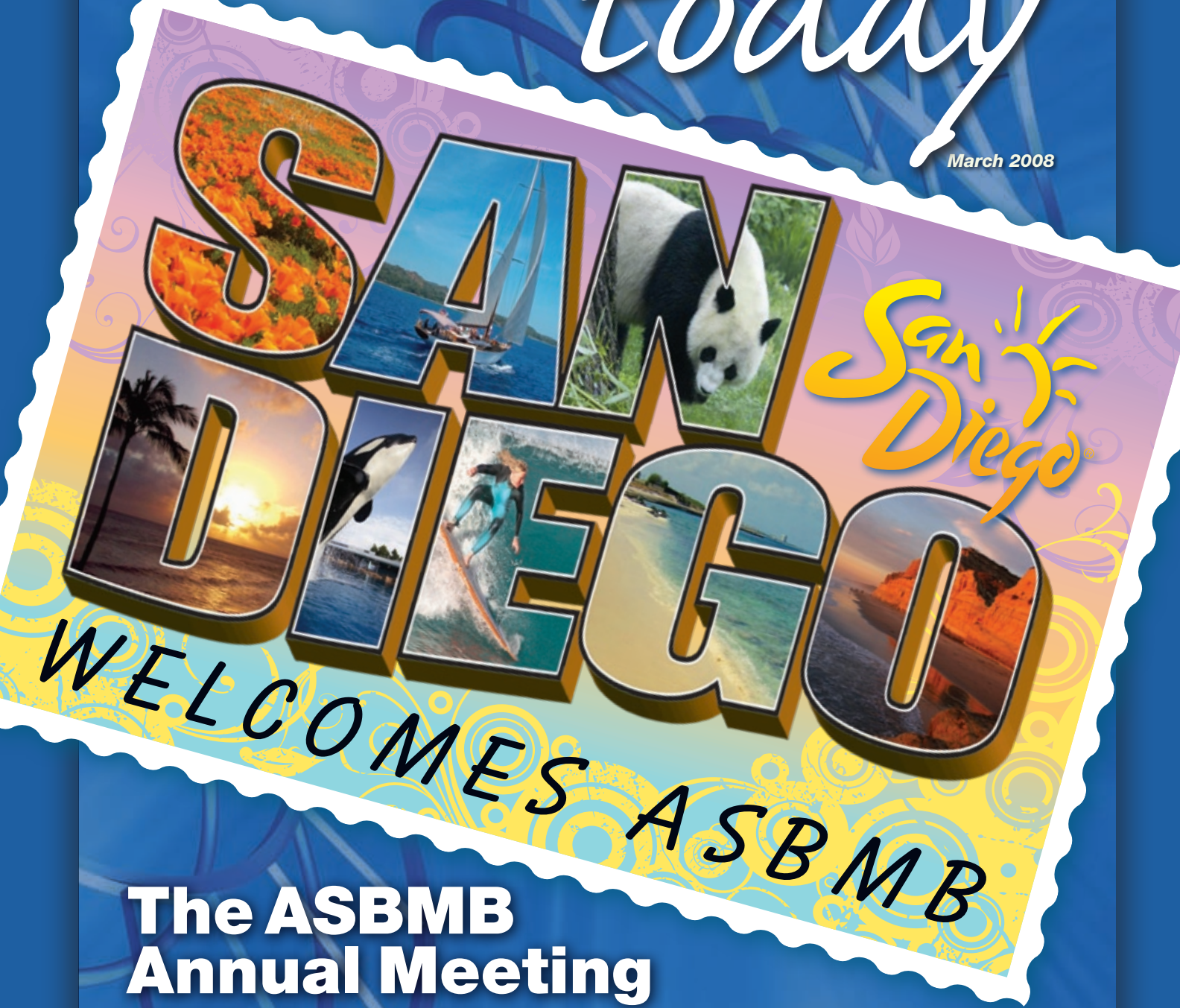
ASBMB ANNUAL MEETING PULLOUT GUIDE INSIDE

ASBMB today

March 2008



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MARCH 2008

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ASBMB's annual meeting will be held April 5 through 9 in San Diego, California. See inside for a pullout meeting guide.

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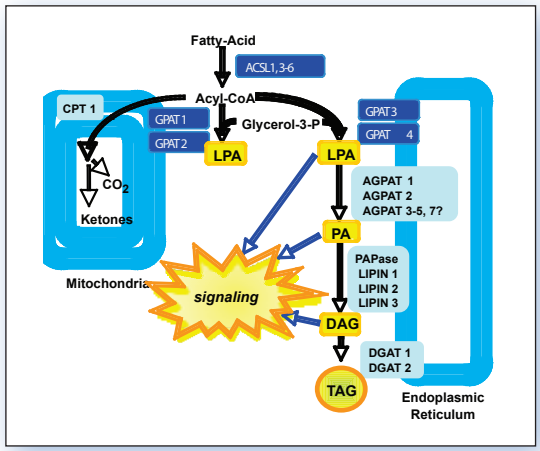

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podcast summary

Listen to the February ASBMB AudioPhiles *MCP* News Podcast to hear about an article that looks at protein phosphorylation in bacteria, a study that uncovers potential urine based biomarkers for coronary disease, and an up close and personal look at snake venom.

Download the podcast at:
http://www.faseb.org/asbmb/media/media.asp

ASBMB today

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ASBMB Today

Nicole Kresge *Editor*
nkresge@asbmb.org

Nick Zagorski *Science Writer*
nzagorski@asbmb.org

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

Barbara Gordon *Executive Director*
bgordon@asbmb.org

Magazine design & production: Amy Phifer

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

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from the **editor**

See You in San Diego!

BY NICOLE KRESGE

The ASBMB annual meeting in San Diego is rapidly approaching, so don't forget to mark your calendars for April 5–9. The meeting will feature numerous scientific symposia that are grouped into smaller "meetings within a meeting" themes, including DNA and RNA Biology, Molecular Structure and Dynamics, Cell Systems and Metabolism, Signal Transduction, and Chemical Biology. There will also be 8 award lectures and numerous poster sessions throughout the meeting.

As always, the ASBMB Education and Professional Development (EPD) and Minority Affairs (MAC) committees have arranged several special sessions for the meeting. The MAC sessions this year focus on mental health issues, including Alzheimer disease, diseases of the central nervous system, and drug abuse. The EPD has organized several workshops as well as a Classroom of the Future symposium. Ellis Bell gives an overview of some of these events in his article on p. 19. ASBMB has also organized a day-long graduate student and professional postdoctoral development program, which you can read more about on p. 15 of this issue.

There are several public affairs events going on at the meeting, including a training session for ASBMB members interested in learning more about local advocacy, and a symposium on peer review at the NIH. More details on these events can be found in Heidi Hamm's President's Message on p. 3.

The meeting will also feature several special events, including an opening reception and dance, a 5K Fun Run, a Minority Scientists Mixer, a Women Scientists Networking event, and a lunchtime workshop titled "How to Publish in the *Journal of Biological Chemistry*." As a tie-in to the workshop, *ASBMB Today* is starting a new series of articles about publishing in the JBC. The first article of the series can be found on p. 16 of this issue.

To help you make the most of your time at the meeting, we've included a special pull-out guide in the center of this issue of *ASBMB Today*. In it, you'll find an overview of the meeting's award lectures, special events, and scientific symposia. For specific information on the sessions and events, visit the ASBMB meeting Web site at www.asbmb.org/meetings.

Nicole Kresge

Public Affairs Events at EB—We Hope to See You There

BY HEIDI HAMM

Although our annual meeting will not be in Washington, D.C., this year, we at ASBMB value public affairs and thus still plan to hold several such events in San Diego in April.

As you know if you are a regular reader of this column, I have been most interested in generating greater activism among ASBMB members at the grass roots level. In that regard, we have established a Local Activists' Network of ASBMB members in the various congressional districts, and we have launched several exciting initiatives to provide this group with support and additional information beyond the public affairs content of *ASBMB Today*. One such activity will be a training session for ASBMB members interested in learning more about local advocacy. This session, entitled "Advocacy for ASBMB Members," will be held on Monday, April 7, from 12:30 to 2:00 p.m. in Room 14B of the San Diego Convention Center.

The training session, organized by the Public Affairs Advisory Committee, will feature a showing of our training DVD, "*Meeting with Your Congressman: A Guide for the Grass Roots Advocate.*" This innovative training DVD has gotten uniformly high marks and was featured in an article in *Associations Now*, the monthly magazine of the American Society of Association Executives. Copies of the DVD will be provided to all attendees. In addition to a discussion of the lessons covered in the DVD, a featured speaker is Gary Kline, a legislative aide to San Diego Congressman Brian Bilbray (R-CA).

EB-Wide Events

ASBMB is also co-sponsoring an EB-wide public affairs event, and we certainly hope that many of you can attend it. On Sunday, April 6, Keith Yamamoto, University of California, San Francisco, and Lawrence Tabak, Director of the NIH's National Institute for Dental and Craniofacial Research, will speak jointly on the efforts of a Working Group of the NIH Director's Advisory Committee to conduct a comprehensive review of the NIH peer review system. The working group held a series of meetings around the country starting last summer, and heard from hundreds of scientists and other NIH stakeholders on what was wrong (and what was right) with the NIH peer review system. A report was presented to the Director's Advisory Committee in December, and Yamamoto and Tabak (who co-chaired the Working Group) will share the results of their efforts and will no doubt be interested in hearing feedback from attendees as well. This session, called "Peer Review at NIH: Making Sure the System Works," will be held at 11:30 a.m. on Sunday, April 6, in Room 16A of the Convention Center.

I also hope those of you interested in public affairs will take the opportunity during the meeting to meet our first ASBMB Science Policy Fellow, Angela Hvitved, a recent Ph.D. graduate from Rice University. Angela joined the ASBMB staff as a Fellow for a year starting on October 1, and works with our Director of Public Affairs, Pete Farnham. Angela has already made a real difference in the public affairs programs of the society, such as beginning a monthly e-newsletter for members of our Local Activists Network. Angela is a pleasure to work with and I'm sure you'll enjoy talking with her.

By the way, we are now soliciting applications for next year's Fellowship. I invite you to nominate your favorite local activist graduate student who is interested in public affairs. You can find an ad with additional details on page 18 of this issue of *ASBMB Today*.

We hope to see you at these and other ASBMB events!

Public Affairs Events at EB

SUNDAY, APRIL 6, 11:30 A.M.

Keith Yamamoto and Lawrence Tabak: "Peer Review at NIH: Making Sure the System Works."

MONDAY, APRIL 7, 12:30 P.M.

Public Affairs Advisory Committee-sponsored training symposium: "Advocacy for ASBMB Members."

FASEB Releases Federal Funding Report, Article on HPV and Cervical Cancer

BY CARRIE D. WOLINETZ

FASEB has released two new publications designed to convey the importance of fundamental biomedical research. On January 29th, FASEB President Robert Palazzo presided over the unveiling of FASEB's annual report, *Federal Funding for Biomedical and Related Life Sciences Research, FY2009*. Developed through consultation with FASEB's 21-member societies and scientific experts, this report makes the case for sustainable funding for six federal science agencies.

The annual report, which serves as the basis for FASEB's research funding advocacy efforts for the next fiscal year, will be distributed to federal lawmakers, health research officials in the administration, and the research community. It is also available online at http://opa.faseb.org/pdf/2008/FedFund09.pdf. The following are FASEB's recommendations.

National Institutes of Health (NIH)

In order to fulfill the extraordinary scientific and medical promise of biomedical research, FASEB urges Congress to make the NIH a priority and respectfully requests that NIH receive $31.2 billion in FY 2009.

National Science Foundations (NSF)

In keeping with the America COMPETES Act of 2007, FASEB recommends an appropriation of $7.33 billion for the NSF in FY 2009.

Department of Energy (DOE)

In keeping with the America COMPETES Act of 2007, FASEB recommends an appropriation of $4.8 billion for the DOE's Office of Science in FY 2009.

Department of Veterans Affairs (VA)

FASEB recommends funding the VA Medical and Prosthetics Research Program at the $555 million level in FY 2009 with an additional $45 million for VA laboratory space renovation.

United States Department of Agriculture (USDA)

FASEB supports funding the USDA's National Research Initiative Competitive Grants Program in FY 2009 at the $257 million level recommended in the President's 2008 budget and the Agricultural Research Service at $1.377 billion.

National Aeronautics and Space Agency (NASA)

FASEB recommends that Congress increase funding for Life Sciences Research (Ground Research, Ground Facilities, and Flight Research) to $39.65 million.

FASEB has also released the latest article in its *Breakthroughs in Bioscience* series, "Viruses, Cancer, Warts and All: The HPV Vaccine for Cervical Cancer." *Breakthroughs in Bioscience* is a collection of illustrated articles, published by FASEB and designed for non-scientists, which explain recent developments in basic biomedical research and how they are important to society. This publication describes the scientific clues that established the connection between human papillomavirus (HPV) and cervical cancer, ultimately resulting in a vaccine against this deadly disease.

Each year, cervical cancer kills more than 250,000 women worldwide. In the United States alone, 11,000 new cases are diagnosed annually. Our story shows how a century of basic science culminated in the first vaccine to prevent cervical cancer and other diseases caused by human papillomaviruses. Decades of fundamental research, from insight into the basic biology of viruses, to findings about how benign growths like warts are formed, to strange pathways involving the legend of the mythical jackalope, eventually led researchers to the breakthrough discovery that some forms of HPV cause cervical cancer. The article also outlines how cutting edge new technologies, from DNA hybridization to generation of virus-like particles, allowed scientists to create an effective and safe vaccine that can prevent the vast majority of cervical cancer cases. Readers will learn how the HPV vaccine works, the role of Pap smears, and what the future of cervical cancer vaccines holds. Quality hardcopies of *Breakthroughs* articles are available, at no cost, to ASBMB members (contact the Office of Public Affairs at cwolinetz@faseb.org or 301-634-7650) or on line at http://opa.faseb.org/pages/Publications/breakthroughs.htm.

Carrie D. Wolinetz is Director of Scientific Affairs and Public Relations for the Office of Public Affairs at the Federation of American Societies for Experimental Biology (FASEB). She can be reached at cwolinetz@faseb.org.

NIH Loses Ground for Sixth Year Running

BY PETER FARNHAM[1]

The Administration rolled out its 2009 budget proposal on February 4, and the news was grim regarding domestic spending—a flat budget, with large increases for military spending and border security necessitating cuts across most other federally funded programs to keep the overall total within last year's spending limits. The Health & Human Services department would suffer a 2% overall reduction. In that context, what happened to the National Institutes of Health was comparatively good—it was only flat-funded, with a proposed budget of $29.307 billion, the same amount as 2008.

The agency's budget briefing for the biomedical research community was held after normal work hours on February 4, and it was very subdued—even funereal—with few moments of optimism. Only about 30 people attended, and although it was by invitation only, gatherings of the community usually number in the hundreds, and Wilson Hall, the large meeting room in Building 1 on the NIH campus, could have easily held dozens more.

John Bartrum, director of the NIH Office of the Budget, apparently drew the short straw and thus had to make the actual presentation, which went on for only about 20 minutes, including a few perfunctory questions. NIH Deputy Director Raynard Kington attended for part of the meeting, accompanied by several other NIH officials. NIH Director Elias Zerhouni did not put in an appearance.

Bartrum pointed out that NIH expects the success rate to fall to 18% overall in FY 2009, the lowest level since records began being kept on this statistic in 1970. He also noted that if the Administration's 2009 request is enacted, the NIH will have lost 13.4% of its purchasing power since FY 2003. The comparable figure for FY 2008 is 10.4%.

9757 competing awards will be available in FY 2009, only 14 fewer than FY 2008 but at the cost of no inflationary increases for noncompeting renewals. NIH will also continue to support new investigators through the Pathways to Independence program and the New Innovator Awards. The Director's Bridge Awards program, designed to help struggling institutions keep previously funded laboratories and research programs from closing, will continue at a level of $91 million. Pre- and post-doctoral trainees will receive a 1% stipend increase. The Common Fund will be funded at $534 million, which represents 1.8% of the NIH budget.

The Clinical and Translational Science Awards program is being boosted by $20 million, a 5.5% increase, although the National Center for Research Resources (NCRR) plans only to fund 6 to 7 of them this year instead of the proposed 12 planned for this year. Unfortunately, the expansion comes at the expense of $6 million in cuts in other NCRR clinical research center programs.

Bartrum also noted that the rate of biomedical inflation for 2008 had been revised from 3.7% to 3.5%, and that for 2009 it was projected to be 3.5% as well.

As was the case last year, funding for the Children's Health Study, in which the health of 100,000 children was to be tracked until they were 21, was zeroed out of the budget due to "competing priorities," according to Bartrum.

The View from the White House

More broadly, some insight as to why NIH had been flat-funded in recent years was gained at the budget rollout for the Office of Science and

Technology Policy, the White House science adviser's office headed by John Marburger.

When a reporter from *Science* magazine asked Marburger for an explanation of the logic behind the lack of an increase for NIH, he replied that NIH is very large and that even with flat funding, NIH can greatly increase its assets through internal reorganization (that is, fewer institutes). Marburger stated that Zerhouni had some great ideas about how to redirect funds within NIH and that Zerhouni should have greater control over the way NIH spends its money.

For example, Marburger cited the Common Fund as a place where Zerhouni should have more funding discretion. Marburger also opined that it was a mistake to double NIH funding over 5 years without having first required the agency to change the way it spends its money. Marburger views NIH's current funding situation as a natural consequence of the agency's lack of planning.

Marburger further characterized biomedical research as an unregulated market, so that after the NIH budget was increased and the overall number of Ph.D.s increased, postdocs are now vying with established investigators for their jobs. Marburger also noted that whereas the NIH budget increased, the National Science Foundation (NSF) and the Department of Energy's Office of Science (DOE) stagnated. This led to the administration's so-called American Competitiveness Initiative (ACI). The proposals under the ACI were largely adopted by Congress and signed into law last year as the America Competes Act. Under this law, funding for the NSF and the DOE's Office of Science will double over 10 years. Marburger said that what has happened to NIH was one of the reasons these budgets were being doubled over 10 years rather than more quickly. He did not address the issue of NIH's precipitous decline in purchasing power over the past 6 years.

FASEB President Bob Palazzo (also a member of ASBMB's Public Affairs Advisory Committee) noted that "our

FASEB Co-Sponsors NIH Briefing for House Freshmen

FASEB partnered with the American Cancer Society, the American Heart Association, the Alzheimer's Association, and Representative Tim Walz's (D-MN) office to sponsor a late January briefing for the House Democratic Freshman class on the impacts of NIH on our nation's health. Congressman Walz is President of the Democratic Freshman class and represents the greater Rochester, MN, area, including the Mayo Clinic.

The briefing was structured to provide members of Congress and their staff an overview of the NIH and allow them a chance to ask questions of the participating directors. The Director of the NIH, Elias Zerhouni, gave a brief presentation on the economic benefits and health impacts of the Institutes' work and three Institute directors spoke briefly about their own programs: Elizabeth Nabel, Director of the National Heart, Lung, and Blood Institute; John Niederhuber, Director of the National Cancer Institute; and Richard Hodes, Director of the National Institute on Aging.

FASEB Director of Legislative Affairs Jon Retzlaff called the meeting "a tremendous success" with 11 members of Congress attending. Several staffers of members who could not make the briefing also attended, and there was not an empty seat in the room when the briefing began. Members showed significant interest in learning more about the NIH and seemed to appreciate the opportunity to directly interact with the directors.

—Peter Farnham

President Gives NSF 13% Boost

In sharp contrast to how the National Institutes of Health was treated in the Administration's budget proposal for FY 2009, the National Science Foundation would receive a 13% boost, mostly to support physical science, engineering, and mathematics programs. These programs were all emphasized in the Administration's American Competitiveness Initiative promoted 2 years ago, which became the America Competes Act (ACA), and which was signed into law in 2007.

Overall, the NSF budget would increase to $6.85 billion, up almost $800 million over 2008.

Most physical science, math, and engineering programs received increases approaching 20%, with the Math and Physical Sciences Directorate (the largest NSF research directorate) receiving a 20.2% increase, increasing to $1.4 billion. And, even though biology programs were not included in the ACA, the Biology Directorate still receives a healthy 10.3% increase, to $675 million.

Education and Human Resources would go up almost 9% to $790 million.

The generous proposed increase for NSF continues a common pattern in presidential budget submissions going back at least to the Reagan administration—when NIH gets poor increases, NSF usually does pretty well (and vice versa). See the accompanying story about NIH for Science Adviser John Marburger's comments on why that is the case this year.

The NSF budget increased about 3% between 2007 and 2008. The administration had proposed an 8% increase for 2008, which Congress increased to more than 10% during the appropriations process last year. However, this generous increase was vetoed in a dispute over total spending. The Administration appears to be trying to make up for lost ground with this year's submission.

For more information about the NSF budget, please visit the agency's home page at www.nsf.gov/about/budget/fy2009/index.jsp

—Peter Farnham

continued progress in medicine and advances in health are dependent upon our investment in basic research. If this proposal moves forward, it would represent the 6th year of essentially flat-funding for NIH. Although President Bush has given lip-service to supporting the search for treatment for diseases like cancer, Alzheimer, and pandemic influenza, this budget again reveals his failure to uphold that commitment. This is an injustice to the patients and their families suffering from conditions for which research funded by NIH is their only hope."

The NIH proposal, like the rest of this final budget proposal of this administration, is likely to be heavily modified by Congress as it begins considering the budget this spring.

If you would like more details on the FY 2009 budget as it pertains to NIH, including funding at specific institutes, go to: http://officeofbudget.od.nih.gov/ui/HomePage.htm

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Peter Farnham CAE is public affairs officer of the Society, a position he has held since 1985. He can be reached at pfarnham@asbmb.org.

[1] *Gretchen Opper, FASEB Office of Public Affairs, also contributed to this story.*

NBME Will Keep Basic Science Med School Exam

BY PETER FARNHAM

In a meeting on the FASEB campus on February 6, Peter Scoles, Senior Vice-President of Assessment Programs for the National Board of Medical Examiners (NBME), told scientists from a half-dozen basic science societies that contrary to reports in the press from last fall, the NBME did not plan to eliminate or downgrade the basic science component of the United States Medical Licensing Examination (USMLE).

ASBMB had written a letter to the NBME on December 10 decrying the proposal (this letter is available for review on the ASBMB website; also see *ASBMB Today*, January 2008, p. 4, for a discussion of the issue). Other basic science societies had also written expressing concern about the proposal.

Scoles noted that none of the supposed decisions had actually been made; they were strictly proposals, and the whole process was fluid and subject to additional input. A participant said that none of the basic science societies had been consulted about the proposed change. Scoles apologized for the lack of communication but blamed it on a misunderstanding of which stakeholders were represented in the groups with whom NBME officials were meeting last year to discuss the various proposals.

Scoles said that it had been 25 years since the licensing examination system had been reviewed, and there had been enormous changes in medical school education in that time. Therefore, it was appropriate to review the current system and assess whether changes were needed, but this was going to be a long process and the earliest that proposed changes were likely to be implemented was 2014.

Under current thinking, the NBME committee charged with evaluating the licensing exam program—called the CEUP—would require that candidates for postgraduate medical training or initial licensing be tested on the scientific foundation of medical practice, application of medical knowledge to patient care, and clinical skills.

Regarding basic scientific knowledge, CEUP notes that:

"The abilities to interpret scientific literature, evaluate evidence, and apply scientific methods to clinical decisions are essential skills for the practice of medicine. To the greatest extent possible, guided by the best available evidence, integration of basic science and clinical medicine should be encouraged in each content domain" of whatever exam regime is developed.

Contrary to last fall's reports, CEUP is "not likely" to specify the number of examinations, assessment formats, score reporting formats, or timing of the exams. Furthermore, students will likely be offered a great deal of flexibility in when they take these exams. These had all been issues of concern to the basic science groups that had written to NBME last year.

ASBMB representatives, and all other participants in the February 6 meeting, seemed pleased at the level of responsiveness displayed by NBME. "The scare is off," said William Merrick, one of ASBMB's representatives to the Council of Academic Societies, a group organized within the Association of American Medical Colleges that represents the interests of societies like ASBMB. "It appears as if there will continue to be three exams, but the three will be combined for a single score, and thus the impact on the teaching of basic science is likely not going to be dramatically affected."

ASBMB will continue to monitor the situation and has invited Scoles to meet with the ASBMB Council during the EB meeting in April. ASBMB will likely provide names of candidates for service on various NBME committees charged with revising the exam over the next several years.

For more information, visit the United States Medical Licensing Examination website at: www.usmle.org/General_Information/review.html

—Peter Farnham

The New Education and Professional Development Web Site: A Wealth of Information

Are you a professor of molecular biology who is wondering about joining the Undergraduate Affiliates Network (UAN)? Are you a biochemistry student contemplating graduate school or a postdoctoral fellow trying to figure out how to get that much-coveted "first job"? What job should you look for anyway? Would you like to reach out to your local schools and get involved with their science education programs? Do you have a research-related ethical dilemma and want to know where to go for more information? Did your cousin ask you to recommend a good book on science over the holidays?

You can find answers to these questions and many more on the newly updated ASBMB Education and Professional Development Committee Web Site (http://www.faseb.org/asbmb/epd/EPD.html). The site is divided into sections containing information on a variety of topics of interest to ASBMB members, including the aforementioned Undergraduate Affiliates Network, ΧΩΛ: the ASBMB Undergraduate Honor Society, The Enzymatic Newsletter, Graduate and Postdoctoral Interests, Professional Development, and Outreach to both the K-12 community and the public.

Highlights:

- A list of Institutes offering degrees in Biochemistry, Molecular Biology, or Chemistry with a biochemistry emphasis, arranged by state
- An article titled, "Planning and Preparing for a Career in the Molecular Life Sciences" by Peter J. Kennelly of Virginia Polytechnic Institute and State University
- An article titled "Biomedical Careers in Industry" by Robert A. Copeland of GlaxoSmithKline Pharmaceuticals
- Resources for those interested in exploring a wide range of career options for scientists
- All the Career Insight Articles published in *ASBMB Today* collated in one place for easy reference
- A wealth of information on K-12 outreach
- A compendium of links to web sites related to a variety of bioethical issues
- A list of over 70 popular science books recommended by your peers

We encourage you to go to the web site to check it out yourself and hope you will find it useful in multiple situations. We welcome comments and/or suggestions at education@asbmb.org.

Richmond Students Are Connecting with Their Futures

BY ANGELA HVITVED

The University of Richmond held its annual "Connect with Your Future" career day for undergraduate students in late January. The goal of the day was to demonstrate to students some of the many ways to utilize a scientific background and how to turn their interest in science into a rewarding career. The event was organized by J. Ellis Bell, a professor of chemistry at the University of Richmond and chair of ASBMB's Education and Professional Development committee.

Panels comprised of science professionals from several different fields were assembled, and many career tracks were represented, including research, education, and science communication, research and development in the private sector, medical professions, and science policy and law. Panelists included several ASBMB members who provided a brief overview of their positions, including their educational backgrounds, pros and cons of their chosen field, and issues of work/life balance before opening the session for students' questions.

Students asked questions regarding a wide range of considerations, from how a given career affects one's personal life to concerns of intellectual independence. Many of them expressed relief at hearing there are often several ways to achieve success in a science-based profession and there are very few "career-ending" decisions.

In addition to bench research, the career options discussed included science administration with a federal agency or business; working in public policy for an association, professional society, or in congress; becoming a patent examiner; or entering the field of science writing or editing.

Feedback from the participating students was very positive. "The students really appreciated the chance for more detailed discussions," Bell said, "and really got a lot out of the insights they got from their discussions. Many students made it to two sessions and heard a good diversity of career options." Bre-Onna DeLaine, a student who participated in the workshop, told *ASBMB Today* that as a result of the session she was considering seeking an internship this summer in Washington. "The speakers were great resources," she said.

ASBMB Staff will be happy to participate in similar events at your institution; please contact Pete Farnham, ASBMB's Director of Public Affairs, at pfarnham@asbmb.org.

Angela Hvitved received her bachelor's degrees in biochemistry and philosophy from Iowa State University and her Ph.D. in biochemistry from Rice University. She is currently the ASBMB science policy fellow and can be reached at ahvitved@asbmb.org.

asbmb member spotlight

Please submit news about yourself to asbmbtoday@asbmb.org

Dey to Receive Carl G. Hartman Award

S. K. Dey, Dorothy Overall Wells Professor in the Department of Pediatrics and the Departments of Cell and Developmental Biology and Pharmacology, Vanderbilt University Medical Center, is the recipient of the Society for the Study of Reproduction's 2008 Carl G. Hartman Award.

Named for a distinguished reproductive biologist, the Hartman Award is the society's highest award. It recognizes a career of research and scholarly activities in the reproductive biology field. Dey will receive the award at the society's annual meeting in Hawaii this spring.

For more than 3 decades, Dey's laboratory has been engaged in defining the molecular and genetic basis of preimplantation embryo development and embryo-uterine interactions during blastocyst implantation. His group has addressed critical roles of growth factors, regulatory molecules, cytokines, and lipid mediators in the uterus and embryo during early pregnancy.

Dey is currently focused on elucidating the critical role of ligand-receptor signaling with endocannabinoids; the roles of $cPLA_2$-COX-2-derived prostaglandins, PPARs, LIF, Hoxa-10; and the roles of developmental genes in implantation and pregnancy establishment. His group is also engaged in studying global gene and protein expression profiles in the uterus and embryo during implantation by employing genomics and proteomics approaches.

Lindquist Awarded 2008 Genetics Society Medal

Susan Lindquist of the Whitehead Institute/Massachusetts Institute of Technology and Howard Hughes Medical Institute in Cambridge, MA, is the recipient of the 2008 Genetics Society of America (GSA) medal given for outstanding contributions in the field of genetics in the last 15 years.

Lindquist is widely recognized for her work in protein folding and the consequences of misfolding, which has important implications for understanding some neurodegenerative diseases and cancers. Through this research she has also worked on heat shock proteins, prions, and amyloids. Her work has provided evidence for a new paradigm in genetics based upon the inheritance of proteins with new, self-perpetuating shapes rather than new DNA sequences.

Lindquist was Secretary of the GSA Board from 1998 to 2000 and director of the Whitehead Institute from 2001 to 2004. She has received numerous awards and honors, including election to National Academy of Sciences in 1997 and the Institute of Medicine of the National Academies in 2006.

The GSA Medal will be presented to Lindquist later this year at a GSA-sponsored model organism meeting.

IN MEMORIAM

Hayato Kihara 1922-2007

Hayato Kihara, 85, died in Ventura, California, on December 26, 2007. A research biochemist, he retired in 1987 as the head of the Lanterman Biochemistry Laboratory in Pomona, California.

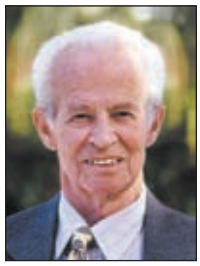
Kihara was born in 1922 in San Leandro, California. He was a student at the University of California, Berkeley, at the start of World War II, but in 1942 was interned at a government relocation camp in Topaz, Utah. He obtained his B.S. from the University of Texas and his Ph.D. from the University of Wisconsin.

Kihara completed postdoctoral studies at the University of California, Berkeley, and in 1963, he established the biochemistry laboratory at Lanterman and developed a highly productive laboratory for the biochemical study of human genetic conditions resulting in mental retardation. He was one of the pioneers in the use of cultured skin fibroblasts for such studies. His lab was instrumental in showing the feasibility of enzyme replacement for metachromatic leukodystrophy (MLD) using cultured cells, an approach currently being tested in MLD patients.

Kihara and his family resided in the Los Angeles area for more than 40 years, where he was active during his retirement in Japanese-American veterans and community affairs, including being a volunteer tutor and teacher of ESL and citizenship classes.

IN MEMORIAM

Gordon Candee Mills 1924-2008



Gordon Candee Mills, age 83, died on January 24, 2008, at Fleet Landing, Atlantic Beach, Florida.

Mills was born in Fallon, Nevada, in 1924. He graduated from the University of Nevada at Reno with a major in chemistry in 1946. He continued his education at the University of Michigan where he obtained his Ph.D. in biochemistry.

In 1950, Mills moved to Memphis, Tennessee, where he was a research associate in the biochemistry department of the University of Tennessee Medical School. In 1955, he accepted a position at the University of Texas Medical Branch at Galveston, where he remained until he retired in 1989. During his tenure he attained the position of full professor within the department of Human Biological Chemistry and Genetics.

During his career, Mills authored over 65 articles on biochemistry. In 1957, he authored a paper on glutathione peroxidase and was later credited with the discovery of the enzyme, having written at least 5 articles on it before anyone else. He was a member of numerous scientific societies and served as president of the Sigma Xi Chapter at the University of Texas. He retired at 65 but continued his research at the university as a professor emeritus.

Retrospective:
Helmut Beinert (1913-2007): A Nonagenerian Par Excellence!

The man whom many would identify as the founder and first proponent of the use of electron paramagnetic resonance (EPR) spectroscopy in biological systems, Helmut Beinert, passed away at the age 94, after a brief illness. His excellent health permitted him to visit his office almost every day at the (former) Institute for Enzyme Research of the University of Wisconsin, where he spent many years of his professional life. His state-of-the-art science had earned him an invitation as an invited speaker for the upcoming 2008 Gordon Research Conference on Iron-Sulfur proteins. As a true pioneer in Bioinorganic Chemistry, and the most prominent researcher in the area of Fe-S proteins for many years, he had been asked to speak on the history of these important proteins.

Beinert helped to install the first EPR spectrometer, equipped with liquid nitrogen cooling to perform experiments down to 77 Kelvin, at the University of Konstanz in the late 1960s. Although the University of Konstanz competed for the recruitment of Beinert, the University of Wisconsin at Madison was able to retain him there where he performed his research for a major portion of his professional life. The Madison campus became the destination for anyone interested in studying metal-containing enzymes, recording EPR spectra of biological samples below 10 K, capturing catalytic intermediates within milliseconds using rapid-freeze techniques, or squeezing the most information from milligram quantities of meticulously prepared proteins in the absence of dioxygen. His laboratory had the appearance of an engineering shop where he and his erstwhile colleague, Ray Hansen, were able to design the instrumentation and develop the techniques required to address biological problems.

Beinert's research career was noted not only by the significance of his discoveries, but also by the fact that he was one of the few well known scientists who consistently performed research with his own hands. In the 1980s, during a period when retirement was mandatory, with the assistance of the administration, Bettie Sue Masters, as Chairman of Biochemistry, recruited Beinert to the Medical College of Wisconsin as a Distinguished Scholar-in-Residence, providing him with salary and endowment support for his NIH-supported laboratory activities. He brought with him Mary Claire Kennedy, S.S.J., who, side-by-side with Beinert, conducted their premier studies on aconitase[1].

In a 1992 paper, they and their collaborators revealed a second aconitase, found only in the cytosol of mammalian tissues, which in its apo-form functions as an iron regulatory protein (IRP1). They characterized the beef liver cytosolic aconitase and demonstrated it to be active in its [4Fe-4S] form with a turnover number similar to that of the mitochondrial aconitase. However, the EPR spectra of the two enzymes were shown to be markedly different, whereas their amino acid composition, molecular weight, isoelectric point, and the sequences of six random peptides clearly showed their physicochemical and structural characteristics to be identical to those of IRP1, but that cytosolic aconitase is distinctly different from mitochondrial aconitase. These experiments revealed a new role for aconitase and a mechanism by which it could be involved in intracellular Fe homeostasis. Mössbauer experiments on Fe-S centers of a number of different proteins, including aconitase, in collaboration with Eckard Münck, revealed mechanistic aspects of the role of the Fe-S clusters in these proteins[2].

Because Beinert collaborated with physicists and explored their advanced techniques for the analysis of complex biomolecules, he was able to address many difficult biological problems. Utilizing EPR, he was able to

address the copper sites in cytochrome oxidase in collaboration with Richard Sands[3]. With both Sands and Münck, physicists by training, Beinert performed interdisciplinary research at the highest level. He also studied the fatty acyl-CoA dehydrogenases in pig liver mitochondria, founding yet another field in intermediary metabolism, which plays a major role in human health[4].

The original acyl-CoA dehydrogenase, medium chain acyl-CoA dehydrogenase (it was then called general acyl-CoA dehydrogenase), was discovered by David Green's group and, as Beinert wrote[4], Green "farmed out" the acyl-CoA dehydrogenase project to him for purification and characterization, which resulted in a series of papers that describe all of the fundamental enzymological aspects of acyl-CoA dehydrogenases. He said "Unexpectedly, but not unfortunately, the acyl-CoA dehydrogenases were a starting point for me into quite a different direction"[4]. During the course of these studies, he discovered long chain fatty acid-specific acyl-CoA dehydrogenase, and later electron-transferring flavoprotein (ETF) and ETF-ubiquinone oxidoreductase that link fatty acid metabolism to the main mitochondrial respiratory chain. Those of us who study enzymes involved in βoxidation marveled at Beinert's biochemical instinct and insights: all of the biochemical properties of the acyl-CoA dehydrogenases and ETF we now know were anticipated by Beinert in the 1950s!

Beinert was born in Lahr, a small town in Baden, Germany, on November 17, 1913. In 1955, he became a U.S. citizen. He received his Abitur in 1932 at a classical German Gymnasium in Heidelberg, Germany, graduating in Greek and Latin. "I was certainly not predestined or even prepared to enter the world of frontline biochemical research," recounted Beinert. "In the close neighborhood, there was the Kaiser-Wilhelm-Institute (KWI), and one day the children of two KWI directors, Prof. Meyerhof (Physiology) and Prof. Hausser (Physics), suddenly appeared in our school"[5]. During his final exams, a rather unique meeting at the KWI occurred entitled, "Lectures and Demonstrations about Foundations and Problems of Biological Oxidation Processes." With almost all the great names in the field in attendance: Warburg, Keilin, Haldane, Krebs, Kuhn, and Meyerhof, it was most likely a momentous event. Beinert then began studying chemistry in Heidelberg and Leipzig and, in 1943, obtained his doctoral degree from the University of Leipzig, while performing his thesis research in the laboratory of Richard Kuhn, at the KWI for Medical Research in Heidelberg.

After working there as a Research Associate until 1945[5], Beinert left for the U.S. He spent several years with the U.S. Air Force School of Aviation Medicine in Randolph, Texas. He then joined the Institute for Enzyme Research at the University of Wisconsin in Madison in 1950, where he became a full professor in 1962. He stayed in Madison until his retirement in 1985 at which time he was recruited to the Medical College of Wisconsin as a Distinguished Scholar-in-Residence. One of the attractions there was the National Biomedical ESR Center, under the direction of James S. Hyde. Beinert served on the EPR Center Steering Committee as a member until his death.

Beinert received many honors and awards during his career, including induction into the National Academy of Sciences in 1980 and the Keilin Medal from the British Biochemical Society in 1985, followed by the Warburg Medal from the German Society for Biological Chemistry in 1994. In the same year, Beinert received the first Honorary Doctoral Degree from the Faculty of Biology from the University of Konstanz.

Throughout his prolific career, Beinert contributed many discoveries and insights to the field of metalloenzymes, redox enzymology, bioenergetics, and Fe homeostasis. His research has formed the basis of much of our information in the field of biological oxidations in the modern textbooks of biochemistry. Beinert is survived by a daughter, Isabel, and son, Hannes. His wife, Elisabeth, passed away in April, 2005.

Beinert, who relished and, in fact, insisted upon remaining involved in his own experiments, will be sorely missed by his many admirers and colleagues. Vivid in our memories is the virtually photographic image of Beinert and Kennedy, side-by-side, performing anaerobic titrations with their custom-constructed equipment as though in another world and another time. We all knew that what would result was quite futuristic![a]

Respectfully,
Bettie Sue Masters, Ph.D.
Mary Claire Kennedy, S.S.J., Ph.D.
Jung-Ja P. Kim, Ph.D.
Peter H. Kroneck, Ph.D.

REFERENCES:

1. Beinert, H., and Kennedy, M. C. (1989) *Eur. J. Biochem.* **186,** 5.
2. Beinert, H., Holm, R. H., and Münck, E. (1997) *Science* **277,** 653.
3. Beinert, H., Griffiths, D. E., Wharton, D. C., and Sands, R. H. (1962) *J. Biol. Chem.* **237,** 2337.
4. Beinert, H. (1988) in *Fatty Acid Oxidation: Clinical, Biochemical, and Molecular Aspects* (Tanaka, K., and Coates, P., eds) p. 1-22, Alan R. Liss, New York.
5. Beinert, H. (1999) in *Flavins and Flavoproteins* (Ghisla, S., Kroneck, P., Macheroux, P., and Sund, H., eds) p. 3, R. Weber Agency for Scientific Publications, Berlin.

FOOTNOTE:

a. For more information on Beinert's research, see his *JBC* Reflection (Beinert, H. (2002) *J. Biol. Chem.* **277**, 37967-37972)

Postdocs and Taxes: *A Primer*

BY KATHLEEN FLINT

Tax time can be a headache for postdocs

who often must piece together multiple sources of income reported by an alphabet soup of W-2 and 1099-MISCs forms. This can be doubly true for international postdocs who may be encountering the U.S. tax system for the first time. With "Tax Day" fast approaching on April 15th, this article provides a brief overview of tax issues for postdocs. It does not, however, constitute tax or legal advice, and postdocs are encouraged to consult a qualified tax professional regarding individual circumstances.

Postdocs of all classifications are responsible for filing a tax return with the Internal Revenue Service (IRS) by April 15th of each year on income earned during the previous calendar year. The primary classifications of postdocs are explained in further detail below. The requirement for filing a tax return is based on the interpretation of federal law, such that any support a postdoc receives that is used to cover "living expenses" (as opposed to, say, tuition and fees) is subject to income tax. How that tax is paid typically depends upon the postdoc's type of funding, employment classification, and citizenship.

Employee Postdocs

"Employee" postdocs are U.S. citizens or permanent residents who are funded on grants or receive a salary from their institution through the "standard" payroll disbursement. (For postdocs who are temporary residents, please refer to the section below on international postdocs.) Employee postdocs will have federal tax withholdings automatically taken out of their paychecks. The amount of this tax withholding depends upon the individual circumstances of the postdoc, including total income, status of dependents, and any tax treaty status for international postdocs.

Tax Withholding

Employee postdocs will determine the amount of this withholding at the start of their appointment by completing a federal withholding form, IRS Form W-4 and, in states with an income tax, an equivalent form for withholding state tax. It is very important that the withholding be calculated in as much detail as possible to avoid paying too much or too little tax over the course of the tax (calendar) year.

Tax Filing

All employee postdocs must file a tax return between January 15 and April 15 for the previous tax year or file for an extension by April 15th to receive more time (however, any tax owed is due at the time an extension is filed). To complete the tax return forms, postdocs will need to have received a W-2 form from their employer that lists their wages and salary accrued for the year. If too little tax has been paid, a postdoc risks a large payment of the balance and possibly a penalty.

Postdoc Fellows: "Non-employee" Postdocs or Postdocs on Fellowships

Postdoctoral fellows receive stipends from fellowships that may be paid through the institution or may be paid directly to the postdocs. These postdocs are typically *not* considered regular employees and so often are not subject to automatic tax withholding. Nevertheless, virtually all postdoc fellowships funded from U.S. sources are subject to income tax because they pay for living expenses.

Estimated Payments

Those fellowships *without* automatic tax withholding are still subject to the IRS requirement that income tax be paid on a regular basis throughout the tax year, and not all at once at the end of the year. Thus, postdocs without withholding should make estimated tax payments each quarter to avoid a penalty. Use IRS Form 1040ES for estimated federal tax calculations and payments and find the equivalent form for estimated state taxes (where applicable).

Tax Filing

Postdocs on fellowships must also file a tax return between January 15 and April 15 for the previous tax year (or an extension for more time). Postdoc fellows and trainees may receive a W-2 or 1099-MISC Form reporting their total fellowship income, or they may receive no summary form at all. In any case, a tax return must be filed, and the fellowship stipend amount should be

reported with gross income. For instructions on reporting taxable fellowship income not included on a W-2, see IRS Publication 970, "Tax Benefits for Education," which has a section on "Reporting Scholarships and Fellowships"[1]. Tax time also provides an opportunity to make sure that the estimated quarterly payments are sufficient to avoid penalties for too little tax paid.

FICA and Fellowships

For fellowships paid through the institution, there is some variation on whether the institution should withhold federal employment taxes: Social Security and Medicare taxes (FICA) and unemployment tax (FUTA). A 2005 IRS ruling implies that all postdoc income be subject to these taxes, including postdoc fellowship income; however, certain fellowships and traineeships, in particular the National Institutes of Health National Research Service Award (NRSA), are not because the research conducted by these postdocs is considered noncompensatory (*i.e.* the stipend is more like a grant than a wage paid for services). Given the initial controversy (and confusion) over these determinations[2-4], the policies governing those supported on fellowships have been determined on a case-by-case basis by the institution's legal counsel. Because of these variations, postdocs should check to determine their own institution's decision.

Self-employment Tax

It can be a complicated question whether postdocs on fellowships are self-employed and are thus required to pay self-employment tax. Most IRS publications for the typical taxpayer suggest that if you receive a 1099-MISC form you should be paying self-employment tax. However, being a postdoc is a bit different from being an independent contractor. There are several tax court cases that deal specifically with postdocs and fellowships, primarily *Spiegelman v. Commissioner of Internal Revenue* (1994, 102 T.C. 394), which says that postdocs supported on fellowships are *not* self-employed. The crux of most of these arguments hinges on whether or not there is a *quid pro quo* or employer-employee relationship between postdoc and institution, and typically postdoc fellows are not required to render services to their institution in exchange for their stipend. However, as with paying FICA, this issue can be complicated. The unofficial rule of thumb is that if your salary shows up in Box 7 for "Non-employee compensation" (as opposed to Box 3, "Other income") there is a higher chance that the IRS will scrutinize your tax return more carefully, expecting you to have paid self-employment tax. Thus, if you are not sure, it is highly advised that you talk to a tax professional.

International Postdocs

International postdocs are subject to U.S. federal and state tax laws; however, qualified residents of some countries may have tax treaties that make them exempt from U.S. taxes or provide other benefits. Those who intend to pay taxes in the U.S. typically have the same automatic tax withholding as employee postdocs. Tax-exempt postdocs, however, may or may not have taxes withheld, depending on the institution and nature of their appointment.

Tax Filing

International postdocs must always file a federal tax return because it provides the vehicle for either claiming tax exemption or for declaring (and perhaps paying) taxes owed. The need to file state tax returns varies widely depending upon the state and the amount of time an individual was physically present there. Those who are tax-exempt but who still have taxes automatically withheld from their paychecks will need to file a tax return to receive a refund of their withholdings.

Resident or Nonresident?

An international scholar's status as a resident or nonresident for tax purposes is different from his or her status for immigration purposes. The IRS determination depends upon several factors, including treaty status, visa status, and the amount of time the scholar was physically present in the U.S. The IRS's guide for Foreign Students and Scholars[5] includes a section on "Residency for Tax Purposes" that can help postdocs determine their status and thus which federal tax form they should use.

The inherent complexity of the postdoc appointment, from its temporary nature to multiple funding sources to its visa implications, means that the financial circumstances of many postdocs will be unique. Although this guide can provide general information, postdocs with more complex concerns are encouraged to seek out professional advice on their individual situation.

Kathleen Flint is Project Manager for the National Postdoctoral Association. She can be reached at kflint@nationalpostdoc.org

DISCLAIMER: *This article is for informational purposes only and does not constitute tax or legal advice. If you want tax or legal advice, please contact a qualified tax professional/lawyer.*

REFERENCES

1. IRS Publication 970 (2007) "Tax Benefits for Education" (accessed on 2/7/08) http://www.irs.gov/publications/p970/ch01.html#d0e1066
2. Benderly, B. L. (2005) "A Taxing Question on Postdoc Pay: New IRS Regulation Demands Deductions from All Postdocs" ScienceCareers.org http://sciencecareers.sciencemag.org/career_development/previous_issues/articles/3500/a_taxing_question_on_postdoc_pay_new_irs_regulation_demands_deductions_from_all_postdocs/
3. Austin, J. (2005) "Americas Weblog: NYU Changes Course (and So Do We)" ScienceCareers.org http://sciencecareers.sciencemag.org/career_development/americas/americas_weblog/nyu_changes_course_and_so_do_we
4. Harding Jr., B. "NRSA Fellows May Be Eligible for Substantial Tax Refunds" (accessed on 2/6/08) http://www.phds.org/nrsa-taxes/
5. IRS Guide for Foreign Students and Scholars (accessed on 2/6/08) http://www.irs.gov/businesses/small/international/article/0,,id=96431,00.html

The 2008 Award for Exemplary Contributions to Education: **Michael F. Summers**


Summers

The ASBMB Award for Exemplary Contributions to Education will be presented to Michael F. Summers, a Howard Hughes Medical Institute (HHMI) investigator at the University of Maryland, Baltimore County. The award, administered annually by the ASBMB Education & Professional Development Committee, is given to a scientist who encourages effective teaching and learning of biochemistry and molecular biology through his or her own teaching, leadership in education, writing, educational research, mentoring, or public enlightenment. Summers will present his award lecture entitled "The Meyerhoff Scholars: A STEM Diversity Program That Really Works!" at the Annual Meeting in San Diego on Sunday, April 6, at 12:30 pm.

Summers graduated from the University of West Florida with a B.S. in Chemistry in 1980. He completed his Ph.D. in Bioinorganic Chemistry 4 years later at Emory University, investigating the role of metals in biology. He then did a postdoctoral fellowship with William Egan at the National Institutes of Health, using nuclear magnetic resonance (NMR) to study coenzymes and nucleic acids.

In 1987 Summers joined the Department of Chemistry and Biochemistry at the University of Maryland Baltimore County (UMBC) as an assistant professor and moved up the ranks to eventually become professor. At UMBC, he became intrigued by the controversy over whether the nucleocapsid protein surrounding HIV's viral core requires zinc to fold and function properly. Using NMR, he found that the nucleocapsid protein binds zinc tightly, enabling the formation of a stable region called a "zinc knuckle." He also showed that zinc knuckles are an important component of mature viruses. In recent years, Summers has uncovered a molecular switching mechanism that plays an important role in HIV infection and has also identified a new class of compounds that inhibit a key protein involved in the transformation of HIV into its mature form. Ultimately his studies should help guide the design of new therapeutic approaches for the treatment of AIDS.

Despite the complex nature of his work, Summers has made a point of assigning key roles to undergraduate students working in his laboratory, especially students from groups traditionally underrepresented in science. "Young people need to have experiences that excite them and motivate their interest in science," explains Summers. "Making our laboratories available to bright young students is important for developing the next generation of scientists, and can be personally very rewarding."

Summers credits much of his success in increasing diversity to UMBC's president Freeman Hrabowski III, who launched the Meyerhoff Scholarship Program in 1988. The program supports minorities and other students who have a strong interest in pursuing Ph.D. degrees in the sciences by providing mentoring, training, academic and career advising, group study, and research opportunities. Summers also currently serves as the director of the UMBC Meyerhoff Graduate Fellows Program. The goal of this program is to increase diversity among students pursuing Ph.D. degrees in the biomedical and behavioral sciences.

"In this day and age of competitive research, it is truly rare to find a young researcher willing to dedicate his/her time and energy to work with undergraduates to the extent that Professor Summers does," says Isiah M. Warner, Vice Chancellor for Strategic Initiatives and professor at Louisiana State University. "It is not unusual to find as many as 25 undergraduates working in his laboratory at any given time."

Utilizing his experience with the Meyerhoff Programs, Summers has also developed the HHMI Scholars Program at UMBC. This effort begins with outreach programs to high-school students, followed by laboratory rotations in a pre-freshman summer, and culminates in independent research in the laboratories of research-intensive scientists, including HHMI Investigators across the nation. Summers anticipates that the outcomes of this program will be even more successful than those of the Meyerhoff Scholars.

In addition to designing and implementing these successful student programs, Summers has collected data to measure recruitment and retention of underrepresented minority students in science and has shown that active, continuous mentoring is essential to keeping

highly talented students on the path to a career in science. He has also spent significant amounts of time publicizing these results and helping colleges and universities set up programs for minority students who are inclined toward science.

"Mike has created opportunities and programs that have altered the lives of countless undergraduate students," says Thomas R. Cech, president of the Howard Hughes Medical Institute. "He has pioneered efforts to recruit and retain students traditionally lost to science, harnessing the power of mentoring and undergraduate research. He has shown by example and critical analysis the steps needed to broaden the diversity of students engaged in science. Finally, he has been tireless in disseminating across the nation the principles and strategies that make such programs successful."

ASBMB to Hold Professional Development Session at 2008 Annual Meeting

In response to the great success of the morning career development session during last year's annual meeting, ASBMB is holding a special 2-day session dedicated to graduate and postdoctoral professional development at this year's meeting.

The program kicks off on Friday, April 4, at 5:00 pm with an invitation-only Graduate/Postdoctoral and Graduate Minority Travel Award Symposium. This symposium will honor the recipients of the ASBMB 2008 Graduate/Postdoctoral and Graduate Minority Travel Awards. The program features a special plenary lecture by 2008 ASBMB William C. Rose Award winner John D. Scott of Oregon Health and Science University, who will give a talk titled, "Management, Manuscripts, Mentorship, and Membership." The lecture will be followed by a poster session in which all travel award recipients will present their work.

The program continues into Saturday with a series of discussions and workshops open to students and postdoctoral fellows who pre-registered for the sessions (see the ASBMB Meetings Website for more details on registration). The morning session, which starts at 9:00 am, will feature a panel discussion on career options for scientists, including patent law, science editing, and industry consulting. This will be followed by a networking luncheon. The afternoon's program will start with oral presentations by some of this year's travel award recipients, and will conclude with a series of afternoon workshops on career and professional development topics ranging from finding the perfect postdoctoral position to time management.

FRIDAY, APRIL 4, 2008*

Graduate/Postdoctoral and Graduate Minority Travel Award Symposium

Keynote Lecture

JOHN D. SCOTT, *OREGON HEALTH AND SCIENCE UNIVERSITY*
"Management, Manuscripts, Mentorship, and Membership"

SATURDAY, APRIL 5, 2008**

Graduate and Postdoctoral Professional Development Program

Career Options: The Bench, the Boardroom, or in Between?

ALEXANDRA NEWTON, *UCSD*
From Discovery to Dissertations—Notes from Academia

NEENA GROVER, *COLORADO COLLEGE*
Primarily Undergraduate Institutions: What Makes a Successful Teacher-Scholar?

JAMES PATERNITI, *AMYLIN PHARMACEUTICALS*
Industry

FENG CHEN, *EDITOR, MOLECULAR CELL*
Science Editing

JOHN J. EMANUELE, *JR., SOMMER BARNARD PC*
Patent Law

Graduate Student and Postdoctoral Professional Development Workshops

JOHN DENU, *UNIVERSITY OF WISCONSIN-MADISON*
Mentoring Your Way to Success

KIM ORTH, *UT SOUTHWESTERN*
Finding the Perfect Postdoctoral Position

ANN MILLER, *UNIVERSITY OF WISCONSIN-MADISON*
Time Management: Achieving Your Goals (and still having time for a life outside of science)

MITI SHAH, *ARIZONA STATE UNIVERSITY*
Making the Most of Your Postdoctoral Experience

LEE LIMBIRD, *VANDERBILT UNIVERSITY/MEHARRY MEDICAL COLLEGE*
The Seasons of Your Career: Evolving an Independent Research Plan While Engaged in Postdoctoral Training

PETER KENNELLY, *VIRGINIA TECH*
Making Your Interview a Successful One

** Friday program by invitation only*
***Advance registration required for participants of Saturday's session*

OFFICE 2007... Friend or Foe?

This article is the first in a series on publishing your research in the *Journal of Biological Chemistry*. The series will address a variety of issues that authors may have when writing and submitting articles to the *JBC*. The articles will be written by Cadmus Professional Communications, a Cenveo Company, who are responsible for the editing, production, and printing of *JBC* articles.

Much to no one's surprise, Office 2007 is now packaged standard on many new computers. It's the Microsoft way! However, buyer beware, the differences between Office 2000 and Office 2003 pale in comparison with the changes in Office 2007. When you open the various programs, familiar by now to most of us, there are some noticeable differences. New features in each application will be a pleasure to some and an annoyance to others.

Let's Start with Word 2007

The most visible difference in Word 2007 is the interface. Word's features and settings have become so numerous over the years that they have become difficult to find. Remember the joy and ease of adding your favorite commands to the toolbars, so many that it sometimes became overcrowded? Well, Microsoft's response to that conundrum is what it calls a ribbon interface (Figure 1). The ribbon is also visible in Outlook, Excel, PowerPoint, and Access.

The ribbon is composed of tabs and drop-down lists; each tab has the commands and icons that are relevant to the context or activity. The larger icons are those for the most commonly used actions like inserting a text box, a table, clip art, or an equation. Along with the large icons are standard tabs in Word 2007, including References and Mailings. Some tabs are program tabs, such as Print Preview. There are also contextual tabs. These tabs change depending on what you are doing on the screen. For example, if you are attempting to style a table, the choices for styles appear.

Adding to the fun, within the tabs are groups like font, paragraph, styles, and editing. Most of these groups have tiny icons in the bottom-right corner called Dialog Box Launchers. Clicking on the Dialog Box Launcher (Figure 2) brings up a more traditional task panel or dialog box.

File types…From .doc to .docx

The default file type in older versions of Word is .doc, and in most cases, you may not even see the extension. In Word 2007, the default is .docx. The x stands for XML (or extensible mark-up language), which is an open standard for sharing files among different applications. By adding the XML, Microsoft is keeping pace with the growing demand for dynamic text and the need to move files easily among applications. XML files are also somewhat smaller than files saved in the binary format. There is less chance of corruption of the XML files because each entity is stored as a separate component. Saving a file in Word 2007 actually creates a zipped file containing XML files, including, for example, one for header information, one for graphics, and one for text. Unfortunately, despite the good intentions, the .docx files are not backward-compatible.

Not uncommon to other upgraded software programs, Word 2007 files cannot be read by lower versions of the program. So consider that co-authors may not be able to read your Word 2007 document unless you save it in an earlier version. Authors who are collaborating with colleagues who have not yet upgraded to Word 2007 may find the incompatibility of the versions frustrating. To avoid the frustration, note that a Word 2007 user can set the default to automatically save documents in an earlier version. For those who would prefer to work in an older version of Word, a converter is also available for download on the Microsoft site: http://www.microsoft.com/down-

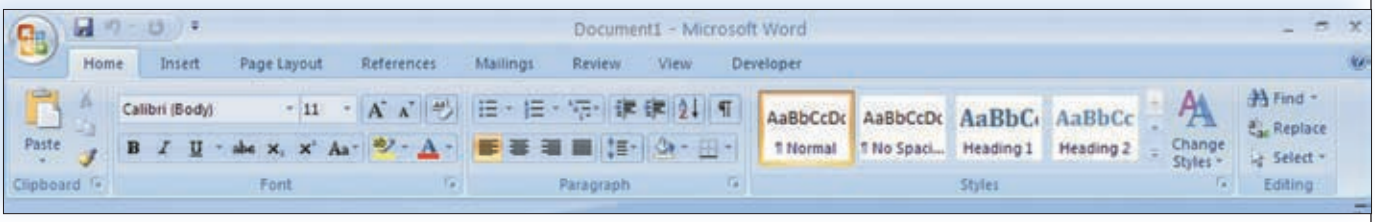


Figure 1: The ribbon.

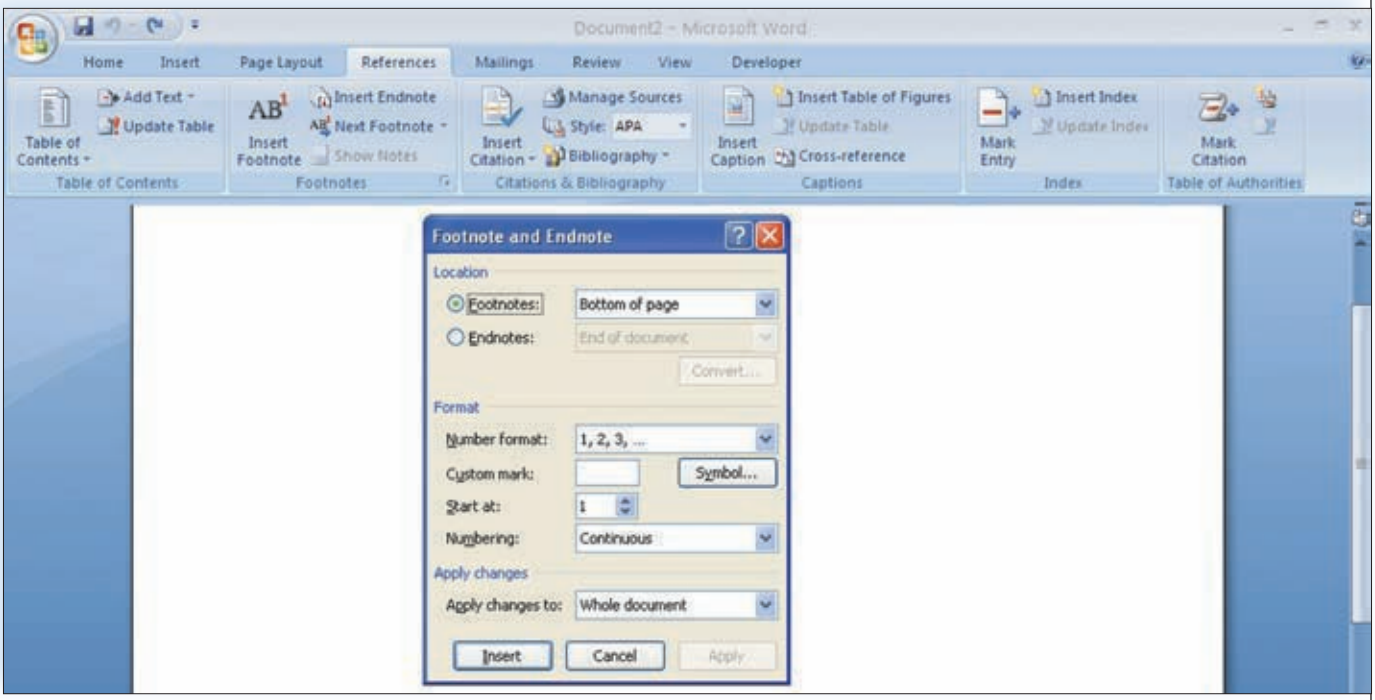


Figure 2: Dialog box launcher.

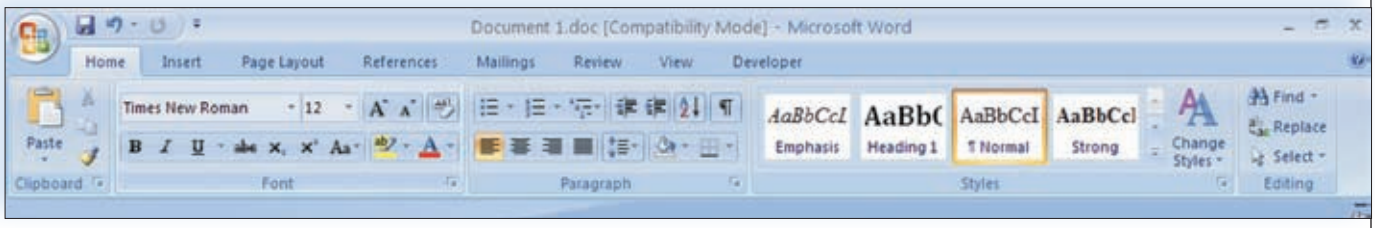


Figure 3: Compatibility mode.

loads/details.aspx?FamilyId=941b3470-3ae9-4aee-8f43-c6bb74cd1466&displaylang=en

Another helpful new feature of Word 2007 is the compatibility mode (Figure 3). If you work in compatibility mode, you can be sure that your Word 2007 files will not have features that are unsupported by earlier versions. Additionally, if you receive a file created in an earlier version of Word from a colleague and open it in Word 2007, the program opens the document in compatibility mode. You can see that you are in compatibility mode at the top of the screen.

Macros, Math Symbols, and Equations

Here is some news about Word 2007 you can be happy about: the macro editor is very similar to that of earlier versions, and the handling of math symbols and equations is far easier than in earlier versions. For macros, if you have developed them in your current (earlier) version of Word,

they will usually work just as well in Word 2007. And, you can simply add them into the normal template. One more thing: if you are a fan of using shortcut keys, you can use them to find or execute most of the same commands as in earlier versions.

For math, earlier versions of Word used a Design Sciences-developed math editor (similar to MathType, which is an add-in) to create formulas and equations. Word 2007 uses Microsoft's own mark-up language for math. Experienced MathType users may find the new equation tools in Word 2007 a bit awkward until they learn how to use them effectively. Authors without MathType experience may find learning to use the equation tools in Word 2007 easier to master than MathType. There is, however, a downside. Equations, although easier for beginners to create, are another feature that may be more difficult to share. When saving math or equations to earlier versions of Word for collaborative authoring, the equations become graphic elements and therefore cannot be edited.

As the answer to the friend or foe question continues to be explored through upcoming issues of *ASBMB Today* in features on Excel, PowerPoint, and Outlook as part of the Office 2007 suite, early adopters need not fret…At this time, Cadmus Communications has no immediate plans to upgrade to Word 2007 for our copyediting staff, but we can certainly accept files from authors who are using the new version. We have been successfully translating files sent in Word 2007 since they started arriving several months ago. Files submitted in Word 2007 will still be converted through our RapidEdit department to have coding and StyList changes applied. Our highly qualified copyediting team will then read your manuscripts and copyedit the files for grammar, spelling, punctuation, and consistency of editorial style according to *JBC* guidelines.

ASBMB 2008/2009 Science Policy Fellowship Program

ASBMB is now accepting applications for its Science Policy Fellowship. The fellowship offers recently graduated PhDs an exposure to a range of activities regarding science policy, and congressional and government relations, by working in the Public Affairs office at ASBMB's Bethesda headquarters. The Fellow will have the opportunity to participate in meetings with Congressional staff as well as being involved with other advocacy organizations. The Fellow will also learn how science policy issues are addressed in the federal government. He or she will work with the Society's Public Affairs Advisory Committee and participate in regular office activities, will write regularly for the Society's monthly magazine, *ASBMB Today*, and will have the opportunity to participate in workshops and meetings directly related to career development.

TERMS

The Society will sponsor one Fellow to work in the ASBMB Office of Public Affairs for one year, beginning September 1, 2008. The Fellow will receive a stipend of $40K, healthcare benefits, and reimbursement of moving expenses up to $1,500. Applicants will be notified in early June.

QUALIFICATIONS

The Fellow will be selected on a competitive basis from applicants having:

- a recently awarded doctorate (i.e. applicant is not beyond post-doctoral stage)
- an interest in the relationship between science, technology and public policy
- flexibility in handling a variety of tasks
- excellent interpersonal and communication skills

HOW TO APPLY

Individuals interested in applying should submit the following no later than April 30, 2008 :

✔ **A resume or CV (no more than 3 pages)**

✔ **A letter of intent (no more than 3 pages) outlining:**

- Why you are applying for this particular program
- What specific policy issues interest you
- What you hope to accomplish as a Fellow
- How this experience would enhance your career
- Your previous participation in civic activities and/or public affairs

✔ **Two letters of reference should be sent directly to ASBMB at the address below. Please include reference contact information with your application.**

PLEASE SEND ALL APPLICATION MATERIALS TO:

Peter Farnham, CAE, Director of Public Affairs, ASBMB, 9650 Rockville Pike, Bethesda, MD 20814

For questions or additional information: pfarnham@asbmb.org • Tel: 301-634-7384 • Fax: 301-634-7126

See You in San Diego!

BY ELLIS BELL

The annual meeting is just around the corner, and scattered across the country 175 undergraduates are busy preparing their posters for the Annual Poster Competition, which will be held on Saturday, April 5. These students will also present their research in the poster sessions at the main meeting, where few people realize they are actually undergraduates. In addition to presenting their posters, a number of undergraduates and faculty from primarily undergraduate institutions will be speaking in the main platform sessions of the various symposia.

The number of undergraduates attending the meeting surprises most people, including the organizers of the various "meetings within a meeting" themes. For the last several years, abstracts submitted by undergraduates have made up over 15% of the total number of submitted abstracts, making undergraduates one of the largest groups of meeting attendees.

The future of the profession is in good hands judging by undergraduate interest in engaging in meaningful research activities. A major goal of the Society membership should be to encourage these students in their endeavors and to help them reach the next stage in the pipeline. I encourage all attendees at the meeting to come to the Undergraduate Poster Competition, wander through the aisles of posters, and talk to these young scientists. Not only will you learn some interesting science, you will also be helping to more fully engage these students in Society activities and the meeting. By the way, it's also not a bad place to do some recruiting for future graduate students—many of the undergraduates in attendance are underclass students and are thinking about which graduate schools to apply.

Please Provide Us with Feedback!

Many members of the Education and Professional Development Committee will be at the meeting, and if you are interested in becoming more involved in the various activities that the committee is promoting please do not hesitate to talk to us. We will be easily identifiable: our name tags will carry the designation "Education and Professional Development Committee Member."

There are a number of issues on which the Committee could use membership input, and scattered around the meeting, particularly at the ASBMB Booth in the Exhibit Hall (booth numbers 1301 and 1303), there will be a number of questionnaires asking your opinion about the following topics:

- **Do you think that a formal affiliation and accreditation program sponsored by ASBMB would be of use? Would you like to hear more about such a program?**
- **What sort of activities do you think would add value for graduate students who join the Society?**
- **Do you think the Society should be more involved in outreach to K-12 teachers and students?**
- **Would ASBMB standardized exams (either comprehensive or theme-specific) be useful to you or your program?**
- **This year marks the first year in recent history where the Education and Professional Development Committee has not held regular symposia every day of the meeting. Instead we are holding one "Classroom of the Future" symposium on Sunday, April 6, and providing more hands on networking and workshop type activities during the "off hours" so as not to compete with the main scientific themes of the meeting. Do you like this change or would you prefer to see Education and Professional Development Symposia scheduled every day of the meeting as we have in the past?**
- **Would you like to see the Society host a "Small Meeting" dedicated to education activities at some other time of the year? What time of the year would be most useful to you?**

If you will not be at the meeting and would like to answer some of the above questions, please send your responses to jbell2@richmond.edu.

Ellis Bell is currently Professor of Chemistry and Chair of the Biochemistry & Molecular Biology Program at the University of Richmond. He is also Chair of the ASBMB Education and Professional Development Committee. His current research focuses on the role of protein dynamics in activity and allosteric regulation of oligomeric dehydrogenases.

Are Molecular Biologists and Biochemists Doing Enough?

BY GEORGE C. HILL

These breast cancer disparities are a national imperative, and many questions need to be answered

While I was teaching and conducting research at Meharry Medical College for 19 years, I had a tremendous graduate student. Once, prior to a lab meeting on a Monday, she casually mentioned to me on the previous Friday that she would not be present for the lab meeting as she had a medical appointment. Later it became clear that she was having a double mastectomy. She came through the surgery, radiation, and chemotherapy well and received her Ph.D. in biomedical sciences in the next few months working on the biochemistry of African trypanosomes. Unfortunately, she passed 12 months later from breast cancer. She was a beautiful African American woman not yet 30 years old. I am now at Vanderbilt University School of Medicine but have never forgotten this young lady.

Given the fact that 1 in 8 women in the United States will have an experience with breast cancer, many of us have probably had loved ones or friends who have been affected by this disease. Breast cancer is the most commonly diagnosed invasive cancer among females in the United States. A recent report from the Centers for Disease Control and Prevention (CDC) described a stabilization in female breast cancer incidence rates from 2001 to 2003 (ending increases that began in the 1980s) and a decline in the number of breast cancer cases diagnosed in 2003. However, for African American women, the increase in incidence has continued.

From numerous studies, it is clear that African American women have a lower incidence of breast cancer compared with white women but die at a higher rate. As seen in the figure, the trends in death rates for female breast cancer reveal an increasing disparity between black and white females. Death rates for white women are substantially lower than those for black women, and this disparity appears to be increasing.

The Institute of Medicine of the National Academies, in a landmark report, *Unequal Treatment: Confronting Racial and Ethnic Disparities in Healthcare*, has noted that racial and health disparities in our country are the result of many factors, including access to care, stereotyping with regard to patients, significant differences in recommendation of specialty procedures, other socio-economic factors such as lower frequency of mammograms with later diagnosis, the patients themselves, and a significant shortage of minority healthcare professionals and biomedical scientists.

A recent study led by Rowan Chlebowski of Harbor-UCLA Medical Center in collaboration with several cancer centers, including Howard University Cancer Center and Fred Hutchinson Cancer Research Center, that was published in the *Journal of the National Cancer Institute* found that breast cancer differences between white and black women persisted even after accounting for numerous risk factors that could influence the development of the disease, like age, body weight, family history of breast cancer, and whether the women received mammograms.

The researchers looked at tumor characteristics and found that black women were more likely than women of all other races to have high grade (aggressive) tumors and tumors without estrogen receptors (ER-negative). Those characteristics make a tumor more difficult to treat. The differences between black and white women in this regard were especially great. They suggested that it remains to be determined whether differences in unidentified environmental exposures, genetic makeup, or other factors lead to the higher frequency of high grade, ER-negative cancers in African Americans.

William Blot, CEO of the International Epidemiology Institute, and other colleagues have noted that the most notable difference in breast cancer among black *versus* white women is the difference in subtype of the tumors, with black women more likely to have estrogen-, progesterone-, and HER2-negative tumors (the so-called triple negative cancers). These types tend to have a more aggressive course and worse prognosis. They also tend to occur at younger ages. Thus, Blot notes that while the overall age-adjusted incidence of breast cancer is lower among black than white

women, the incidence of breast cancer at younger ages, and the incidence of triple negative breast cancers, is higher among blacks than whites. These breast cancers, as with most cancers that occur at younger ages, also may be more likely to have a genetic origin. This is a research area ripe for investigation.

It is important that we as biochemists, pharmacologists, molecular biologists, biomedical scientists, and physicians get on board and investigate these serious issues. These breast cancer disparities are a national imperative, and many questions need to be answered. Are there biological differences in breast cancers from different ethnic groups? Are there molecular mechanisms that may contribute to incidence and outcomes in African Americans?

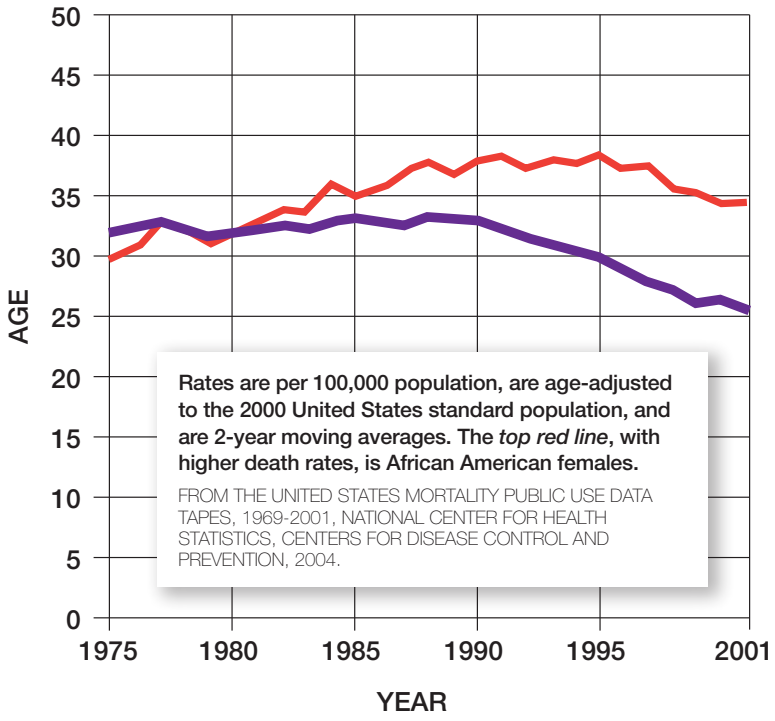
What breast cancer susceptibility variants might be identified through epidemiological studies such as the Southern Community Cohort Study led by Meharry Medical College, Vanderbilt University Medical Center, and the International Epidemiology Institute and over 20 community health centers throughout the southeast? Recruiting 90,000 volunteers, this is the largest population-based study ever undertaken to find the reasons for cancer and later other health disparities. What is the role of obesity and nutrition? What is the genetic basis for more aggressive cancers that are ER-negative in African American women? Other questions are certainly apparent.

We must also recognize that by increasing the number of medical school graduates who are now under-represented in medicine and also increasing the number of graduate students and postdoctoral fellows from these backgrounds, we will increase the number of scientists who have a strong interest, will conduct research, and will submit proposals to address these health disparities. We are improving, but there is a significant shortage of such under-represented individuals in our research-intensive institutions in the professoriate that can make significant contributions. As emphasized in the W. K. Kellogg Foundation-supported Sullivan Commission on Diversity in the Healthcare Workforce Report entitled *Missing Persons: Minorities in the Health Professions*, addressing this crisis is essential for the health of the United States.

We as scientists have a major responsibility to investigate breast cancer and other racial health disparities affecting many ethnic groups. We have the knowledge and technology to make a difference. We need to determine in our laboratories, centers, institutes, and departments what we can do in this fight, and we need to strategically expand our research expertise and energies in this area and find the answers.

My graduate student was a fantastic person. She, Vanita, was like many of our current and past students and postdoctoral fellows--eager to pursue research questions. Her determination and perseverance were amazing. I never heard her complain. She had a love for learning. In her memory, and in memory of many others, we can and we must make a difference.

Trends in Death Rates for Female Breast Cancer (1975-2001)



Rates are per 100,000 population, are age-adjusted to the 2000 United States standard population, and are 2-year moving averages. The *top red line*, with higher death rates, is African American females.

FROM THE UNITED STATES MORTALITY PUBLIC USE DATA TAPES, 1969-2001, NATIONAL CENTER FOR HEALTH STATISTICS, CENTERS FOR DISEASE CONTROL AND PREVENTION, 2004.

George C. Hill is the Levi Watkins, Jr., Professor and Associate Dean for Diversity in Medical Education, and Professor of Microbiology and Immunology at Vanderbilt University School of Medicine. He conducts research on the biochemistry of African trypanosomes. He has been elected to the Institute of Medicine of the National Academy of Sciences and the Academy for Microbiology and formerly served as Dean of the School of Graduate Studies and Vice-President for Research at Meharry Medical College.

How I Stopped Following What I "Should" Do and Started Doing What I Love to Do

BY SJANE CHIN

I was a third year biochemistry Ph.D. graduate student when I realized that I wanted to leave bench science. At the time, I had no idea that I would take 4 additional years to gather enough data, write my dissertation, and complete my doctorate. I had my first taste of what Matt Groenig called "School Is Hell," and I began to seriously consider an alternative scientific career.

The irony was that I chose this path. I had taken the road of least resistance. I majored in biology because I did well in biology during school, and people said it was logical to continue. I had limited information, worse yet I had limited self-knowledge. I went with what people said was safe and kept this mindset during the early years of my professional career. In other words, I traded my "School Is Hell" journey for multiple sequels of "Work Is Hell."

I would get bored with a career and transition for another. All the while, I dreaded that inevitable day when the "honeymoon" ended and I would also get bored with this next career. My resume read like a serial job hopper: I had a career in industry R&D, pharmaceutical sales, and medical affairs (as a medical science liaison). Finally, I got bored of getting bored. After 2 years of intense self-reflection, I took a risk: I quit a six-figure job and started a consulting business. Through trial and error, I realized that achieving full potential requires both intimate self-knowledge and being in the right "space" to exercise your talents.

My time spent in trial and error was not in vain, as it culminated in my writing a guide on the mechanics of an alternative science career transition. *5 Lessons in PhD Career Transitions* distilled what I and other scientists had learned in our own transitions.

Know Your Strengths

These are useful ways to start your career exploration, but what if your "ideal" job is not on the list? Let's go a step further from an entrepreneurial mindset, what if your "ideal" job does not yet exist because you have not yet created it? You will not find your best suited job ideas and career options on a pre-made template or a list generated from statistical averages.

The most important ingredient when exploring career options and designing your career is introspection; in other words, know yourself. Know your strengths, your thought processes, and your values. Your strengths are your natural assets. Your thought processes are the mechanics through which you may apply your assets to generate new fields of possibilities. Your values determine what gives you a feeling of meaning and satisfaction in a career.

You may identify your strengths by taking assessments designed for this purpose, committing to periodic introspection, and working with a coach or a mentor.

Let Go of What You "Should" Want

If you have ever felt trapped in a career, then you probably were following a series of "shoulds" during your career. I got good grades in science at school, therefore I "should" want to major in

Chin

Jane Chin received her B.S. in Microbiology from Cornell University in Ithaca, New York, and her Ph.D. in Biochemistry from Roswell Park Cancer Institute at the University of Buffalo, New York. After spending more than a decade working in various functions in the pharmaceutical industry, Chin became an entrepreneur and created several businesses, including the Medical Science Liaison Institute. She is interested in how scientists explore what they want to do with their lives. Chin shares some of her creative adventures through life at www.JaneChin.com.

science in college. I "should" want to continue with a science program in graduate school. I "should" want to pursue a career as a scientist. This series of "shoulds" caught up with me by my third year in graduate school.

Those of you who are prospecting a career transition, either out of the traditional career track or into an alternative scientific career, may find yourself surrounded by negative reinforcements, where your peers or advisors continually remind you of these "shoulds."

In this situation, you want to be very selective of the company you keep. Your support network may include a coach or mentor who is supportive of your transitional aspirations. You may want to pair up with a "transitional buddy," a peer who has similar transitional goals. You may want to keep quiet the details of your transition from those who are not directly affected by your decision.

Make Your Ph.D. Work for You

One of the most common challenges that scientists write me about is the "catch-22" when they desire a transition into non-research scientific careers. Many postdocs today do not receive the optimal types of skill training to be more competitive in alternative scientific careers. They need formal training plus on-the-job continuous training.

Many scientists may not realize what skills they already have that may be desirable to prospective employers. As a result, they have not learned to see the skills they do have from a non-research, non-academic angle. More importantly, scientists do not receive training on how to communicate these skills to hiring managers who do not have a background in academic research. This creates a perception by some employers that scientists do not have transferable skills beyond bench research.

It becomes the scientists' imperative to translate the diverse skills they have acquired in the process of conducting research and working in a lab environment into new situations where they may successfully apply their skill sets. When communicating with prospective employers, scientists need to learn the jargon or language that hiring managers recognize.

Put a Price Tag on Procrastination

If procrastination is really a matter of time management, personal organization, or prioritization, then the wealth of publicly available seminars and scheduling tools should solve this problem. However, the source of procrastination is rarely a lack of knowledge in organizing time or priorities. The source of procrastination is fear: fear of the unknown, fear of failure, fear of public opinion. These are a few fears that plague professionals in transition and sometimes cut off their initial momentum.

Many postdocs in transition start out with great momentum: researching, reflecting, and reviewing their transitional goals. Then a curious but common phenomenon occurs: they begin to stall and procrastinate. Some will ask questions like, "Should I do another experiment?", "Should I do another postdoc?", or "Should I go back to school and get a business degree?" In most circumstances, these options are valid questions. In transitional circumstances, however, these options are frequently used as a delay tactic from leaping into the unknown.

Putting a price tag on procrastination is a constructive reality check. Postdocs can calculate how much being a postdoc is "costing" them annually by taking the difference between their overall compensation and that of an entry level position in a general field, for example, in sales. If this reality check isn't enough to jump-start a procrastinator's momentum, she may work with a coach or mentor who can help hold her accountable for tasks.

Create Your Opportunities

Do you believe that you "have what it takes, but just need an opportunity?" If so, you may join ranks with many Ph.D. scientists who desire a career transition but assume that once their resumes are polished, their next step is to wait for their "lucky break." Ph.D. scientists aren't the only ones making this dangerous assumption, people in career transition can keep waiting to bump into the right people at the right time that will give them the right opportunities.

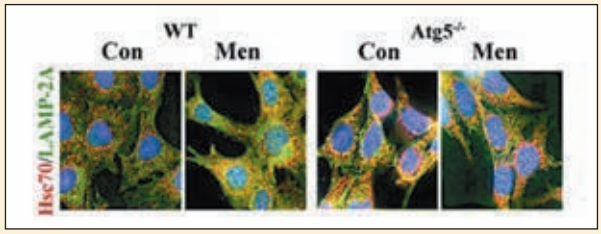
Networking is an essential skill for creating opportunities. Network at job fairs and industry conferences or trade/association meetings. Network with recruiters. Networking is a skill of "connecting with the connectors." The better you become at networking, the more likely you're able to connect with people who may point you in the right direction and refer you to others who may have the opportunities you are looking for. You usually do not directly meet contacts that have the opportunities you desire at networking events unless you are at an industry conference aimed at these constituents.

Conclusion

By preparing yourself mentally and systematically, you can act on your strengths and talents, and triumph in transitioning. Then you too can begin doing what you truly love to do and achieve your full potential.

Balancing Apoptosis and Autophagy

Experimental studies have produced disparate results implicating macroautophagy in both promoting and protecting against programmed cell death. The speculation is that the role of macroautophagy may be based on cell type. The authors of this paper reveal that this may not be the case. Using mouse embryo fibroblasts with RNA interference knockdown of the autophagic gene *Atg5*, they show that inhibiting macroautophagy can produce multiple end results in the same cell type, depending on the context. Atg5$^{-/-}$ mouse embryonic fibroblasts (MEFs) had increased activation of caspase-dependent apoptosis in response to death receptor ligands, possibly due to the inability of the cell to envelop apoptotic mitochondria. In contrast, the loss of macroautophagy made MEFs more resistant to the intrinsic apoptosis pathway following menadione-generated oxidative stress or UV radiation; this intrinsic protection was due to an upregulation of chaperone-mediated autophagy, which could sequester oxidized molecules. Overall, these results suggest that macroautophagy engages in a complex relationship with apoptosis, and the specific stimuli that trigger cell death may govern the cell's response.



Cells lacking macroautophagy produce higher levels of chaperone-mediated autophagy in response to menadione

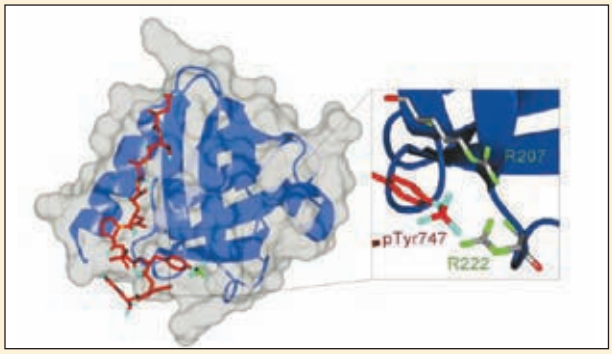
Loss of Macroautophagy Promotes or Prevents Fibroblast Apoptosis Depending on the Death Stimulus

Yongjun Wang, Rajat Singh, Ashish C. Massey, Saul S. Kane, Susmita Kaushik, Taneisha Grant, Youqing Xiang, Ana Maria Cuervo, and Mark J. Czaja

J. Biol. Chem. 2008 **283**, 4766–4777

Integrin On, Integrin Off

Integrin receptors play a fundamental role in cell movement and adhesion by providing a physical connection between the cytoskeleton and extracellular matrix to enable bi-directional signaling through the cell membrane. Two important integrin ligands inside the cell are talin and Dok1, both of which bind to the cytoplasmic tail of the integrin β3 subunit but act in opposite fashion; talin is a positive regulator of integrin activation, whereas Dok1 is a negative regulator. In this paper the authors used both x-ray crystallography and NMR spectroscopy to investigate the molecular interactions of these competing ligands. They found that Dok1 and talin both bind to the integrin β3 NPLY motif, but unlike talin, Dok1 does not interact with the membrane proximal region upon binding and therefore does not initiate integrin activation. Additional experiments revealed that talin has three times as much affinity for the integrin tail as Dok1, but upon phosphorylation of integrin Tyr-747, binding preference shifts dramatically to Dok1. These results suggest that tyrosine 747 phosphorylation acts as a switch to regulate integrin activation.



Model of Dok1 complexed with the integrin β-tail

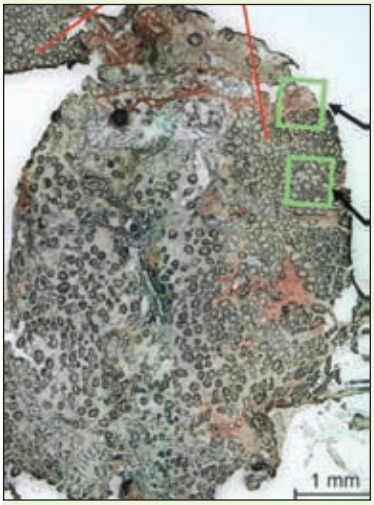
An Integrin Phosphorylation Switch: The Effect of β3 Integrin Tail Phosphorylation on Dok1 and Talin Binding

Camilla L. Oxley, Nicholas J. Anthis, Edward D. Lowe, Ioannis Vakonakis, Iain D. Campbell, and Kate L. Wegener

J. Biol. Chem. 2008 **283**, *5420-5426*

Lipid Changes in Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is an X-linked, severe degenerative genetic disease that is caused by the absence of expression or the truncation of dystrophin, a protein involved in a transmembrane complex of proteins. This lack of dystrophin causes rapid degeneration of skeletal, smooth, and cardiac muscle. In this *JLR* paper, the authors compare human striated muscle from children with and without DMD using cluster-time-of-flight secondary ion mass spectrometry imaging. They found that the DMD-affected muscles displayed different distributions of the lipid ions in dystrophic cells and severely damaged areas. Vitamin E and phosphatidylinositols concentrated within the cells, whereas intact phosphocholines accumulated over the most damaged areas of the dystrophic muscles, together with cholesterol and sphingomyelin species. Fatty acyl chain composition, on the other hand, varied depending on the region. Thus the ion images allowed the authors to differentiate the regions where the accumulation of different compounds occurred in dystrophic cells, severely damaged areas, or adipocytes.



Human striated muscle from a DMD patient

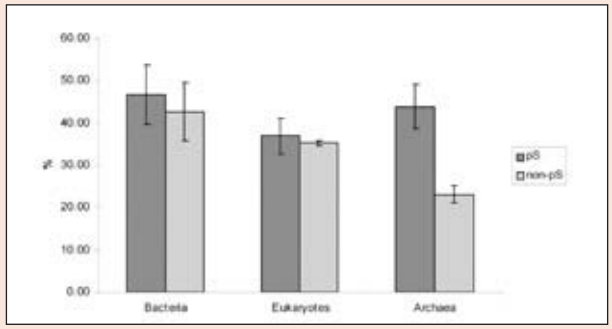
Lipid Mapping in Human Dystrophic Muscle by Cluster-Time-of-Flight Secondary Ion Mass Spectrometry Imaging

Nora Tahallah, Alain Brunelle, Sabine De La Porte, and Olivier Laprévote

J. Lipid Res. 2008 **49**, 438-54

Bacterial Phosphorylation

The addition of phosphate groups to proteins is generally considered to be the major regulatory post-translational modification in eukaryotic cells. Increasing evidence has also shown that this modification is present and functional in prokaryotes. In this *MCP* paper, the authors looked at the phosphoproteome of the Gram-negative bacterium *Escherichia coli* using high accuracy mass spectrometry combined with phosphopeptide enrichment. They were able to find 81 phosphorylation sites on 79 *E. coli* proteins. The authors also compared the *E. coli* phosphoproteome with that of the Gram-positive bacterium *Bacillus subtilis* and found that despite their phylogenetic distance, the two bacterial phosphoproteomes demonstrate a striking similarity in size, classes of phosphorylated proteins, and distribution of phosphorylation sites. Surprisingly, both phosphoproteomes showed significantly higher conservation levels than a random protein population, with several phosphorylation sites being conserved from Archaea to humans, suggesting this modification plays an important role in prokaryotes as well as eukaryotes.



The evolutionary conservation of phosphoserine in *E. coli*

Phosphoproteome Analysis of *E. coli* Reveals Evolutionary Conservation of Bacterial Ser/Thr/Tyr Phosphorylation

Boris Macek, Florian Gnad, Boumediene Soufi, Chanchal Kumar, Jesper V. Olsen, Ivan Mijakovic, and Matthias Mann

Mol. Cell. Proteomics **2008** 7, *299–307*

Rosalind Coleman: Regulating Triacylglycerol in the Body

BY NICK ZAGORSKI

Coleman

When Rosalind Coleman started her own lab, her chosen research specialty–triacylglycerol synthesis–wasn't on many scientists' radar. "When you went to the annual lipid meetings back in the 70s and 80s, most of the interest would lie with phospholipids and cholesterol," she says. "Neutral lipids like triacylglycerols were not considered that appealing." Part of the problem came from the difficulty of working with triacylglycerols; the enzymes were all membrane-bound and impossible to purify, and likewise the substrates were highly hydrophobic. Also, triacylglycerols weren't functionally very thrilling because their primary role was simply for fat storage– which seemed like a boring concept to many investigators.

This was all well and good for Coleman, currently Professor of Nutrition and Pediatrics at the University of North Carolina in Chapel Hill. As a researcher and physician, Coleman had to balance her new lab with her clinical responsibilities, so focusing in a field that most people weren't interested in would let her move at a slower pace as she established herself. And, she adds, "It also meant that there was plenty of work to be done on this topic, giving me a wide range of research directions."

The direction Coleman has since taken is understanding the mechanisms that regulate the amount of triacylglycerols in tissues, especially those in the liver; her work has shed light onto how activating fatty acids with coenzyme A (CoA) partitions them toward metabolism or storage, as well as how multiple enzymes work at each step of the synthesis process to control the concentration of lipid intermediates.

At the same time, this whole field has taken an unexpected direction. "In recent years people have discovered that triacylglycerols are connected with leptin and appetite control, realized that fatty liver is not a benign problem, and discovered that the phenomenon most closely associated with the level of insulin resistance was the amount on triacylglycerols in non-fat cells." Neutral lipid researchers like Coleman are now at the forefront of some of the fastest rising health issues in the United States, namely obesity and diabetes.

"I just helped organize the first FASEB summer conference on lipid droplets and neutral lipids this past August," she says, "and it was amazing who showed up; so many researchers in fields like parasitology and virology that you wouldn't think to associate with lipids." All this new attention does mean Coleman may have to pick up the pace a bit, but she doesn't mind at all. "It's wonderful to be working in such an exciting area."

In a Man's World

Coleman began her undergraduate studies at Harvard University in 1960, a little unsure about her future aspirations. After all, she points out, growing up in the 1950s did not provide for too many female role models with professional careers. "I didn't really know any women who had jobs other than teaching, except one who was a child psychologist," she says. "So I thought I would give it a try." Her introductory psychology course left her divided, however. On the one hand, the material was fascinating, but on the other hand, it was a bit too ambiguous. "The results were so often open to a range of interpretations, and I liked it better if you could do one test, and get one outcome."

That same year, Coleman had a far more positive experience with her required introductory biology course, which was taught by George Wald, a future Nobel winner (Chemistry, 1967) who was renowned for his research into retinal pigments and vision. "I remember Wald being one of the most inspiring lecturers I ever

heard," she says, "and I think others would agree because his previous students would keep coming back to hear his talks on the chemistry of life and the meaning of death."

After finishing Wald's course, Coleman decided to pursue a major in biology and began taking laboratory courses, which also strongly appealed to her. For one, they catered to her desire to do experiments that produced concrete results. "Although," she adds, "I also liked them so much because sometimes I was the only one in the lab whose experiments worked."

Unfortunately, in what may reflect another sign of the time, Coleman didn't receive much encouragement from faculty or colleagues to pursue her biology training in graduate school despite her skill and enthusiasm. "And still being young and undecided, I really wanted someone to tell me I would make a good scientist," she says. So, in a decision she admits was not her first choice, Coleman enrolled at Case Western Reserve School of Medicine to obtain her M.D.

A Metabolic Switch

Coleman settled on pediatrics as her specialty and began her residency at Duke University Medical Center in 1972. She favored pediatrics for many reasons, not the least of which was that she enjoyed being in an area where patients actually followed her advice. "One of my big frustrations in medicine was trying to provide my best guidance to people and then frequently finding out that they had ignored you," Coleman says. "But, if you told parents that same medical advice for their children, they tended to listen and would do things for their children they wouldn't do themselves."

During this time, Coleman also became interested in the biology and defects underlying growth and development. "I ended up doing a fellowship in what we called metabolic diseases but now refer to as inborn errors of metabolism." She began asking around how to continue studying these disorders, and was informed that because they were pretty rare she couldn't go into private practice.

> *"After nearly a decade in medicine, the change to a basic research environment took a bit of adjustment"*

Rather, she should stay in academic medicine and do post-doctoral research in a lab. Not many words could have been sweeter to Coleman, who began looking for possible labs at Duke. Although no one there specifically focused on inborn errors of metabolism, she soon found a good fit with lipid biochemist Robert Bell, who gave her a project looking at enzymes of triacylglycerol synthesis in rat fat cells.

After nearly a decade in medicine, the change to a basic research environment took a bit of adjustment—Coleman notes in the beginning she needed help even turning on the pH meter–but one she relished very quickly. "Compared with some of the stressful times I had as a pediatrician, the atmosphere was relaxing," she says. "I would come in and get a gratifying result almost every day, I wasn't sleep-deprived, and I had a mentor who was absolutely terrific." Her knack for getting experiments to work remained intact as well; within 6 months she had enough material for her first article, a *JBC* paper characterizing the enzyme that catalyzes the final step in triacylglycerol biosynthesis.

"At that point, I felt so positive that I became committed to continuing with research," she says, and in 1978 she finished her post-doc training with Bell and became an assistant professor at Duke. She continued to study the enzymes and regulation of triacylglycerol synthesis, while also seeing patients with metabolic disorders and conducting some clinical work on glycogen storage disease and defective β-oxidation (the breakdown of fatty acids into 2-carbon acetyl-CoA units). She remained at Duke until 1991, and then relocated to nearby Chapel Hill to work for her good colleague Steven Zeisel, who had just been appointed Chair of University of North Carolina's Department of Nutrition.

Sorting the Fat

Over her long and distinguished research career, Coleman has discovered that what appeared to be a relatively straightforward synthesis pathway, the attachment of three acyl chains to a glycerol 3-phosphate, is in fact highly regulated and quite complex. One of her main areas of interest has been acyl-CoA partitioning.

When fatty acids enter a cell, they can undergo multiple metabolic fates: burned for energy, integrated into phospholipids, or stored for future use. The first order of business for all options, however, is to 'activate' the fatty acid by attaching a CoA molecule to create an acyl-CoA.

The enzymes that handle this are acyl-CoA synthetases; numerous different types exist, and their expression varies in different tissues as well as under different dietary conditions. Coleman has shown that this assortment of synthetases help channel fatty acids to the appropriate destination depending on the cell's needs and thus may be closely tied with several of the metabolic disorders she has studied.

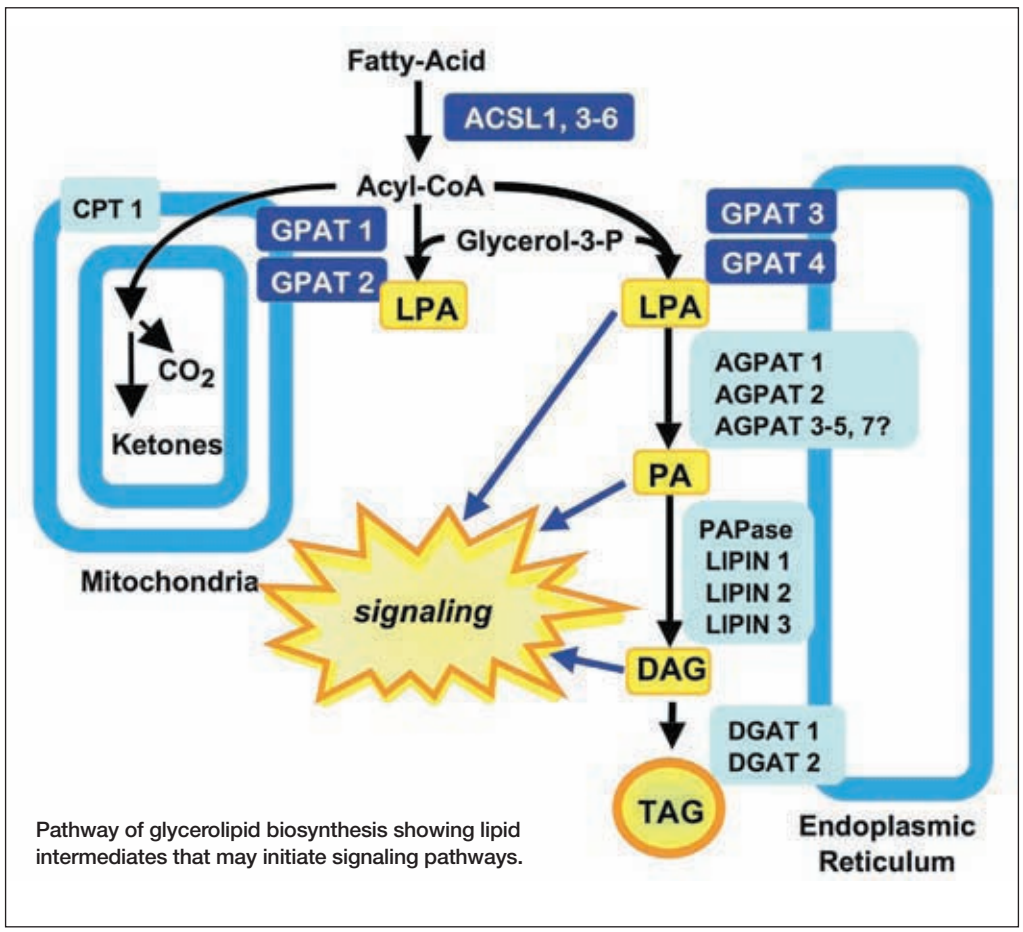
However, this multifaceted regulation is not limited to fatty acid activation. "If you look at the synthesis of most molecules, like glucose or amino acids, each step in the pathway is generally carried out by a single specific enzyme," says Coleman. "But one of the surprising things we've uncovered is that each of the four main steps in triacylglycerol synthesis is catalyzed by enzymes with multiple isoforms, each encoded by a different gene." Coleman and others have developed several knock-out mice of these triacylglycerol genes and found that they cannot compensate for each other. "That seems to imply that each isoform has special properties to help it carry out a specific job, and we're in the process of using our mouse models to tease out exactly what these jobs are."

Coleman hypothesizes that the peculiar nature of this pathway arises from the nature of the intermediates in triacylglycerol synthesis. "The three molecules you create along the path are lysophosphatidic acid (LPA), then phosphatidic acid (PA), then diacylglycerol (DAG)," she notes. "These three intermediates—LPA, PA, DAG—also happen to be major signaling molecules in kinase cascades." By having multiple isoforms, a cell might be able to better regulate this overlap and prevent pathways from interfering with each other.

Coleman notes DAG

Out of Focus: Collecting the Bet

As if the lack of encouragement from faculty wasn't enough, Coleman even received a bit of pessimism from her House tutor at Harvard (undergraduate residencies at Harvard follow an English University model where students and faculty live and learn together). "After I announced my decision to go into medicine, my tutor–he'll remain nameless--bet me a dinner that I wouldn't complete medical school," she says. Coleman adds that the tutor's response was not mean-spirited, "we actually got along well and were good friends; he just thought I wouldn't have the gumption to stick it out." Although the tutor did enter a different area of biology, Coleman ran into him at a large conference years later. "So I went up to him after he gave his lecture and let him know it was time to pay up."



Pathway of glycerolipid biosynthesis showing lipid intermediates that may initiate signaling pathways.

is especially interesting as it can activate protein kinase C and inhibit parts of the insulin signaling pathway. Her lab, in fact, has recently shown that overexpressing glycerol-*sn*-3-phosphate acyltransferase-1, the enzyme that carries out the first step of triacylglycerol synthesis, in the liver of rats resulted in increased DAG levels, the onset of fatty liver, and insulin resistance. As excess DAG can also be produced by a high fat diet, these findings raise a tantalizing connection. "It puts forth the idea that altered triacylglycerol synthesis is a critical mechanism that links obesity with diabetes," she says.

Coleman hopes that relating finds like these might help her in another role she picked up in 1999, when she became Associate Director of University of North Carolina's Clinical Nutrition Research Center. Her main duties at the Center are to encourage junior faculty to get into nutritional research through pilot grants aimed at funding innovative, nutrition-related projects that investigators can work on in coordination with their primary research. At the least, these grants may stimulate scientists to think more about nutrition and health, but it's also possible they could lead to a long and exciting career.

Nick Zagorski, Ph.D., a graduate of The Johns Hopkins and Cornell Universities, is a science writer for ASBMB. He can be reached at nzagorski@asbmb.org.

BIBLIOGRAPHY

Coleman, R. A. (2007) How do I fatten thee? Let me count the ways... *Cell Metab.* **5**, 87-89.

Coleman, R. A., Reed, B. C., Mackall, J. C., Student, A. K., Lane, M. D., and Bell, R. M. (1978) Selective changes in microsomal enzymes of triacylglycerol phosphatidylcholine, and phosphatidylethanolamine biosynthesis during differentiation of 3T3-L1 preadipocytes. *J. Biol. Chem.* **253**, 7256-7261.

Coleman, R. A., Lewin, T. M., Van Horn, C. G., and Gonzalez-Baró, M. R. (2002) Do long-chain acyl-CoA synthetases regulate fatty acid entry into synthetic versus degradative pathways? *J. Nutr.* **132**, 2123-2126.

Lewin, T. M., Schwerbrock, N. M., Lee, D. P., and Coleman, R. A. (2004) Identification of a new glycerol-3-phosphate acyltransferase isoenzyme, mtGPAT2, in mitochondria. *J. Biol. Chem.* **279**, 3488-3495.

Li, L. O., Mashek, D. G., An, J., Doughman, S. D., Newgard, C. B., and Coleman, R. A. (2006) Overexpression of rat long chain acyl-CoA synthetase 1 alters fatty acid metabolism in rat primary hepatocytes. *J. Biol. Chem.* **281**, 37246-37255.

Nagle, C. A., An, J., Shiota, M., Torres, T. P., Cline, G. W., Liu, Z. X., Wang, S., Catlin, R. L., Shulman, G. I., Newgard, C. B., and Coleman, R. A. (2007) Hepatic overexpression of glycerol-*sn*-3-phosphate acyltransferase 1 in rats causes insulin resistance. *J. Biol. Chem.* **282**, 14807-14815.

Lewis Cantley: Mapping the Phosphatidylinositol 3-Kinase Pathway

BY NICK ZAGORSKI

Cantley

While an undergraduate at West Virginia Wesleyan College in the late 1960s, Lewis Cantley got caught up in a radical movement, but not the one most people might assume. Rather, Cantley's intrigue stemmed from the chemiosmotic hypothesis, Peter Mitchell's scientifically radical 1961 theory that cellular ATP synthesis was connected to an ion gradient across mitochondrial membranes. "I remember how exciting the whole theory sounded," he says. "And how it started as a controversial and not well accepted idea, but despite the skepticism researchers like Mitchell and Efraim Racker discovered the evidence to prove the idea."

Perhaps fittingly, Cantley began his research career by studying some enzymes involved in ATP synthesis, an endeavor that would eventually lead to his own radical, textbook-revising discovery years later. In 1987, while studying the activity of a phosphatidylinositol kinase he had purified, Cantley found that it placed its phosphate group on the 3-position of the inositol ring, which was completely unprecedented. "In over 30 years of research in this area, phosphate groups had only been identified on the 4- and 5-positions of inositol rings," he says. Only 38 years old and a relative scientific novice who had recently been turned down for tenure at Harvard, Cantley faced an uphill battle to validate his newly identified phosphatidylinositol 3-kinase (PI3K).

Two decades (and many accolades) later, it can be safely surmised that this particular battle was won. Cantley, now back at Harvard as Professor of Systems Biology at Harvard Medical School and Director of the Beth Israel Deaconess Cancer Center, has not only proven the existence of PI3K and its lipid products, but he has also shown that the PI3K signaling pathway participates in numerous key processes, including cell growth, cell division, and metabolism. Many battles remain to be fought, however, and Cantley has combined classical biochemistry, peptide screening, and mass spectroscopy in his lab's pursuit of understanding the biochemical pathways that regulate normal cell activities and how defects in these pathways lead to disease.

Pump It Up

After graduating from West Virginia Wesleyan in 1971, Cantley, who grew up enjoying chemistry and math, went to Cornell University for his Ph.D. work in biophysical chemistry. And although he didn't join the lab of Efraim Racker, the pioneer in mitochondrial ATP synthesis, he managed to contribute to this growing area of research working with Gordon Hammes in the department of chemistry. Under Hammes, Cantley studied the kinetics of the F_1-ATP synthase and the chloroplast homolog (CF1).

In 1975, Cantley completed his dissertation and took a post-doctoral position at Harvard with Guido Guidotti, who studied the plasma membrane Na^+/K^+-ATPase. "This gave me the opportunity to continue looking at ATP-coupled membrane transport systems, although Guidotti's lab was definitely more biologically oriented than Hammes'," says Cantley. "I could see I was on the slippery slope of turning into a biologist." Interestingly, at that point Cantley had almost no formal training in biology, although his time in the Hammes lab provided some exposure. "I think I absorbed enough biology by osmosis that I didn't need to take any actual courses."

While studying the kinetics of the Na^+/K^+-ATPase, Cantley noticed that when ATP was added to the enzyme to initiate ATP hydrolysis, there was a burst of activity and then the enzyme quickly died, even in conditions where only a small fraction of the ATP was consumed and no significant product was made. Other labs had made this

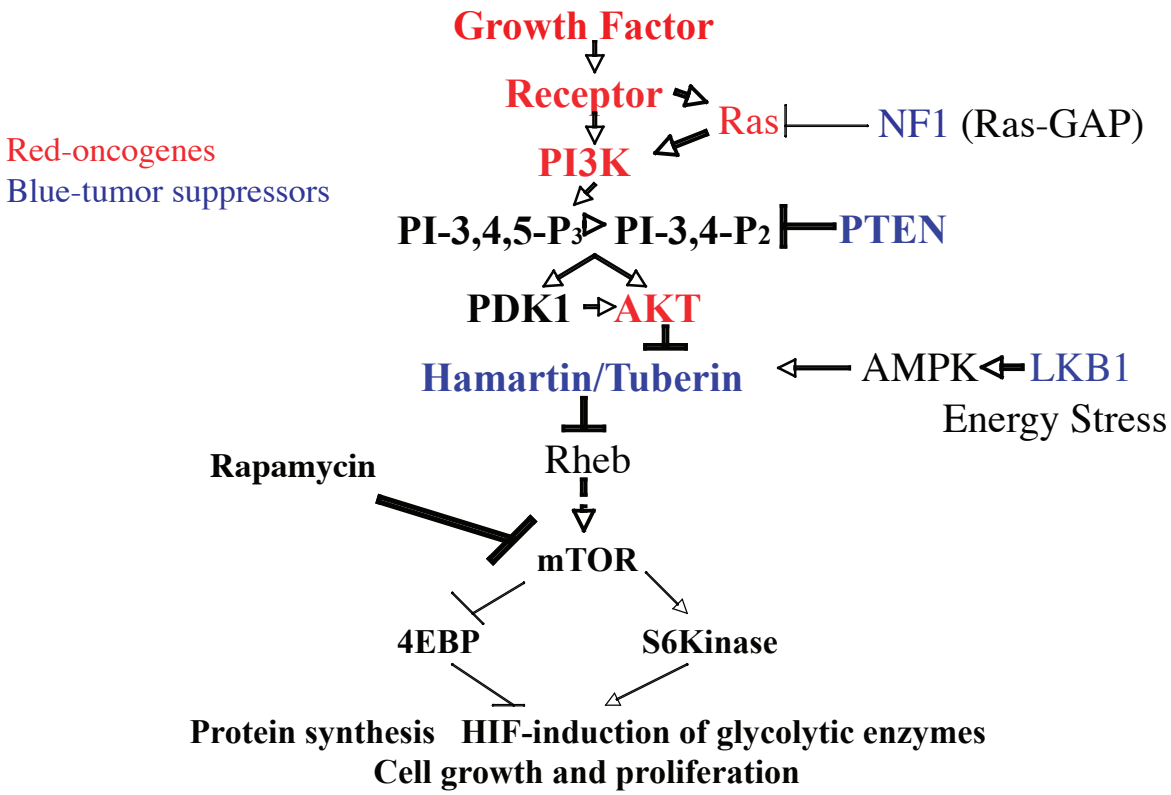
same observation and attributed this to the enzyme being unstable. Being trained in enzyme kinetics, however, Cantley realized that this didn't make sense and further explored this phenomenon.

One day he ran out of Sigma Grade ATP and found an old bottle of Boehringer Mannheim ATP to use instead. To his shock, the Na^+/K^+-ATPase activity continued indefinitely when this ATP was used. Cantley ultimately discovered that Sigma Grade ATP was contaminated with minute amounts of vanadate (Sigma promptly revised their process for ATP purification to get rid of the vanadate). He went on to show that vanadate was a very potent inhibitor of Na^+/K^+-ATPase because it mimicked the transition state that phosphate undergoes during the formation of a phosphorylated intermediate on the enzyme. His discovery led to the use of vanadate as an inhibitor of other enzymes that form phosphorylated intermediates (*e.g.* phosphotyrosine phosphatases and some lipid phosphatases such as PTEN).

Following his postdoc, Cantley started his own lab at Harvard where he continued probing the Na^+/K^+-ATPase, although now he was investigating the connection between growth factors and cation transport. He had observed that vanadate could inhibit the differentiation of a leukemia cell line, suggesting that changes in pump activity might affect cell growth. Coupled with another observation that ATPase activity was different in synthetic membranes depending on whether or not the lipid phosphatidylinositol was phosphorylated, it led Cantley to think that growth factor receptors, which have kinase activity, might regulate the Na^+/K^+-ATPase through lipid phosphorylation.

In 1983, Cantley's colleague Raymond Erikson reported that his Src oncoprotein, a tyrosine kinase, could not only phosphorylate proteins but glycerol as well. Because glycerol and phosphatidylinositol had similar chemical structures, Cantley believed he had found the centerpiece to his argument. A collaboration with Erikson's laboratory revealed that the purified Src

PI3K is central to a signaling network that controls cell growth



protein had an activity that could phosphorylate phosphatidylinositol. Further collaborations with Tom Roberts and Brian Schaffhausen revealed that other oncoproteins had associated phosphatidylinositol kinase activity and that this activity correlated with cell transformation.

Pip, Pip, Hooray!

It only took 1 mm for Cantley to decide to change the course of his research. (While reviewing phosphatidylinositol kinase assay results with his graduate student, Malcolm Whitman, they noticed that the lipid produced by the Src-associated phosphatidylinositol kinase had a slightly different migration position from the expected product, PI-4-P. With help from Peter Downes, they went on to show that the product of the enzyme was PI-3-P.) His first order of business would be difficult: trying to win over a skeptical research community. After accomplishing this through several reproductions of his results and purifying the PI3K enzyme, he set upon a far easier task: characterizing the PI3K signaling pathway.

Cantley was eager to follow the PI3K trail because, he notes, "It wasn't just Src; we had found several activators of PI3K that could induce cell transformation." Over the years, this association has certainly borne out. "Currently, we know that 25% of all breast and colorectal tumors have altered PI3K activity," Cantley says. "As an oncoprotein, it's second only to RAS in terms of prevalence."

One of Cantley's first insights into the PI3K pathway was showing that phosphatidylinositol-3-P, the lipid that jump-started the whole thing, was a bit of a red herring in cell signaling. Rather, in response to cell-stimulating agents like platelet-derived growth factor and polyoma virus middle T antigen (which can induce cancer transformation), PI3K added a 3-phosphate onto existing phosphoinositides. These resulting products, PI-3,4-bisphosphate and PI-3,4,5-trisphosphate (PI-3,4-P_2 and PIP_3 for short), were the true messengers that helped alter cell activity.

In a way, Cantley has come full circle, returning to his first graduate school projects modeling glucose metabolism and ATP homeostasis.

Over the past several years, Cantley has been linking these lipid second messengers to the activation of Akt and mammalian target of rapamycin (mTOR). This pair of protein kinases plays a central role in regulating cell growth, survival, and proliferation, and in addition to their role in cancer, their activity can result in enlarged organs. A collaboration with Seigo Izumo's laboratory led to the finding that the level of activity of PI3K and AKT in the heart determined the size of the heart. Similar studies in flies led to the same conclusion, and these studies suggested that the *Drosophila* homolog of mammalian mTOR was downstream of Akt.

These two proteins didn't interact, however, which meant any connection had to be indirect. The bridge proved to be a protein called tuberin, which joins with its partner hamartin to form a complex that inhibits a Ras-like GTP-binding protein, Rheb, that in turn activates mTOR and consequently cell proliferation. However, Cantley found that Akt could phosphorylate tuberin and turn off its function, thus enhancing mTOR activity.

The Akt-tuberin-mTOR connection opened up another exciting avenue when Cantley discovered that the LBK1 protein also fed into the tuberin complex. "LKB1 acts like a cell's energy monitor," Cantley explains. "It senses when cells are running low on ATP and shifts cell activity to prevent

Out of Focus: Be Careful What You Wish For

Because he was unsure whether or not his method of screening for SH2 domain binding motifs with a degenerate peptide library would work, Cantley did what most PIs would do: assign it as a rotation project. Then, after prospective student Sunny Songyang managed to identify the binding domain for PI3K, Cantley joked "Ok, your thesis project will be to identify the optimal peptide sequences for all the other known SH2 domains." Of course, when Songyang came back to Cantley 1 month later to report that he had finished 15 of the 20 known SH2 proteins, the joke had turned. Says Cantley, "I realized then I better find some other projects if I wanted to keep Sunny around."

total energy depletion." In fact, LKB1 is critical for maintaining glucose concentrations in the liver; without it, the popular anti-diabetes drug metformin won't work. "We've known for a while that PI3K signaling is activated by the insulin receptor and connected with diabetes," Cantley says. "But as we uncover more details, it seems clear that metabolic disorders and cancer are intimately linked."

In a way, Cantley has come full circle, returning to his first graduate school projects modeling glucose metabolism and ATP homeostasis. And even though he no longer works with cation transporters, he is pleased to know that other research has shown that PIP_2 and PIP_3 can indeed regulate transporter activity. "The PI3K picture is finally beginning to make a little sense," he says, although he does point out that there is still a great deal to learn about this intricate pathway. "And when you consider that humans have three different classes of PI3K, with multiple isoforms, it becomes more complex still."

Peptide Predictors

To help figure out the complexity of PI3K interactions, Cantley has been employing many screening techniques to tease out critical binding sites. This initiative began in 1991, while Cantley was preparing a review article for *Cell* highlighting the recent advances connecting oncogenes and signaling pathways. He had previously found that a mutation of a single Tyr residue of polyoma middle T could prevent PI3K binding. "Now, as I was comparing polyoma middle T to other proteins that bound PI3K, I noticed they had a similar sequence motif around the Tyr residue needed for PI3K binding." Specifically, the similarity occurred in the three amino acids immediately following the phosphorylated tyrosine.

Going back to his early training in biophysical chemistry, "I like to ask myself why things happen as they do," Cantley hypothesized that these slight differences in sequence affected binding specificity of Src homology 2 domain (SH2)-containing proteins. Ideally, he could design synthetic peptides and measure their binding affinity, "but with 20 amino acids, even a 3-residue sequence required assembling 8000 different peptides, which was beyond my time and budget," he says.

To circumvent this, Cantley devised an approach where he would create all 8000 simultaneously using degenerate peptides and pass the mixture through an SH2 affinity column. He could then take the material that stuck and sequence the peptides. Because the samples would be mixed, the Edman sequencing procedure would only relate the abundance of each amino acid at a given position rather than the sequences of individual peptides, but that could still reveal preferential binding motifs. Cantley and his graduate student Zhou (Sunny) Songyang started with the SH2 domain of PI3K, which produced a predicted sequence of phospho-Tyr-(Met/Val)-*X*-Met; these were the exact sequences on several PI3K-binding proteins with which Cantley worked. Studies into other SH2 proteins revealed that related SH2 proteins recognized similar sequences, although each family member had its own unique combination.

"I remember thinking, "Wow, this actually worked," says Cantley, who decided to expand his peptide library to identify the optimal substrates for all protein kinases. Cantley and Songyang used a variation of the previous approach, synthesizing a 9-residue-long peptide library (over 2.5 billion combinations) that was briefly exposed to a given protein kinase. They could then isolate and sequence phosphate-containing peptides. This approach confirmed that individual tyrosine kinases have their own special recognition site, which highlights a remarkably rapid evolution for this small but important protein family.

These peptide libraries have greatly helped Cantley and other researchers connect the dots in kinase signaling cascades, as they could predict cellular pathways simply by looking at the sequences of specific proteins. Of course, it's critical to perform the biochemistry to prove whether these pathways are real, but the libraries have provided no shortage of experiments. "I like to think of these peptides as hypothesis generators," says Cantley.

Nick Zagorski, Ph.D., a graduate of The Johns Hopkins and Cornell Universities, is a science writer for ASBMB. He can be reached at nzagorski@asbmb.org.

BIBLIOGRAPHY

Auger, K. R., Serunian, L. A., Soltoff, S. P., Libby, P., and Cantley, L. C. (1989) PDGF-dependent tyrosine phosphorylation stimulates production of novel polyphosphoinositides in intact cells. *Cell* **57**, 167-175.

Cantley, L. C., Josephson, L., Warner, R., Yanagisawa, M., Lechene, C., and Guidotti, G. (1977) Vanadate is a potent (Na,K)-ATPase inhibitor found in ATP derived from muscle. *J. Biol. Chem.* **252**, 7421-7423.

Carpenter, C. L., Duckworth, B. C., Auger, K. R., Cohen, B., Schaffhausen, B. S., and Cantley, L. C. (1990) Purification and characterization of phosphoinositide 3-kinase from rat liver. *J. Biol. Chem.* **265**, 19704-19711.

Shaw, R. J., Kosmatka, M., Bardeesy, N., Hurley, R. L., Witters, L. A., DePinho, R. A., and Cantley, L. C. (2004) The tumor suppressor LKB1 kinase directly activates AMP-activated kinase and regulates apoptosis in response to energy stress. *Proc. Natl. Acad. Sci. U.S.A.* **101**, 3329-3335.

Shaw, R. J., Lamia, K. A., Vasquez, D., Koo, S. H., Bardeesy, N., Depinho, R. A., Montminy, M., and Cantley, L. C. (2005) The kinase LKB1 mediates glucose homeostasis in liver and therapeutic effects of metformin. *Science* **310**, 1642-1646.

Shioi, T., McMullen, J. R., Kang, P. M., Douglas, P. S., Obata, T., Franke, T. F., Cantley, L. C., and Izumo, S. (2002) Akt/protein kinase B promotes organ growth in transgenic mice. *Mol. Cell. Biol.* **22**, 2799-2809.

Songyang, Z., Blechner, S., Hoagland, N., Hoekstra, M. F., Piwnica-Worms, H., and Cantley, L. C. (1994) Use of an oriented peptide library to determine the optimal substrates of protein kinases. *Curr. Biol.* **4**, 973-982.

Sugimoto, Y., Whitman, M., Cantley, L. C., and Erikson, R. L. (1984) Evidence that the Rous sarcoma virus transforming gene product phosphorylates phosphatidylinositol and diacylglycerol. *Proc. Natl. Acad. Sci. U.S.A.* **81**, 2117-2121.

Tee, A. R., Fingar, D. C., Manning, B. D., Kwiatkowski, D. J., Cantley, L. C., and Blenis, J. (2002) Tuberous sclerosis complex-1 and -2 gene products function together to inhibit mammalian target of rapamycin (mTOR)-mediated downstream signaling. *Proc. Natl. Acad. Sci. U.S.A.* **99**, 13571-13576.

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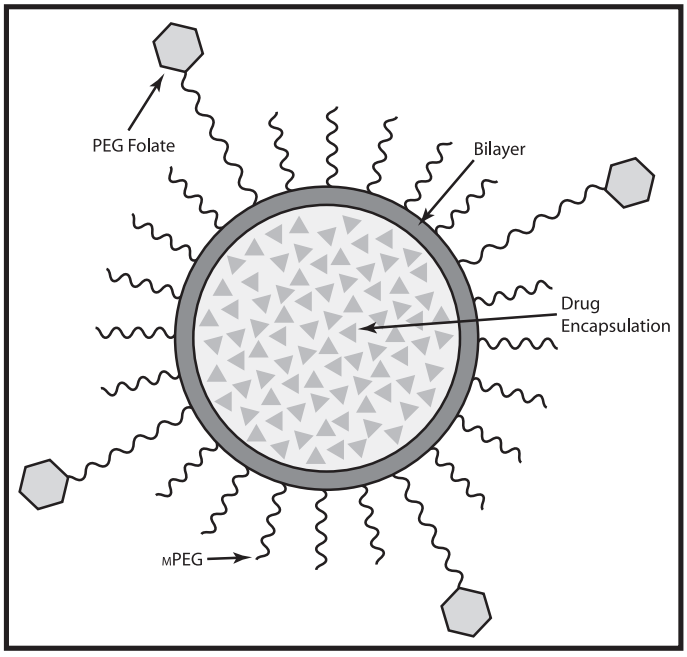

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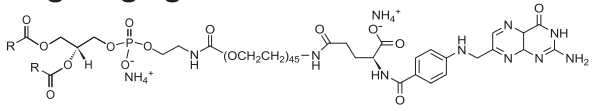

DSPE-PEG(2000)Folate — Avanti Number 880124

Hilgenbrink, A.R. and P.S. Low. (2005). Folate receptor-mediated drug targeting: from therapeutics to diagnostics. *J Pharm Sci* 94:2135-46.

Folate targeted drug delivery has emerged as an alternative therapy for the treatment and imaging of many cancers and inflammatory diseases. Due to its small molecular size and high binding affinity for cell surface folate receptors (FR), folate conjugates have the ability to deliver a variety of molecular complexes to pathologic cells without causing harm to normal tissues.

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scientific meeting calendar

MARCH 2008

American Society for Neurochemistry 2008 Annual Meeting
MARCH 1–5, 2008
SAN ANTONIO, TX
asneurochem.org/

US HUPO 4th Annual Conference
MARCH 16–19, 2008
BETHESDA, MD
www.ushupo.org
E-mail: ushupo@ushupo.org
Tel.: 505-989-4876

Genomes to Systems 2008
MARCH 17–19, 2008
MANCHESTER, UK
www.genomestosystems.org/

42nd Annual Scientific Meeting of the European Society for Clinical Investigation (ESCI)
MARCH 26–29, 2008
GENEVA, SWITZERLAND
www.esci.eu.com/default.asp?page=meetings&file=future

Annual IACUC Conference Ethics and Compliance in Animal Care and Use Programs: *Current Challenges and Future Directions*
MARCH 27-28, 2008
ATLANTA, GA
www.primr.org

KEYSTONE SYMPOSIUM—Nuclear Receptors: Orphan Brothers
MARCH 30–APRIL 4, 2008
WHISTLER, CANADA
www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=956

KEYSTONE SYMPOSIUM—Nuclear Receptors: *Steroid Sisters*
MARCH 30–APRIL 4, 2008
WHISTLER, CANADA
www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=957

APRIL 2008

ASBMB Annual Meeting *in conjunction with EB2008*
APRIL 5–9, 2008
SAN DIEGO, CA
Contact: ASBMB 2008, 9650 Rockville Pike, Bethesda, MD 20814-3008
www.asbmb.org/meetings
E-mail: meetings@asbmb.org
Tel.: 301-634-7145

Vascular Biology 2008 in conjunction with American Society for Investigative Pathology at Experimental Biology 2008
APRIL 5–9, 2008
SAN DIEGO, CA
www.navbo.org/vb08.htm

SHORT COURSE: *Principles and Applications of Immunocytochemistry*
APRIL 5, 2008
SAN DIEGO, CA
This is a technique-oriented course for novice and experienced investigators.
http://immunocytochem.wordpress.com/ for information

INTERNATIONAL CONFERENCE ON CELLULAR AND MOLECULAR BIOLOGY
A satellite meeting of the 4th World Congress on Cellular and Molecular Biology
APRIL 6–8, 2008
INDORE, INDIA
Please submit your CV and proposal to:
E-mail: ak_sbt@yahoo.com

Arteriosclerosis, Thrombosis, and Vascular Biology Annual Conference 2008
APRIL 16–18, 2008
ATLANTA, GA
www.americanheart.org/presenter.jhtml?identifier=1201

MAY 2008

Proteomics Informatics Course at the Institute for Systems Biology
MAY 12–16, 2008
SEATTLE, WA
http://www.proteomecenter.org/nav.course.05.08.php
Email: info@proteomecenter.org

2008 ATS International Conference
MAY 16–21, 2008
TORONTO, CANADA
http://www.thoracic.org/

Keystone Symposium—G-Protein Coupled Receptors
MAY 18–23, 2008
KILLARNEY, IRELAND
www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=908

Gordon Research Conference on Thiol-based Redox Regulation and Signaling
MAY 25–30, 2008
IL CIOCCO, ITALY
Chair: Ruma Banerjee.
Vice Chair: Roberto Sitia
www.grc.org
E-mail: rbanerje@umich.edu

JUNE 2008

FASEB Summer Research Conferences
JUNE – SEPTEMBER 2008
VARIOUS LOCATIONS
http://src.faseb.org

American Diabetes Association 68th Scientific Sessions
JUNE 6–10, 2008
SAN FRANCISCO, CA
http://scientificsessions.diabetes.org

90th Annual Meeting of the Endocrine Society
JUNE 15–18, 2008
SAN FRANCISCO, CA
www.endo-society.org/apps/Events/Event.cfm?EventID=1253

33rd FEBS Congress & 11th IUBMB Conference
JUNE 28–JULY 3, 2008
ATHENS, GREECE
www.febs-iubmb-2008.org

JULY 2008

Trends in Enzymology 2008
JULY 2–5, 2008
ST MALO, FRANCE
Organizers: Susan Miller and Bernard Badet
Website: http://TinE2008.org
E-mail: TinE2008@icsn.cnrs-gif.fr

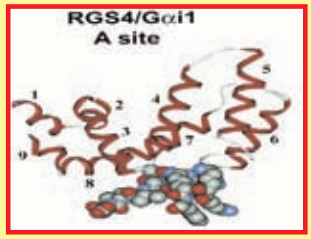
3rd RGS Colloquium

April 4-5, 2008, San Diego, CA

Organized by: Michael Koelle, PhD and Richard R. Neubig, MD, PhD

This is a Satellite Meeting to Experimental Biology 2008

Topics and Speakers include:



RGS Structure/Function

John Tesmer, University of Michigan

Roles of RGS proteins and RGS homology domains in signaling scaffolds

John Sondek, University of North Carolina at Chapel Hill

R7-family RGS proteins

RGS Targeting/Cellular Localization

John R. Hepler, Emory University

RGS proteins as multifunctional scaffolding proteins in cell physiology

Kendall J. Blumer, Washington University School of Medicine

Post-translational modifications regulating RGS protein shuttling

Kirill Martemyanov, University of Minnesota

Macromolecular complexes of RGS9 - master regulators of G protein signaling in retina and striatum

Marilyn G. Farquhar, University of California at San Diego

Roles of RGS-PX1 in endocytosis and G protein signaling

Andrew Tinker, Royal Free & University College Medical School

The molecular basis of the pleiotropic effects of RGSs in the regulation of G-protein gated K+ channels

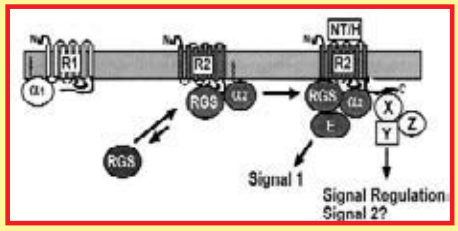
Novel Interactions/Functions

Vladlen Slepak, University of Miami

Structure and function of Gbeta5-R7 complexes: 10th anniversary

Peter Chidiac, University of Western Ontario

Novel regulatory properties of RGS2



Additional speakers will be selected from meeting registrants based on their submitted abstracts

RGS Action In Vivo

John H. Kehrl, National Institute of Allergy and Infectious Diseases

Insights into RGS protein function from the analysis of RGS and Gi alpha knock-out mice

John Traynor, University of Michigan

RGS proteins as a potential drug target for depression

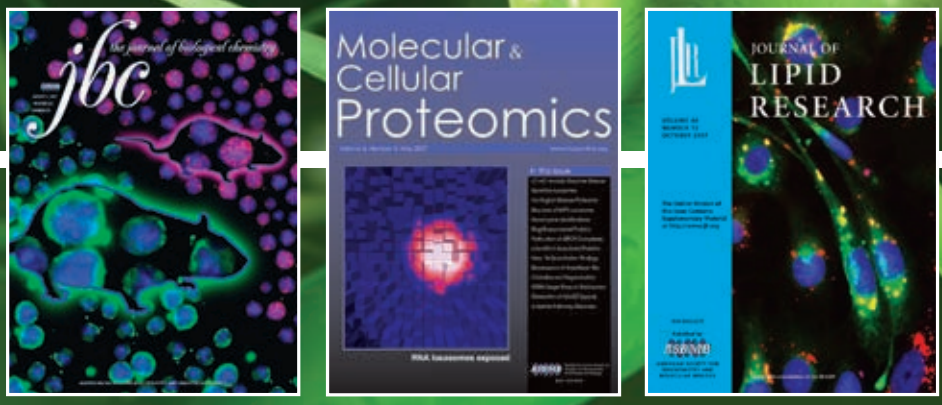
Vanna Zachariou, University of Crete

A role of RGS9, RGS4, and RGSz in addiction and analgesia

Register for this meeting at:

http://www.aspet.org/public/meetings/meetings.html

We anticipate, but cannot guarantee, being able to provide some funds to assist junior scientists with travel to the meeting. See website for details.



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www.jlr.org Most-Cited Journal Devoted to Lipids

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