

JANUARY 2007

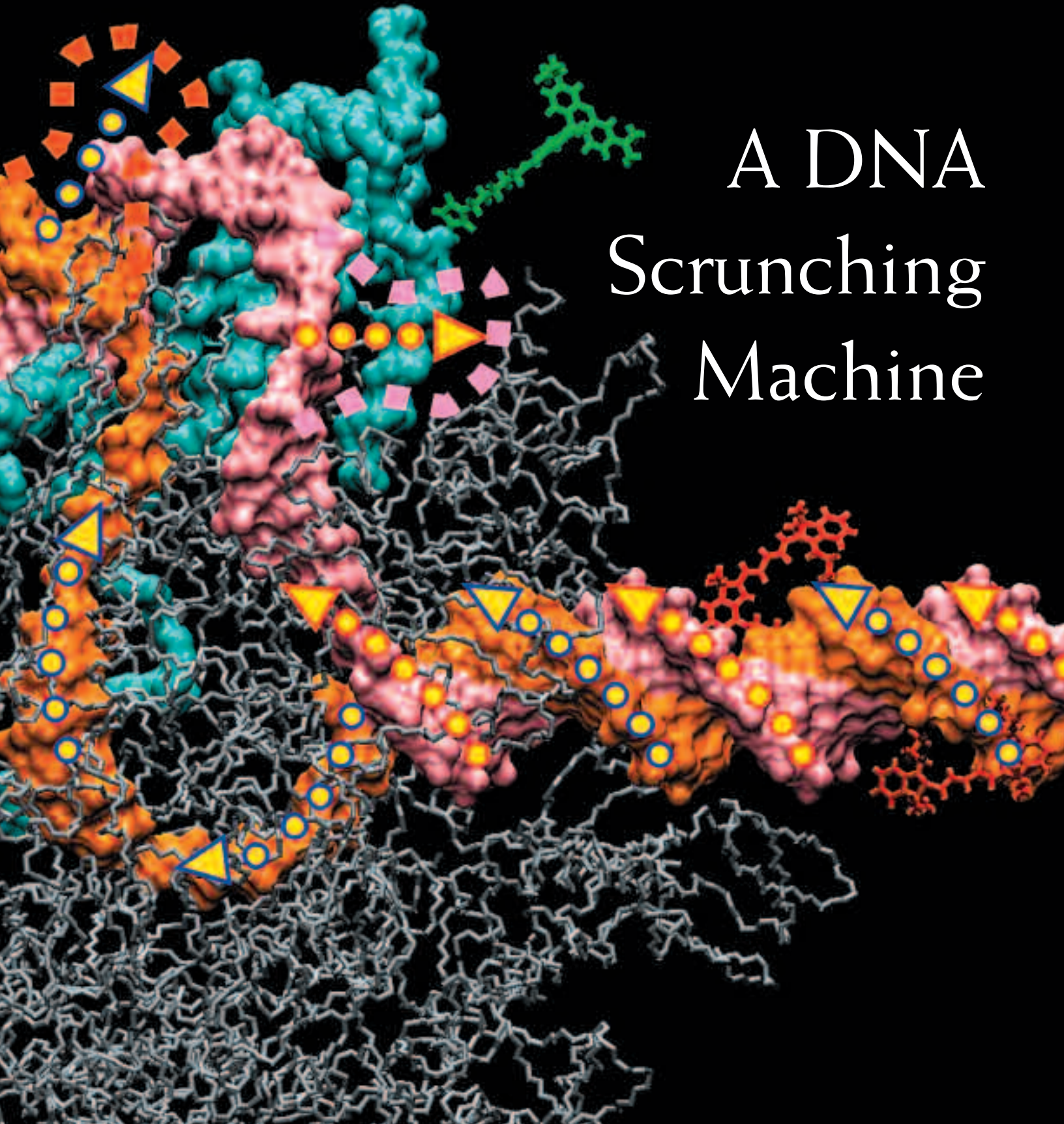
www.asbmb.org

ASBMB *Today*

Constituent Society of FASEB

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

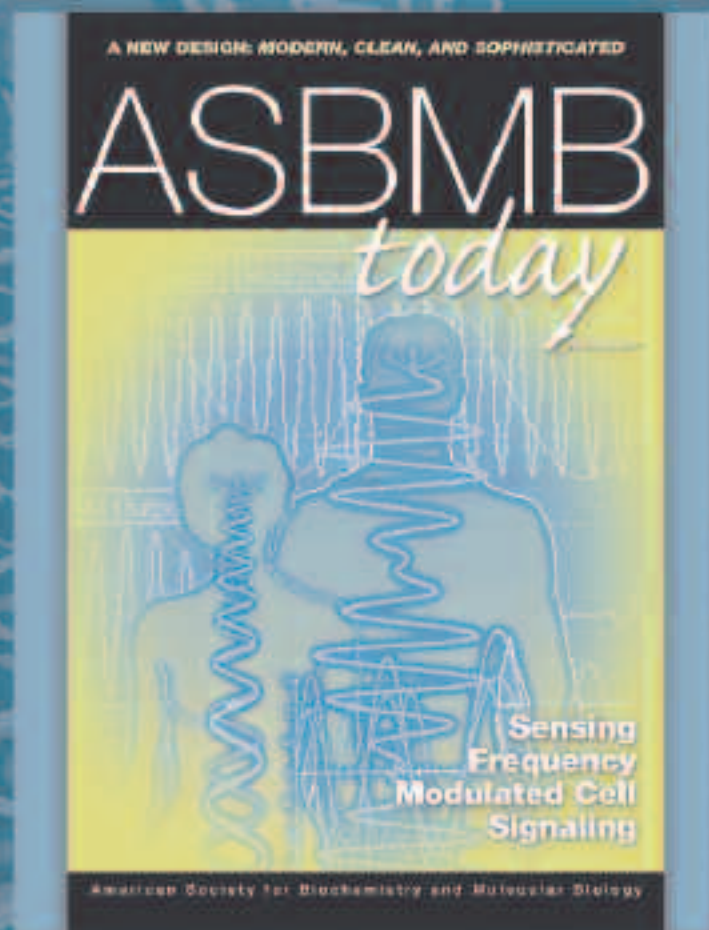
A DNA Scrunching Machine



COMING THIS FEBRUARY

**A new and improved
member only publication**

**Important news, enlightening features,
& key information from ASBMB –
*all in a new modern package.***



ASBMB

American Society For
Biochemistry And

Not yet a member? Please join us.
www.asbmb.org

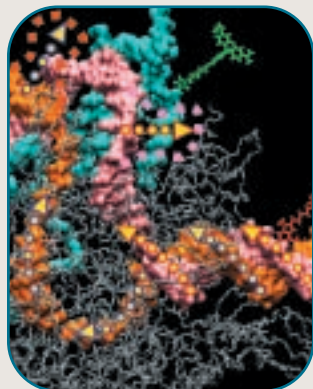
ASBMB Today

AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

JANUARY 2007
Volume 5, Issue 10

features

- 5 ASBMB Receives Teagle Foundation Grant
- 7 AAAS Announces 2006 Fellows
- 8 Immunoglobulin G Antibodies Activate Lysosome/Phagosome Targeting
- 10 Ron Evans Chosen for Fritz Lipmann Lectureship
- 11 Research!America Receives Schachman Award
- 12 An Interview with Toni Scarpa
- 14 Micro Molecules Contribute Mightily to Heart Problem
- 15 Education and Professional Development: New Year's Resolutions and Challenges
- 16 Biomedical Careers in Industry: A Few Tips for the Newcomer (Part 2)



ON THE COVER:

18 Initial transcription by RNA polymerase proceeds through a "DNA scrunching" mechanism



AWARDS FOR PUBLICATION EXCELLENCE

AWARDS OF EXCELLENCE:

MOST IMPROVED MAGAZINE

COLUMNS & EDITORIALS

DESIGN & LAYOUT



BRONZE AWARD WINNER 2003

departments

- 2 Letters
- 3 From the Desk of the President
- 4 News From the Hill
- 6 Washington Update
- 20 Spotlight on Members
- 22 ASBMB BioBits
- 24 Biotech Business
- 26 Career Opportunities
- 27 For Your Lab
- 28 Calendar

23





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

Officers

Heidi E. Hamm	President
Judith S. Bond	Past-President
Peggy J. Farnham	Secretary
Merle Olson	Treasurer

Council Members

Joan W. Conaway	Councilor
Robert A. Copeland	Councilor
Kuan-Teh Jeang	Councilor
John D. Scott	Councilor
William S. Sly	Councilor
Kevin Struhl	Councilor
Suzanne Pfeffer	Councilor
Linda Pike	Councilor

Ex-Officio Members

J. Ellis Bell

Chair, Education and Professional Development Committee

Laurie S. Kaguni
Chair, Meetings Committee

George Hill
Chair, Minority Affairs Committee

Benjamin F. Cravatt
Michael Rosen
Co-chairs, 2007 Program Committee

William R. Brinkley
Chair, Public Affairs Advisory Committee

Ralph A. Bradshaw
Deputy Chair, Public Affairs Advisory Committee

Shelagh Ferguson-Miller
Chair, Publications Committee

Herbert Tabor
Editor, JBC

Ralph A. Bradshaw
Al Burlingame
Co-Editors, MCP

Edward A. Dennis
Editor, JLR

Editorial Advisory Board

Irwin Fridovich
Richard W. Hanson
Bettie Sue Masters
J. Evan Sadler
Robert D. Wells

ASBMB Today

9650 Rockville Pike,
Bethesda, MD 20814-3996
Phone: 301-634-7145; Fax: 301-634-7369

Nicole Kresge nkresge@asbmb.org
Editor

Nancy J. Rodnan nrodnan@asbmb.org
Director of Publications

For information on advertising
contact FASEB AdNet at 800-433-2732
ext. 7157 or 301-634-7157, or
email adnet@faseb.org.

Proving that More Money Really Means Better Health

To the Editor:

Reading Heidi Hamm's "Update on Peer Review" in the November 2006 issue of *ASBMB Today*, I was struck by her imprecation to researchers to communicate to the public, and especially to members of Congress, the benefits of NIH-funded scientific research. What especially gave me pause was the statement that many Americans "do not understand that a stagnant NIH budget means that much important research does not get done, research that would likely lead to breakthroughs in combating disease and developing new treatments."

That sounds like a compelling argument, so much so that one wonders how we could have such a problem. Who could be opposed to breakthroughs in combating disease? But, particularly as scientists, it is fair to ask: What is the evidence? More pertinently, if we ASBMB members are out there proselytizing and are asked to explain how we are so sure that more money means better health, how should we respond?

Rest assured that skeptics exist. Daniel Sarewitz of Columbia University, reviewing Daniel Callahan's *False Hopes: Why America's Quest for Perfect Health is a Recipe for Failure* (1), has written, "One might reasonably posit that the results of biomedical research are applied through the health care system to create a healthier, longer-lived population. Careful studies of the determinants of public

health, however, fail to reveal such clear connections...Indeed, historical and individual country studies invariably demonstrate that the health of a population increases more or less in concert with socioeconomic development, and that within any given society the prime determinant of health is relative social status." And in his book, "Science, Money, and Politics: Political Triumph and Ethical Erosion," Daniel Greenberg quotes a federal official as saying, "With the possible exception of veterans, farmers, and college students, there is no group that squeals more loudly over a reduction of federal subsidies than scientists. They are the quintessential special interest group."

I share Dr. Hamm's desire for NIH funding that is adequate to support the research infrastructure that has been built over the past decades—my research was supported by NIH for nine years, but now it's not, and I would very much like to have NIH support again. But I believe that if we are too incautiously evangelical in our pleas for support and make arguments that we cannot support, we may lose credibility. We need to present succinct and cogent arguments for continued support. Such arguments should include, beyond the near term benefits to public health and projected benefits that we cannot be sure of, the value of our educational infrastructure and contributions that research funding makes to that, and the role of federally funded research in dri-

Continued on page 9



Dr. Heidi E. Hamm
ASBMB President

ASBMB Local Advocates— Get Ready for FY 2008

By now you have probably heard the news—the NIH will be flat-funded again in 2007. Thus, for the 4th year in a row since the doubling, NIH funding will fail to keep up with inflation. Since the doubling of NIH's budget was completed in 2003, the agency has lost almost 11 % in purchasing power

Obviously, this situation cannot continue without dire consequences for biomedical research, and ASBMB is taking a number of steps to try to turn this around for FY 2008. But time is short. The President will release his budget proposal for 2008 in early February 2007. Thus, we need all the help we can get from you, our members. To bring some direction to this effort, ASBMB has established a Local Advocate program and we would like you to be a part of it. Here is where we are on the program so far.

ASBMB Local Advocates

Late last summer we sent around a survey asking ASBMB members to volunteer to serve as advocates for biomedical research with their senators and in their local Congressional districts. A lot of you responded, for which we are grateful. We could certainly use more of you, however (more on that later). But for the moment, the staff has analyzed the responses, and here are the numbers. As you will see, we have a good start on a national advocacy list, but we still have some gaps.

First, about 220 of you with identifiable contact information have volunteered to serve. Unfortunately, some of you who responded did not provide us with an e-mail address or any other

identifying information, so we have no way of contacting you. If you are one of the dozen or so respondents who fall in this category, we want to hear from you. There is always room for more local advocates. An additional dozen or so of you who responded are not ASBMB members. While we are happy you support ASBMB's efforts, we would of course like you to join the Society. Thus, we will be inviting you to join.

Responses from across the Country

We had respondents from 40 states, in 116 different Congressional districts. This is slightly over one-quarter of the House of Representatives. Most respondents came from university towns and urban areas, which tend to be heavily Democratic. Thus, 92 of the districts in which we have local advocates are represented by Democrats. In a "blue" House, this will work to our benefit the next two years.

16 of the House districts where we have local advocates are represented by freshmen who won election for the first time in November. All but one are Democrats. However, there will be at least 36 more districts represented by freshmen in the next Congress (possibly more depending on the outcome of several races still undecided as of this writing). These are important people to cultivate early in their tenures; ***we will be seeking ASBMB members to take on local advocacy in these districts as well.***

In the 40 states where we have local advocates, 34 Senators are Republican, and 46 are Democratic. The 10 states where we have no coverage include Alaska, Idaho, Mississippi, Montana,

Nebraska, New Mexico, Rhode Island, South Dakota, West Virginia, and Wyoming. While these are small states in terms of population and representation in the House (these states contain a total of 21 congressional seats), some of the Senators representing them are very powerful. These include incoming Appropriations Chair Robert Byrd (D-West Virginia), ranking minority Appropriations member Thad Cochran (R-Mississippi), as well as appropriators Tim Johnson (D-South Dakota), Ted Stevens (R-Alaska), Pete Domenici (R-New Mexico), and Larry Craig (R-Idaho). Most of these senators will no doubt continue on the Appropriations Committee next year. ***It is thus very important that we get ASBMB members in these states.***

The Senate also will have 10 freshman members. We have coverage for 8 of these, but need additional members to work with Senators-elect Sheldon Whitehouse (D-Rhode Island) and Jon Tester (D-Montana).

In short, we have garnered a pretty good response for our initial effort but could use a lot more volunteers. Many of the 116 districts are covered by only one ASBMB local advocate; we could always use more. Thus, if you have not volunteered to participate in this effort, please consider doing so.

In coming weeks, we will also be contacting ASBMB members in the states and districts where we need coverage but don't have it. Please consider volunteering if you are asked.

To volunteer, all you need to do is send an e-mail to our public affairs officer, Pete Farnham, at

Continued on page 4

2007 Funding: Democrats Go with Long Term CR

The incoming chairmen of the House and Senate Appropriations Committees announced on December 11 that they would fund all remaining 2007 appropriations bills under a long term Continuing Resolution (CR) that would last through the rest of the fiscal year, that is, until October 1, 2007. Funding for all programs in the relevant appropriations bills would thus be at or close to the level under which they were funded in 2006, which ended this past September 30.

Thus NIH can expect a fourth consecutive year of funding at a rate less than inflation, which will erode the doubling of the budget (1999-2003) even further. NIH will very likely be funded at approximately \$28.5 billion.

This decision was reached because during the last Congress, only 2 of the 11 appropriations bills were signed into law. The House passed all appropriations bills by mid-summer, but the Senate refused to act on most of them, and the Republican leadership, in the waning days of the 109th Congress, was unable to reach agreement on getting them passed before the Congress ended. Instead, Republicans decided to let the incoming Democratic majority deal with the 9 unpassed bills as their first item of business in January.

However, Congressional Democrats decided that, rather than waste valuable time dealing with last year's business when they had other issues they wanted to deal with, they would simply fund all remaining 2007 appropria-

tions bills at last year's levels (more or less). Senator Robert Byrd (D-West Virginia) and Representative Dave Obey (D-Wisconsin) noted in their statement announcing the decision that "It is important that we clear the decks quickly so that we can get to work on the American people's priorities, the President's anticipated war funding request, and a new budget.


"Unfortunately, there are no good options available to us....we have decided to dispose of the Republican budget leftovers by passing a year long joint resolution. We will do our best to make whatever limited adjustments are possible within the confines of the Republican budget to address the nation's most important policy concerns. We intend to work with the leadership of both parties in both houses to do what we can to resolve last year's disputes and turn to the challenges facing us in the new fiscal year."

Byrd and Obey acknowledge that this was a "far from ideal" solution but decided it was the best way to dispose of this "unfinished business" quickly.

On the plus side, there will be no Congressional earmarks in the joint funding resolution; rather, a moratorium on earmarks will be put in place until a reform package is developed that contains standards for "transparency and accountability."

Footnote: NIH Reauthorization Passes


In a piece of rare good news out of the 109th Congress, the NIH Reform

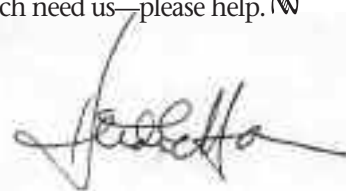
Act of 2006 was passed just before adjournment. The bill authorizes funding for NIH for 2007, 2008, and 2009 that would restore the erosion its budget has suffered since 2003 and pave the way for continued real growth. Outgoing Energy & Commerce Committee Chairman Joe Barton (R-Texas) was very grateful for the assistance in passage he received from FASEB and other organizations in Washington with interests in the NIH. The bill calls for 6.7% growth in 2007, 8.3% growth in 2008, and additional funds "as required" for 2009. The President is expected to sign the bill into law. 

President continued...

Continued from page 2

pfarnham@asbmb.org, and give him your contact information, including the Zip code (9-digit if possible) of the address where you are registered to vote, i.e., your residence if it differs from your place of business (of course, this presupposes that you are a U.S. citizen).

We can make a difference for biomedical research next year if we can mobilize a significant number of ASBMB members to become active local advocates. We thank those of you who have volunteered to be a part of this effort and urge as many of the rest of you as possible to sign up. NIH and biomedical research need us—please help. 



ASBMB Receives Teagle Foundation Grant

By Nicole Kresge

The Teagle foundation aims to strengthen liberal education by marshalling the intellectual and financial resources to ensure that today's students have access to challenging, wide-ranging, and enriching college educations.

In November 2006, the American Society for Biochemistry and Molecular Biology (ASBMB) received a \$75,000 grant from the Teagle Foundation to evaluate the Biochemistry and Molecular Biology major and to consider how our discipline supports the broad goals of a liberal education. The grant was one of six awarded by the Teagle Foundation to groups thinking about the disciplines in undergraduate education.

The Teagle Foundation was established in 1944 by Walter C. Teagle, longtime president and later chairman of the board of Standard Oil Company, now Exxon Mobil Corporation. The foundation provides leadership for liberal education, marshalling the intellectual and financial resources necessary to ensure that students have access to challenging, wide ranging, and enriching college educations.

Since 1992, ASBMB has supported a recommended curriculum for the bachelor's degree in Biochemistry and Molecular Biology¹. This curriculum has been modified in the years since it was developed to emphasize skills rather than coursework. The leaders of ASBMB would like to ensure that the curriculum is incorporated into biochemistry and molecular biology programs and would also like to know how biochemistry and molecular biology contribute to a liberal education.

The Teagle Foundation grant will allow ASBMB to assess how its recommended curriculum is being received and implemented in different types of institutions and evaluate the success of their graduates. To do this, the Society will convene a working group that includes biochemistry and molecular biology faculty who teach undergraduates, representatives from institutions that further train and employ their graduates, and agencies and writers supporting their work. The group will be headed by Adele Wolfson of Wellesley College, former chair of ASBMB's committees on Education and Equal Opportunities for Women.

"I have always been convinced that science is an essential part of the liberal arts," says Wolfson. "In recent years, as there has been more and more focus on how students learn and on imparting skills rather than facts, I have seen how good science courses naturally include the kind of active learning and critical thinking that all disciplines are being urged to incorporate."

Other people who have committed to this project include: Trevor Anderson (University of KwaZulu-Natal, South Africa), Ellis Bell (University of Richmond, Chair of ASBMB's Educational and Professional Development

Committee), Judith Bond (Penn State Medical School, Past President of ASBMB), Rod Boyer (Hope College Emeritus), Robert Copeland (Glaxo Smith-Kline), Barbara Gordon (Executive Director, ASBMB), Heidi Hamm (Vanderbilt University, President of ASBMB), Nicole Kresge (Science Writer, ASBMB), and Peter Rubenstein (University of Iowa College of Medicine).

The group will also consider the essential elements of an undergraduate major in Biochemistry and Molecular Biology and how new research on how people learn and other elements such as communication, collaboration across diverse communities, and ethical considerations can be best incorporated into the curriculum.

"We will showcase our findings at both a national meeting and in our publications," explains Wolfson. "We expect that these will be useful to members in that they will facilitate discussions about student learning and essential skills imparted in Biochemistry and Molecular Biology undergraduate courses on various campuses. We hope to work together with various institutions to assess graduates' success in their subsequent education and careers, and this in turn will guide development of new courses and materials." ❧

1 Voet, J. G., Bell, E., Boyer, R., Boyle, J., O'Leary, M., and Zimmerman, J. K. (2003) Recommended Curriculum for a Program in Biochemistry and Molecular Biology. *Biochem. Mol. Biol. Educ.* 31, 161-162



FASEB Tackles Issues Related to Benefits for Postdoctoral Researchers

Carrie D. Wolinetz, Ph.D., FASEB Office of Public Affairs

The Training and Career Opportunities subcommittee of FASEB's Science Policy Committee (SPC) has long been interested in issues related to the career development and quality of life issues of postdoctoral fellows (postdocs). As part of this ongoing effort, the subcommittee has recently been focused on the issue of health benefits for postdocs. In response to an NIH proposal to modify the tuition and benefits allowance associated with the Ruth L. Kirschstein National Research Service Award (NRSA), the subcommittee helped develop a FASEB position urging NIH to separate tuition costs from those allocated for health benefits. This was to minimize the risk that benefits received by NRSA awardees would be diminished, and the position was subsequently adopted by NIH. Similarly, the subcommittee recently developed a statement, approved by the SPC, in support of uniform health benefits for postdocs within the same institution. The statement, which was ratified by the FASEB Board of Directors and cosigned by the Association of American Medical Colleges, is as follows:

"The Federation of American Societies for Experimental Biology (FASEB) and the Association of American Medical Colleges (AAMC) strongly believe that every effort must be made to recruit and retain talented scientists to the biomedical research enterprise. It is critical, therefore, that our nation's young investigators view science as an attractive and viable career option that offers postdoctoral researchers compensation commensurate with their education, experience, and contribution to the research enterprise. Access

to affordable health care is an essential component of this support.

"Many institutions have found it difficult to provide the same health benefits to all postdocs because of their differential classification as 'employees' or 'non-employees' according to the source of funding for their position. Employee postdocs may have access to the same benefits plans as other employees at their institution, while non-employee postdocs may not. Indeed, non-employee postdocs may be limited to inferior plans or no plan at all. This system not only limits their access to adequate health coverage, but it creates inequity among postdocs within and across institutions even though they have the same level of expertise and perform the same type of work.

"Rectifying this situation requires action by both training and funding institutions. Universities and other training institutions must provide the same benefits to all postdocs regardless of their funding source. Training program administrators are encouraged to look toward institutions such as the University of California and Case Western Reserve University as models for the successful implementation of these plans.

"For their part, funding institutions must provide non-employee postdocs with the financial resources to purchase comprehensive health benefits packages that are on par with those offered to employee postdocs. FASEB and AAMC appreciate the National Institutes of Health's (NIH) commitment to the health of trainees, including their recent decision to modify the Ruth L. Kirschstein National Research

Service Award (NRSA) policy by making health benefits an allowable cost within the Training Related Expenses and Institutional Allowance categories of the institutional and individual NRSA fellowships. We urge NIH to sustain this commitment by ensuring the additional funding to these categories is sufficient to cover the cost of health benefits.

"As leading advocates for research and training in the biomedical sciences, FASEB and AAMC strongly believe that postdoctoral researchers must have funding for and access to comprehensive health care coverage. By working together to provide these critical benefits, funding and training institutions can enhance the attractiveness of careers in biomedical research."

Currently, the FASEB Training and Career Opportunities subcommittee is considering additional projects to further address issues related to career development of postdocs, including expansion and enhancement of its Individual Development Plan (IDP), a self-guided tool for use by postdocs and their mentors. Other possibilities include creating resources for use by postdoctoral program administrators and career counselors at universities, expressly designed to meet the needs of postdoctoral scientists, or partnering with FASEB societies and FASEB's Career Resources Department to provide professional development workshops for trainees and mentors at scientific meetings. More about the IDP and work of the FASEB Training subcommittee may be found at <http://opa.faseb.org/pages/PolicyIssues/training.htm>.

AAAS Announces 2006 Fellows

Several ASBMB members have been awarded the distinction of AAAS Fellow, an honor bestowed upon American Association for the Advancement of Science (AAAS) members by their peers.

This year, 449 AAAS members have been awarded this honor by AAAS because of their scientifically or socially distinguished efforts to advance science or its applications. The new Fellows will be inducted at the Fellows Forum in February during the 2007 AAAS Annual Meeting in San Francisco.

ASBMB congratulates the following ASBMB members for this achievement:

Barbara A. Baird, Cornell Univ.

Dipak K. Banerjee, Univ. of Puerto Rico

Shelagh M. Ferguson-Miller, Michigan State Univ.

James R. Halpert, Univ. of Texas

Barry Honig, Columbia Univ.

Arthur Horwich, Yale Univ.

Barbara B. Kahn, Beth Israel Deaconess Medical Center

Kenneth Keegstra, Michigan State Univ.

Thomas J. Kelly, Sloan-Kettering Inst.

Bruce E. Kemp, St. Vincent's Inst. of Medical Research

Judith Kimble, Univ. of Wisconsin

Amy S. Lee, Univ. of Southern California

Arthur J. Lustig, Tulane Univ. Health Sciences Center

Kenneth J. Marians, Memorial Sloan-Kettering Cancer Center

Steven L. McKnight, Univ. of Texas

Janet E. Mertz, Univ. of Wisconsin

Carol S. Newlon, Univ. of Medicine and Dentistry of New Jersey

Timothy W. Nilsen, Case Western Reserve Univ.

Ann M. Stock, Center for Advanced

Biotechnology and Medicine

William A. Toscano Jr., Univ. of Minnesota

Teresa S. F. Wang, Stanford Univ.

Eleanore T. Wurtzel, Lehman College, The City Univ. of New York

Ning-Sun Yang, Academia Sinica

Barbara A. Baird, Cornell Univ.

David Penfield Ballou, Univ. of Michigan Medical School

Carol Ann Fierke, Univ. of Michigan

Kenneth Allen Johnson, Univ. of Texas, Austin

Jack F. Kirsch, Univ. of California, Berkeley

Gaetano T. Montelione, Rutgers Univ.

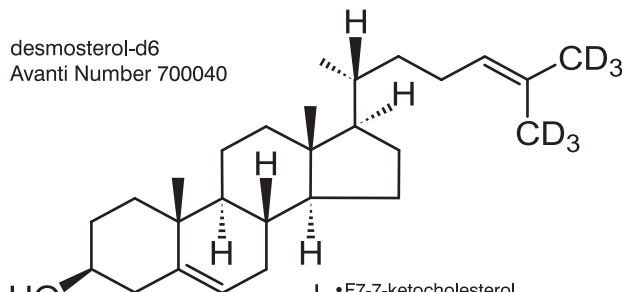
Mary Fedarko Roberts, Boston College

Steven R. Tannenbaum, Massachusetts Inst. of Technology

Christian P. Whitman, Univ. of Texas, Austin

Cholesterol, Sterols & Oxysterols + Fluorescent, Fluorinated & Deuterated Derivatives - from Avanti®

desmosterol-d6
Avanti Number 700040



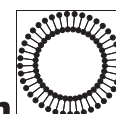
- Cholesterol (Ovine Wool)
Avanti Number 700000
- Cholesterol (Plant Derived)
Avanti Number 700100
- 25-NBD Cholesterol
Avanti Number 810250
- F7-cholesterol
Avanti Number 700002
- F7-5,6 α -epoxycholestanol
Avanti Number 700003
- F7-5,6 β -epoxycholestanol
Avanti Number 700004

- F7-7-ketocholesterol
Avanti Number 700005
- F7-7 α -hydroxycholesterol
Avanti Number 700007
- F7-7 β -hydroxycholesterol
Avanti Number 700006
- 7-ketocholesterol
Avanti Number 700015
- 15-ketocholestene
Avanti Number 700008
- 15-ketocholestanone
Avanti Number 700009
- 25-hydroxycholesterol
Avanti Number 700019

- 27-hydroxycholesterol
Avanti Number 700021
- 6 α -hydroxycholestanol
Avanti Number 700030
- 3 β -hydroxy-7-oxo-5-cholestenoic acid
Avanti Number 700026
- 7 α -hydroxy-3-oxo-4-cholestenoic acid
Avanti Number 700027
- 15 α -hydroxycholestene
Avanti Number 700010
- 15 β -hydroxycholestene
Avanti Number 700011
- 15 α -hydroxycholestanone
Avanti Number 700012
- 15 β -hydroxycholestanone
Avanti Number 700013
- 3 β ,7 α -dihydroxy-5-cholestenoic acid
Avanti Number 700028
- 3 β ,7 β -dihydroxy-5-cholestenoic acid
Avanti Number 700029
- 3 β ,27-dihydroxy-5-cholesten-7-one
Avanti Number 700022
- 7 α ,27-dihydroxy-4-cholesten-3-one
Avanti Number 700023
- 7 α ,27-dihydroxycholesterol
Avanti Number 700024

- 7 β ,27-dihydroxycholesterol
Avanti Number 700025
- Cholesterol-D7
Avanti Number 700041
- 4 β OH-Chol-D7
Avanti Number 700042
- 7 α OH-Chol-D7
Avanti Number 700043
- 7 β OH-Chol-D7
Avanti Number 700044
- 24OH-Chol-D6
Avanti Number 700049
- 25OH-Chol-D3
Avanti Number 700050
- 6 α OH-Cholestanol-D7
Avanti Number 700045
- 7-Ketochole-D7
Avanti Number 700046
- 5,6 α -Epoxy Chol-D7
Avanti Number 700047
- 5,6 β -Epoxy Chol-D7
Avanti Number 700014
- 24,25-Epoxy Chol-D6
Avanti Number 700048

To order from Avanti® phone 205-663-2494,
Fax 800-229-1004, or Email orders@avantilipids.com



Avanti®
POLAR LIPIDS, INC.

FROM RESEARCH TO cGMP PRODUCTION - AVANTI'S HERE FOR YOU

Immunoglobulin G Antibodies Activate Lysosome/Phagosome Targeting

by Dr. Axel Nohturfft

Around the turn of the 20th century an epic controversy was fought on the question of how the body defends itself against infections. In one camp were the "cellularists," led by zoologist Elie Metchnikoff, who believed the principal instruments of the immune system to be white blood cells that engulf and digest invading microorganisms. Their opponents, called "humoralists," disagreed and argued instead that the chief weapons of the immune system were soluble molecules called antibodies.

As it turned out, the truth lies in the middle, a possibility that was first proposed by Wright and Douglas in 1903 and popularized by George Bernard Shaw in the preface to his play "The Doctor's Dilemma":

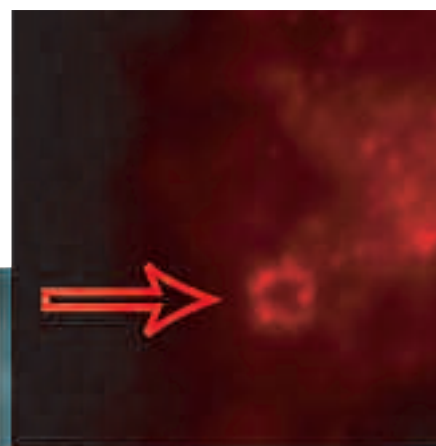
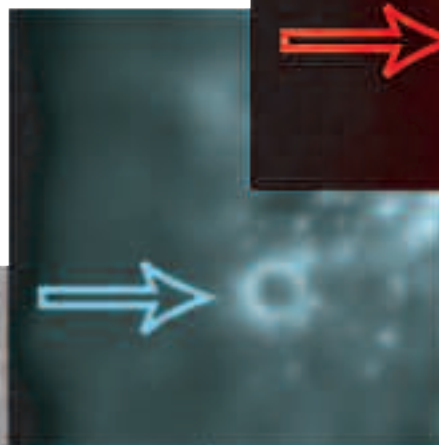
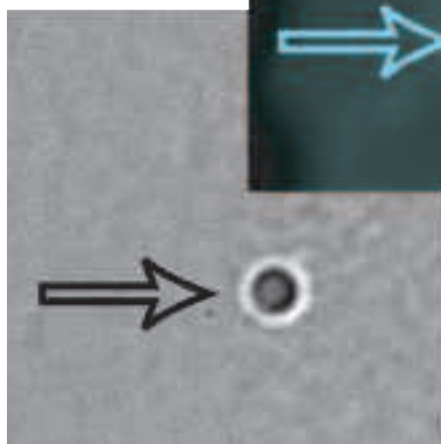
"...Sir Almroth Wright, following up on Metchnikoff's most suggestive biological romances, discovered that the white corpuscles or phagocytes...do their work only when we butter the disease germs appetizingly for them with a natural sauce which Sir Almroth named opsonin ..."

Amoeba-like phagocytes such as neutrophils, macrophages, and dendritic cells are our first line of defense against microbes that enter the body. Phagocytes can swallow microbes whole and store them in membrane-bound phagosomes where the prey is slowly digested. Digestion requires the fusion of phagosomes with lysosomes, which deliver hydrolytic enzymes as well as proteins involved in acidification, microbe killing, and presentation of antigens to T lymphocytes.

If an infection persists other cells of the immune system will mount a second line of defense and begin to

secrete molecules that potentially stimulate the ability of phagocytes to do their work. Among these stimulants are the humoralists' antibodies as well as cytokines such as interferon- γ .

Following their discovery by Behring and Kisato in 1890, antibodies were found to be globular proteins comprising different classes, the most important of



Mouse macrophage with a phagosome surrounded by docked lysosomes.

which is referred to as immunoglobulin G, or IgG. The immune system produces billions of different IgG antibodies, each of which can avidly bind to another foreign molecule.

IgG molecules have two domains. One domain binds foreign antigens, while the other is recognized by specific receptors on the surface of phagocytes. IgG thus enhances the recognition of microbes by phagocytes and potentially accelerates their engulfment. Following Sir Almroth Wright's suggestion, IgG and other phagocytosis-stimulating "sauces" such as complement are still referred to as opsonins.

In addition to "buttering" germs for phagocytosis, antibodies prevent disease by neutralizing bacterial toxins, a function that is crucial for example in the body's defense against diphtheria. Another trick up the sleeve of the immune system is the ability of phagocytes to produce their own toxins, reactive oxygen species and nitric oxide, to kill microbial intruders, a process strongly enhanced when microbes are covered with antibodies.


In a paper appearing in the November 28, 2006, issue of the *Proceedings of the National Academy of Sciences* we are now describing yet another aspect of IgG's ability to promote the destruction of foreign particles. When IgG binds to receptors on phagocytes, a signal is transmitted to the cytoplasm that activates the merger of phagosomes with lysosomes. We speculate that

IgG-induced activation of the lysosome/phagosome targeting pathway is particularly important in the defense against microbial intracellular pathogens. Many of these pathogens survive in phagocytes by blocking lysosome/phagosome fusion; examples of public health importance include microbes responsible for tuberculosis, toxoplasmosis, salmonellosis, and chlamydia.

We found that the IgG-induced boost of lysosome/phagosome targeting required the activity of protein kinase C (PKC), an enzyme that had already been shown to mediate other IgG-enhanced processes, such as particle engulfment and generation of microbicidal oxygen species. PKC thus emerges as a central coordinator of IgG-induced stimulation of phagocyte function.

Similar to processes in other parts of the cell, lysosome/phagosome targeting proceeds in three sequential steps referred to as tethering, docking, and fusion. The cytosolic face of phagosomes is topologically equivalent

to the plasma membrane where fusion is often regulated in response to extracellular signals. In most cases of regulated exocytosis, influx of calcium ions leads to rapid fusion of already docked vesicles. According to *in vitro* data, the effect of IgG on lysosome/phagosome targeting is different in that the antibodies appear to specifically stimulate the tethering step. Microscopy studies are currently under way to test this conclusion *in vivo*.

Few examples of extracellular signals affecting membrane tethering are known. However, according to a recent paper by Gonzalez and McGraw in the October 2006 issue of *Molecular Biology of the Cell*, insulin promotes the movement of glucose transporters to the surface of adipocytes in part by activating the tethering of transporter-carrying vesicles to the plasma membrane. Whether activation of membrane tethering is a rare phenomenon or a more widespread device remains to be seen. 



Dr. Axel Nohturfft

ASBMB member Axel Nohturfft is an associate professor in the Department of Molecular and Cellular Biology at Harvard University. After finishing his undergraduate degree at the Free University of Berlin in 1993, Nohturfft moved to Canada, where he spent the early 1990s doing research at the University of Victoria in British Columbia. From there, he immigrated to the United States for a Ph.D. in Biochemistry, which he completed at the University of Texas Southwestern Medical Center in Dallas in 1998. He remained at the University of Texas as a postdoctoral fellow until he accepted a position as assistant professor in the Department of Molecular and Cellular Biology at Harvard University in 2001.

Nohturfft has published more than 20 times and is the recipient of multiple honors and awards, including a 2004 Merck-Wiley Award and a 2002 Searle Scholarship. His professional memberships include the Faculty of 1000. His research focuses on lipid distribution within cells and the mechanisms behind membrane biogenesis, as well as phagocytosis as a real life function of the immune system.

Letters Continued ...

Continued from page 2

ving the biotechnology industry that is a vital part of our economy.

As to the first item—near term benefits to public health—I can think of some concrete examples (for example, yesterday I heard at a seminar that the FDA is working on incorporating research results on genetically based contraindications into labeling of specific drugs), but it might be helpful to have a publicly accessible list of tangible benefits that have

derived from NIH- and NSF-funded research. Maybe such a list already exists. Could the ASBMB help in some way with this?

Randy Morse
Chief, Laboratory
of Developmental Genetics
Wadsworth Center, Albany, NY

1. D. Sarewitz, *Journal of Health Politics, Policy, and Law*, Volume 25, No. 5, October 2000, 988-991.

Ronald M. Evans Chosen for Fritz Lipmann Lectureship

Ronald M. Evans, professor in the Gene Expression Laboratory and March of Dimes Chair in Developmental and Molecular Biology at the Salk Institute for Biological Studies, has been chosen for the ASBMB Fritz Lipmann Lectureship. The lectureship was established by friends and colleagues of Fritz Lipmann and is awarded every other year for conceptual advances in biochemistry, bioenergetics, or molecular biology.

Fritz Lipmann was a former ASBMB president and recipient of the 1953 Nobel Prize in Physiology or Medicine. The award provides a plaque, \$3,000, and transportation and expenses to the 2007 ASBMB Annual Meeting to present a lecture. The first recipient of the lectureship was Joan A. Steitz in 1989. Other past awardees include Christopher T. Walsh, Rodrick MacKinnon, Heidi Hamm, and Steven Fesik.

Evans is known for his discoveries and characterization of nuclear receptor hormone receptors, the establishment of the nuclear receptor superfamily, and the elucidation of their universal mechanism of action, a process that governs how lipophilic hormones and drugs regulate virtually every developmental and metabolic pathway in animals and humans.

Evans obtained his BA and Ph.D. from the University of California, Los Angeles, School of Medicine in 1970 and 1974, respectively. After working on myeloid leukemia viruses he became a postdoctoral fellow with James Darnell at the Rockefeller University in New York studying the transcriptional regulation of human adenovirus leading to the identification of the first eukaryotic promoter


for messenger RNA. In 1977 he joined the faculty of The Salk Institute where he is now an investigator of the Howard Hughes Medical Institute and professor in the Gene Expression Laboratory. Since 1996 he has held the March of Dimes Chair in Molecular and Developmental Biology. Evans also holds adjunct professorships at the University of California, San Diego, in the Departments of Biology, Biomedical Sciences, and Neuroscience.

At Salk, Evans isolated the growth hormone gene to study its transcriptional regulation by steroid and thyroid hormones. These lipid soluble hormones control fundamental aspects of physiology including sugar, salt, and fat metabolism; basal metabolic rate; and reproduction. In 1982, with Palmiter and Brinster, he created the first transgenic growth hormone "supermouse." In 1985 his group cloned and characterized the first nuclear hormone receptor, the human glucocorticoid receptor. His subsequent isolation of the thyroid, mineralocorticoid, and retinoic acid (vitamin A) established the existence of the nuclear receptor superfamily. Though the ligands for nuclear receptors are chemically and biosynthetically distinct, the homology of their receptors revealed the existence of an underlying unity in their mechanism of action. This work led to the principles of DNA recognition, receptor heterodimer formation, and the discovery of the DNA coding mechanism for hormone response elements.

Over the past 10 years, Evans has focused on the characterization of the so-called "orphan" members of the nuclear receptor family for which no physiologic ligands were known. He



isolated the first orphan receptors (ERR1 and -2) as well as the unexpectedly important retinoid X receptor (RXR). He pioneered biochemical and molecular techniques that led to the identification of the RXR ligand 9-cis RA, the first new hormonal lipid since the isolation of aldosterone in 1952. He also isolated and characterized the xenobiotic sensor SXR that acts as a molecular gateway to control the catabolism and clearance of steroids, bile acids, oxidized lipids and numerous prescription drugs.

Evans has received numerous awards in recognition of his contributions to research. These include the First Bristol-Myers Squibb Award in Metabolic Research (2000), the March of Dimes Prize in Developmental Biology (2003), the General Motors Cancer Research Foundation Alfred P. Sloan Medal (2003), the Keio Medical Science Prize (2003), Albert Lasker Basic Medical Research Award (2004), Glen T. Seaborg Medal, UCLA (2005), the "Grande Medaille d'Or" from the French Academy of Sciences (2005), and the Gairdner Award (2006). Evans is a member of the National Academy of Sciences, the Institute of Medicine, and the American Academy of Arts and Sciences and was named the 1994 California Scientist of the Year. 

ASBMB Annual Meeting

April 28 - May 2, 2007 in Washington, DC

Research!America—Recipient of 2007 Schachman Public Service Award

By Peter Farnham, CAE, ASBMB Public Affairs Officer

Research!America, one of the most effective advocacy organizations in the country for biomedical research since its founding in 1989, was selected as the 2007 recipient of the Howard K. Schachman Public Service Award. “A great way to end the year when it hasn’t been all that great a year for funding,” said Mary Woolley, president of Research!America, in a conversation with *ASBMB Today* shortly after learning the news.

“Research!America is truly honored to be the 2007 recipient of the Howard K. Schachman Public Service Award,” Dr. Woolley said, “To be considered in the company of the past honorees is an honor in itself. We look forward to continued collaboration with ASBMB to make research a higher national priority.”

Dr. Woolley will be accepting the award on behalf of Research!America—the first organization to receive the award—at the ASBMB annual meeting this May in Washington, D.C. The award ceremony and her address will occur on Tuesday, May 1, 2007, at 12:30 pm.

The Schachman Award, established by the ASBMB in 2001, recognizes dedication to public service in support of biomedical science, as exemplified by the award’s namesake, Howard K. Schachman, who served as chairman of ASBMB’s Public Affairs Advisory Committee for more than 10 years (1989-2000) and made numerous contributions to biomedical research policy in both governmental and non-governmental capacities.

The Schachman Award is given annually, and candidates are considered by the Society’s Public Affairs Advisory Committee. The award consists of a permanent keepsake, an honorarium of \$5,000, an opportunity to deliver a talk or lecture at the Society’s annual meeting, and travel

Dr. Mary Woolley, president, Research!America, will accept the Schachman Award on behalf of the organization at the spring 2007 editorial board meeting.



expenses to the meeting. Past recipients are the Honorable Sherwood Boehlert (2006), Senators Tom Harkin and Arlen Specter (2005), philanthropist and biomedical research advocate John Whitehead (2004), former NIH Director Ruth L. Kirschstein (2003), and the Honorable John Edward Porter (2002).

Research!America, according to its website, “is the nation’s largest not-for-profit public education and advocacy alliance working to make research to improve health a higher national priority. Founded in 1989, Research!America is supported by more than 500 member organizations that represent the voices of more than 125 million Americans.” Its public opinion polls, advocacy programs, and publications reach the public and decision makers to help advance medical and health research.

Research!America’s member organizations represent stakeholders in basic, behavioral, biotech, clinical,

health services, prevention and public health, and therapeutic research from both the public and private sectors. Research!America provides a voice for strong, increased investment in the National Institutes of Health and Centers for Disease Control and Prevention as well as growth in the research investment of the Agency for Healthcare Research and Quality and the National Science Foundation.

The organization has been gauging Americans’ attitudes toward medical and health research for more than a decade. It also works to raise awareness of the importance of effective collaboration among the nation’s government, industry, academic, and philanthropic research sectors.

To learn more about Research!America, visit its website at www.researchamerica.org.

ASBMB Today congratulates Research!America and looks forward to many more years of collaboration on health research advocacy. ∞

An Interview with Toni Scarpa

The following are questions posed to Dr. Toni Scarpa, director of the NIH Center for Scientific Review, by ASBMB President Heidi Hamm.

The ongoing reorganization of NIH study sections seems to be nearing completion. How is the new structure working out, and do you foresee any further changes or reorganizations in the near future?

The reorganization of our Integrated Review Groups (IRG) and their respective study sections was a major effort for NIH and the scientific community. The significantly positive effects include the facts that it (1) realigned peer review with changes in science by making the study sections broader, (2) removed “entitlements” from narrowly focused study sections, and (3) diluted the presence or the appearance of the “old boys’ network.”

Does it work well now? Yes, in many cases. However, a number of study sections were unchanged by the process and remain too narrowly focused, whereas others become far too broad, covering a wide range of scientific areas. As a result, these study sections have become too unwieldy, with up to 70 reviewers.

What are we going to do? In addition to the mandatory external reviews of each IRG every five years, we have taken two very important steps:

(1) Early in 2006, we initiated new rigorous workshops for reviewing one of our IRGs every month, involving CSR leadership and appropriate chiefs and scientific review administrators (SRAs) as well as program staff and members of the study sections. During this review, if problems are identified, they are fixed immediately. If the per-

ceived problems are substantial, we work up a proposal with the scientific community in that scientific area and present a plan to the NIH Peer Review Advisory Committee. For instance, we created one new study section after conversations with several ASBMB members.

(2) In 2007, we will hold six open house workshops focused on our scientific review areas. Leaders from professional societies and disease groups and study section chairs will be invited to participate. There will be many opportunities for them to provide input on whether specific areas of science are being appropriately reviewed and to discuss possible alternatives.

NIH is moving toward an electronic submission process for all grants. Tell us about electronic reviewing. What are your plans for this?

By February 2007, the majority of NIH grant applications will be submitted electronically. This is a major step, which is overdue and highly desirable. However, just receiving applications electronically doesn’t save time for us. We must change what we do after the application is received to save time and resources. Thus we are reengineering the system. A major goal is to automatically assign applications directly to IRGs and study sections using text fingerprinting and artificial intelligence software. Preliminary pilots using this technology have been very promising, so we plan to be fully operational by June 2007. This will save several weeks in the review process.

Will study sections continue to have to meet face to face, or will real time “meetings” over the Inter-

net be a viable alternative? The idea of “chat rooms” has been raised to facilitate meetings without actually having to travel to Bethesda for regular study section meetings. This and other examples of using modern communications tools might make study section service less of a burden and thus encourage more participation. Can you tell us about your plans in this regard?



Dr. Toni Scarpa

Image courtesy of the NIH

Face-to-face study section meetings have been synonymous with NIH peer review and have served the scientific community and the American people incredibly well. Unfortunately, because of the increased pace of science and the decreased number of applications that reviewers are willing to review, our study sections have become increasingly large, with about 50 reviewers, of which only ~20 are chartered members. The result is a dilution of the good chemistry found in the original study sections.

There is no plan to abolish face-to-face meetings. The plan, already in motion, is to provide additional review platforms. We are having some success with video enhanced reviews, using mini-cameras and associated software, and also with asynchronous electronic reviews, using secure online discussion (chat) boards. The review process for both is much the same: the reviewers review their applications and post preliminary scores and critiques online. The difference is that, instead of traveling to a meeting, they discuss the applications on camera or on a secure Web site after 2-3 days.

Why are we doing it? It is not so much to save costs (the technology is very costly). We are pursuing these alternatives to better our ability to recruit the best reviewers, since many are unwilling to come to Washington for 2-3 days three times a year. So far, using these new platforms has increased our ability to recruit clinical colleagues (especially in surgical specialties) and others. We have carried out several dozen pilot experiments, and it is clear that both platforms have great potential and have been very well received by certain groups (e.g. physicists.)

What is the best review platform? Clearly, in my view, the best platform is the one that allows us to recruit the best reviewers for a particular study section. After all, our reviews are only as good as our reviewers are. I thus think our duty is to provide our reviewers with different kinds of review platforms so that each group can find the one that is most effective.

A recent member survey we conducted revealed many questions and concerns about the review process. One item we are wondering about is a shorter, more standardized application. Are there any plans for moving toward this? This might help expedite the review process.

Yes. I have read the survey and note that other societies are requesting shorter applications for R01, R21, and fellowship funding. Indeed, many have pointed out that our R01 application is 2-5 times larger than those used by similar funding institutions in the United States and abroad.

At CSR, a major driver is the desire to recruit and retain the best review-

ers. At the moment, we are using 18,000 a year, and the large majority of these reviewers are ad hoc reviewers. On average, a reviewer spends over 7 hours just to read an R01 application. If the application were shorter, reviewers will be encouraged to review more in the same time span they dedicate to us. Hence, we will use fewer reviewers, the study sections will have fewer reviewers, and we could be more selective in recruiting ad hoc reviewers. Another advantage of a shorter application is that it could be focused more on significance and impact and less on experimental detail.

We have established a new NIH committee to consider a shorter R01 application. Both our advisory committee and the NIH Director's Leadership Forum have given their unanimous and enthusiastic support for this effort. A request of information was posted in the NIH Guide¹, seeking input from the scientific community. During the first 3 days, NIH received 1,200 responses, with 80 percent of them in favor of shortening the application.


Shortening the R01 application would have a major cultural effect on applicants and reviewers; hence, your input is welcomed and appreciated.

Another alternative for expediting the process might be increasing the number of reviewers. We have come up with a list of hundreds of ASBMB members who have expressed a willingness to serve on study sections and are curious as to when or if you plan to begin taking advantage of this spirit of volunteerism among at least some ASBMB members.

Yes, we have been asking societies to submit lists, and we have gratefully accepted 20 so far. We are setting up a clearing house office just to handle, distribute, and track the wonderful volunteers who are stepping forward to help us. So we are very, very grateful.

Are there other issues you would like to discuss with our membership?

One that may be of interest to your membership is that we are making progress in shortening the time² between application submission and the posting of scores and summary statements. As many may know, we are conducting a pilot where over 600 new investigators who submitted applications in February 2006 were eligible to reapply for the next review round in July rather than wait until November. The pilot is ongoing, but the preliminary data are very encouraging. Fourteen percent of these researchers took advantage of the shortened cycles to reapply in the next round, saving four months. We are still collecting and examining the data. If all goes well, we will offer this option to all new investigators and then to all R01 applicants. This should be possible since once most all NIH applications will be submitted electronically as of February 2007.

Ultimately, it would be important to provide our first response (scoring and reviews) no later than four months from the date of application. 

¹ Request for Information (RFI): Possible Page Limit Reduction For the Research Plan Section of the Research Project Grant (R01) Application, NIH Guide, Nov. 9 2006: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-014.html>

² <http://cms.csr.nih.gov/NewsandReports/ShortCycle.htm>

Micro Molecules Contribute Mightily to Heart Problem

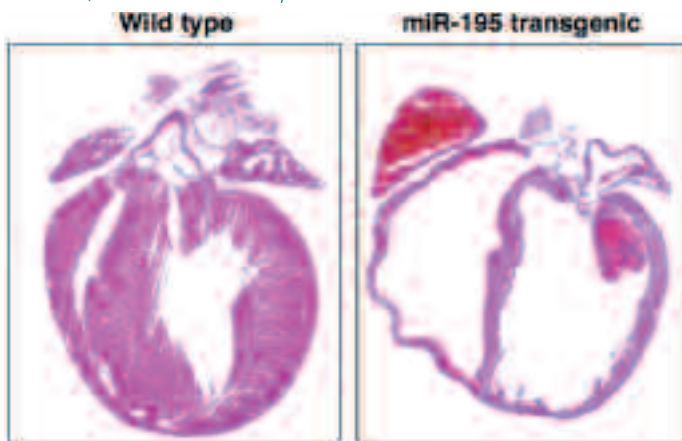
Researchers at the University of Texas Southwestern Medical Center have discovered that tiny bits of RNA play a large role in causing enlargement of the heart, which is a major risk factor for heart failure and sudden death.

Their findings, published in the November 28 issue of the *Proceedings of the National Academy of Sciences*, are part of a fast growing research field revealing the importance of micro ribonucleic acids, or miRNAs, in numerous bodily functions, including cancer, cell death, and cell growth.

"They [miRNAs] haven't been studied for very long," said Dr. Eric Olson, senior author of the study. "These particular micro RNAs aren't just markers of heart failure. They're actually able to cause the disease, at least in mice. This is the first evidence for the involvement of micro RNAs in adult heart disease."

Eventually, manipulating micro RNAs might be a way to treat heart disease, the researchers reported. A micro RNA can be blocked with a short complementary fragment of genetic material engineered to attach to RNA and neutralize it.

Heart from wild type mouse and transgenic mouse with over-expression of miR-195, which causes heart failure.



ASBMB member Eric N. Olson attended Wake Forest University and received a B.A. in Chemistry and Biology in 1977, a Ph.D. in Biochemistry in 1981, and an honorary doctorate in 2003. After postdoctoral training at Washington University School of Medicine, he joined the Department of Biochemistry and Molecular Biology at The University of Texas M. D. Anderson Cancer Center in 1984 and became professor and chairman in 1991. In 1995, he founded the Department of Molecular Biology at The University of Texas Southwestern Medical Center at Dallas. He holds the Robert A. Welch Distinguished Chair.

Olson's honors include the Basic Research Prize and Founding Distinguished Scientist Award from the American Heart Association, the Pasarow Medical Research Award in



Dr. Eric N. Olson


Cardiovascular Disease, the Gill Heart Institute Award, the Lucian Award for Research in Cardiovascular Disease, the Outstanding Investigator Award from the International Society for Heart Research, and the Pollin Prize in Pediatric Research. He is a member of the American Academy of Arts and Sciences, the National Academy of Sciences, and its Institute of Medicine. Olson served as editor-in-chief of *Developmental Biology* from 1995 to 2005 and belongs to numerous editorial boards.

The process of identifying the damage-causing micro RNAs started with the researchers investigating whether any micro RNAs were present at abnormal levels in diseased, enlarged hearts of mice. They found 28 such micro RNAs

and focused on 16 that were similar to those found in humans and rats. The researchers found that some of the same micro RNAs are present at abnormal concentrations in diseased human hearts, suggesting that these micro RNAs also play a role in human heart disease.

Olson's team eventually zeroed in on one micro RNA, called miR-195, which had both visible and functional effects on the heart. These effects were established by creating genetically modified mice that had higher than normal amounts of miR-195. Those mice had misshapen hearts and decreased pumping power.

In addition, adding miR-195 to heart cells cultured in dishes made the cells larger and more disorganized.

Because some of the micro RNAs studied are known to be involved in other cell processes, the researchers speculate that these particular RNAs play a role in cell division or growth of heart muscle cells. Further research is needed to determine the mechanism by which miR-195 causes the heart to enlarge, Olson said. 

New Year's Resolutions and Challenges

By Dr. J. Ellis Bell

What are the goals of education in the molecular life sciences? What are the responsibilities of scientists and educators? Aren't we all educators in one sense or another, whether we are on the faculty in a medical center, in the Chemistry or Biology Department of a small college in the Midwest, working in a drug company, or we are a patent lawyer or science writer, or even a merchant banker or real estate agent? Hopefully if you studied biochemistry and molecular biology in college, you have a lifelong fascination with how cells work, whether they are plant, animal, or bacterial. Biochemistry may have had its roots in bread and beer, but in today's world it can fairly claim a central position in every aspect of the life sciences, and increasingly in nanotechnology. In the past several decades biochemistry and molecular biology have surpassed chemistry as the second most popular undergraduate degree in science in many institutions. Not because it's an "easy" degree to obtain (with its combination of both biology and chemistry with a sound basis in math and physics its far from "easy"), but because it's a fascinating topic that almost anyone can relate to at some level. It is largely because of this ability for people to relate to issues in the life sciences that makes it such a powerful vehicle for education, which in turn makes it so important that all of us in the molecular life sciences are constantly aware of our responsibilities as educators.

Everyone talks about the crisis facing the country in science education—not enough students are being trained (educated—are these terms really interchangeable?) in the sciences, not enough students are going on into the workforce with scientific training, not enough students pursue science degrees, there is not enough diversity in the profession, the general public is

perceived as being scientifically illiterate and susceptible to pseudo-science. The funding agencies and principal investigators worry about why legislators don't understand the need for increased budgets.

Whose responsibility is it to educate people in the life sciences? I'm pretty sure it is the job of the faculty in the various colleges and universities that offer degrees in biochemistry and molecular biology to educate both undergraduate majors in these areas and the remainder of the student body (through general education courses etc.), but whose job is it to educate the rest of the population—the K–12 students, the folks who managed to go through college without taking a course in biochemistry, those who went to college before biochemistry and molecular biology became so popular, those who didn't go to college, those who don't keep up with the literature and don't know how exciting the times are in this discipline? I suggest that it is our job, the job of each and every one of us that call ourselves biochemists or molecular biologists. It is our job to be aware of the need to continually educate/excite the public about our discipline—why we do the science, what it takes to do the science, and to explain what the rewards are of doing the science or understanding the science. It is our job to get involved with outreach: to the K–12 school system, to under-represented minorities in the profession, to the general public and to the students in our labs and classrooms, whatever their goals in life.

In response to the crisis discussed above, in the coming year the American Society for Biochemistry and Molecular Biology, through its Education and Professional Development Committee, will be promoting and supporting action on a number of fronts. In *ASBMB Today*

each month there will be articles related to these issues to, we hope, provide examples of how every institution and every individual member of the Society can help. These articles will range from how to start a biochemistry and molecular biology club or program in K–12 or college to how to prepare for various careers that use the skills and knowledge that come from training in the life sciences. In between there will be articles about steps each and every one of us can take to help broaden participation, reach out to more students (at every level of their education), as well as highlights of successful programs around the country.

The Challenge: To remember that every generation of students we train may have a quite different set of career aspirations than we have, but the theme that unites us is our excitement about the life sciences and that for the long term future of the science we must educate not only ourselves but our students to be involved with outreach to the public in general—as researchers, we talk about being life-long learners, as responsible scientists we must also be life-long educators.

The New Year's Resolution: In addition to the inevitable "lose a few extra pounds" my resolution is to spend a little less time "teaching" and a little more time "educating": we tend to assess our effectiveness by how many facts we teach people rather than how many things they end up understanding. If we want people to value what we "teach" them we must take the time to make sure they really understand it. In the age of information technology, facts are a dime a dozen: education is about appreciating and understanding those facts, where they came from, what they can tell us, and how they can lead to new understanding in the future. We need to change the way we assess what our students are learning! 🎯

Biomedical Careers in Industry:

By Robert A. Copeland, Ph.D.

In part 1 of this series we discussed the differences between academic and industrial science that one is likely to encounter in making the transition between these two environments. We also presented a summary of the key skills that are highly valued in the industrial sector and which are looked for in potential job candidates. One of the overarching themes that was presented is that industrial science, at least in the pharmaceutical industry, is a highly collaborative venture, requiring scientists of diverse expertise to come together as a project matrix team. This reflects the complexity of the drug discovery and development process, which requires very different scientific and medical expertise at different points in the process; this is summarized in the drug discovery roadmap, illustrated in Figure 1.

In this second part of the series we shall discuss some of the frequent misconceptions that students and other academic scientists often have about scientific careers in industry. We end this series with some general comments on finding happiness and fulfillment in one's professional life.

Frequent Misconceptions about Industry

When I speak with students and postdoctoral researchers who are considering an industrial career I often encounter some common misconceptions about industry. Let me set the record straight here by addressing some of the more common of these misconceptions.

Scientists in industry have no freedom to work on their own

ideas. This could not be further from the truth. Industry seeks to hire bright and motivated people who will be the source of new ideas and directions for the company. No one today, in any employment sector, has unfettered freedom to work on projects that cannot be justified. In academic settings, research must be funded, usually through government sources. Thus, academic researchers must convince funding agencies of the value of their proposed research. Likewise, ideas for projects in industry must be funded by management, and it is up to the scientist to justify this investment of resources by showing the value of their proposed research to the company. In both sectors, good ideas get resources, and clever people find creative ways to work on interesting and germane research topics.

Industrial scientists can't publish or otherwise obtain external recognition for their work. It is true that companies must maintain their competitive advantages over competitors, and sometimes this means keeping certain information out of the public domain, at least temporarily. In the pharmaceutical industry, for example, the chemical structures of drug candidates are not usually disclosed until late in development (i.e. during clinical trials) or when the drug is brought to market. Most other information is considered less proprietary and is typically published at some point by industrial scientists. Most companies encourage their scientists to publish and otherwise communicate their work to the external community. This proves to be very beneficial to the morale of their creative scientific staff.

Publishing, however, is not encouraged merely to benefit individual scientists. The company also benefits from such external communications by showcasing the high quality work of its employees. This helps to bolster the overall reputation of the company, helping in recruiting future employees, garnering favor with potential investors, and generally enhancing the scientific credibility of the company.



There are no opportunities for teaching/mentoring in industry.

Having been in both the academic and industrial settings in my own career, I can honestly say that I do far more teaching and mentoring as an industrial scientist than I ever did as a full time faculty member. In industry, teaching and mentoring are not separate job functions, but are integral parts of doing research within the context of project matrix teams. Beyond this, anyone with any supervisory responsibility is expected to mentor, both scientifically and in terms of career guidance, those who report to him or her. Teaching and mentoring is a daily activity of successful scientists in industry. This does not take place in a traditional classroom, but it is a real and valued part of our profession.

Career advancement in industry requires moving out of the laboratory and into management.

Scientists who demonstrate talents in supervising others and in managing science can advance their careers in industry by moving into a manage-

A Few Tips for the Newcomer (Part 2)

ment track. This, however, is not the only means of career advancement and fulfillment within the industrial sector. Most companies, at least within the pharmaceutical industry, offer dual career ladders, allowing talented individuals to advance either along a management or scientific track. Professional fulfillment does not always require a change in job title or responsibilities. One can also grow a career by continuing to expand the repertoire of skills and experiences one has within a particular job title (i.e. growing in breadth rather than in a hierarchical, linear fashion). Whether one chooses an industrial or other career path, eventually one is likely to make the transition from being in the laboratory, conducting experiments with one's own hands, to supervising those who do the actual laboratory work. Faculty members in academics function as managers of science, although they seldom are referred to by such titles. Think about your own academic experience; how often have you seen a full professor working at the bench? Progression from the laboratory to some form of management is an almost inevitable consequence of success in science.

Some general advice

My focus in this brief article has been to clarify the role of biomedical scientists in the industrial sector. I have personally found great fulfillment in applying my own scientific talents to the pursuit of new medicines within the pharmaceutical industry. I believe this industry offers many exceptional opportunities for those who want to contribute to human health. Others

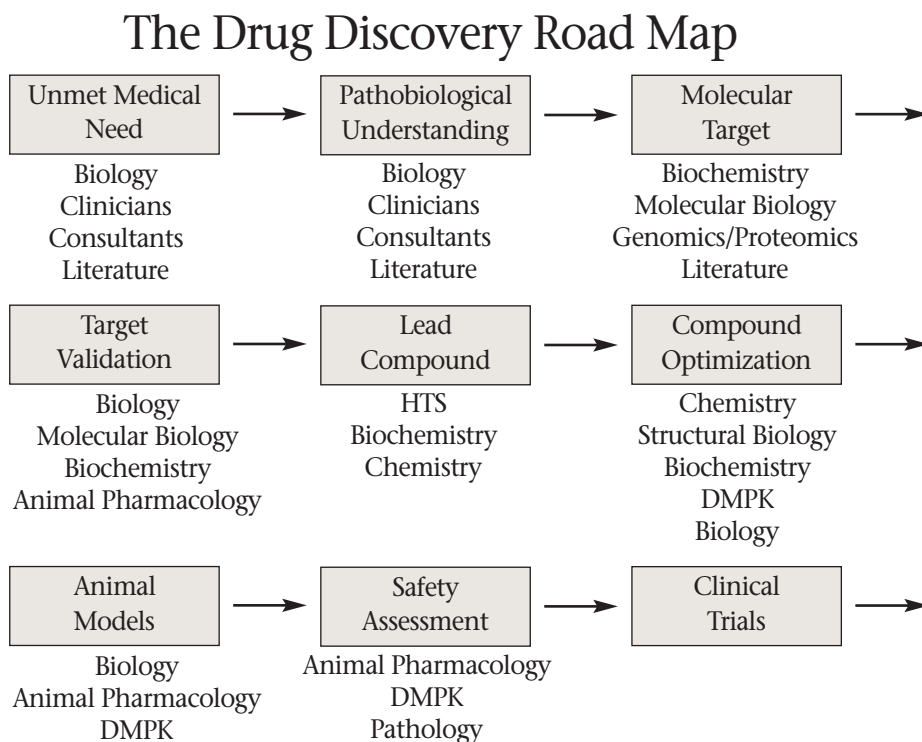


Figure 1: The Drug Discovery Roadmap, illustrating the different stages of a drug discovery project and the different expertise required by the project matrix team at each of these stages.

will find different paths to professional fulfillment in teaching, academic research, government service, and other venues. Whatever your individual professional path, however, I believe there are some universal keys to career happiness. I will close this article by offering some key points that I have found useful to remember in my own career:

Work in an atmosphere that you find comfortable.

Make sure your value system is not incompatible with that of your employer.

Balance career with other life needs (e.g., family, hobbies, etc.).

Know what you want out of life, and seek employment that provides a path to your goals.

Identify role models and seek them out as mentors.

Be adaptive to change.

Be a problem solver, not an expert on a specific method or area.

Commit to life-long learning.

Always remember that your career is in your own hands.

Don't look to others to advance your career – be proactive.

Distinguish yourself at the job and externally.

Network with talented people. ☞

Robert A. Copeland, Ph.D., is vice president of Enzymology and Mechanistic Pharmacology at GlaxoSmithKline Pharmaceuticals. He is also an adjunct professor in Biochemistry and Biophysics at the University of Pennsylvania as well as an ASBMB Council member. Copeland can be reached at robert.a.copeland@gsk.com.

Nanotech Tools Yield DNA Transcription

Rutgers University researcher Richard H. Ebright and his collaborators have solved one of the longstanding mysteries surrounding DNA transcription. The breakthrough, described in two articles in the November 17 issue of the journal *Science*, reveals important structural information about the gyrations of DNA during transcription and the effects of those gyrations on the process.

Transcription is carried out by RNA polymerase, which synthesizes an RNA copy of DNA. The papers by Ebright and collaborators define, for the first time, the mechanism by which RNA polymerase begins synthesis of RNA and the mechanism by which it breaks free from its initial binding site and moves along DNA to continue synthesizing RNA.

The results establish that, during transcription initiation, RNA polymerase remains stationary at its initial binding site and “reels in” adjacent DNA segments, unwinding the segments and pulling the unwound DNA strands into itself. This mechanism, termed “DNA scrunching,” enables RNA polymerase to acquire and accumulate the energy it needs to break its binding interactions with the initial binding site and to begin to move down the gene.

“Our findings were made possible by newly developed single-molecule methods,” said Ebright. “These methods enabled us to analyze and manipulate individual molecules of the machine, one by one, as they carried out reactions.”

The discoveries, which significantly advance our understanding of the structure and function of RNA polymerase, set the stage for new opportunities to combat bacterial diseases.

“For six decades, antibiotics have been our bulwark against bacterial infectious diseases, but this bulwark now is collapsing,” said Ebright. “For all major bacterial pathogens, including tuberculosis, strains resistant to current antibiotics have emerged.”

Ebright explained that his laboratory at Rutgers’ Waksman Institute of Microbiology has two parts. One part seeks to understand RNA polymerase; the other part uses that understanding to develop new classes of antibacterial agents that function by inhibiting bacterial RNA polymerase. “There is a direct information flow from our basic research to our applied research,” he said. “Our basic research identifies new vulnerabilities within the bacterial version of the machine; our applied research exploits those vulnerabilities.”

One of the studies reported in *Science* was conducted by Ebright’s laboratory in conjunction with Shimon Weiss’ laboratory at the California NanoSystems Institute of the University of California-Los Angeles (UCLA). The study by the Rutgers/UCLA team used single-molecule fluorescence spectroscopy. The researchers attached pairs of fluorescent tags to key structural elements of RNA polymerase and then monitored changes in distance between tags in single molecules of RNA polymerase as transcription occurred. The researchers showed that, during initial transcription, RNA polymerase does not move to

reach adjacent DNA segments and does not stretch to reach adjacent DNA segments (as had been proposed two decades ago in models termed “transient excursions” and “inchworming”). Instead, the researchers showed that RNA polymerase remains stationary and pulls adjacent DNA segments into itself.

The other study reported in *Science* was conducted by Ebright’s laboratory in collaboration with Terence Strick’s laboratory at the Institut Jacques Monod in Paris. The study by the Rutgers/Paris team used single-molecule nanomanipulation. The researchers used “magnetic tweezers” to hold, stretch, and twist a single molecule of DNA having a single start site for transcription. They then read out changes in the conformation of the DNA molecule, in real time, as transcription occurred. The researchers showed that the RNA polymerase unwinds adjacent DNA segments and pulls unwound DNA into itself during initial transcription (“scrunching”). In addition, the researchers showed that RNA polymerase re-winds this unwound DNA when it leaves the start site and begins to move down the gene

Richard H. Ebright, Ph.D., is an investigator of the Howard Hughes Medical Institute, laboratory director at the Waksman Institute of Microbiology, and professor of Chemistry and Chemical Biology at Rutgers University. His research focuses on




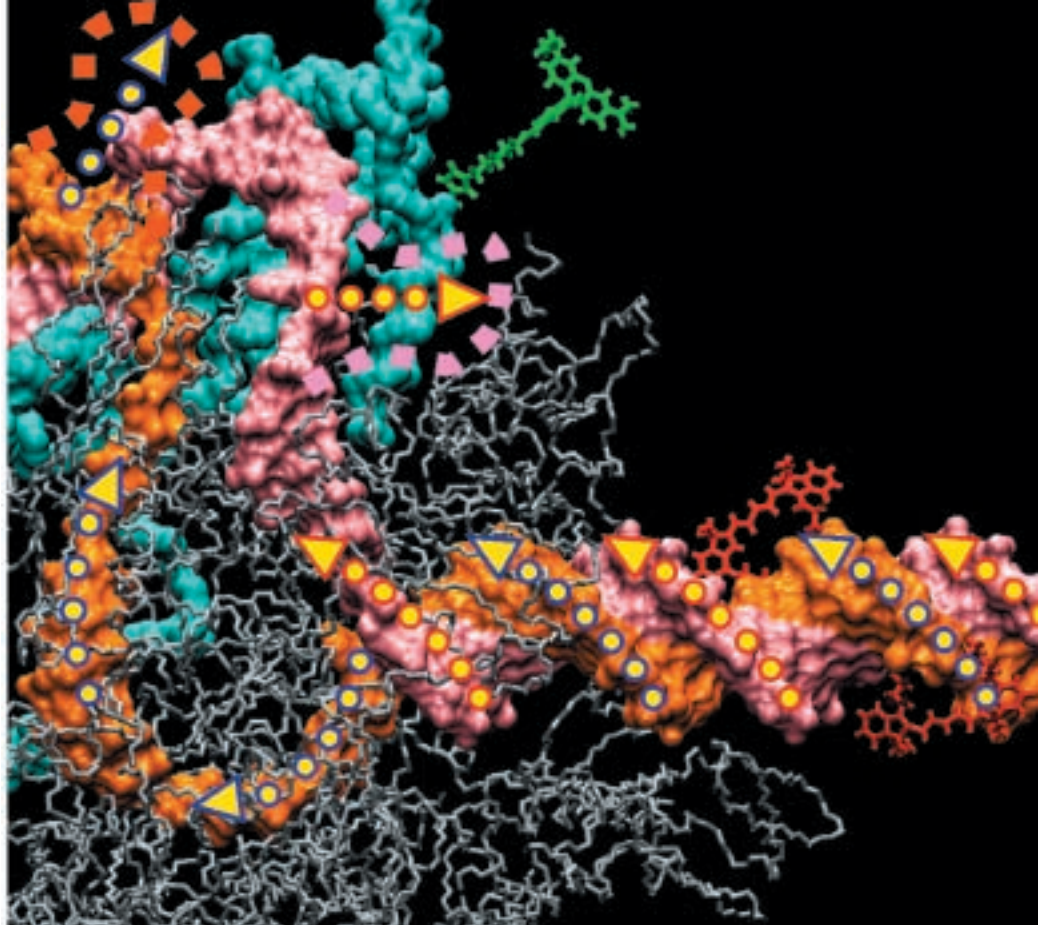
Dr. Richard H. Ebright is a Junior Fellow of the Harvard University Society of Fellows. He has received the Searle Scholar Award, the Schering-Plough Award of the American Society for Biochemistry and Molecular Biology, and the Walter J. Johnson Prize. He is a Fellow of the American Association for Advancement of Science and of the American Academy of Microbiology.

scopy, single-molecule spectroscopy, and single-molecule nanomanipulation techniques. Ebright received his A.B. and Ph.D. degrees from Harvard University. He performed graduate research at Harvard and the Institut Pasteur and was a

Breakthrough

("unscrunching"). Finally, the researchers showed that this process of scrunching and unscrunching occurs every time that transcription initiation occurs, indicating that the process is an obligatory part of transcription initiation.

Taken together, the two studies answer the longstanding question of how RNA polymerase acquires the energy required to break its interactions with, and leave, the start site. It acquires this energy by unwinding DNA and pulling unwound DNA during initial transcription. As DNA is unwound, energy is stored in the system, in the same manner, Ebright notes, as winding the rubber band of a rubber-band-powered airplane stores energy. Eventually, there is sufficient energy stored in the system that RNA polymerase is able to break its interactions with the start site, to shoot forward, and, at the same instant, to rewind the unwound DNA. 



Initial transcription by RNA polymerase proceeds through a "DNA scrunching" mechanism, in which the enzyme remains stationary on promoter DNA and pulls into itself downstream DNA. Image provided by Achilles Kapanidis, Shimon Weiss, and Richard H. Ebright.



APPOINTMENTS FOR RESEARCH & POSGRADUATE STUDY FREE RADICAL & ANTIOXIDANT BIOLOGY



Applications are invited from fresh PhD graduates or experienced post-doctoral scientists to join Professor Barry Halliwell's research team in the area of free radical and antioxidant biology (http://medicine.nus.edu.sg/bioweb/acad_staff/barry_halliwell.html). Current projects include:

- 1) Determination and evaluation of specific biomarkers of oxidative stress in human studies
- 2) The role of metals and oxidative damage in atherosclerosis and neurodegenerative diseases
- 3) Basic mechanisms of ageing- the importance of oxidative damage and the impact of antioxidants
- 4) Isolation, development and therapeutic use of natural antioxidants.

The Department of Biochemistry has teaching commitments to medical, dental and science students. There are three major research interests in the Department namely Neurobiology, Molecular and Cellular Mechanisms underlying Human Diseases and Molecular Mechanisms of the action of toxic agents. Within these areas, we are particularly anxious to strengthen the area of Oxidant and Antioxidant Biology. The Department has a strong research tradition and active collaborations with other research institutes in Singapore and with many leading Universities worldwide. Prof Halliwell's group is located in excellent purpose-built accommodation on the Neurobiology floor at the new Centre for Life Sciences building (<http://www.ols.nus.edu.sg/index.shtml>). Salary ranges are as follows:

- 1) Research Fellow (B) : S\$3,400 to S\$7,050 per month (all-inclusive)
- 2) Research Fellow (A): S\$4,000 to S\$7,910 per month (all-inclusive)

(Travel Assistance/Settling-in Allowance and housing allowance may be given at the discretion of the Principal Investigator).

Interested parties should submit their applications, supported by a resume and names of three external referees to:

Professor Barry Halliwell, Department of Biochemistry, Yong Loo Lin School of Medicine, National University of Singapore
8 Medical Drive, MD7 #02- 03, Singapore 117597, Fax: (+ 65) 6775 2207, E-mail: bchbh@nus.edu.sg. Only shortlisted candidates will be notified.

The research group also has space for well-qualified undergraduates to undertake PhD programmes with generous scholarship funding (<http://www.nus.edu.sg/ngs/index.shtml>).

Aebersold, Nissen, Elected to EMBO

Ruedi Aebersold of the Swiss Federal Institute of Technology and Poul Nissen of the University of Aarhus in Denmark are 2 of the 49 new members elected to the European Molecular Biology Organization (EMBO).

EMBO elects new members annually on the basis of scientific excellence. Its membership comprises over 1,200 of the world's finest researchers. The lat-

est scientists to join the fold come from 14 different countries and represent a broad cross-section of the molecular life sciences community. 44 of the new members are based in Europe, while 5 distinguished scientists from the USA and China receive the special honor of associate membership.

Aebersold is one of the pioneers in



Dr. Ruedi Aebersold

the field of proteomics and is known for developing a series of methods that have found wide application in analytical protein chemistry and proteomics. Nissen's research focuses on the structure of cellular proteins connected with protein synthesis and transport across the membrane.



Dr. Poul Nissen

Steitz Receives Keio University Medical Science Prize

Thomas A. Steitz, investigator at the Howard Hughes Medical Institute and Sterling Professor of Molecular Biophysics and Biochemistry at Yale University, received the 11th Keio Medical Science Prize in a ceremony and commemorative symposium on November 1, 2006, at Keio

University in Tokyo, Japan.

The award, given to researchers in recognition of their outstanding achievements in the fields of medical or life sciences, is the only prize of its kind awarded by a Japanese university. Steitz will receive a certificate of merit, a medal, and 20 million yen (approximately 173,706 American dollars).

Steitz was honored for determining the high resolution crystal structures of the large ribosomal subunit and its substrate complexes, giving structural

insights into the mechanism by which it synthesizes polypeptides using only RNA. From this work, he and his collaborators established the structures of several antibiotics in complex with the large ribosomal subunit and showed how these antibiotics stop peptide synthesis.



Dr. Thomas A. Steitz

Lindquist, Morse, and Young Part of *Scientific American* Top 50

Susan L. Lindquist, Daniel E. Morse, and Richard A. Young have been named to the 2006 "*Scientific American* 50," the magazine's annual list of individuals, teams, companies, and other organizations whose accomplishments demonstrate outstanding technological leadership. The list, selected by the board of editors of *Scientific American*, appeared in the magazine's December issue.

Lindquist and Young are both professors at the Massachusetts Institute of Technology and members of the

Whitehead Institute for Biomedical Research. Lindquist was named to the *Scientific American* 50 for her discovery that prions play a critical role in maintaining a class of adult stem cells that produce mature blood cells. Young and postdoctoral fellow Laurie A. Boyer were both cited for recent work in which they analyzed the genomes of human embryonic stem cells and identified key molecules responsible for the cells' unique attributes.

Morse is a professor of molecular



Dr. Susan Lindquist



Dr. Daniel E. Morse



Dr. Richard Young

genetics and biochemistry and director of the Institute for Collaborative Biotechnologies (ICB) at the University of California, Santa Barbara. He was recognized for putting molecules that mimic the enzymes of marine sponges onto gold surfaces to create catalytic templates for growing semiconductor films.

George C. Hill Becomes Chair of Minority Affairs Committee

Recently, George C. Hill, Ph.D., was appointed the new chair of ASBMB's Minority Affairs Committee (MAC). He assumed this position when Dr. Juliette B. Bell stepped down in April 2006. The mission of the MAC is to increase cultural diversity in the fields of biochemistry and molecular biology by increasing participation, visibility, and status of minorities within ASBMB. Members of the Committee are appointed by the president of the ASBMB for three-year terms.

Hill is currently a professor in the Department of Microbiology and Immunology and the Levi Watkins, Jr. professor and associate dean for Diversity in Medical Education at the Vanderbilt University School of Medicine. Hill received his Ph.D. from New York University when working on the electron transport systems in African trypanosomes with Dr. Seymour Hutner. He was an NIH Research Fellow at the University of Cambridge in 1972 prior to joining the faculty at Colorado State University, where he established a pioneering research program on the molecular biology and biochemistry of differentiation in African trypanosomes. In 1983, Hill joined the

faculty at Meharry Medical College, where he served as the director of the Division of Biomedical Sciences, dean of the School of Graduate Studies and Research, and vice president for Sponsored Research while continuing his research. He was elected a member of the Institute of Medicine of the National Academy of Sciences in 1998 and a Fellow of the American Academy of Microbiology in 2002. He was selected a "Giant in Science" for his efforts to motivate minority students into biomedical research.



Dr. George C. Hill



Faculty Appointments



The National University of Singapore invites applications for full-time tenure-track Assistant Professor and tenured Associate Professor/Full Professor appointments in the Department of Biochemistry.

The Department of Biochemistry has teaching commitments to medical, dental and science students and has an active postgraduate research programme. There are three major research interests in the Department namely Neurobiology, Molecular and Cellular Mechanisms underlying Human Diseases and Molecular Mechanisms of the action of toxic agents. Within these areas, we are particularly anxious to strengthen the area of Oxidant and Antioxidant Biology. The Department has a strong research tradition and active collaborations with many research organizations in Singapore and worldwide. The Department has excellent facilities for research in biochemistry and molecular and cell biology and competitive grant funding for excellent projects and programmes is easy to obtain.

We are looking for outstanding faculty members who possess a PhD degree, or an approved basic medical degree with a recognized higher academic/professional qualification, with track record of high calibre, self-directed research, preferably in the areas listed above. However outstanding applicants in other areas are welcome to apply.

All faculty members are expected to teach undergraduate and/or graduate courses (although new appointments have a very light teaching load to allow them to establish their research programmes), supervise graduate students, and conduct vigorous research programs that generate external funding and scholarship and intellectual output typical of that of a world-class university.

Interested parties should submit their applications, supported by a resume, detailed research plan and names of three or more external referees to:

HEAD, Department of Biochemistry, Yong Loo Lin School of Medicine
National University of Singapore, 8 Medical Drive, MD7 #02- 03
Singapore 117597, Fax: (+ 65) 6 779 8842
E-mail: bchhead@nus.edu.sg

Only shortlisted candidates will be notified.

By Nicole Kresge

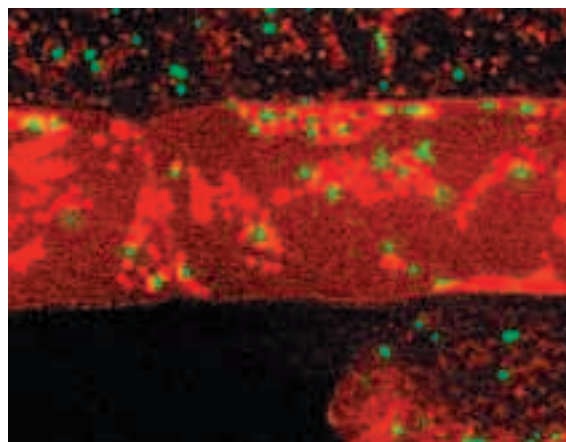
ASBMB Bio Bits

Identification of a Peroxisomal Acyl-activating Enzyme Involved in the Biosynthesis of Jasmonic Acid in Arabidopsis

Abraham J. K. Koo, Hoo Sun Chung, Yuichi Kobayashi, and Gregg A. Howe

J. Biol. Chem. 2006 281: 33511-33520.

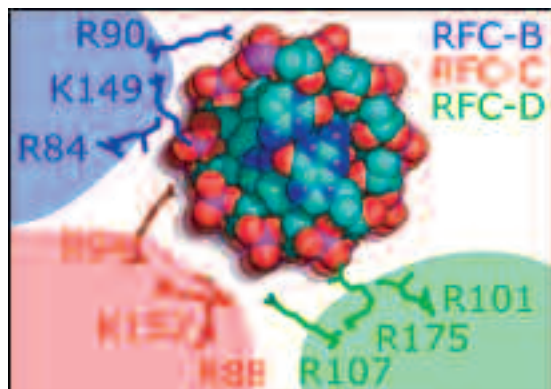
Jasmonic acid is a signaling molecule that regulates a wide range of developmental and defense-related processes in higher plants. It is synthesized from linolenic acid via an enzymatic pathway that begins in the plastid and terminates in peroxisomes. In this paper, the authors use co-expression analysis to identify genes that are coordinately regulated with known jasmonic acid biosynthetic components in *Arabidopsis*. Among the candidate genes uncovered by this approach is a 4-coumarate:CoA ligase-like member of the acyl-activating enzyme gene family that the authors named OPC-8:0 CoA Ligase1. Using a combination of genetic, biochemical, and cellular evidence, they show that OPC-8:0 CoA Ligase1 is involved in peroxisomal jasmonic acid biosynthesis. These findings establish a clear physiological role for OPC-8:0 CoA Ligase1 in the activation of jasmonic acid biosynthetic precursors and indicate that OPC-8:0 is a physiological substrate for the activation step.



OPC-8:0 CoA Ligase1 is targeted to peroxisomes.

The Replication Factor C Clamp Loader Requires Arginine Finger Sensors to Drive DNA Binding and Proliferating Cell Nuclear Antigen Loading

Aaron Johnson, Nina Y. Yao, Gregory D. Bowman, John Kuriyan, and Mike O'Donnell

J. Biol. Chem. 2006 281: 35531-35543.

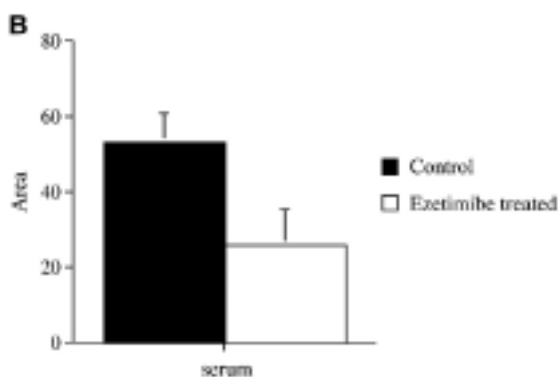
Residues in the central chamber of RFC are required for DNA binding.

During DNA replication, DNA polymerase is tethered to DNA via a clamp, which is placed onto the DNA by a clamp loader. In eukaryotes, the pentameric clamp loader known as replication factor C (RFC) uses energy from ATP binding and hydrolysis to recruit a clamp called proliferating cell nuclear antigen (PCNA), break one clamp interface, and topologically link the clamp to primed template DNA. RFC contains four ATP sites with four associated arginine fingers that sense ATP binding and catalyze ATP hydrolysis. In this paper, the authors mutated the arginine fingers on RFC to determine the role of the fingers and their ATP sites in the PCNA loading mechanism. They show that none of the arginine fingers are needed for PCNA interaction and ring opening. However, their results demonstrate that certain ATP sites on RFC play distinct roles downstream of the PCNA opening.

Ezetimibe Inhibits the Incorporation of Dietary Oxidized Cholesterol into Lipoproteins

Ilona Staprans, Xian-Mang Pan, Joseph H. Rapp, Arthur H. Moser, and Kenneth R. Feingold

J. Lipid Res. 2006 47: 2575-2580.



Epoxy cholesterol levels in serum decrease with ezetimibe treatment.

The typical Western diet contains substantial quantities of oxidized cholesterol. When ingested, oxidized cholesterol is absorbed by the small intestine and then incorporated into lipoproteins, which are more susceptible to further oxidation. There is strong evidence that oxidized lipoproteins play a key role in the pathogenesis of atherosclerosis. In this article, the authors determined the effects of ezetimibe on the levels of oxidized cholesterol in the serum following a test meal containing oxidized cholesterol. Ezetimibe is a recently developed drug that reduces serum and low density lipoprotein cholesterol levels by inhibiting the absorption of cholesterol in the small intestine. The authors found that ezetimibe, at 10 mg per day for one month, markedly reduced the levels of oxidized cholesterol in the serum after feeding a test meal containing either α -epoxycholesterol or 7-ketocholesterol, two of the predominant oxidized cholesterols found in the diet.

Identification and Characterization of New Protein Chemoattractants in the Frog Skin Secretome

Baptiste Leroy, Gerard Toubeau, Paul Falmagne, and Ruddy Wattiez

Mol. Cell. Proteomics 2006 5: 2114-2123

The vomeronasal organ is a chemosensory organ present in most vertebrates and is involved in chemical communication. Snakes possess a highly developed vomeronasal system that is used in various behaviors such as mating, predator detection, and prey selection. In this paper, the authors used a proteomics approach to identify and characterize proteins from the frog cutaneous mucus proteome that are involved in prey recognition by snakes of the genus *Thamnophis*. They purified and characterized two proteins from the frog skin secretome that elicit the vomeronasal organ-mediated predatory behavior of *Thamnophis marcianus*. Both of these proteins belong to the parvalbumin family. Moreover functional studies of these proteins revealed for the first time their presence in a physiological extracellular fluid as well as a $\text{Ca}^{2+}/\text{Mg}^{2+}$ dependence of their chemoattractive properties.




A bioassay in which a lure (cooked macaroni coated with 10 μl of protein sample) is presented to a snake.

Drugmakers to Pay FDA to OK Ads

The U.S. Food and Drug Administration (FDA) has struck a deal with pharmaceutical companies under which the companies would pay the agency fees for vetting their TV advertisements in exchange for speedier reviews. Fees from the proposed agreement would help pay for new staff to be hired by the FDA to review the industry's TV ads.

The agreement would be proposed in tandem with a separate, five-year pact setting new user fees to be paid by drug makers to the FDA when the agency reviews their applications to market new medicines. That agreement is expected to require the industry to pay substantially more money to the FDA, with a large portion going to fund drug safety initiatives.

The deals are not final because FDA's parent agency, the Department of Health and Human Services, has not yet signed off on them. In addition, the agreements must be approved by Congress to take effect. Both would begin in the government's fiscal year 2008, which starts on October 1, 2007.

The FDA is expected to get more than \$300 million in user fees in fiscal year 2007, the last year of the current arrangement. The figure would increase by about one-third in fiscal year 2008 under the proposed agreement. 


Generic Drugs May Gain from Stronger Democrats

The newly empowered Democrats' vow to cut healthcare costs might spell bad news for the brand name pharmaceutical industry but could provide

new momentum for generic drug rivals. Boosting the generics industry may prove to be a politically palatable way to follow up on the party's campaign promises.

Jake Hansen, a vice president at generic drug manufacturer Barr Pharmaceuticals Inc., says that because of the shift in Congress, 2007 could be the most important year to the generics industry since 1984—when Congress passed the law that opened the door to the modern generics business.

Early in November 2006, Barr Pharmaceuticals Chief Executive Bruce Downey said that Democrats might be more likely to pass legislation that sets a path for approval of cheaper copies of biotech medicines, a major priority for generic manufacturers.


A top official at rival generic maker Teva Pharmaceuticals Industries Ltd. said that both parties had become supporters of the less expensive drugs as a means to control rising healthcare costs. 

(Taiwan) China Synthetic in US\$821 Million Drug Royalty Agreement

In the biggest drug royalty agreement ever involving a Taiwanese company, a U.S.-based subsidiary of China Synthetic Rubber reached a 15-year royalty sharing deal valued at up to US\$821 million.

Synpac Inc. of Research Triangle Park, North Carolina, agreed on royalty payments with Genzyme Corp. of Cambridge, Massachusetts, over Myozyme, a drug therapy used to fight Pompe disease. The deal will pay Synpac between US\$423 million and US\$821 million over 15 years, depend-


ing on the success of the drug, China Synthetic said in a statement to the Taiwan Stock Exchange.

The company said Myozyme has received approval for use in the U.S. and Europe. The drug itself consists of the human enzyme acid a-glucosidase (GAA), which is encoded by the most predominant haplotype of the gene, according to Genzyme. 

Novartis Plans Chinese R&D Center

Novartis has unveiled plans to build a \$100 million integrated biomedical Research & Development center in Shanghai's Zhangjiang Hi-Tech Park. The center will become an integral part of the Novartis global research and development network.

The new facility will focus initially on the infectious causes of cancer endemic in China and Asia. It will also work to combine Western technology and drug discovery approaches with those of traditional Chinese medicine.


Scientists will initially work in a 5,000-square-meter start-up facility that is expected to open in May 2007. Construction of a permanent 38,000-square-meter facility for approximately 400 scientists will begin in July 2007. 

Pfizer Drug Snag Could Cause Delays for Others

The failure of Pfizer's much anticipated drug torcetrapib, intended to increase high density lipoprotein cholesterol levels, is likely to invite greater scrutiny of all new heart drugs and could delay for at least five years the introduction of other drugs in the

same class. Also, analysts predict Pfizer will make more job cuts and push for more merger and licensing deals as a result.

The world's largest drug maker said that it was ending development of torcetrapib, its experimental drug to raise "good" cholesterol, after increased deaths and heart problems were found among patients taking the drug in a late stage trial.

Pfizer is expected to rev up its acquisition efforts to plug the hole left by torcetrapib, which Pfizer had said had the potential to become as big a drug as Lipitor, the world's top-selling medicine with annual sales approaching \$13 billion. 


Biotech Companies Enter New Era with More Products

With about 300 medical products on the market and nearly 400 more in late stage tests, Northern California biotechnology companies are on the cusp of a commercial explosion, according to a report by the industry group BayBio.

But competition from other states and countries where it is cheaper to operate with fewer government regulations could woo many local companies elsewhere, according to several experts.

"We are starting to see part of a brain drain" of Bay Area biotechnology talent heading to Singapore, China, India, and other nations, warned Dr. Daniel Perez, a BayBio board member and venture partner with Bay City Capital, a San Francisco investment firm.

The report includes data from 900 life science companies from Santa Bar-


bara to Sacramento, although most of the businesses are in the Bay Area. About 60% of the companies have fewer than 50 employees, and many continue to struggle financially. Nonetheless, the industry is quickly evolving into a commercial powerhouse, the report concluded. 

Roche Unveils New Nanotech Diagnosis Tool

Swiss pharmaceutical group Roche Holding AG unveiled a new method using nanotechnology to track patients' responses to treatments by monitoring their genes. The new method detects active genes directly by using sensors attached to tiny silicon cantilevers which are only 450 nanometers thick and therefore react with extraordinary sensitivity, the company said.

"This promising new technology takes us a step nearer to tailoring treatment directly to patients' needs, hopefully with ever fewer adverse effects," Ulrich Certa, head of functional genomics at the Roche Center for Medical Genomics, said in a statement.

The study was completed by researchers from Roche and the National Center of Competence in Research at the new Swiss Nanoscience Institute (SNI) in Basel, and was published in the December issue of the journal *Nature Nanotechnology*.

"Because the method also works within minutes, it could be used as a real-time sensor for continuously monitoring biomedical processes [and] for detecting rapidly replicating pathogens that make prompt diagnosis essential," Roche said. 


CDC Contracts for New, Faster Bird Flu Tests

The U.S. Centers for Disease Control and Prevention (CDC) has awarded \$11.4 million to four U.S. companies for developing new, quick tests for influenza.

The idea is to come up with reliable, on-the-spot tests for H5N1 avian influenza, the CDC said in a statement. Current quick tests can tell if a person is infected with influenza A or B, but they do not identify the strain, and reports suggest the tests miss influenza in patients infected with H5N1.

Currently, to test for H5N1, samples from the patient must be sent a specialized testing lab, and testing can sometimes take more than a week. This would be too slow to stop the spread of a pandemic, experts say.

The companies that received the money are: Sunnyvale, California based Cepheid, which got \$2.4 million; San Diego-based Nanogen, which won \$4.5 million; Marlborough, Massachusetts-based Iquum, which got \$3.8 million; and Gaithersburg, Maryland-based MesoScale, which won \$706,000.

"During the next year, the four companies will work to create tests that would detect seasonal human influenza viruses and differentiate influenza A H5N1 from seasonal human influenza viruses within 30 minutes," the CDC said. "Because influenza viruses are constantly changing, the tests would also need to be quickly adapted if the virus mutates over time or if new viruses emerge that have the potential to cause a pandemic." 

Career Opportunities

Research Associate

Research Associate wanted to conduct research on apolipoproteins, gene regulation & experimental gene therapy to understand the molecular basis of disease. Must have Ph.D, M.D. or other degree which involves Biochem. , Mol. Biol. & Physiology, & 2 yrs. exper. w/ in vivo mouse models, incl. exper.w/ cell & tissue culture techniques, lipid profile analyses, immunoblotting & radioactive labeling techniques. Send resume to Anne Plunkett, Administrative Assistant, Boston University School of Medicine, Section of Molecular Genetics, 715 Albany Street, W509, Boston, MA 02118.

Chairperson of Biochemistry and Molecular Biology

Michigan State University invites applications and seeks nominations for a Chairperson of the Department of Biochemistry and Molecular Biology. An outstanding scientist is sought to

provide leadership that capitalizes on, but is not limited to, existing areas of research strength in genes and signaling, plant biochemistry, and structural and computational biology. Evidence of leadership in interdisciplinary research is an important qualification. It is anticipated that the candidate will contribute to and build upon the highly collaborative research atmosphere within the department and among the science departments, many of which are located in adjacent buildings. A growing medical science community offers additional research opportunities. State-of-the-art support facilities are available to enhance the new chairperson's research program.

The selected individual will be an experienced scholar with a vigorous well-funded research program and creative ideas for strengthening undergraduate and graduate programs (the department has 300 undergraduate majors and more than 100 graduate students). More information about the department is

available at www.bmb.msu.edu.

Applications will start being reviewed on January 15, 2007, and will continue to be considered until a suitable candidate is identified. Women and minorities are encouraged to apply. Send cover letter and C.V., including names of three individuals that could be contacted for a recommendation, to:

Lee Kroos
Chairperson Search Committee
Biochemistry and Molecular Biology
Michigan State University
East Lansing, MI 48824-1319
bmbsrch@msu.edu

Assistant Professor

Institute of Biochemical Sciences, National Taiwan University invites applications for two ASSISTANT PROFESSOR or higher positions. For details please visit our website at <http://homepage.ntu.edu.tw/~ibs/english/job.htm>

Why join ASBMB?



**BECAUSE WE ARE YOUR PEERS.
12,000 PEOPLE JUST LIKE YOU.**

We're experts in our industries and professions.

We work in the areas of biochemistry, molecular biology, pharmacology, physiology, nutrition, anatomy and proteomics.

We come from diverse backgrounds and have dedicated our professional lives to working in the biological and molecular biology fields.

For information and membership application go to:
www.asbmb.org/membership

For Your Lab/For Your Lab/For Your Lab

The information in For Your Lab has been provided by manufacturers and suppliers of laboratory equipment. For further information about any of these products listed contacts are listed at the bottom of each panel. When contacting any of these companies, please mention that you saw their product in *ASBMB Today*. Please note that a listing in *ASBMB Today* does not imply an endorsement by the American Society for Biochemistry and Molecular Biology or by any of its members or staff.

Manufacturers and suppliers, to include your products in For Your Lab contact Molly at adnet@faseb.org or 301-634-7157 (direct) or 1-800-433-2732 ext. 7157.

G = STORM

THE CUTTING EDGE THERMAL CYCLER SOLUTION

G-Storm – purpose built for the demands of cutting edge molecular biology, the new benchmark of thermal cycler excellence. Superb thermal performance characteristics are perfectly balanced with ease of operation ensuring that routine and gradient use never becomes a chore.



Distributed by BLNmarketplace.com. For more info please email info@blnmarketplace.com, or call 703-757-0327

IGLOO SOLUTIONS

YOUR COLD STORAGE IMPROVEMENT CENTER

Organize and maximize your LN2 and freezer space with our rack and box storage systems. Protect, Identify and locate your precious samples with our



Brady labels, printers, barcode scanners and our inventory management software. Use our remote alarm systems to add additional security to your cold storage units.

Distributed by BLNmarketplace.com. For more info, please email info@blnmarketplace.com, or call 703-757-0327

POLAR CRYOGENIC SYSTEMS = PCS

LN2 STORAGE FOR DEMANDING LABS

PCS is designed to meet the storage and security specifications required by today's labs. We offer a unique and versatile line of LN2 freezer systems with storage capacities from 750 to 40,000 2ml vials. Our systems are capable of both vapor and immersion phase environments, as well as both manual and auto fill controllers.

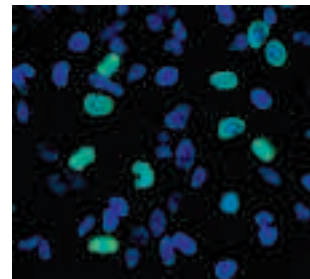


Distributed by BLNmarketplace.com. For more info, please email info@blnmarketplace.com, or call 703-757-0327

BETHYL LABORATORIES, INC.

PHOSPHO-SPECIFIC ANTIBODIES

Bethyl Laboratories offers over 60 phospho-specific antibodies with various validated applications, including western blot, immunoprecipitation, immunofluorescence, and immunohistochemistry. These antibodies are directed specifically against modified proteins. The key attribute is that they do not recognize the unphosphorylated form of the protein.



For more information, please visit us at www.bethyl.com

Calendar of Scientific Meetings

JANUARY 2007

BioSysBio 2007: Bioinformatics, System Biology, Synthetic Biology Incorporating the Young Bioinformaticians Forum

January 11-13 • Manchester, UK
For information: www.biosysbio.com
Email: JohnCumbers@biosys.com; Ph: 44-0-207-617-7824

Keystone Symposium—Obesity: Peripheral and Central Pathways Regulating Energy Homeostasis

January 14–19 • Keystone, CO
Website: www.keystonesymposia.org

Sanibel Conference

January 19-22 • Sundial Beach Resort, Sanibel Island, Florida
Imaging Mass Spectrometry
Program Chairs: Richard Caprioli, Ron Heeren, and Markus Stoeckli, For information contact: ASMS
505-989-4517; asms@asms.org; www.asms.org

FEBRUARY 2007

Keystone Symposium on Ubiquitin and Signaling

February 4-9 • Big Sky Resort, Big Sky, Montana
For information: www.keystonesymposia.org/Meetings/ViewMeetings.cfm•MeetingID=860
info@keystonesymposia.org; Ph: 800-253-0685 or 970-262-1230

Proteomics and Pathology—Joint Congress of the Spanish Proteomics Society and the European Proteomics Association

February 10-14 • Valencia, Spain
For Information: www.proteomics-valencia2007.ibv.csic.es/
Email: catedrasg@cac.es; Ph: 34-96-197-46-70

Keystone Symposium on PI 3-Kinase Signaling Pathways in Disease

February 15-20 • Hilton Santa Fe/Historic Plaza, New Mexico
For information: www.keystonesymposia.org/Meeting/ViewMeetings.cfm•MeetingID=864
info@keystonesymposia.org; Ph: 800-253-0685 or 970-262-1230

Keystone Symposia: Bioactive Lipids in the Lipidomics Era

February 20-25 • Taos, New Mexico
For information: www.keystonesymposia.org

German Society for Fat Science (DGF): Oleochemicals Under Changing Global Conditions

February 25-27 • Hamburg
For information: www.dgfett.de/meetings/hamburg/index.html

MARCH 2007

Biophysical Society 51st Annual Meeting

March 3–7 • Baltimore, MD
Website: www.biophysics.org/

U.S. HUP0 2007

March 4-8 • Seattle
For information contact: www.ushupo.org
Email: USHUPO@USHUPO.org; Ph: 505-9899-4876

Cell Signaling and Proteomics

March 22–27 • Steamboat Springs, CO
Website: www.keystonesymposia.org/Meetings/

Keystone Symposia Metabolic Syndrome and Cardiovascular Risk

March 27-April 1 • Steamboat Springs, Colorado
For information: www.keystonesymposia.org

4th International Symposium on Diabetes and Pregnancy

March 29-31 • Istanbul, Turkey
For information: www.kenes.com/dip07/ref=old
Email: dip07@kenes.com

RNAi2007: The Expanding Roles of Small RNAs

March 29-30 • St. Anne's College
Woodstock Road, Oxford, UK
Organizer: Dr. Muhammad Sohail
Ph: +44(0)1865 275231
Fx: +44(0)1865 275259 (Switchboard)
Email: Muhammad.sohail@bioch.ox.ac.uk
www.libpubmedia.co.uk/Conferences/RNAi2007/Home.htm

Association for Biomolecular Resource Facilities

Mar 31-April 3 • Tampa Convention Center, Florida
For information contact: www.faseb.org/meetings/default.htm
Email: ncopen@faseb.org; Ph: 301-634-7010

APRIL 2007

3rd European Symposium on Plant Lipids

April 1-4 • York, UK
Website: www.eurofedlipid.org/meetings/index.htm

Second Workshop on Biophysics of Membrane Active Peptides

April 1–4 • Lisbon, Portugal
Website: www.biophysicsmap.com

American Society for Biochemistry and Molecular Biology Annual Meeting in Conjunction with EB2007

April 28–May 2 • Washington, DC
Contact: ASBMB 2007, 9650 Rockville Pike, Bethesda, MD 20814-3008
Ph: 301-634-7145
Email: meetings@asbmb.org
Website: www.asbmb.org/meetings

2nd International Congress on Prediabetes and the Metabolic Syndrome

April 25–28, 2007 • Barcelona, Spain
www.kenes.com/prediabetes2007;
Email: prediabetes2007@kenes.com

MAY 2007

7th International Symposium of the Protein Society

May 12–16, 2007 • Stockholm-Uppsala, CA Sweden
www.proteinsociety.org/pages/page02b.htm
E-mail: cyablonski@proteinsociety.org
Tel.: 301-634-7277

National Lipid Association Annual Scientific Sessions
May 31–June 3 • Scottsdale, AZ
Website: www.lipid.org/chapters/swla

JUNE 2007

55th ASMS Conference on Mass Spectrometry

June 3-7 • Indianapolis
For information contact: ASMS, 505-989-4517
asms@asms.org; www.asms.org

Mitosis Spindle Assembly and Function A FASEB Summer Research Conference in Honor of Dr. B. R. Brinkley

June 9 -14 • Hyatt Grand Champions Resort and Spa, Indian Wells, California
Applications from students and post-docs are especially welcome! For additional information contact the organizers:
Dr. Conly L. Rieder, rieder@wadsworth.org or
Dr. Robert E. Palazzo, palazr@rpi.edu.

76th Annual EAS Congress European Atherosclerosis Society

June 10-13 • Helsinki, Finland
The Congress aims to create a stimulating atmosphere for exchange of the latest scientific and clinical knowledge in the field of atherosclerosis and cardiovascular diseases.
Deadline for submission of abstracts: November 30, 2006
For more information contact: Kenes International, EAS 2007
17, rue du Cendrier; P.O. Box 1726
CH-1211 Geneva 1, Switzerland
Ph: +41 22 908 0488; Fax: +41 22 732 2850
Email: eas2007@kenes.com
Website: www.kenes.com/eas2007

20th American Peptide Symposium—20th Jubilee Peptides for Youth

June 22-27 • Montreal, Canada
For information: www.americanpeptidesociety.com/index.asp?
Email: 20thAPS@UMontreal.ca
Ph: 819-564-5346

JULY 2007

XXIst Congress of the International Society on Thrombosis and Haemostasis

July 6–12, 2007 • Geneva, Switzerland
www.isth2007.com

32nd FEBS Conference: Molecular Machines and their Dynamics in Fundamental Cellular Functions

July 7-12 • Vienna, Austria
Abstracts to be considered for lectures must be received by January 31, 2007. All presenting authors of abstracts chosen for a main talk will receive a registration fee waiver.
For registration information: <http://FEBS2007.org/>
For Sponsor and Exhibitor information: Email: Info@febs2007.org

Life Sciences 2007, the first joint meeting of the Biochemical Society, the British Pharmacological Society, and The Physiological Society.

July 8-12 • The SECC, Glasgow, UK
The key themes of this major meeting are:
Cancer, Exercise, Ion Channels
Cardiovascular Bioscience, GPCR, Metabolism
Central Nervous System, Imaging, Signaling
Education, Inflammation
Abstract deadline: February 26, 2007
Earlybird registration deadline: April 27, 2007
Website: <http://www.lifesciences2007.org/>

2007 ASBMB Annual Meeting

April 28 – May 2, 2007 • Washington, DC
Held in conjunction with EB 2007

Organized by: Benjamin F. Cravatt, The Scripps Research Institute, Michael K. Rosen, University of Texas Southwestern Medical Center and the 2007 ASBMB Program Planning Committee

Early Registration Deadline: March 2, 2007

Preliminary Program

Genome Dynamics

From Genome to Epigenome

– Modification and Repair

- *Methylating and De-methylating DNA*
- *Recombining and Modifying DNA*
- *Making and Re-making DNA*
- *Telomeres and Telomerase*

The Chromosome Cycle

- *Centromeres and Kinetochores*
- *Chromatin Structure and Remodeling*
- *Chromosome Duplication and Cohesion*
- *Chromosome Segregation and Aneuploidy*

RNA

- *Molecular Recognition and Enzymology of RNA*
- *RNA-Based Gene Regulation*
- *Small RNAs*
- *RNA Modification: Mechanism and Function*

Protein Synthesis, Folding and Turnover

- *Molecular Mechanisms of Protein Biosynthesis*
- *Co- and Post-Translational Folding*
- *Protein Modification and Turnover*
- *Ribosome and Translation*

Structure and Design

Macromolecular Structure and Dynamics

- *Conformational Transitions and Protein Aggregation*
- *Experimental and Computational Dynamics*
- *Protein-Lipid Interface*
- *Structural and Mechanistic Evolution*

Enzymes – Mechanism and Design

- *Structural Enzymology*
- *The Role of Dynamics in Enzyme Catalysis*
- *Computational Studies of Mechanistic and Dynamical Aspects of Enzyme Reactions*
- *Enzyme Design*

Extracellular Matrix at Multiple Biological Scales

- *Extracellular Matrix at the Cellular Scale*
- *Extracellular Matrix at the Molecular Scale*
- *Extracellular Matrix at the Organism Scale*
- *Extracellular Matrix at the Tissue Scale*

Chemical Biology

- *Chemical Biology of Cell Death*
- *Fragment Based Drug Discovery*
- *Chemistry and Cell Biology of Natural Products*
- *Antibiotics for the 21st Century*

Cell Systems

Metabolism

- *Metabolic Sensing and Signaling*
- *Molecular and Cellular Aspects of Metabolic Disease*
- *Mitochondria in Health and Disease*
- *Aging and Metabolism*

Organelle Dynamics

- *Golgi Structure and Biogenesis*
- *Membrane Biogenesis*
- *Mitochondrial Dynamics*
- *Nuclear Dynamics*

Systems Biology

- *Modeling of Cell Systems*
- *Molecular Profiling of Cell Systems*
- *Proteomics of Cell Systems*
- *Mathematical Biology*

Signaling

Biochemistry and Signaling of Lipids

- *Biogenesis, Transport and Compartmentalization of Lipids*
- *Chemical Probes of Lipid Systems*
- *Lipids as Transcriptional Regulators*
- *Specific Protein-Lipid Interactions*

Signaling Pathways Controlling Cell Structure and Fate

- *Cytokine and Growth Factor Signaling*
- *DNA Damage Signaling*
- *Cell Cycle*
- *Signaling to the Cytoskeleton*

Public Affairs Advisory Committee Sponsored Symposium

Sponsored by EB participating societies

- *NIH at the Crossroads: How Diminished Funds Will Impact Biomedical Research and what Scientists Can Do About it*

Education and Professional Development Committee Sponsored Symposia

- *Classroom of the Future II*
- *Science at Undergraduate Institutions*
- *Graduate Student/Postdoctoral Starting Faculty Transitions*
- *Preparing for a Successful Career in Industry*

Minority Affairs Committee

Sponsored Symposia

- *Best Practices in Program Assessment*
- *Infectious Diseases in Minority Populations – Hepatitis C*
- *Genetic Diseases in Minority Populations – Sickle Cell Anemia*
- *Infectious Diseases in Minority Populations – Tuberculosis*



ASBMB
Chemistry of Life