal name, and you don’t have to first click your way to the journal’s own online site.

The result when you enter those three numbers will be a full article citation, accompanied by a link to the abstract and—in most cases for recent articles—a link to the full-text. For HighWire-hosted journals, the citation will also show if you have access to the full-text, and if not, whether and for what fee you can purchase the full-text. Since over 420,000 full-text articles are free at the HighWire site, there is a good chance you’ll have full-text access.

From the HighWire Portal home page at http://highwire.stanford.edu just enter the year, volume and page in the search entry boxes in the center of the home page—no need to enter author or any other text. (See Quick Search at top center of the home page shown here.) If your article is in one of the 330+ HighWire-hosted journals, click on the appropriate radio button below the year; if not or if you don’t know whether the journal is a HighWire-hosted journal, just click on the “HighWire + Medline” radio button:

You might wonder why you don’t have to give a journal name. In most cases, the year, volume and first page information is enough to limit a search result—even in twelve million entries—to just 1 - 5 possible citations. So the search result you will see when you type in those three numbers will be small enough that you can pick out the right article much faster than you could type in a journal name or go to a journal’s home page to search. In fact, if you don’t have all three of the numbers—perhaps a citation you were given wasn’t complete—typing even two of them will typically get you a result that is just a page or two of search results to scan.

Next month we’ll look at Advanced Searching capabilities in the new portal.

Patent for Graft Made From Tissue-Engineered Biomaterial

Cook Biotech Inc., West Lafayette, Indiana, has been granted a patent for a medical graft made from tissue-engineered submucosa that is useful in promoting regrowth and repair of damaged or diseased neurological tissue structures.

“Small intestine submucosa is showing outstanding clinical results as surgical graft material used to repair and support many internal soft tissues,” stated Mark Bleyer, president and CEO of Cook Biotech. The patent covers several neurological products in development, including one that will be used to repair the dura mater.

Small intestine submucosa is animal-derived and carefully processed to produce a safe, sterile and biocompatible material. Cook uses a manufacturing process designed to maintain the integrity of the naturally occurring tissue. The process creates a matrix which acts as a scaffold for tissue growth and, over time, is replaced with the body’s own tissue.
Swiss Research Giant Moving Headquarters to Boston

Swiss drug giant Novartis AG is moving its worldwide research headquarters to Cambridge, Massachusetts, where it is providing a major boost to the region’s attempt to establish itself as the nation’s premier center for biomedical research.

The Novartis Institute for Biomedical Research, Inc. (NIBRI) will initially hire 400 scientists and lease 255,000 square feet of lab space owned by the Massachusetts Institute of Technology. Novartis pegged its initial investment at $250 million and said all worldwide research activities performed in Europe, the U.S., and Japan will be led out of Cambridge by its new head, Mark Fishman, M.D., currently Professor of Medicine, Harvard Medical School, Chief of Cardiology and Director of Cardiovascular Research at Massachusetts General Hospital.

Novartis is planning to expand the Cambridge site, with the goal of creating one of the most important research campuses in the world, which will be focusing on the discovery of new drugs for diabetes, cardiovascular, and infectious diseases.

Germany Leads Europe in Biotech Business

According to a recent Ernst & Young report, Germany now has the most biotechnology companies in Europe, 333 compared with 271 companies in the UK and 240 in France. This is a dramatic change, considering recent German attitudes toward biotechnology.

In Germany, public opposition to biotechnology and genetic engineering was strong throughout the 1980s and early 1990s. The government reacted with strict regulations on biotechnological research, which led large pharmaceutical companies such as Bayer, Hoechst, and BASF to set up research sites abroad and enter into cooperation with leading U.S. research institutions, including Massachusetts General Hospital, and biotech companies such as Genentech. Responding to this corporate drift over the Atlantic and changing public opinion about biotechnology, the German Federal Ministry of Education and Research set in motion a program to stimulate entrepreneurship in biotechnology.

Having noted the successful development of U.S. clusters of biotech business and research institutions, such as can be seen in Boston, North Carolina, San Diego, and the San Francisco Bay Area, Germany encouraged the commercialization of biotechnological research in 17 regional clusters. These regions brought scientists, researchers, government officials, technology transfer agencies, and pharmaceutical and chemical company executives together to establish coordination centers that link together all activities.

The top regions—Munich, Cologne, and Heidelberg—received 25 million euros ($22,942,500) from the national program in addition to loan funding and research grants up to 50% of the cost of a research project. Other regions received varying amounts from state governments and other sources, and one of these, Berlin, is now one of Germany’s biotech hot spots.

San Francisco Vying for Biotech Business

In the wake of the dot-com downturn, cities all around San Francisco Bay have been wooing biotech as one of the few industries that’s still building, but for San Francisco itself, the courtship is not just economics. It’s a matter of wounded civic pride.

Although the University of California at San Francisco has spawned dozens of biotech companies, so far none has landed in the city. Even worse, many of UCSF’s offspring have set up just over the city line in South San Francisco, home of industry pioneer Genentech.

San Francisco’s Mayor Willie Brown has pitched the city’s virtues to numerous biotech executives, and Nancy Pecota, CFO of Signature BioScience which moved to San Francisco last month, has been quoted as being pleasantly surprised by the help she received from city officials. However, some of those being courted see a downside to relocating in San Francisco.

Brian Oppendike, an executive with South San Francisco-based FibroGen, told the San Francisco Chronicle’s Tom Abate, “Payroll taxes are a big issue.” Given that most biotech firms run deficits and operate on invested capital, he explained, it’s tough to justify paying taxes to San Francisco when other cities don’t demand them.
Biggest Gene Bank Granted 45 Million Pounds

The largest genetic database in the world, which will take DNA samples from half a million Britons to form a vast BioBank for medical research, has been awarded £45 million ($34,956,000) in funding from the government and the Wellcome Trust.

BioBank UK, which will hold genetic information and medical records from 500,000 volunteers aged between 45 and 69, will be an aid to scientists investigating conditions such as heart disease, cancer and Alzheimer’s. It will combine details of people’s lifestyle and genetic background to help researchers to unravel the complex interplay between genes and environment that governs most of the most serious human diseases. Information from the database, which will be the largest of its kind in the world, is expected to ultimately lead to improved diagnosis, treatment, and preventive strategies for many disorders.

Professor Sir George Radda, Chief Executive of the Medical Research Council, said: “This exciting project may one day herald a new era of medicine. In 20 years time, we may see individualized approaches to disease prevention and treatment.”

Professor Sir John Pattison, Director of Research and Development at the Department of Health, said: “This initiative will create a crucial national resource for clinical researchers that will help them to better understand susceptibility to the common diseases of adult life. In turn, it will help us to know how to adopt healthier lifestyles and so reduce the burden of ill-health.”

Tight Genes Good For Treating Disease

By compressing genes to under 25 nanometers, Cleveland-based Copenicus Therapeutics (CT) has advanced delivery of gene-therapy drugs that could one day help thousands of cystic fibrosis sufferers live longer, healthier lives.

CT’s methods seek to clear this hurdle and, along with it, a major stumbling block on the way to better treatments for genetic-based diseases such as cancer or even skin disorders like psoriasis.

If CT’s treatments are approved by the FDA, CF patients could receive the aerosol form of this therapy within four years. According to CT, the overall market for genetic therapies will be $12 billion by 2007. The CF market alone is $2.5 billion and, although it is still only spending venture capital dollars at the moment, CT’s take of this market could be substantial.

Novel Screening Strategy Designs Compounds with Increasing Potency Against Cancer

Knowledge of how one drug triggers death by apoptosis in colon cancer cells led Cell Pathways, Inc., Horsham, Pennsylvania, to develop a unique screening algorithm for the discovery of increasingly more potent anticancer compounds.

W. Joseph Thompson, Vice President of Research and Discovery for Cell Pathways, says studies with the company’s first-generation drug, exisulind (Aptosyn), led to the discovery of a novel role for PDE5 (cyclic GMP phosphodiesterase 5) in cell growth and the design of compounds with selectivity for cancer cells over normal ones. His remarks were made at the 2002 Apoptosis: Commercial Opportunities conference in San Diego, April 28 to May 1.

“Exisulind, a metabolite of the non-steroidal anti-inflammatory drug (NSAID) sulindac, was initially developed based on clinical observations from the 1980s that high doses of sulindac (400 mg) could shrink and prevent the formation of precancerous colon polyps,” said Thompson. “Research with exisulind found that it selectively triggered apoptosis in colon cancer cells through a novel mechanism of action quite distinct from sulindac’s inhibitory effects on COX enzymes and prostaglandins—effects that exisulind lacks.”
The Challenge
Facing Public Research Universities

“Is the public research university dead?” That was the question asked by University of Minnesota President Mark G. Yudof in an article written for The Chronicle of Higher Education.

In that article, Yudof noted that a College Board survey reported that public colleges and universities last year raised tuition fees by an average of 7.7%—the highest rates in eight years and more than twice the rate of inflation. For this year, the National Conference of State Legislatures reports that 43 states are experiencing revenue shortfalls with more than half considering budget cuts, and at least nine governors have warned universities to expect midyear cuts in their appropriations.

These developments are only the latest in a long-term trend toward decreased state support. As a result, students at public research universities can expect to pay higher fees, and the role of such institutions faces fundamental change. The gap between professors’ salaries at public and private universities, for example, has grown from $1,400 in 1980 to $22,100. As a result, public institutions find it increasingly difficult to compete for the best faculty members, those who, in turn, attract the brightest students and significant research dollars.

Both federal and state policy makers are pushing for students to shoulder a larger share of their higher-education expenses. Rather than provide operational support to universities, they encourage higher tuition charges, with the result that students at public research universities are paying more. At the University of Minnesota, for example, tuition covers nearly two thirds of the direct cost of their instruction, compared with the one third that their peers paid 25 years ago.

As state support erodes, flagship research universities face other challenges. Many local businesses now operate more globally and are less oriented toward state or regional concerns. In addition, businesses are creating their own educational programs, such as Motorola University or Dell University, to focus on specific workforce needs. Moreover, increased enrollment in higher education over the past 30 years, and the growth of regional universities within states to meet that demand, has further diluted state support, as even when such institutions have limited research capacities they still are competing for state dollars.

Where will such trends lead? The 21st century will see the evolution of a hybrid public research university, one with roots in both the public and private spheres. That new hybrid will confront significant new challenges.

The first will be to convince the public and decision makers—governors, legislators, and regents—that tuition must increase significantly to keep public research universities viable and competitive with private research universities. Universities will have to demonstrate that it is “worth it” to their regional economy and society, as well as to students, to charge more in order to support a high-quality research institution.

The University of Minnesota President asked, “What can be done about professional degree programs that usually cost far more money than tuition will ever generate, for example, those in medicine, dentistry, and veterinary science?”

He concluded his comments with the following observation:

The author William Arthur Ward once said, “The pessimist complains about the wind; the optimist expects it to change; and the realist adjusts the sails.” Unfortunately, we at public research universities and our supporters have fallen into a pattern of blaming the circumstances of the day—this year’s economy, the current legislature or governor, or the media—for our dwindling share of state resources, rather than focusing on our future over the long haul. Keeping public research universities relevant and thriving will be no easy task, and we should start by recognizing that the long-term political winds have shifted.

“What can be done about professional degree programs that usually cost far more money than tuition will ever generate, for example, those in medicine, dentistry, and veterinary science?”
**Faculty Position:**
The Department of Anatomy, Physiology and Cell Biology, School of Veterinary Medicine, University of California, Davis is recruiting an Assistant/Associate Professor of Veterinary Anatomy/Cell Biology. DVM or equivalent preferred. PhD required with advanced training in vertebrate anatomy/physiology/cell biology/molecular biology or associated field, such as bioengineering, orthopedics or pathology. Responsibilities will include teaching in the DVM professional curriculum. Demonstrated research record with potential to develop an independent research program in the area of musculoskeletal biology and ability to secure extramural funding. Salary dependent on qualifications and experience. Submit letter of intent, a curriculum vitae and the names of 3 references to Charles G. Plopper, Chair, Department of Anatomy, Physiology and Cell Biology, School of Veterinary Medicine, University of California, Davis, CA 95616, Attn: Terry Davison. To receive fullest consideration, applications must be received by August 15, 2002; position open until filled. AA/EOE.

**Postdoctoral Associate,**
The University of Iowa Health Care, Department of Internal Medicine, Pulmonary, Critical Care and Occupational Medicine Division.
Postdoctoral position available for training related to Molecular and Cellular Biology of the lung. Postdoctoral position also available for training in Translation Research related to the lung. Requires an M.D. or a Ph.D. Those interested in applying should contact: Gary W. Hunninghake, M.D., University of Iowa College of Medicine, 200 Hawkins Drive, C33 G General Hospital, Iowa City, IA 52242, Phone: (319) 356-4187, Fax: (319) 353-6406. Women and minorities are encouraged to apply.

**University of Michigan Health System Postdoctoral Position**
NIH funded Postdoctoral position at University of Michigan Medical Center is available NIH funded immediately to study the physiology of the enteric nervous system. Applicants should have a strong background in neurophysiology. Experience in electrophysiology, cell culture and molecular biology is required. Interested applicants should submit curriculum vitae to:

Michael, W. Mulholland, M.D., Ph.D., University of Michigan Health System, 1500 E. Medical Center Drive, 2920 Taubman Center, Ann Arbor, MI 48109-0331 USA, Fax: 734-936-5830.

The University of Michigan is a non-discriminatory Affirmative Action Employer and strongly encourages females and minorities to apply.

**Molecular Targets for Dietary Intervention in Disease**

For more information, contact: Growth Factor and Signal Transduction Conferences, Symposium Office, Iowa State University, 3208 Molecular Biology Building, Ames, Iowa, 50011-3260. Tel: 515-294-7978, Fax: 515-294-2244, Email: gfst@iastate.edu. Or visit http://molebio.iastate.edu/~gfst/phomepg.html

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Calendar of Scientific Meetings

JUNE 2002

50th Annual American Society for Mass Spectrometry
June 2–6 • Orlando, FL
Conference on Mass Spectrometry and Allied Topics
Contact: The American Society for Mass Spectrometry
http://www.asms.org; E-mail: office@asms.org; Tel.: 505-989-4517

HPLC 2002: 26th International Symposium on High Performance Liquid Phase Separations and Related Techniques
June 2–7 • Montreal, Quebec, Canada
Contact: HPLC Secretariat; E-mail: hplc2002@ums.lan.mcgill.ca
http://www.medcor.mcgill.ca/hplc2002; Tel.: 514-398-3770

Beyond Genome: In Silico Biology—Bioinformatics and Genome Research Proteomics
June 2–7 • San Diego, CA
Contact: Cambridge Health Institute; http://www.healthtech.com
E-mail: chi@healthtech.com; Tel.: 617-630-1300

45th Annual Canadian Federation of Biological Societies Meeting
Themes: Neurological Development; Physical Activity, Nutrition and Chronic Disease
June 12-15 • Palais des Congres, Montreal, Canada
Contact: wantonious@cfbs.org; Website: http://www.cfbs.org

Symposium on Research Responsibility and Undergraduates
Co-sponsored by ORI, the Council on Undergraduate Research and Sigma Xi, The Scientific Research Society, this symposium will focus on ethical issues for faculty doing research with undergraduates, and ways to instill ethical research behavior in undergraduates. Website: http://www.cur.org/conferences.html.

Proteomes: Structures, Changes, Interactions, and Function
June 20-23 • Iowa State University, Ames Iowa
Contact: Plant Sciences Symposium Office;
Ph. 515-294-7978; Fx. 515-294-2244; email: bmb@iastate.edu
Website: http://molebio.iastate.edu

RAPS National Biotechnology Conference
June 24–26 • San Diego, California
Contact: AAPS Meetings; Fax: 703-243-9532
Email: Meetings@aaps.org

International Conference: Genomics, Proteomics and Bioinformatics for Medicine
June 22–29 • Moscow, St. Petersburg, Russia
Contact: Professor A. I. Archakov; E-mail: gpbm2002@ibmh.msk.su
http://www.ibmh.msk.su/gpbm2002/; Tel.: 7-095-246-6980

JULY 2002

Trends in Sample Preparation 2002
June 30–July 4 • Seggau-Castle, Austria
Contact: Institute for Analytical Chemistry
http://www.analytchem.tugraz.at/acmr/en/events/home.html
E-mail: trisp@analytchem.tu-graz.at.at; Tel.: 43-316873-8301

European Cells and Materials: ECM III Cartilage & Joint Repair
Tutorials, Basic Research, and Clinical Methods
July 1-3, 2002 • Congress Centre, Davos, Switzerland
http://www.aofoundation.org/events/ao/ecm/organiser.shtml

AUGUST 2002

Tissue Remodeling
August 1-4 • Iowa State University, Ames, Iowa
Contact: Growth Factor and Signal Transduction Conferences
Ph. 515-294-7978; Fx. 515-294-2244; Email: gfst@iastate.edu
Website: http://molebio.iastate.edu

American Society of Cell Biology: Nontraditional Functions of Ubiquitin and Ubiquitin-like Proteins
August 11-14 • Colorado Springs, Colorado
Contact: Delia Zielinski, ASCB; Ph: 301-347-9300
Fx: 301-347-9310; Email: dzielinski@ascb.org

SEPTEMBER 2002

5th Siena Meeting “From Genome to Proteome: Functional Proteomics”
September 2–5 • Siena, Italy
Contact: Denis Hochstrasser; E-mail: pallini@mailsrv.unisi.it
http://www.unisi.it/eventi/proteome

Computational Biophysics:
Integrating Theoretical Physics and Biology
September 7-12 • San Feliu de Guixols, Spain
Contact: Dr. J. Hendekovic, European Science Foundation
Ph. +33 388 76 71 35; Fx. +33 388 36 69 87;
Email: euresco@esf.org

14th Meeting Methods of Protein Structure Analysis
September 8–12 • Valencia, Spain
Contact: Juan J. Calvete; http://www.mpsa2002.ibv.csic.es
E-mail: mpsa2002@ibv.csic.es
Molecular Targets for Dietary Intervention in Disease
September 19-22 • Iowa State University, Ames, Iowa
Contact: Growth Factor and Signal Transduction Conferences
Ph: 515-294-7978; Fx: 515-294-2244; email: gfst@iastate.edu; Website: http://molebio.iastate.edu

7th International Symposium on Dendritic Cells
September 19-24 • Bamberg, Germany
Contact: Prof. Dr. Alexander Steinkasserer
Ph: ++49-9131-853-6725; Fx: ++49-9131-853-5799;
e-mail: steinkasserer@derma.imed.uni-erlangen.de
Website: http://www.dc2002.de/

European Conference on Computational Biology 2002
in conjunction with the German Conference on Bioinformatics 2002
October 6–9 • Saarbruecken, Germany
Contact: http://www.eccb2002.de
E-mail: eccb.organizers@bioinf.uni-sb.de

Metabolic Engineering IV: Applied System Biology
October 6-11 • II Ciocco, Castelvecchio Pascoli Tuscany, Italy
Contact: United Engineering Foundation; Ph: 212-591-7836
Fax: 212-591-7441; Email: engfn@aoi.com
Website: http://www.engfn.org
Registration: http://www.engfn.org/2ay.html

9th Midwest Platelet and Vascular Biology Conference
October 11-13 • Washington University School of Medicine,
St. Louis, MO
Abstract and registration due August 15, 2002
Website: http://www.biochem.wustl.edu/mwpc9/index.html

Federation of Analytical Chemistry and Spectroscopy Societies
October 13–17 • Providence, Rhode Island
Contact: FACSS National Office; http://www.facss.org

The 18th International Conference on Arginine and Pyrimidines
October 13-17 • Giza, Cairo, Egypt
Biennial conference on all aspects of biochemistry and genetics of uptake and metabolism of arginine and pyrimidines.
Contact: Ahmed T. Abdelal, Georgia State University
Email: aabdelal@gsu.edu; Website: http://www.cas.gsu.edu/icap

The Applications of Proteomics
October 16–18 • Lille-Villeneuve d’Ascq, France
Contact: French Society for Electrophoresis and Proteomic Analysis; Tel.: 33-3-20-43-40-97; http://www.sfe-ices.org/
E-mail: hubert.hondermarck@univ-lille1.fr

18th Asilomar Conference on Mass Spectrometry
October 18–22 • Asilomar, Pacific Grove, CA
Contact: American Society for Mass Spectrometry
http://www.asms.org; E-mail: office@asms.org; Tel.: 505-989-4517

Fourth HUGO Pacific Meeting and Fifth Asia-Pacific Conference on Human Genetics
October 27–30 • Pattaya, Chonburi, Thailand
Contact: Tel.: 66-2-8892557-8; http://www.mu-st.net/hugothy

ABSTRACTS

18th Asilomar Conference on Mass Spectrometry
October 18–22 • Asilomar, Pacific Grove, CA
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October 27–30 • Pattaya, Chonburi, Thailand
Contact: Tel.: 66-2-8892557-8; http://www.mu-st.net/hugothy

ARAP Annual Meeting and Exposition
November 10-14 • Toronto, Ontario, Canada
Contact: AAPS Meetings, Fax: 703-243-9532 Email: Meetings@aps.org

First Human Proteome Organizational (HUPO) Congress
November 21–24 • Versailles, France
Contact: http://www.hupo.org

13th International Conference on Genome Informatics
December 16–18 • Tokyo, Japan
Contact: http://giw.ims.u-tokyo.ac.jp/giw2002/
E-mail: giw@ms.u-tokyo.ac.jp

Keystone Symposium, Proteomics: Technologies and Applications
March 25–30 • Keystone Resort, Keystone, Colorado
Contact: Paul Lugauer; http://www.keystonesymposia.org
E-mail: info@keystonesymposia.org; Tel.: 970-262-1230 ext. 111

American Society for Biochemistry and Molecular Biology Annual Meeting in Conjunction with EB2003
April 11-15 • San Diego, California
Contact: EB2003 Office; Ph: 301-530-7010
Fx: 301-530-7014; Email: eb@faseb.org
Website: http://www.faseb.org/meetings/eb2003

16th International Mass Spectrometry Society Conference
August 31–September 5 • Edinburgh, Scotland, United Kingdom
Contact: John Monaghan; E-mail: johnmonaghan@ed.ac.uk
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