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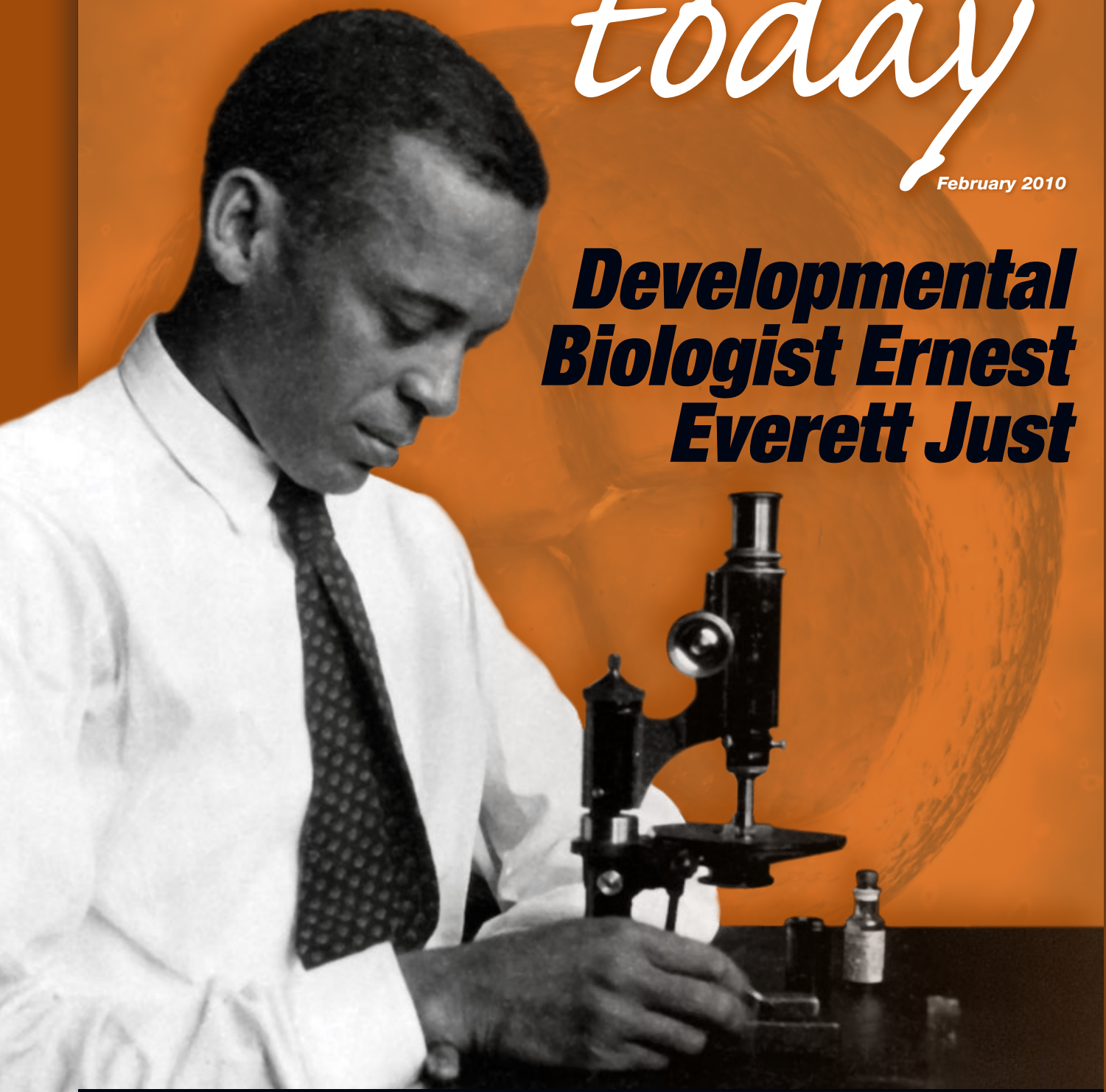
ASBMB today

February 2010

Developmental Biologist Ernest Everett Just



American Society for Biochemistry and Molecular Biology

2010 ASBMB Annual Meeting




Get Ready to Meet in California!

DEADLINES APPROACHING

Early Registration: February 24, 2010
Late Breaking Abstracts: February 24, 2010

SPECIAL EVENTS

ASBMB 5K Fun Run, *early registration required*
Minority Scientists Welcome Reception
How to Publish in the JBC Workshop
Opening Reception and Dance

Anaheim Awaits
April 24–28, 2010

www.asbmb.org/meeting2010

ASBMB
American Society for Biochemistry and Molecular Biology

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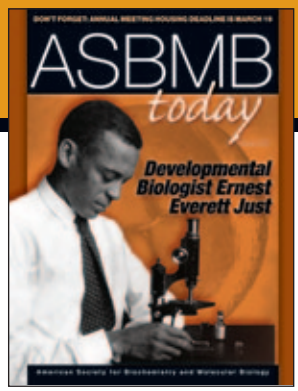

FEBRUARY 2010

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Ernest Everett Just made seminal contributions to the study of fertilization and early development in marine mammals. 22

PHOTO CREDIT: THE MARINE BIOLOGICAL LABORATORY ARCHIVES.

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podcast summary

This month's ASBMB podcast features Journal of Biological Chemistry Paper of the Week author Jason Fish discussing a unique transcriptional control mechanism for endothelial nitric oxide synthase in hypoxia.

To hear this and other podcasts, go to www.asbmb.org/Interactive.aspx.

ASBMB today

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ASBMB
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2008 APEX AWARDS FOR PUBLICATION EXCELLENCE

letters *to the editor*

Letter for "Advice and Dissent"

Dear Greg,

Your editorial in ASBMB Today (December 2009) struck me as being a bit confused. Your denunciation of the British politician for not following the recommendation of a scientist to effectively reduce penalties on marijuana use shows a lack of understanding of the functions of the panel of experts and the politicians. The former are charged with giving their opinions on the best course their government should take, while the latter are charged with setting policy. Opinions, whether scientific or not, will probably be influenced by the biases, or call them the values, of the experts, and, like all scientific evidence, are inherently incomplete. Policies reflect many things, values (social, religious, economic, etc.) above all, but also fears as to the results of following the panel's recommendations. Politicians are, after all, elected to set policies and to be held responsible for their consequences. If the consequences are bad, no one will remember the panels or who was on them, only the politician(s).

I think you are right, however, that legalization ("decriminalization") of pot is indeed a flashpoint dividing liberals from conservatives. Liberals tend to stress all the good things they believe will ensue from some proposed change, while conservatives tend to think of all the bad things that might result. As a card-carrying conservative myself (the deuce or trey of clubs, probably), I tend to stress the latter.

To me, there are too many questions involving effects of higher dosages of active ingredient, especially upon the young, and control over suppliers to feel assured of the overall benefits of such a course. Then too, there is a generally ignored question of the social irresponsibility of illegal drug users. Not all changes, however passionately advocated, merit support.

John M. Brewer
Professor of biochemistry and molecular biology
University of Georgia

Letter for Education Issue

Dear Dr. Petsko,

Two articles that appeared in the October issue ("A Teachable Moment" and "Student-Centered Education in Molecular Life Sciences") have been very good motivation to share some observations. I was very fortunate to be a participant at the American Society for Biochemistry and Molecular Biology-sponsored conference at Colorado College last August, centered on improving education in the molecular life sciences. As described in Neena Grover's and Marilee Benore Parsons' article, the meeting was incredibly informative and stimulating. Spanning three days, there was ample time to have insightful discussions with those who have been at the forefront of the drive to transform our lecture and laboratory courses. It was also highly beneficial that there were faculty from both smaller, primary undergraduate institutions as well as larger research universities, both types of schools having their own special circumstances that affect the ways in which we implement our curricula.

As a result of conversations with J. Ellis Bell, Joseph Provost and Neena Grover spanning five years, numerous articles in Biochemistry and Molecular Biology Education and the Journal of Chemical Education, as well as several publications by the National Research Council, I had been formulating a transformation plan for our department's upper-division biochemistry laboratory

course from a primarily methods-and-techniques format into a inquiry-based "gene-to-protein" experience. Making such a sweeping change can be a very daunting task, especially when trying to overcome the inertia of more conservative departmental colleagues. In her closing talk, Neena fervently urged us to evaluate how we are teaching our courses and to make small, subtle changes and then evaluate the efficacy of those changes to enhance our students' educational experience.

With this advice resonating in my brain, on the flight back to Tucson, Ariz., I outlined two small projects I would introduce to our laboratory course during the upcoming semester. One project was designed to be an open-ended, inquiry-based assignment originating from interesting results the students would encounter in the early part of the semester. In the assignment, student groups would choose an experiment they would like to conduct, do the appropriate literature research on methods we had not covered in the course, design their experiments and finally carry them out with the relevant data analysis. The project would culminate in brief oral presentations by each group. The data collected in the fall semester would be passed on to the students in the spring classes, serving as a new starting point.

Two outcomes of this project are worth noting. First, several students made excellent suggestions about further experimentation that could be conducted to tie up some loose ends, and they volunteered to do the work on their own time (a rarity in my experience). Second, a young Hispanic student told me that since our department has a two-semester senior thesis requirement for a B.S. in biochemistry, she had contemplated switching majors or opting for the nonthesis B.A. throughout most of the semester. However, as a result of the work she had done on tandem mass spectrometry analysis of Escherichia coli periplasmic proteins during "the special project," she had become very excited about scientific research and was making a concerted effort to get into a mass spec lab for her thesis project.

So, for those who are waffling about transforming their courses, I reiterate Neena's advice: Make small, incremental changes in your courses first (a suggestion also made by Jennifer Loertscher in the December 2009 ASBMB Today concerning implementation of POGIL modules in pre-existing lecture courses), diplomatically ignore those with an "if it ain't broke, don't fix it" attitude, and, finally, in honor of the BCS season, "Just Do It!" You and your students will be very glad you did.

Finally, ASBMB should be very highly commended for taking a leadership role in not only advocating making substantive changes in the way we teach our undergraduates but also for its efforts to engage undergraduates in research and scientific investigation through the auspices of the Undergraduate Affiliate Network, the ΧΩΛ undergraduate honor society and encouragement of our highly motivated and talented students to fully participate at the annual meetings.

James T. Hazzard
Senior lecturer in chemistry and biochemistry
The University of Arizona

A Harsh Climate*

BY GREGORY A. PETSKO

I might as well come right out and say it: I don't care whether global warming is caused by manmade greenhouse gas emissions. And neither should you.

Before you start reaching for your laptops, iPhones and BlackBerrys to fire off scathing e-mails, give me a moment to explain why I made this statement and what it really means. I bet that, when I'm through, you will agree with me.

This column is being written because of the confluence of two events. One is a meeting in Copenhagen of representatives of most of the world's nations, aimed at formulating a new global strategy for dealing with the climate crisis. The talks have ground to a halt as I write this because the group of developing countries, known as the G-77, has accused the United States and other industrialized states of forsaking the Kyoto Protocol, the current climate agreement that imposes greenhouse gas emissions on nearly every developed nation.

The second event is "Climategate," the release of illegally hacked e-mails between climatologists. As an example of giving aid and comfort to the enemy, Climategate hardly could be improved upon. In late November, a computer file including more than 1,000 e-mails sent either from or to members of the University of East Anglia's Climate Research Unit was stolen and released on the Internet. The e-mails contain language that opponents of emission curbs have seized upon as alleged examples of data manipulation and outright fraud on the part of climate researchers. For example, one e-mail apparently sent by the head of the CRU, Phil Jones, refers to using "Mike's Nature trick of adding in the real temps to each series for the last 20 years… to hide the decline." The CRU is one of the leading research units on climate change, and its data had a major role in the Fourth Assessment Report of the Intergovernmental Panel on Climate Change, released in 2007, that provided unequivocal evidence for global warming (see Figure 1).

Of course, scientists use the word "trick" all the time as a shorthand term for a method or algorithm, but professional skeptics rarely bother themselves with the way scientists work. It seems likely that the files were stolen to undermine the Copenhagen talks, but my assessment is that there are so many other contentious issues in that meeting that this is a relatively minor matter for most of its participants. Nevertheless, Jones has stepped down as head of the CRU pending an internal investigation. In my view, he instead should have been made to write on the blackboard 1,000 times: "I will never put anything into an e-mail or text message that could be embarrassing to me or to my organization if it were read by someone else, and, if I don't believe this, I should ask Tiger Woods."

One of the most sensible things I have read about the climate debate is an opinion piece by Stewart Brand in the Dec. 15, 2009, edition of The New York Times. He argues that the popular depiction of the combatants as belonging to two camps, the alarmists and the skeptics, is fallacious. There are actually four sides: "denialists," a group consisting of people with a right-wing political agenda who assert that the claim that global warming is caused by manmade emissions is a lie and is not based on sound science; "skeptics," a group largely composed of scientists who argue that climate science, particularly large-scale modeling, is far too imperfect to form the basis of a consensus; "warners," another group of scientists who believe that the best climate models accurately predict a looming planetary disaster and that human production of greenhouse gases is the primary cause; and "calamatists," a collection of environmental activists whose agenda, like that of the denialists, is ideologically driven, but in the opposite direction: they have a neo-luddite view of industrialization and believe the denialists are evil. As Brand, a self-described warner, points out, understanding from which of these camps any given argument springs is useful in distinguishing propaganda from science and appeals to emotion from evidence-based assertions.

Yet even Brand misses what I think is the crucial point, the point I want to make in this column, which is that you can't win a war if you are fighting in the wrong field. And in the war over climate change, which should be fought in the field of science, the denialists and the calamatists have dragged us into battle on their turf.

When you're in a fight with an opponent who is not above using invective and illogic, the worst mistake you can make is letting the other side define the terms of the debate. That's exactly what has happened in the argument about climate change. For decades, the denialists

insisted that the Earth was not getting warmer. Short-term fluctuations were meaningless, they asserted. Climate modeling was worse than useless. The doomsayers were just trying to push a liberal political agenda, and so on. But after massive amounts of data were collected and analyzed by the Intergovernmental Panel on Climate Change, it became clear, on the release of its report in 2007, that no sensible person could deny that a dramatic rise in the planet's average temperature had been occurring for at least a century (see Figure 1). Largely thanks to Al Gore, this information also reached the general public, whose reaction even the staunchest denialists could not ignore.

So they did what clever, unprincipled losers often do: They changed the issue. Of course the Earth is getting warmer, they said (blithely ignoring the fact that they had said exactly the opposite the day before), but human activities have nothing to do with it. It's entirely due to natural causes, and people who assert that manmade greenhouse gases are causing the problem are employing flawed science, deliberately distorting the facts (Climategate), and are using fear to advance the same old, tired environmental activism. Because global warming is not a manmade phenomenon, there is no scientific or political reason to limit manmade greenhouse gas emissions. Sarah Palin (why am I not surprised?) is one of the leaders of this chorus, stating recently that climate change occurs naturally "like gravity," while warning that reducing greenhouse gas emissions will mean "job losses" and "economic costs." (This is the same ex-Alaska governor who, before becoming a national political figure, said in July 2008, "Alaska's climate is warming. While there have been warming and cooling trends before, climatologists tell us that the current rate of warming is unprecedented within the time of human civilization. Many experts predict that Alaska, along with our northern latitude neighbors, will warm at a faster pace than any other areas, and the warming will continue for decades." I don't know whether to laugh at that kind of soulless opportunism or just cry.)

This strategy is actually working, to some extent. It's much harder to establish the cause of something than it is to prove that something is happening, and the data supporting manmade emissions as the leading driver of climate change are not nearly as persuasive, or as immune to challenge, as the data demonstrating the fact of global warming. And scientists, foolishly, have allowed that to become the center of the climate crisis debate. I say foolishly because, in so doing, they have given up the victory that they already won.

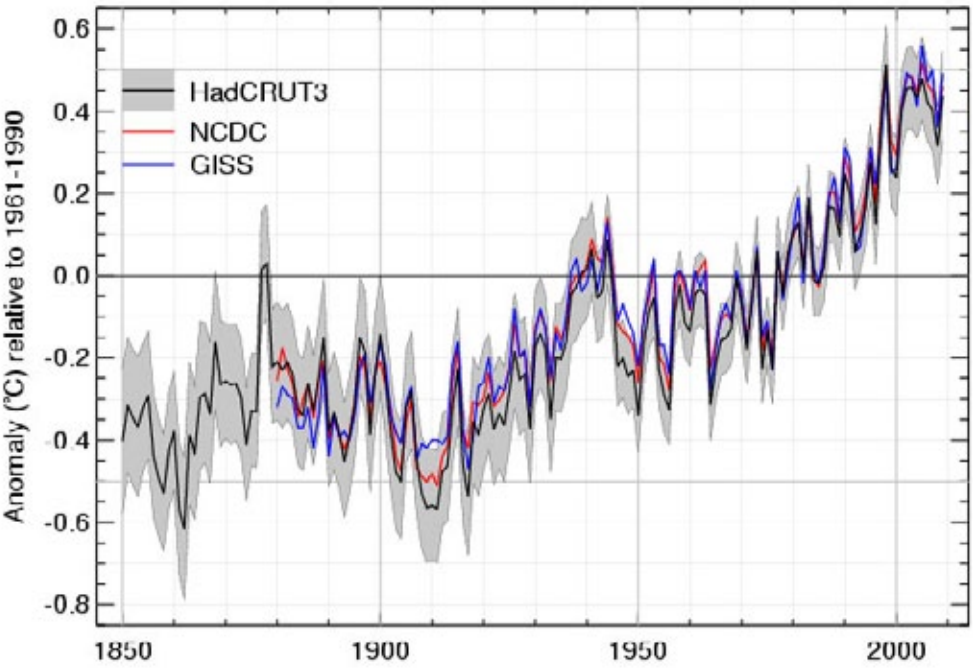

Figure 1. Unequivocal evidence for a warming planet. Global surface temperature trend from three global datasets: NOAA (NCDC Dataset), NASA (GISS dataset) and combined Hadley Center and Climate Research Unit of the University of East Anglia (UK) (HadCRUT3 dataset). The data clearly indicate a dramatic and accelerating warming trend over the past 150 years. Reproduced from the World Meteorological Organization (http://www.wmo.int/pages/index_en.html).

The denialists have conceded the fact of climate change. And here is my central point: Once you admit that the Earth is warming rapidly, it does not matter in the least whether that trend is due to manmade causes or not.

Regardless of its origin, a rapidly changing climate is a very bad thing. We have built an entire civilization on the assumption of long-term climate stability. We grow wheat in Kansas rather than in the Yukon, because Kansas has an ideal climate for growing

wheat, and the Yukon is too cold, and we assume that will still be the case 10 years from now. We build our cities on the coast, because that is convenient for shipping goods, and we assume the coastline won't suddenly move 10 miles inland. We don't have air conditioning in many homes in Northern California, because we assume the average temperature won't suddenly rise by several degrees, making summer unbearably hot. We assume that England won't have a yearly climate like Lapland, even though its position on the globe might lead one to expect otherwise, because the Gulf Stream will always be there off the west coast, keeping things moderate. Every one of these assumptions fails in the event of significant global warming. One reason I prefer the term "climate crisis" to "climate change" or "global warming" in discussing this problem is because our dependence on stable long-term climate patterns means that any change in those patterns represents a potential catastrophe on a planetwide scale.

It doesn't matter what the cause of that crisis is; once you accept the fact that the crisis is coming, the only thing that matters is how to prevent it or slow it down. And the only way we have of doing that at the moment is to reduce our greenhouse gas emissions. Put another way, human activity may not even be causing the Earth's temperature to rise, but human activity is the only means we have of doing something about it.

A simple analogy may make this point clearer. Suppose we learned tomorrow that there was one chance in 10 that a huge asteroid, recently discovered, was going to crash into the Earth in five years, killing a billion people and raining debris in such amounts as to blot out sunlight significantly for a year. (A similar event is thought to have led to the extinction of the dinosaurs.) Would anyone in his or her right mind argue that, because we couldn't prove that human activity was responsible for the asteroid, there was no reason to hurt our economy by spending hundreds of billions of dollars firing nuclear-tipped rockets at it to destroy it or alter its course? Yet that's exactly what the denialists are trying to argue now, in the case of a climate crisis that has at least an equal probability of globally devastating consequences.

True, our climate models can't predict with certainty that the steps being considered in Copenhagen will retard, halt or reverse the current warming trend. But they represent all we can do at the moment. If global warming is being caused primarily by greenhouse gases, as many thoughtful scientists believe, then the Copenhagen measures will do a lot. If global warming is actually caused by, say, sunspots or something similar, reduction of emissions may not do so much. But everyone agrees that the Copenhagen strategy will do something, and my point is that something simply has to be done.

I hope you see now why I started this essay as I did. We should not be debating whether human activity is responsible for global warming or not. Given that even the denialists and skeptics have conceded the fact of global warming, the debate should be over the most effective means of doing something about it. This means, I am afraid, not just limiting our discussion to controls on CO_2 emissions. We need to look seriously at developing technologies for carbon sequestration, alternative fuels and carbon-neutral technologies for transportation and energy production. Much of this will involve engineering microorganisms and plants, so genomics is going to be very important in enabling these technologies as we grapple with the crisis. I also see no escape from at least investigating ideas for geoengineering — solutions involving deliberate changing in sunlight absorption, carbon capture and temperature reduction on a continent- or planetwide scale. My gut reaction to geoengineering is that it is a terrible idea, born as much of hubris as desperation, that should be shelved permanently because we will never have the kind of models that would guarantee beforehand that it could be done safely. But the fact is, we don't know what we don't know when it comes to such projects, and, given the severity of the climate crisis, if someone wants to propose that we should at least begin to study such solutions to determine the extent of our ignorance and the possibility that we might someday be able to employ them, I wouldn't say no.

So, the next time you find yourself in a debate with someone over the climate crisis, and they say that we shouldn't reduce CO_2 emissions because there is no definitive proof that manmade greenhouse gases are the cause of global warming, respond by saying, "Then if an alien race were threatening to exterminate mankind, you wouldn't do anything to try to stop them because human activities weren't the cause of the alien invasion, is that right?" And they'll reply, "Of course not! But this is completely different." And you'll say, "No, it's not. Let me explain why."

Given the harsh climate that has developed around the subject of global warming, you probably won't convince them that they're wrong. But at least you'll be having the right argument. XXX

* This article originally appeared in Genome Biology (2009) 10, 115 and was reprinted with permission from BioMed Central.

FASEB Makes Budget Recommendations

Releases Federal Funding Report, Statement on NIH

BY CARRIE D. WOLINETZ*

The Federation of American Societies for Experimental Biology is taking its message of support for biomedical researchers to both Congress and the federal science agencies. On Jan. 28, FASEB President Mark O. Lively presided over the unveiling of FASEB's annual report, "Federal Funding for Biomedical and Related Life Sciences Research, FY2011." Developed through consultation with FASEB's 23 member societies and scientific experts, this report makes the case for sustainable funding for five federal science agencies: the National Institutes of Health, the National Science Foundation, the U.S. Department of Energy, the U.S. Department of Veterans Affairs and the U.S. Department of Agriculture.

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.

A summary of FASEB's recommendations for the five agencies is detailed below:

National Institutes of Health

In order to fulfill the extraordinary scientific and medical promise of biomedical research, FASEB urges Congress to make the NIH a priority and recommends that it receive **$37 billion** in fiscal 2011.

National Science Foundation

FASEB recommends an appropriation of **$7.68 billion** for the National Science Foundation in fiscal 2011.

U.S. Department of Energy

In keeping with President Obama's vision for doubling the DOE Office of Science budget, FASEB recommends an appropriation of **$5.24 billion** in fiscal 2011.

U.S. Department of Veterans Affairs

FASEB recommends funding the VA Medical and Prosthetics Research Program at the **$1 billion** level in fiscal 2011, including $700 million for research and $300 million for infrastructure.

U.S. Department of Agriculture

FASEB supports funding the USDA's Agriculture and Food Research Initiative at **$500 million** in fiscal 2011.

NIH Statement

In response to a September 2009 town hall meeting at which NIH Director Francis Collins pledged to maintain a "wide-open" dialogue with agency constituents, FASEB submitted a statement to NIH regarding balance and optimization of the agency portfolio, focusing on three major issues.

First, FASEB urged NIH to stimulate innovation in the biomedical research enterprise through the sustained support of science and scientists and emphasized that higher paylines and success rates allow investigators and study sections to take more risks.

Second, the statement highlighted how the percentage of the NIH budget for Research Project Grants and R01 awards has declined and requested an explanation for how the agency will address that issue in the future. FASEB also noted that since the end of the NIH budget doubling in 2003, the actual number of R01 awards has fallen 7.4 percent (from 28,743 to 26,621).

Finally, FASEB recommended that NIH enhance investigator-initiated research across the full spectrum of basic, translational and clinical research and that it resist calls for redistribution of funding resources unless there are appropriate increases in the budget.

Carrie D. Wolinetz (cwolinetz@faseb.org) is director of scientific affairs and public relations for the Office of Public Affairs at FASEB.

*Tyrone Spady of FASEB's Office of Public Affairs contributed to this article.

For more information:

FASEB's annual report: http://bit.ly/5DgaD9

FASEB's statement on the NIH: http://bit.ly/4ZbvYo.

Visiting Congress at Home

Your Member of Congress Is Home Most of the Time — Why Not Visit Then?

BY PETER FARNHAM

Question: What federal officials, while ostensibly based in Washington, D.C., actually spend the bulk of each year — almost three quarters of it — back in their home states? The answer: senators and members of Congress.

This is a fact frequently overlooked by many society government relations programs and, by extension, their members. Many societies tend to concentrate their congressional visit activity in Washington with "Hill Day fly-ins" and other Washington-based efforts. However, because the overwhelming majority of a congressional member's time is spent in his or her congressional district, it is an essential part of any advocacy strategy to try to meet with him or her when he or she is home. The advantages are obvious: It saves time and money and increases one's chances of getting "face time" with the elected official.

The following are some suggestions on how to arrange a home-office meeting.

Tips on Meetings at Home

Contact the local office. All members of Congress maintain at least one local district office and sometimes more, depending on the geographical size of the district. In addition, senators usually have several scattered around the state. Go to the congressional member's Web site (you can find it at www.house.gov or www.senate.gov) and find the address and phone number of the office nearest you. Contact that office, introduce yourself and ask when it might be possible to get some time with the member. Congressmen frequently arrange group meetings when in their districts. They may devote one or two days a month to meeting with anyone who wants to come see them.

Plan to go with a group. Your chances of meeting with the member will increase if you go as part of a group. (Students, in particular, make excellent ambassadors.) However, make sure that your delegation includes at least some constituents: If you show up with a bunch of foreign graduate students, that is not going to have as much of an impact as if you show up with voters.

Do some research. Once you have arranged a date and time for your meeting with the local office staff, you need to do research, especially if you don't know much about your Congress member's positions

on issues of concern to you. The member's Web site is a good place to start. You also can contact the American Society of Biochemistry and Molecular Biology staff members in Washington. They can easily provide you with information on the member's voting record and district as well as his or her level of support for research and the amount of federally funded biomedical research in your district or state. Many members do not realize the magnitude of the federal commitment to biomedical research: All states have at least some federally funded research conducted at colleges and universities.

Pre-meeting for the group. It is helpful if all members of the delegation get together a day or two before the official meeting to go over what to say and to review handout materials they plan to drop off. Each should rehearse a brief introductory statement of no more than a few sentences, telling who he or she is, where he or she works and the type of research he or she does. Plan to explain research in simple terms; do not use a lot of jargon. In addition, make sure to have an "ask" in mind. Members of Congress expect to be asked for something — to vote for or against a particular bill or to support or oppose a particular position — so don't be bashful about having one. The ASBMB staff will be happy to provide you with some possible requests.

The Day of the Meeting

Show up on time. Make sure everyone in your party shows up on time. If you do not arrive as a group (i.e., if you plan to arrive at the meeting location separately), make sure everyone knows the location of the meeting and knows how to get there. Share cell phone numbers in case there is some kind of problem.

Get to the point. After your introductory statements, it is best if you get to the point as soon as it seems appropriate. (The member may want to talk a bit about local matters, sports or other topics as ice-breakers.) Make your case as succinctly and clearly as possible. If the member asks questions, this is good; it is a sign that he or she is engaged and listening. Try to answer the questions as clearly as possible. If you do not know the answer, don't hesitate to say so, and promise to get back to him or her as soon as possible with the answer.

Ending the meeting. Most meetings like this last 15 minutes or so; if you get a half-hour, you are very fortunate. When wrapping up, leave contact information for all of the group members and a document restating your "ask." This should be no more than a single page or tri-fold brochure. It is also helpful to offer to arrange a visit to your lab or place of business. These visits are excellent opportunities for the member to get out into the community in a highly visible way and experience a working research laboratory.

Following up is important. After the meeting, your group should go over what was said and make particular note of any commitments the member made. If there were questions you couldn't answer, make sure you find the answers as soon as possible. You should also write a thank-you note restating your message.

Finally, get to know your member beyond this single meeting. Drop him or her a note occasionally to comment on a public issue. Perhaps make a campaign contribution, if you share his or her politics. At a minimum, make an effort to develop and maintain a friendly and courteous relationship.

2010 Is Important

This year is shaping up to be a very important one politically. There will be a fierce battle fought for control of the House and Senate, and much is at stake that affects ASBMB interests. We hope you will make an effort in 2010 to contribute to the dialogue. Remember, whether you participate in it or not, such a dialogue will be going on.

The ASBMB staff is fully prepared to assist you in any way in arranging such meetings, and we hope you will take advantage of the resources we can provide.

Peter Farnham (pfarnham@asbmb.org) is director of public affairs at ASBMB.

Congressional District Work Periods for 2010

The following are the remaining regularly scheduled "district work periods" when House and Senate members will be back in their districts and states. These are in addition to the four days each week they are home when Congress is in session. Note that Congress will adjourn in late September or early October to allow time for members to campaign at home in advance of the November elections.

Feb. 15 – 19
March 29 – April 9
May 31 – June 4
July 5 – 9
Aug. 9 – Sept. 10
Oct. – adjournment expected early in the month

Rules and Views

BY KYLE M. BROWN

Science policy issues increasingly dominate the national agenda. Whether describing a clean-energy economy or a war on cancer, politicians and policymakers are often talking about science. With so many important decisions to be made, the federal government must rely upon the expertise of scientists to make policy recommendations. While many agencies employ scientific experts, executive agencies need the expertise and opinions of citizen scientists, and, by law, the agencies have to listen.

The Rules

Executive agencies, like the National Institutes of Health and the Environmental Protection Agency, are empowered by Congress to regulate the practices of individuals, industries and agency officials. But legislators rarely have the time or expertise to legislate on highly specific and technical issues. Congress, therefore, empowers executive agencies to make specific, legally binding policy decisions, known as rules.

Rules related to science policy can pertain to a wide range of issues. Some rules apply to the guidelines and practice of research. More frequently, rules pertain to societal issues upon which scientific data and expertise must weigh in.

Comments, Please

Before a rule can be enacted, the agency must solicit comments from the public. Since 1946, the Administrative Procedures Act has dictated that a "general notice of proposed rule-making shall be published in the Federal Register," the U.S. government's official daily publication (1). Once a rule is proposed, individuals and groups are given at least 30 days to submit comments to the agency.

Regulations.gov provides an easy way for scientists and the general public to comment on proposed regulations.

Why Us?

Scientists have an interest in the rule-making process because it affects their research. But perhaps more importantly, comments from scientists are particularly important because of their specialized expertise. A quick search on Regulations.gov at the time this article was written revealed that 147 proposed rules were open for public comment, and 46 of those had been posted by scientifically focused agencies such as the NIH, the EPA, the National Science Foundation, the National Oceanographic and Atmospheric Association and the Department of Energy. While thousands may comment, evidence-based comments from scientists are particularly useful in crafting the best federal regulations.

Scientists also can share their expertise to provide agencies with information that will inform the drafting of proposed rules. While not necessarily required by law, agencies often issue notices of proposed rule-making, allowing the public to submit comments and information that will aid in the formulation of a proposed rule. By submitting information directly to agencies, scientists can help ensure that policymakers have the best information available when drafting new rules.

Comments Matter

Many scientists may worry about the time commitment involved in responding an agency's comment request and whether that comment is likely to have an impact. While practices vary from agency to agency, comments are read and often get public responses. For example, the EPA recently published 11 volumes containing more than 500 pages of responses to the more than 1,000 comments it received on regulating greenhouse gas emissions under the Clean Air Act (2). If they do not appropriately consider and respond to the comments they receive, federal agencies make themselves vulnerable to lawsuits.

A Seat at the Table

President Obama has brought science and scientists back into the policymaking fold. Steven Chu's appointment as U.S. secretary of energy and the new importance of the President's Council of Advisors on Science and Technology are just two prominent examples. But effective, thoughtful science policy will be created with the advice of the entire scientific community, one public comment at a time.

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FOOTNOTES

1. Rulemaking provisions of Administrative Procedures Act: http://www.archives.gov/federal-register/laws/administrative-procedure/553.html
2. http://www.epa.gov/climatechange/endangerment.html

Retrospective: Edwin G. Krebs (1918–2009)

Our Beloved "Reluctant" Biochemist

BY JOHN D. SCOTT

Edwin G. Krebs, a giant of biochemistry in the 20th century, died Dec. 21 in Seattle. He was 91. His discovery of protein phosphorylation as a regulatory mechanism (with Edmond Fischer) touched all aspects of biomedical science and profoundly influenced therapeutic approaches now widely used in clinical care. Ed's life story epitomizes his commitment to family and colleagues, excellence in research and service to the biochemical community.

Ed Krebs was born in Lansing, Iowa, on June 6, 1918, the son of a Presbyterian minister and a schoolteacher. His father died suddenly when Ed was 15 and, at the height of the Great Depression, the family moved to Urbana, Ill., for financial reasons. It was there that Krebs completed high school and earned a degree in chemistry from the University of Illinois in 1940. As an undergraduate, he became enamored with organic chemistry but eventually chose to become a physician, largely because he won a scholarship to attend Washington University School of Medicine in St. Louis.

The principal responsibility of a medical school during the war years was to train physicians for the armed forces. However, Krebs also was encouraged to participate in "medical research." After graduating from medical school in 1943 and doing 18 months of residency training in internal medicine at Barnes Hospital in St. Louis, Krebs went on active duty as a medical officer in the Navy. After being discharged from the Navy in 1946, Krebs returned to St. Louis with plans of becoming an academic internist. However, all of the hospital positions were filled by returning veterans, and, as a temporary measure, Krebs was advised to study basic science as a postdoctoral fellow at Washington University. Largely because of his background in chemistry, he was accepted into the laboratory of future Nobel laureates Carl and Gerty Cori in the department of biochemistry. After two years in the Cori lab doing research on the interaction of protamine with rabbit muscle phosphorylase, Ed became so captivated with biochemistry that this intially reluctant biochemist never returned to internal medicine. The next step was to find a permanent faculty position.

During his naval service, Ed's ship had gone to Seattle. The tranquil waters of the Puget Sound and the natural beauty of the city left a lasting impression. So, in 1948, he happily accepted a position as assistant professor of biochemistry in the fledgling University of Washington School of Medicine. Under the capable leadership of Hans Neurath, the department of biochemistry was being expanded to incorporate expertise in protein chemistry and enzymology. This included the recruitment of Edmond Fischer in 1953— a talented and charismatic Swiss biochemist with experience in the enzymatic analysis of potato phosphorylase. Thus, a lifelong friendship and a formidable research partnership was forged.

Together, Ed (Krebs) and Eddy (Fischer) determined the mechanism by which 5′-AMP served as an activator of phosphorylase *b*. They found that ATP was required for phosphorylase activation and, in a somewhat unusual experiment, discovered that calcium, leaching from filter paper used to clarify the extract, was an important co-factor. By using gamma-^{32}P-labeled ATP, they demonstrated that phosphate was incorporated into a specific serine residue of phosphorylase, thereby yielding the activated phosphorylase form. This landmark paper was published in the Journal of Biological

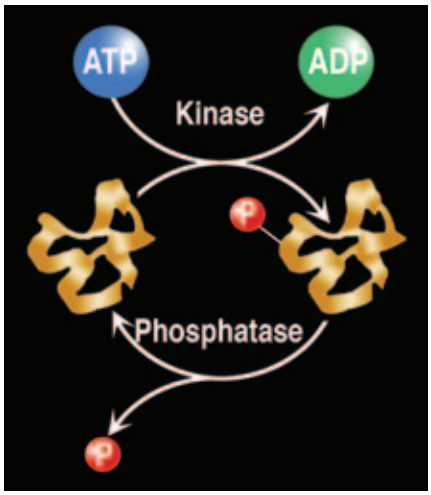
Chemistry in 1955 (1). Subsequently, Krebs, Fischer and colleagues confirmed that this phosphorylation is mediated by a phosphorylase kinase, which is itself controlled by a cAMP-responsive kinase, leading to the idea of a kinase cascade. In 1968, Krebs purified this cAMP-dependent protein kinase (PKA).

At this point in his career, interests in teaching and certain aspects of administration motivated Krebs. In 1968, he was attracted by the opportunity to become the founding chairman of the department of biological chemistry at the University of California, Davis, and stayed for a period of eight years. Ed also embarked on his long association with the American Society for Biochemistry and Molecular Biology, initially by joining the editorial board of the Journal of Biological Chemistry. In 1972, he became associate editor for the journal and remained in this position for more than 20 years. He also served as the president of ASBMB in 1985. In 1977, he returned to the University of Washington as chairman of the department of pharmacology. What he liked most about both positions, he said, was the responsibility of selecting good faculty members for the departments. At UW he was also appointed an investigator for the Howard Hughes Medical Institute.

After achieving his goals as department chair in 1983, Krebs refocused his efforts on research and training junior scientists. At this later stage in his career, he set his sights on solving new problems in signal transduction. His laboratory contributed to the analysis of phosphotyrosine signaling events and published key findings that were instrumental in the discovery of a new phosphorylation cascade— the MAP kinase pathway.

Krebs received many major scientific awards for his insights into the principles governing cellular regulation in health and disease. Among those honors were election to the National Academy of Sciences (1973), the Passano Foundation Award (1988), the Horwitz Prize (1989), the Lasker Research Award (1989), the 3M Life Sciences Award (1989) and the Welch Award in Chemistry (1991). At age 74, he and Edmond Fischer were honored with the 1992 Nobel Prize in Physiology or Medicine for the discovery they made almost 40 years before and its ongoing influence in many scientific and biomedical fields.

In 1997, Ed finally closed his lab but remained a fully committed ambassador for biomedical research at the University of Washington. He was frequently spotted wandering the halls of the medical center on his way to hear the latest and greatest results in a research seminar. Ed is survived by his wife of 64 years, Virgina (Deedy) Krebs, children Sally, Robert and Martha and several grandchildren.



This iconic image depicts the protein phosphorylation-dephosphorylation process as elucidated by Edwin Krebs and Edmond Fisher in their seminal 1955 Journal of Biological Chemistry paper (1).

Edwin G. Krebs will certainly be remembered for his keen intellect, astonishing research productivity and iconic status within the biomedical research community. He was a beloved mentor to numerous students and postdoctoral fellows. Those who were privileged to work closely with him will remember him fondly as a kind and gentle mentor who passed on extraordinary insights in a quiet and dignified manner. The legacy of this self-proclaimed "reluctant biochemist" should be a wonderful inspiration to the next generation of our profession.

Below, we offer reflections from several of Krebs' friends and colleagues.

I was very saddened by the passing of Ed Krebs. Even though I had not seen Ed for several years, I still considered him a close friend.

We are all familiar with his monumental work on protein phosphorylation. Less known is his importance to biochemistry as a member of the editorial board and as an associate editor of the Journal of Biological Chemistry. His influence on the development and operations of the JBC was particularly important during this period of rapid expansion for the journal. We always depended on his advice and thoughtful consideration both on the overall operation of the journal and on the review of specific manuscripts. Authors often commented on the thoroughness and fairness of his reviews.

We had many wonderful interactions over the years, due in large part to his commitment to the JBC. Ed was a superb scientist and a nice person, and I— and all of the associate editors— feel lucky to have known and worked with him.

Herbert Tabor
Editor
Journal of Biological Chemistry

I enjoyed working with Ed Krebs for five years as an associate editor of JBC. I had known him when he was a faculty member of the department of biochemistry at the University of Washington School of Medicine

in Seattle, but I saw him in a new role with JBC. He always had good advice in matters we considered at our associate editor meetings.

Robert L. Hill
James B. Duke professor of biochemistry
Duke University

Ed Krebs and Ed Fischer were two icons in the field of reversible phosphorylation. When my laboratory group started its work on protein phosphatases, they were both very welcoming to me and to members of my group. Their personalities made the field better, and they set the standard for exemplary scientific behavior. I also had the privilege of giving the Ed Krebs Lecture a few years ago, an event I still remember very fondly and treasure to this day.

Jack Dixon
Professor of pharmacology, cellular and molecular medicine and professor of chemistry and biochemistry
University of California, San Diego

I was so sad to hear of the passing of Ed Krebs. He was one of the true gentlemen in science. I owe any success that I have had to his willingness to take on a young and very naïve scientist from Wyoming as a postdoctoral fellow. His lab was a place where you could propose and pursue your own projects under his subtle, but always insightful, guidance. I remember once returning from an interview for a faculty position that I was not offered, probably due in part to my inherent laconic personality. Ed gently pulled me aside, put his arm around my shoulders and said, "Bob, the next time you go on a job interview, take some amphetamines."

Robert Geahlen
Professor of medicinal chemistry and molecular pharmacology
Purdue University

My fondest memories of Ed involved our annual laboratory research retreats. These were held over a couple of days and nights in a place called Pack Forest, a conference center that was owned by the University of Washington's School of Forest Resources. It was not the Hilton. It was a former logging camp, where you slept in bunkhouses, showered in a communal bathhouse, gave your research presentations in a big log cabin heated by a stone fireplace and ate hearty food in a rustic cafeteria. Away from the office, the phone, etc., Ed doffed his coat and tie and donned his jeans and flannel shirt. He joined us for hikes, softball (he broke his hand one year) and Frisbee. There, he'd let his guard down a little and share stories about life. The one that sticks in my mind was the awkward moment when he arrived in Seattle to start work at the UW in the late '40s. There, he was greeted by several reporters wishing to get the first interview with the son of Sir Hans Krebs...

When I arrived as a postdoc in Seattle, I was thoroughly intimidated by this great man. Even the most innocuous conversations were awkward as I tried to get to know him. Then, one evening when the lab was quiet, I was just finishing a cartoon I had drawn that depicted one of my fellow postdocs, Don Tinker, dressed in a tutu, wielding a magic wand. Ed walked past me on his way out. Behind me, I heard him softly repeat the words of the caption — "Tinker Bell" — followed by a quiet chuckle. I had discovered Ed's dry but wicked sense of humor.

Peter Kennelly
Professor and head of biochemistry
Virginia Polytechnic Institute and State University

My postdoctoral experience with Ed Krebs molded my scientific career. Ed was a very kind gentleman. He had a special knack for telling you that your ideas or interpretations were wrong in an unobjectionable way. He was careful to not overtly dictate any of his ideas to his scientific group, but he made suggestions and nourished his thoughts carefully in order to guide young scientists toward the right goals. Sometimes, I was proud to have a good idea, but I came to realize later on that the idea actually came from Ed. I remember just a few times that he was persistent in directing my research toward a specific direction, but, even then, he did it in a congenial manner, and he was practically always right.

Ed will be sorely missed in the scientific world, especially in the field of signal transduction. I miss my wonderful mentor and good friend.

Jackie D. Corbin
Professor of molecular physiology and biophysics
Vanderbilt University Medical Center

For me, Ed was a hands-off adviser. He gave people tremendous freedom — there was certainly ample opportunity to sink or swim in his lab. Ed had a heavy journal editor role, so we did not see a lot of him in the laboratory, but every now and then he would drift in for coffee. The one time Ed came into the laboratory on a Saturday, we were so pleased to see him and be noticed for our diligence, but it came with an unexpected cost. He was there to centrifuge some terrible homemade wine, and we had to taste it in little glass beakers.

Between his hearing aid and my Australian accent, I am not sure he understood a thing I said for the first six months. When I first met Ed, I was struck by his being so low key and devoid of any "brilliant façade," but then I came to realize that nothing but clear thinking and com-

mon sense ever parted from his lips. While somewhat remote, he was immensely likeable, someone whose value just kept growing on you.

His weekly laboratory meetings were of tremendous value and provided the real mentoring environment. Ed was keenly interested in politics and the U.S. economy. He was a strong critic of the infamous U.S. Sen. William Proxmire and his "Golden Fleece" awards. Perhaps the best illustration of his political interests was at a plenary lecture at a Gordon Conference, where he traced the development of the protein phosphorylation field over his long career and what was happening in politics in the U.S. at the time of each major scientific development.

We remember Ed with fondness and enduring thanks for the impact he had on science and our lives.

Bruce E. Kemp
Pehr Edman fellow in protein chemistry and metabolism
St. Vincent's Institute of Medical Research

My time with Ed Krebs as a postdoc in the mid-1970s in both Davis and Seattle had a great influence on my scientific development. Ed had a "hands-off" approach to science that focused on providing resources for a large lab with mostly postdocs, each with a different, mostly self-directed project that had minimal overlap with other projects. This freedom had a broadening impact on postdocs, and, for myself, it formed the model for my own laboratory. Ed expected each person to have passion for his or her work and once commented that he was disappointed to drive by the lab late on a Saturday evening and find no lights on. We postdocs then decided to leave the lights on 24/7.

Ed was a traditional "ice bucket biochemist" and enzymologist, and I was his first postdoc with a cell biology background. I think he was initially not sure what to make of "biochemistry without a license," but that skepticism vanished when we were quickly able to show by microinjecting protein kinase A into Xenopus oocytes that changes in kinase activity could fully account for all the in vivo actions of cAMP in an important biological process. For myself, I learned how to purify enzymes, beginning with phosphorylase kinase, from kilograms of tissue, and this experience served me well in later years when purifying mitotic enzymes (Cdks), whose characterization had eluded others for many years. It was an amazing time in science, because, although Krebs and Fischer had shown the critical importance of phosphorylation in glycogen metabolism, it was not thought to be of much importance for other aspects of biology. At the end of my postdoc, it was reported that the Src oncogene encoded a protein kinase— a finding that linked kinases to cancer and ultimately led the way to the current realization that protein phosphorylation controls virtually all biological processes. It was one of those rare times in science when one happens to be working on something that turns out to be much more important than initially believed.

Although Ed received many honors during his lifetime, his gentle nature was very unassuming, and he exhibited little interest in scientific politics or in going to meetings. He had a long-standing presence in ASBMB as associate editor of the JBC and felt that there was no need to search for "higher impact" journals if the work was sound. Throughout his life, he kept focused on key questions in glycogen metabolism, even after vastly increased support from Howard Hughes Medical Institute and winning the Nobel Prize. To the end, he felt that there were many questions still unanswered about the regulation of metabolism by protein phosphorylation, and he wanted to continue working on them.

James L. Maller
Professor of pharmacology
University of Colorado School of Medicine

I was fortunate to have Ed as my Ph.D. mentor from 1966 to 1970. Two specific pieces of advice that influenced my career come to mind. The first was when I was a student in Ed's lab and was concerned that another lab was working on the same project. Ed's advice was that any time you are working on an important project, there will be strong competition, so find some niche where you have an advantage and pursue that aspect. The second was as a professor at Vanderbilt (University) when we were both Howard Hughes investigators. There had been a change in Hughes leadership, and I was concerned about whether or not they would continue to fund my research. Ed told me to not worry about what Hughes wanted, just make sure my research was outstanding— if so, it would all work out. He was right! Ed's legacy will continue through the many young scientists he mentored.

Tom Soderling
Senior scientist, Vollum Institute
Professor of biochemistry
Oregon Health and Science University

Thinking of Ed always brings a smile to my face. While others will rightfully comment on his brilliant scientific insight, his administrative skills and his role as a mentor, what particularly stands out in my memory is Ed's unusual sense of humor. About 10 years ago, I brought a star-struck graduate student to meet Ed, who proceeded to talk to her about research that he had done "during World War I." Afterward, he professed to me his amusement that the student had not caught the historical error. This, and many other incidents, always

left me wondering whether Ed was kidding around in a given situation. He kept such a straight face that one could never tell. Once, during a whiskey-laced late-night card game at one of our Pack Forest retreats, Ed told me that I had a good poker face. Coming from him, this was quite a compliment!

I thank Ed for many things, including his anecdotes of agricultural pursuits, his tutelage in antique hunting and his mentoring in how to write manuscript reviews, but most of all I thank him for demonstrating how a great scientist can be a great human being.

Kathryn E. Meier
Director of program in nutrition and exercise physiology
Washington State University

It is a pleasure to remember Ed Krebs as a friendly and passionate teacher and science supervisor. His pioneering work on protein kinases as modulators of cellular functions served as a basis for my later investigations. He cordially shared his knowledge of biochemical methodology and readily participated in discussions on protein kinases and protein phosphatases. Much of what I and my colleagues were able to accomplish was made possible by his intuitive research.

Franz Hofmann
Emeritus professor of pharmacology
Technische Universität München

I was on a plane from Durham, N.C., to Seattle, Wash., to start my postdoc in Ed's lab when Mount St. Helens first erupted. It was an apt introduction to my time in Ed's lab. It was May 1980, and tyrosine phosphorylation of pp60src recently had been described. There followed a rapid explosion in our knowledge of protein tyrosine kinases, and Ed's lab was the ideal place to be during this revolution. Ed was supportive of his postdocs who ventured into this new area, and he helped us apply the knowledge he had acquired in decades of studies on protein kinases to these new members of the family. He was rigorous in his approach to data but kind and patient at the same time. He was a wonderful mentor to whom I always will be grateful.

Linda J. Pike
Professor of biochemistry and molecular biophysics
Washington University School of Medicine

When I began working with Ed, his only directive was "find a protein kinase cascade— I know it exists." This initiated studies that led to the discovery and characterization of MAP kinases and MAP kinase kinases. I could not have become a professor without Ed's generosity in accepting me in his lab when my options were limited.

One of the most important lessons that Ed taught us by example was how to conduct ourselves as citizens within the scientific community. Our work on various projects led to competitive interactions with scientists at other institutions and sometimes within our own lab. Ed maintained a balanced approach to scientific competition, treating whomever he met as a colleague and showing him or her great respect and kindness. There were very few people who Ed disliked, and he always was able to find strengths in every person. I recall sessions in his office when Ed pulled out letters and other documents from his past that illustrated in various ways "how to handle oneself with aplomb." Ed valued this deeply, and, in doing so, he set a high standard for fairness, collegiality and professional conduct, which continues to influence investigators throughout the field of signal transduction.

What I remember most fondly about Ed was his keen sense of humor. We'd have to pay close attention in order to pick up his hilarious observations, which were often delivered as soft, understated commentaries, as well as the occasional practical joke. The year was 1991 and Bill Clinton had generated controversy during the primaries with statements about his drug use. To kick off the annual Krebs & Fischer lab retreat at Mt. Rainier, Ed stood up and confessed to the group that "I too have used pot, but that was before I became a professor."

Natalie Ahn
Associate professor of chemistry and biochemistry
University of Colorado at Boulder

Ed Krebs was one of those people whose accomplishments were so numerous and so extraordinary that, paradoxically, they were easy to overlook because they formed such a huge part of our scientific world. But, every time we teach or do research on the regulation of pretty much anything that goes on inside the living cell, the chances are good that we are either talking about or building on his work.

Gregory A. Petsko
Gyula and Katica Tauber professor of biochemistry and chemistry
Brandeis University

John D. Scott (scottjdw@u.washington.edu) is a Howard Hughes Medical Institute investigator and the Edwin G. Krebs-Speights professor of cell signaling and cancer biology at the University of Washington School of Medicine.

REFERENCE

1. Fischer, E. H., and Krebs, E. G. (1955) Conversion of Phosphorylase B to Phosphorylase A in Muscle Extracts. *J. Biol. Chem*. **216**, 121 – 132.

Kozarich Garners Distinguished Scientist Award

John W. Kozarich, chairman and president of ActivX Biosciences Inc., received the 2009 Distinguished Scientist Award from the San Diego section of the American Chemical Society for his work on identifying protein kinase and protease targets for screening drug candidates. The award, created in 1992, also recognizes Kozarich's contributions to academic and industrial research, teaching, corporate leadership, mentoring young scientists and philanthropy.

In addition to his role at ActivX, Kozarich is chairman of the board at Ligand Pharmaceuticals Inc., chief scientific adviser at Kyorin Pharmaceutical Co. Ltd. and adjunct professor of biotechnology and chemical physiology at The Scripps Research Institute. He previously held faculty positions at the University of Maryland and Yale University School of Medicine, and, from 1992 to 2001, he was vice president at Merck Research Laboratories, where he was responsible for a number of research programs.

Kozarich is internationally known for his work on enzyme mechanisms and the chemistry of DNA-cleaving antitumor drugs and has received numerous awards and served on many committees in the academic, government and business sectors.

Schreiber Receives Wheland Medal

Stuart L. Schreiber, Morris Loeb professor of chemistry and chemical biology at Harvard University, has received the 2009-2010 Wheland Medal from the University of Chicago's department of chemistry.

The medal, awarded every other year in memory of the physical-organic chemist George Wheland, recognizes a scientist who has made outstanding contributions to chemistry. Past recipients include Frank H. Westheimer, Harden M. McConnell, Nelson Leonard, Fred Wudl, Robert L. Baldwin and Robert H. Grubbs.

Schreiber is director of chemical biology and founding member of the Broad Institute of Harvard University and the Massachusetts Institute of Technology, where he is also a Howard Hughes Medical Institute investigator. He is best known for having developed systematic ways to explore biology, especially disease biology, using small molecules and for his role in the development of the field of chemical biology. He discovered principles that underlie information transfer and storage in cells, specifically discoveries relating to signaling by the phosphatase calcineurin and kinase mTOR, gene regulation by chromatin-modifying histone deacetylases and small-molecule probes of difficult targets and processes that directly relate to human disease.

Richard Presented with Schoellkopf Award

John P. Richard, professor of chemistry at the State University of New York, Buffalo, was named the winner of the 2009 Jacob F. Schoellkopf Award, given annually by the American Chemical Society Western New York section for outstanding work and service in chemistry or chemical engineering. Richard was cited for his "outstanding research in the field of physical organic and bioorganic chemistry; specifically, the study of reaction mechanisms of biologically significant enzymatic and non-enzymatic reactions."

Richard's early work focused on the mechanisms of organic reactions in water that serve as models for enzyme-catalyzed reactions. These include nucleophilic substitution and proton transfer reactions at carbon and catalysis of phosphate diester hydrolysis by metal ion complexes. His research program since has expanded to include studies of the mechanisms for the stabilization of reactive intermediates at the active sites of enzymes, such as beta-galactosidase, triosephosphate isomerase, isopentenyl pyrophosphate isomerase and orotidine 5'-monophosphate decarboxylase. This has led to work that defines the critical role of flexible protein loops in stabilizing reactive enzyme-bound intermediates.

Paulson Honored with Karl Meyer Award

James C. Paulson, professor of chemical physiology and molecular biology at The Scripps Research Institute, was named the recipient of the Society for Glycobiology's 2009 Karl Meyer Award.

The award, established in 1990 to honor Karl Meyer and his outstanding contributions to the field of glycobiology, is given to well-established scientists with active research programs who have made widely recognized contributions to the field of glycobiology.

Paulson is known as a leader in the chemical biology of carbohydrates and the biological function of glycoproteins and lectins. In his more than 30 years of research, he has made seminal discoveries and contributions to glycobiology. He was one of the first to use chemo-enzymatic synthesis of glycans as a tool to elucidate the functions of glycan binding proteins. His lab was also the first to clone and produce a family of recombinant sialyl transferases, which allowed large-scale synthesis of this synthetically challenging class of carbohydrates. His success in cloning of the first full-length glycosyltransferase, ST6Gal I, was a major achievement: It revealed the topology of glycosyltransferases with N-terminal signal anchors tethering the catalytic domain oriented to the lumen of secretory organelles and led to the production of recombinant glycosyltransferases for use as synthetic tools.

Steiner Wins Manpei Suzuki International Prize

Donald F. Steiner, A. N. Pritzker distinguished service professor emeritus in the departments of medicine and biochemistry and molecular biology at the University of Chicago, has been awarded the Manpei Suzuki Diabetes Prize for 2009.

The prize, now two years old, is the largest award for diabetes research. It was established to commemorate the 15th anniversary of the Manpei Suzuki Diabetes Foundation, and it honors "those who have enlightened researchers in the field of diabetes around the world with their original and excellent scientific achievements." The prize includes a certificate of honor and $150,000.

The prize's selection committee cited Steiner's outstanding achievements over many years of research, including the discovery of proinsulin and characterization of the proinsulin processing pathway, clinical applications of a C-peptide radioimmunoassay for measuring endogenous insulin production and identification of a point mutation in the insulin gene causing various abnormalities in glucose metabolism.

"I am highly honored," said Steiner. "It's humbling to be recognized by my peers and gratifying to receive an award of this stature for my life's work. I'm very grateful to my colleagues for the nomination and to the Manpei Suzuki Diabetes Foundation for this distinction."

IN MEMORIAM:
Robert Wenthold

Robert J. Wenthold, a neuroscientist who had been scientific director of the National Institute on Deafness and Other Communication Disorders, died Oct. 30 in Bethesda, Md. He was 61.

Wenthold was born in Cresco, Iowa. He graduated from Loras College in Dubuque, Iowa, and received a doctorate in biochemistry from Indiana University in 1974. He did postdoctoral work at the National Institutes of Health and later became a faculty member at the University of Wisconsin. In 1984, he joined what was then called the National Institute of Neurological and Communicative Disorders and Stroke as a senior investigator. Five years later, he moved to the new NIDCD and became its director in 1998. There, he was a vital force in helping to build the institute's intramural research program. He also started a collaborative graduate student training program between the University of Maryland and the NIDCD, which later became a model for the Graduate Partnerships Program at the NIH.

Wenthold published widely and was a highly cited researcher in brain science. In 1989, he cloned a member of the family of receptors for glutamate, and, a year later, he developed the first antibodies to these receptors.

Schauer Shares Lifetime Achievement Award

Roland Schauer, professor of biochemistry emeritus at the University of Kiel in Germany, has been honored with the Society for Glycobiology's 2009 Rosalind Kornfeld Award for Lifetime Achievement in Glycobiology. He shares the prize with Mary Catherine Glick of the University of Pennsylvania.

The Kornfeld Award was established in 2008 to honor Rosalind Kornfeld's distinguished scientific career and service to the Glycobiology Society. It is given to scientists who have, over their professional lifetimes, made significant contributions that have had a large impact on the field.

Over the past 40 years, Schauer has contributed to the knowledge about the occurrence, structure, biosynthesis and functions of sialic acids. He discovered many new members of this sugar family and has isolated, characterized and cloned several of the key enzymes involved in the biosynthesis and degradation of a number of these compounds. In addition, he shed light on many of the functions of the sialic acids, such protecting cells from phagocytosis or serving as receptors for certain viruses. His work also has helped researchers understand many of the phenomena in which sialic acids are critically important, such as the control of cell and glycoprotein lifetime in the circulatory system, the adhesion of infectious agents to host cells and the recruitment of leukocytes to sites of inflammation.

IN MEMORIAM:
Francis LeBaron

Francis Newton LeBaron passed away Nov. 2 in Cape Cod, Mass., at age 87.

Born in Framingham, Mass., LeBaron attended the Massachusetts Institute of Technology. After graduating, he entered the U.S. Navy and served in the North Pacific on the USS Watts during World War II.

After being discharged from the navy, LeBaron obtained a master's degree from Boston University and a doctorate in biochemistry from Harvard University. After a postdoctoral fellowship in England and 10 years of research in neurochemistry of the brain at McLean Hospital in Belmont, Mass., he moved to Albuquerque, N.M., to help set up the University of New Mexico Medical School. He eventually served as chairman of the biochemistry department at the university while continuing his research on the aging of the brain.

LeBaron helped to establish the American Society for Neurochemistry and served on the editorial boards of several scientific journals. After retirement from the University of New Mexico, he lived in Blue Hill, Maine, for a year and became a certified yacht surveyor.

54 ASBMB Members Elected AAAS Fellows

Fifty-four members of the American Society for Biochemistry and Molecular Biology have been awarded the distinction of American Association for the Advancement of Science Fellow, an honor bestowed on AAAS members by their peers. These individuals will be recognized for their contributions to science and technology at the Fellows Forum to be held during the AAAS annual meeting in February. The new fellows will receive a certificate and a blue-and-gold rosette as a symbol of their distinguished accomplishments.

We congratulate the following ASBMB members for this achievement:

Section on Agriculture, Food and Renewable Resources

- **Joseph Chappell,** *University of Kentucky*
- **Donald P. Weeks,** *University of Nebraska-Lincoln*

Section on Biological Sciences

- **Etty (Tika) Benveniste,** *University of Alabama at Birmingham*
- **Ing-Ming Chiu,** *The Ohio State University*
- **Pierre A. Coulombe,** *The Johns Hopkins University*
- **Harry A. Dailey Jr.,** *University of Georgia*
- **Ross E. Dalbey,** *The Ohio State University*
- **John E. Donelson,** *University of Iowa*
- **Timothy Donohue,** *University of Wisconsin-Madison*
- **David Draper,** *The Johns Hopkins University*
- **Peggy Farnham,** *University of California, Davis*
- **Sandra J. Gendler,** *Mayo Clinic*
- **Mark Gerstein,** *Yale University*
- **Alfred L. Goldberg,** *Harvard Medical School*
- **Erich Grotewold,** *The Ohio State University*
- **Vincent J. Hilser,** *University of Texas Medical Branch at Galveston*
- **Mary Hunzicker-Dunn,** *Washington State University*
- **Jerry Kaplan,** *University of Utah School of Medicine*
- **Marc W. Kirschner,** *Harvard Medical School*
- **John H. Nilson,** *Washington State University*
- **Donald R. Ort,** *University of Illinois at Urbana-Champaign*
- **Cynthia B. Peterson,** *University of Tennessee, Knoxville*
- **Stephen W. Ragsdale,** *University of Michigan Medical School*
- **John Scott,** *University of Washington*
- **Andrey S. Shaw,** *Washington University in St. Louis*
- **Charles J. Sherr,** *St. Jude Children's Research Hospital*
- **Gerald I. Shulman,** *Yale School of Medicine*
- **Gail Entner Sonenshein,** *Boston University School of Medicine*
- **Michael Robert Stallcup,** *University of Southern California*
- **Michael F. Summers,** *University of Maryland, Baltimore County*
- **Liang Tong,** *Columbia University*
- **Judith L. Van Houten,** *University of Vermont*
- **Xiao-Fan Wang,** *Duke University Medical Center*
- **Dennis R. Winge,** *University of Utah*

Section on Chemistry

- **Hagan Bayley,** *University of Oxford*
- **Tadgh P. Begley,** *Cornell University*
- **Richard A. Cerione,** *Cornell University College of Veterinary Medicine*
- **Michael H. Gelb,** *University of Washington*
- **Francis S. Millett,** *University of Arkansas*

Section on Medical Sciences

- **Michael L. Dustin,** *New York University School of Medicine*
- **Laurie Glimcher,** *Harvard School of Public Health*
- **Billy Gerald Hudson,** *Vanderbilt University School of Medicine*
- **David Levy,** *New York University School of Medicine*
- **Maurine Linder,** *Cornell University*
- **Vassilios Papadopoulos,** *McGill University*
- **Roger Matthew Perlmutter,** *Amgen Inc.*
- **Susan R. Ross,** *University of Pennsylvania*
- **Jonathan D. Smith,** *Cleveland Clinic*
- **Eric Verdin,** *University of California, San Francisco*

Section on Neuroscience

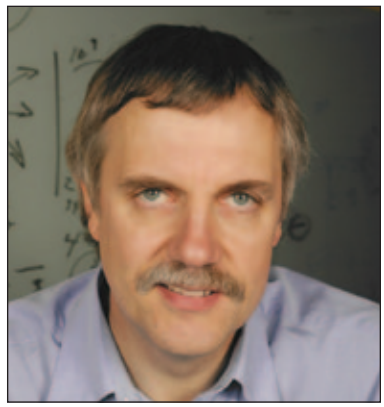
- **William A. Catterall,** *University of Washington*
- **Don W. Cleveland,** *University of California, San Diego*

Section on Pharmaceutical Sciences

- **John F. Carpenter,** *University of Colorado Denver*
- **Robert J. Linhardt,** *Rensselaer Polytechnic Institute*
- **Ruiwen Zhang,** *University of Alabama at Birmingham*

Aebersold Receives Sober Lectureship

BY ANGELA HOPP AND NICK ZAGORSKI



Ruedi Aebersold, a pioneer in proteomics and systems biology, has been named the recipient of the 2010 American Society for Biochemistry and Molecular Biology Herbert A. Sober Lectureship, recognizing outstanding biochemical and molecular biological research with particular emphasis on the development of methods and techniques to aid in research.

As part of his award, Aebersold, a professor at the Institute for Molecular Systems Biology at the Swiss Federal Institute of Technology Zürich with a joint appointment at the University of Zürich, will present an award lecture titled "Mapping and Measuring Molecular Networks in Cells" at 8:30 a.m. Sunday, April 25, at the 2010 annual meeting in Anaheim, Calif.

For the past 30 years, Aebersold, who received his doctoral degree in cell biology from the University of Basel in 1984, has been developing tools and techniques that have been invaluable in the fields of analytical protein chemistry, systems biology and proteomics, a technique that allows researchers to compare the proteomes of two different cell populations, for example cells grown in different media.

His group's efforts have led to the emergence of both gel-free protein identification and quantitative mass spectrometry, perhaps best exemplified by his development of isotope-coded affinity tag proteomics. In addition, Aebersold has created a host of computational tools to assist researchers in analyzing mass spectrometry-derived proteomics data, such as the Trans-Proteomic Pipeline, a program that estimates the percentage error in a dataset.

As Fuchu He, president and director of the Beijing Proteome Research Center, succinctly put it, "The series of his contributions has fueled the proteomic revolution. The methods he developed are now used in thousands of laboratories around the world and are contributing to an explosion of new biological and clinical knowledge."

Aebersold's impressive career has spanned two continents. After his Ph.D. studies in Basel, he worked as a postdoctoral fellow and senior research fellow at the California Institute of Technology, had professorships at the University of British Columbia and the University of Washington and co-founded the Institute for Systems Biology in Seattle (with Lee Hood and Alan Aderem) in 2000 before returning to Switzerland in 2004.

In addition to building technologies for other researchers to use, Aebersold and his team have been employing ICAT and other proteomic approaches in their own comparative studies of protein expression in cells under different conditions. Some specific areas of study include large-scale analyses of post-translational protein modifications, an examination of abnormal protein expression in cancerous cells and systematic studies of how cells respond to external stimuli.

These comparative protein profiles will lead to a more robust understanding of the biochemical processes that regulate cell physiology and also could lead to new prognostic and/or diagnostic biomarkers for disease.

Aebersold, who is also an associate editor for Molecular and Cellular Proteomics, has received numerous awards for his work, including the American Society for Mass Spectrometry Biemann Medal, the Pehr Edman Award, the Michael Widmer Award, the World Technology Network Award for Biotechnology, the Genome Technology Award in Proteomics and the Human Proteome Organization achievement award.

"He has inspired a whole generation of young scientists at the University of Washington, the Institute for Systems Biology and the ETH-Zurich, as well as indirectly through his publications and his active engagement in many leading professional organizations," said Gilbert S. Omenn, professor of internal medicine, human genetics and public health at the University of Michigan Medical School and vice president of HUPO.

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Tesmer Wins ASBMB Young Investigator Award

BY ANGELA HOPP AND NICK ZAGORSKI

John Tesmer, a research associate professor at the Life Sciences Institute and the department of pharmacology at the University of Michigan Medical School, has been named the winner of the 2010 American Society for Biochemistry and Molecular Biology Young Investigator Award (formerly known as the ASBMB/Schering-Plough Research Institute Award), which honors outstanding research contributions to biochemistry and molecular biology by individuals who have no more than 15 years of postdoctoral experience.

Tesmer will present an award lecture titled "Structural Analysis of Heterotrimeric G Proteins and G Protein-Coupled Receptor Kinases" at 8:30 a.m. Monday, April 26, at the 2010 annual meeting in Anaheim, Calif.

G protein-coupled receptor signaling pathways are responsible for a wide range of intracellular events and are an intense area of biological and pharmaceutical study. Researchers studying GPCR owe a lot to Tesmer and his group, who provided insight into GPCR signaling through their structural and functional analyses of G proteins.

Tesmer's impressive array of contributions began in 1997, when he solved the atomic structure of RGS4 in a complex with Gαi1 while he was a Howard Hughes Medical Institute postdoctoral fellow working with Stephen R. Sprang at the University of Texas Southwestern Medical Center at Dallas. This was the first structure of a regulator of G protein signaling, as well as the first structure of an RGS protein in complex with its target. Shortly thereafter, Tesmer solved the crystal structure of Gαs, both alone and in complex with the catalytic domains of adenylyl cyclase, the latter providing the first structure of a G protein-effector complex.

Since then, Tesmer, who double majored in biochemistry and English at Rice University and received his doctorate in biological sciences from Purdue University, has never looked back.

"Protein crystallography is often an extremely time-consuming, high-risk approach to answering questions about the molecular mechanisms of signal transduction," said University of Michigan colleague Alan R. Saltiel. "However, in a very short time [John] has elegantly addressed many fundamental questions of heterotrimeric G protein signal transduction. His success is a clear demonstration of his perseverance, expertise, clear-mindedness and ability to effectively synergize with collaborators."

Sprang, currently a professor and director of the Center for Biomolecular Structure and Dynamics at the University of Montana, agrees wholeheartedly. "Tesmer was among the most productive and creative postdoctoral fellows with whom I have had the honor to work," he said. "Since he began his independent career as a junior faculty member at UT-Austin, and now at the University of Michigan, John has become a recognized leader in the structural biology of G protein signaling. Indeed, I would say with confidence that he is currently the most productive structural biologist working in this area."

Today, Tesmer, who always has been scientifically intrigued by the processes by which cells sense extracellular signals, channels that productivity to determine various structures of signaling proteins regulated by heterotrimeric G proteins, particularly those that contain RGS homology (RH) domains.

Two of his favorite targets are GRK2, a kinase that is important for myocardiogenesis and regulation of heart contractility (for which he recently determined the atomic structure of GRK2 in complex with Gβγ) and leukemia-associated RhoGEF, or LARG, a protein that activates RhoA and thus represents one of the few well-defined links between heterotrimeric G proteins and small-molecular-weight G proteins. His group is currently working on determining the atomic structures of various fragments and complexes of LARG to better understand the mechanism of signal transduction from Gα13 to RhoA.

The 2010 ASBMB Young Investigator Award will add to the impressive honors already bestowed on this young and exciting researcher, including the Lyndon B. Johnson Research Award from the American Heart Association in 2000, a Cottrell Research Scholar award in 2002 and the University of Texas College of Natural Sciences Teaching Excellence Award in 2004.

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Herschlag Named Rose Award Recipient

BY ANGELA HOPP AND NICK ZAGORSKI

Daniel Herschlag, professor of biochemistry, chemistry and chemical engineering at Stanford University, has been awarded the 2010 American Society for Biochemistry and Molecular Biology William C. Rose Award in recognition of his outstanding contributions to biochemical and molecular biological research and a demonstrated commitment to the training of younger scientists.

Herschlag will present an award lecture titled "How Enzymes Work" at 8:30 a.m. Tuesday, April 27, at the 2010 annual meeting in Anaheim, Calif.

Integrating concepts and techniques from physics, chemistry and biology, Herschlag and his lab team seek to unlock the fundamental behaviors of RNA and proteins and, in turn, how these behaviors determine and affect biological processes. Herschlag is perhaps most famous for his groundbreaking research in RNA structure, folding and catalysis, particularly his discoveries concerning the mechanisms and thermodynamics of group I and hammerhead ribozymes.

"Herschlag has set the standard for excellence in this field," notes colleague Carol A. Fierke, chairwoman of the University of Michigan's department of chemistry. "His studies using single-atom substitution and kinetic analysis to identify metal binding sites in ribozymes are a tour de force. Additionally, [he] provided the first direct demonstration of the role of binding interactions in chemical catalysis in ribozymes; these studies elegantly demonstrated the role of binding energy in stabilizing both ground-state and transition-state interactions."

Of course, as Fierke and others will point out, ribozymes represent just a portion of Herschlag's superb body of research. He is also one of the foremost experts on the mechanisms of both naturally occurring and enzyme-catalyzed phosphoryl transfer reactions and a leader in advancing research into RNA chaperones. He has provided tremendous insight into the general nature and evolution of enzyme catalysis.

In this latter area, Herschlag is well known for identifying the implications of a property he termed "catalytic promiscuity"— in which proteins in the same superfamily often display low levels of activity toward reactions catalyzed by other members within the superfamily— for the evolution and design of new enzymes.

In addition to his scientific contributions in the fields of RNA, enzymes and RNA enzymes, Herschlag also has demonstrated an equal level of commitment to training younger scientists. Says Rick Russell, associate professor of chemistry and biochemistry at the University of Texas and former postdoctoral fellow in Herschlag's lab, "Dan has been committed to doing everything necessary to mentor his group members at the highest possible level in all aspects of training, from designing and interpreting the experiments to preparing the presentation."

"I am continually amazed at how willing Dan is to donate his time to provide guidance, and I am amazed at how effective his guidance is across this wide range of scientific areas," Russell continued. "I know of no other scientist who is so willing and eager to assist students in this way."

Herschlag received his undergraduate degree in biochemistry from the State University of New York at Binghamton in 1982, during which time he also co-edited the campus literary magazine.

After a year of conducting research into the enzymology of glycopeptide synthesis with John Gander at the University of Minnesota (and learning a little quantum mechanics on the side), Herschlag began his graduate studies at Brandeis University. There, he began looking into phosphoryl transfer reactions under the direction of William Jencks.

After receiving his doctoral degree in 1988, Herschlag did postdoctoral research at the University of Colorado at Boulder under Thomas Cech, where he got his first taste of the recently discovered RNA enzymes. He then went on to join the Stanford University biochemistry department in 1993, where he has remained ever since.

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Ernest Everett Just: Experimental Biologist *Par Excellence*

BY W. MALCOLM BYRNES

For almost 40 years after the end of World War II, the work of Ernest Everett Just, an African-American biologist known for his studies of fertilization and early development in marine invertebrates, lay forgotten, buried in the scientific literature. Then, in 1983, Kenneth R. Manning, a historian of science at Massachusetts Institute of Technology, published a prize-winning biography titled "Black Apollo of Science: The Life of Ernest Everett Just" (1). Stephen Jay Gould (2) favorably reviewed Manning's book and wrote a column in the magazine Natural History about Just (3). Since then, a number of events have taken place that have brought increased attention to Just: A stamp honoring him was issued; symposia were held in his honor, the most recent at Howard University in 2008; and, in 2009, a special issue of the journal Molecular Reproduction and Development dedicated to Just was published (4). Yet still, E. E. Just and his contributions remain largely unknown to biologists.

A Career in Fertilization and Development

Born in 1883 in Charleston, S.C., Just attended the Kimball Union Academy, a boarding school in Meriden, N.H., graduating in 1903. He then enrolled at Dartmouth College and graduated magna cum laude in 1907 as an esteemed Rufus Choate scholar. He immediately accepted a teaching position at Howard University in Washington, D.C., where he quickly rose through the academic ranks, becoming full professor in 1912. He chaired the department of zoology at Howard and, with the help of the Rosenwald Fund, established a master's program in that field.

In 1909, Just began making annual summer excursions to the Marine Biological Laboratory in Woods Hole, Mass., where he worked under renowned embryologist Frank R. Lillie. Almost from the beginning, his work was significant. His first paper (5) showed that the sperm entry point determines the first cleavage plane in the egg of the marine annelid Nereis limbata. The body of work for his doctoral degree, which he obtained from the University of Chicago in 1916, was based on his study of the breeding habits of N. limbata and Platynereis megalops (another annelid) and the fertilization reaction of the sand dollar Echinarachnius parma. While at the MBL, he rose from student apprentice to internationally respected scientist.

Just was known at Woods Hole and beyond for his uncanny ability to coax marine invertebrate embryos to develop normally, and many sought his advice on the proper handling of marine animal eggs and embryos. He compiled a set of indices of normal development based mainly on the timing and quality of fertilization envelope separation, allowing him to predict with great certainty whether or not development would be normal for a given egg. In 1939, he published a laboratory manual, "Basic Methods for Experiments on Eggs of Marine Animals" (6), which applied his deep storehouse of knowledge on egg handling.

Not content with simply studying the marine life around Woods Hole, in 1929 Just traveled to the Stazione Zoologica Anton Dohrn in Naples, Italy, to investigate fertilization in several European sea urchins and to determine whether the Mediterranean annelid Nereis dumerilii was the same as the North American species Platynereis megalops, as some had postulated. (It was not.) Then, in 1930, he received in invitation by Max Hartmann, the famous German embryologist, to visit the Kaiser-Wilhelm Institut für Biologie near Berlin. An invitation of this kind extended to an American was unprecedented, but the Germans saw an affinity between Just's work and their own. They wanted to see if his ideas about the importance of the cell cortex (the structured layer just beneath the cell surface) could be applied to protists such as Amoeba

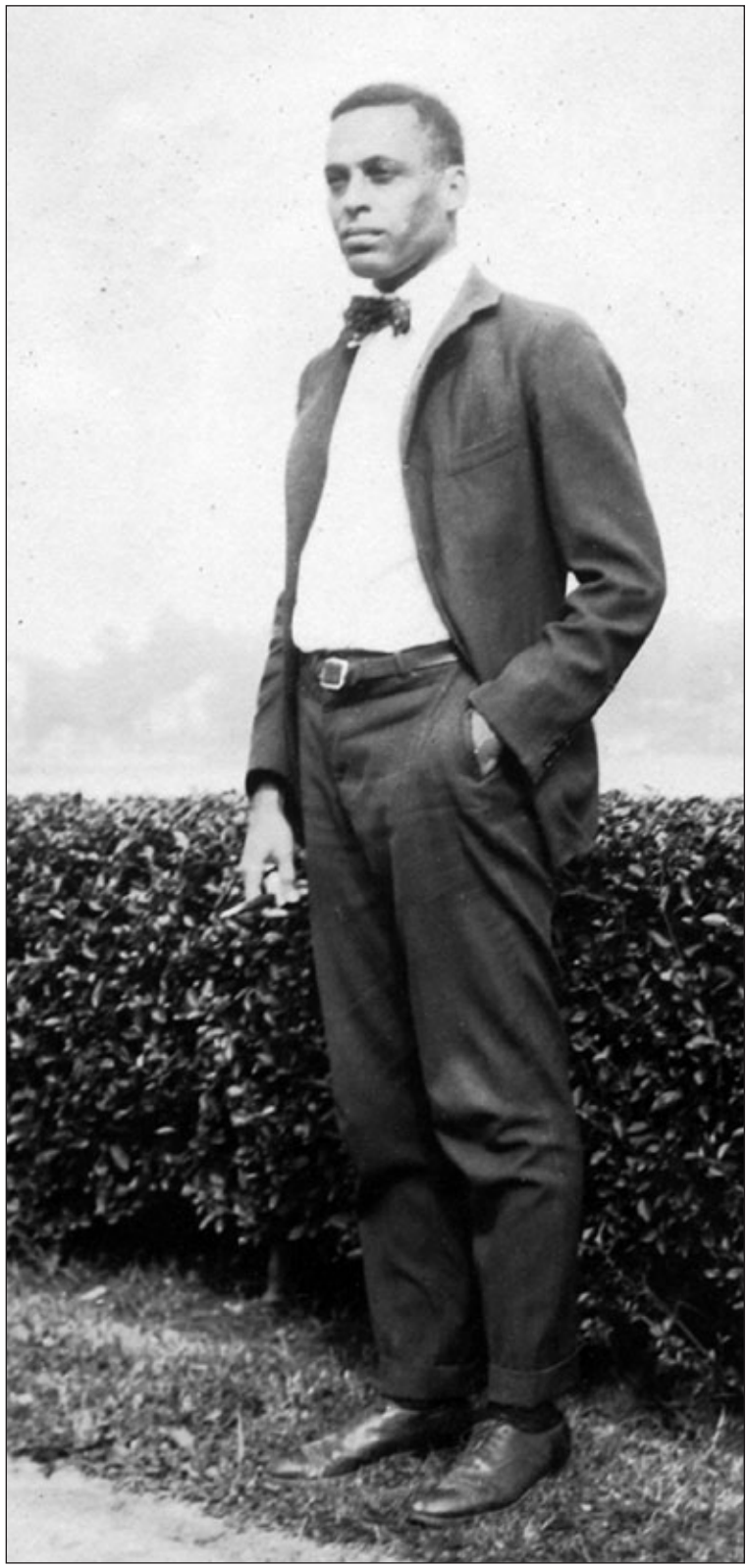
proteus, which they had been studying.

Altogether, Just made nine excursions to Europe. In addition to his trips to Berlin and Naples, he traveled to the Sorbonne in Paris, where he spent some time completing his second book, "The Biology of the Cell Surface" (7), which brought his scientific work and his general ideas together as one synthetic whole. Of the 70 articles he published over the course of his 30-year career, several were in German journals, including one in Naturwissenschaften that, for the first time, correlated changes in cell adhesiveness with developmental stages during the early embryonic cleavage process (8). After 1936, Just's papers became increasingly philosophical. This reflected both his desire to apply his ideas about the importance of the cell surface more broadly and his increased willingness to challenge those American counterparts (notably Thomas Hunt Morgan and Jacques Loeb) whom he saw as too reductionistic.

In 1938, bereft of funding and rejected by many of his American colleagues because of his opposition to their reductionistic views, Just initiated a self-imposed exile in Europe. He took up research at the Station Biologique at Roscoff, a small French fishing village on the English Channel. But in 1940, the Nazis invaded the region around Paris, including Roscoff, and Just was forced to leave. He returned to the United States and Howard University. In 1941, however, he fell tragically ill with pancreatic cancer, and, by the end of October, he died.

Challenging Established Views

It is clear from Just's writings that he believed that life arose out of the complexity and structural integrity of living systems. In "The Biology of the Cell Surface" (7), he wrote that "life is the harmonious communion of events, the resultant of the communion of structures and reactions." Just rejected purely mechanistic explanations, yet he also was not a vitalist. Rather, he took the middle position (3), embracing what is known as "organicism," or materialistic holism, which posits that cells and organisms are "more



Ernest Everett Just outside the Marine Biological Laboratory in 1921.

PHOTO CREDIT: THE MARINE BIOLOGICAL LABORATORY ARCHIVES.

than the sum of their parts" (9). According to this view, the properties of any level of organization (molecule, cell, tissue, whole organism) depend on the properties of the parts of the level below, as well as on the properties of the whole into which they are integrated. Moreover, properties are said to emerge out of the organizational complexity of the living system. This approach to biological investigation has much in common with what is known today as integrative systems biology, in which a top-down view is just as important as a bottom-up view for understanding the system.

A Variety of Scientific Contributions

Just's contributions lay in several areas, including (a) the role of environmental factors in development; (b) the fast and slow blocks to polyspermy during fertilization; (c) experimental parthenogenesis; and (d) embryo morphogenesis.

Role of Environmental Factors in Development

Just investigated the effect of a number of variables – dilute or concentrated sea water, ultraviolet irradiation, temperature, hydration or dehydration — on embryo development. He was intimately familiar with the natural history and breeding habits of the animals whose eggs he studied, and he strove to apply what he learned about development in natural settings to the laboratory. He was very much concerned with what he called the "normality" of the egg, i.e., how well its condition in the laboratory corresponds to the natural, fertilizable state. In these respects, Just's work shares much in common with what is known today as ecological developmental biology (see 10, 11), which focuses on development in its natural environmental context.

Fast and Slow Blocks to Polyspermy

Using only a light microscope, Just was able to observe the detailed structural changes that occur at the egg surface during fertilization. As early as 1919, he observed the "wave of negativity" that sweeps over the egg cell at the onset of fertilization envelope separation, preventing fertilization by more than one spermatozoon (polyspermy). He correctly reasoned that it was this wave, not the physical separation of the envelope, that is responsible for the initial block to polyspermy. Thus, Just is credited with being the first to infer what is known as the "fast block to polyspermy," a phenomenon that subsequently has been shown to be due to a shift in egg cell membrane potential. Just also observed the "slow block to polyspermy," a mechanical block which occurs as a result of the formation of the fertilization envelope itself. Just is best known for his inference and documentation of these two blocks to polyspermy.

Experimental Parthenogenesis

While at Woods Hole, Just investigated the effect of a number of factors on the artificial activation of eggs in the absence of sperm, a phenomenon known as experimental parthenogenesis. His work there led to the public disagreement he had with Jacques Loeb, a prominent biologist at the Rockefeller Institute for Medical Research (now Rockefeller University) in New York. Loeb believed that, by tapping into the power of parthenogenesis, humans could gain mastery over nature and engineer it to their benefit. Just was strongly opposed to Loeb's reductionism, but he also was critical of what he considered to be Loeb's sloppy experimental technique, which he felt had led Loeb to conclusions that were not valid. Just proved that the method of experimental parthenogenesis Loeb pioneered, known as the double treatment method, in which the egg is treated with hypertonic sea water and then butyric acid, was not sound. He showed that the order of treatment was entirely inconsequential and that only one of the two agents was needed to induce parthenogenesis. But what Just rebelled against most was Loeb's notion that the egg's activation was the result of something being done to the egg. In contrast, Just believed that the critical, operative feature behind the activation was an intrinsic property of the egg itself, namely its "independent irritability." Moreover, this property of the egg was an epiphenomenon of the ectoplasm (the structured layer below the cell surface), which Just believed played the dominant role in development, heredity and evolution.

Embryo Morphogenesis

There is evidence that two of Just's discoveries influenced some of the work for which pioneering embryologist Johannes Holtfreter is best known (12). First, Just's discovery of the developmental stage-dependent adhesiveness of the blastomeres of the starfish cleavage embryo (8) contributed to Holtfreter's discovery of tissue affinity, which is critically important during amphibian morphogenesis. Second, Just's discovery of the independent irritability of the egg cell, mentioned above, strongly informed Holtfreter's elucidation of autoinduction, the process by which amphibian gastrula ectoderm is induced by nonspecific agents to form neural tissue. An acknowledgment of these contributions extends the impact of Just's work into the area of embryo morphogenesis, and it connects his work to important embryo research that is taking place today.

As an organicist, Just was squarely in the company of other classical embryologists, who held similar views. What made Just different from his peers was his unflinching willingness to take on giants of biology in his quest — fueled by his conviction about the importance of the cell periphery — to defend the holistic integrity of the developing organism. For instance, at the 1935 American Society of Zoologists meeting in Princeton, N.J., he publicly challenged Nobel laureate Thomas Hunt Morgan for his gene-centered view of development. Morgan had proposed that genes arranged in linear arrays on chromosomes are both the units of inheritance and the controllers of the developmental process. In opposition, Just presented his own cytoplasm-centered "theory of genetic restriction" to explain how differentiation occurs during development. Although ultimately incorrect, Just's explanation nonetheless contained some elements of truth. Indeed, today we are learning that differential gene expression is a multi-faceted process with epigenetic, as well as genetic, components.

Many researchers and instructors, including Ernest Everett Just, played horseshoes at the Marine Biological Laboratory during the summers.

PHOTO CREDIT: ALFRED HUETTNER AND THE MARINE BIOLOGICAL LABORATORY ARCHIVES.

An examination of the life and work of E. E. Just provides several insights relevant to us today. First, although Just experienced crushing inequalities due to his being black in early 20th-century America, he nonetheless made significant contributions to biology. These contributions still resonate today in several areas: fertilization research, the emerging field of ecological developmental biology, integrative systems biology, epigenetics (in the broad sense) and embryo research. Second, Just did not hesitate to challenge prominent biologists whom he felt were incorrect in their overtly nucleocentric or reductionistic view of the cell or organism. Thus, Just's example provides support to all young scientists today whose work leads them to challenge the accepted paradigms. Third, Just emphasized the importance of preserving the integrity of the cell or organism under investigation in the laboratory. "The cell is never a tool," he wrote. It is a living system and not a machine that can be used to "prove a theory" (7). As we biochemists and molecular biologists go about our work to understand the molecular structure and function of living systems, we would do well to heed Just's words. The top-down view should always be kept in mind.

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Heart Matters

BY NICK ZAGORSKI

On Valentine's Day, people's thoughts naturally turn to hearts, though typically of the chocolate or candy variety. However, this holiday should also serve as a reminder of the importance of the human heart, quietly beating more than 100,000 times and pumping almost 2,000 gallons of blood not just this day, but every day of the year. Unfortunately, unlike love, the heart is not everlasting; recent statistics suggest that this year, more than 1 million people in the U.S will experience a new or recurrent heart attack, more than 400,000 will die from coronary heart disease and bad hearts will total some $300 billion in direct and indirect costs.

However, with increased understanding of how the heart works, these numbers can surely improve. So, in honor of this special heart-related holiday, the American Society for Biochemistry and Molecular Biology is highlighting some of our members who devote their time to heart-related research, looking to make heart defects, disease and failure a thing of the past.

Kenneth Walsh

Director, Whitaker Cardiovascular Institute, Boston University School of Medicine

In the arena of cardiovascular research, most scientists fall into one of two camps: those who study the "cardio" and those who study the "vascular." Not many have focused their efforts on the interplay of the two, which Kenneth Walsh finds somewhat unusual.

"In the body, these two systems, heart muscle and blood vessels, are talking to each other all the time," he says, "whether it's in response to physiological stimuli like exercise, in response to some injury or during normal growth, so the heart and vasculature can keep pace with the rest of the body."

The mechanisms behind this inter-tissue communication are the major theme underlying Walsh's lab at Boston University. His methods involve a two-pronged approach, first identifying critical proteins or pathways through bioinformatics (as Walsh says, "mining the cardiac secretome"), then validating uncovered molecules using genetic models.

In several instances, the new molecules have proved to be potential biomarkers for pathological conditions, such as in Walsh's recent work identifying follistatin-like 1 as a factor that may determine the susceptibility of the heart to ischemic injury.

And, Walsh is definitely interested in pursuing diagnostic or therapeutic avenues, because, as he says, "I don't just want to cure heart disease in mice."

Another area Walsh's group currently is exploring — and another overlooked field, in his view — is how metabolic dysfunction, especially associated with obesity and diabetes, affects the heart's activity. As Walsh notes, obese individuals have hearts that are larger than the predicted body-heart size ratio, causing hypertension and other problems.

"It's a big driver of cardiovascular disease, yet, at cardiovascular meetings, you really won't see a lot of metabolic talks," Walsh says. "It's starting to catch on, but, considering the clinical significance of the problem, it's still vastly underrepresented."

That's why Walsh has made the metabolic-cardiovascular connection an initiative not just in his group, where's he's studying the role of the adipose-derived cytokine adiponectin in inflammation and heart disease, but also at

Kenneth Walsh took over as the third director of Boston's Whitaker Cardiovascular Institute in February 2008 and is looking to enhance translational research efforts.

the Whitaker Cardiovascular Institute, which he currently directs.

"It's a very collaborative environment, with a tremendous amount of expertise, and we're still growing," Walsh says proudly of the institute. "And being located in the heart of Boston, one of the best places to do biomedical research, is rewarding as well."

"I think the only drawback right now is that my duties keep me away from the lab often, and I like working with my hands," he continues. "But I think my lab is better served when I am working in my office."

In looking back, though, Walsh sometimes wonders how he reached this point. After all, 30 years ago, he was just a young and headstrong biochemistry student working under Daniel Koshland without much knowledge or interest in cardiovascular research.

Then, when he received his first faculty appointment in the physiology department at Case Western Reserve University, he was surrounded by colleagues who worked in the cardiovascular field, so he started going with the flow, in a manner of speaking.

As for taking on a leadership role, Walsh notes: "I guess I've always been good at two things: chemistry and getting people to work together."

Journal of Biological Chemistry research highlight: Cardiac-specific Deletion of LKB1 Leads to Hypertrophy and Dysfunction. *JBC* **284**, 35839-35849.

Eric N. Olson

Professor and chairman of the department of molecular biology, University of Texas Southwestern Medical Center

It's appropriate that one of Eric N. Olson's favorite tunes to play with his rock band, the Transactivators (in which Olson plays guitar and harmonica), is Neil Young's "Heart of Gold." While each organ in the human body is a complex, fascinating and, in most cases, essential physiological machine, in Olson's view, any discussions as to which organ should be considered the most vital begins and ends with the heart.

"The heart is incredibly unique," he says. "It performs nonstop rhythmic contractions every second, and it's a wonderful model for understanding how genes are coordinately regulated and control organ formation. Plus, adult cardiac cells never divide, making them an ideal system to study the cell cycle."

"Oh, and of course, unlike some other organs, the heart lacks an intrinsic mechanism to repair itself," he adds. "So, cardiovascular disease still remains the No. 1 killer in the United States, while congenital heart defects are the most common birth defects seen in humans: They occur in about 1 percent of all live births."

Eric N. Olson and Willie Nelson. The iconic singer/songwriter and his wife, Annie, established a professorship to support Olson's work on cardiac stem cells.

It's the latter statistic that has been a driving force for Olson's research at UT-Southwestern; since arriving in 1995 from the M.D. Anderson Cancer Center, his group has been hard at work identifying the genes and transcription factors responsible for forming the heart in developing embryos and analyzing how defects in those genetic networks lead to congenital heart disease.

The work has been a natural progression from Olson's earlier — and continuing — studies into skeletal and smooth muscle differentiation, through which he discovered several transcription factors involved in that process and realized many of them had similar roles in cardiac muscle.

Olson combines genetic and biochemical approaches to discover novel cardiac transcription factors, including mutational studies in Drosophila, which has turned out to be an excellent model organism for studying heart defects. "It may not seem readily apparent, but many key muscle transcription factors were first discovered in fruit flies," he says, noting that the fruit fly heart, a simplistic linear pump, closely resembles the heart tube in early mammalian embryos.

Olson notes that his field has been quite dynamic recently (due in no small part to his efforts, which include

the discovery of the transcription cofactor myocardin and the identification of both calcineurin and histone deacetylases as regulators of cardiac hypertrophy). "We've made some dramatic progress this past decade," he says. "We've gone from knowing virtually nothing about the molecular blueprint for heart development to knowing most of the regulators involved, though we still need to tease out how they all fit together."

A new wrinkle in that blueprint, and one that's been a significant focus of Olson's work the past few years, is the emerging role of microRNAs in heart development and disease. From identifying the importance of miR-126 in vascular integrity to miR-133's role in cardiomyocyte proliferation, "we've managed to uncover a treasure trove of new regulators that affect virtually every process associated with heart disease," he says, "such as fibrosis, hypertrophy and atrophy and blood vessel formation."

Combining the potential power of RNA silencing with existing technologies for delivering therapeutics to the heart, Olson is preparing to take these microRNA discoveries to the treatment stage; he even started up a biotech company, called miRagen Therapeutics, to help him with this process.

Journal of Biological Chemistry research highlight: Down Syndrome Critical Region-1 Is a Transcriptional Target of Nuclear Factor of Activated T Cells-c1 within the Endocardium during Heart Development. *JBC* ***282***, 30763-30679.

Daria Mochly-Rosen

Professor of chemical and systems biology, Stanford School of Medicine

In an unusual twist, a run-of-the-mill lecture at a conference became the catalyst for Daria Mochly-Rosen's foray into an exciting new line of research.

In the mid-1990s, Mochly-Rosen showed that different isozymes of protein kinase C were located in discrete subcellular regions of cardiac muscle cells and that shutting off individual isozymes with peptides could make the cells beat faster or slower. This finding confirmed her hypothesis that PKC isozymes have unique localizations in all cells, mediated by binding to isozyme-specific anchoring proteins known as receptors for activated C-kinase, or RACKs.

The identification of RACKs helped explain the mystery of how the many similar-appearing forms of PKC could mediate a range of processes in diverse — and, in the case of heart muscle, even opposite — ways.

"However, when I presented these results at an American Heart Association conference, I noticed a lot of uninterested scientists in the audience," she says. Afterwards her colleague Joel Karliner of the University of California, San Francisco, informed her that cardiologists didn't really care about heart rate, because they had perfectly good ways of managing it.

"So I asked him what cardiologists did care about, and he told me heart attacks," Mochly-Rosen says. However, she was hardly familiar with this area. (A biochemist by training, she had primarily worked with heart cells because their beating was an easy phenotype to observe.) "But then Joel told me not to worry — he would ask one of his cardiology fellows, Mary Gray, to join my lab."

Since then, Mochly-Rosen always has had at least one physician in her lab at Stanford University to help with her research into PKCs role in heart function, and her group has uncovered a lot of valuable information, including the fact that either activation of epsilon PKC or inhibition of delta PKC can protect the heart from ischemia damage. In fact, one of the delta PKC inhibitor peptides she used in her earlier heart rate studies (delta V1-1) is now in phase II clinical trials for heart attack treatment.

"The people at the AHA conferences are a bit more attentive when I speak now," she jokes.

In the past couple of years, Mochly-Rosen has turned her attention to one of the proteins activated by PKC; through a proteomic approach aimed at understanding how epsilon PKC is heart-protective, she identified aldehyde dehydrogenase 2 as an epsilon PKC target. She then confirmed a causal relationship between epsilon PKC and ALDH2 (alcohol dehydrogenase) by developing a small molecule activator of ALDH2 and showing that this activator produced the same cardioprotective effects in rat models as epsilon PKC activation.

Daria Mochly-Rosen was introduced to protein kinase C through her postdoctoral mentor, Daniel Koshland, and has since been instrumental in uncovering this enzyme's role in heart function.

Mochly-Rosen and her lab are now looking at exactly why PKC turns on ALDH2 to protect the heart. However, the importance of ALDH may be the key to the complex role of alcohol in relation to the heart, as alcohol consumption has been linked to both beneficial and damaging cardiac effects.

At the least, this new revelation gives Mochly-Rosen her own change in perspective. "I always thought ALDH was a boring enzyme; it was always active and seemed to have a simple function," she says. "But now I know better."

Journal of Biological Chemistry research highlight: RBCK1, a Protein Kinase CβI (PKCβI)-interacting Protein, Regulates PKCβ-dependent Function. *JBC* **282**, 1650-1657.

Mark A. Sussman

Professor of biology, San Diego State University

When Mark A. Sussman completed his doctoral studies at the University of Southern California, he asked one of his thesis committee members on what area of science his postdoctoral fellowship should focus. "He told me to do something completely different than my graduate school research, because my postdoc was my last opportunity to be stupid, scientifically speaking."

So, Sussman put his dissertation on viral immunology on the bookshelf and pursued his interests in the cytoskeleton, first with Velia Fowler at The Scripps Research Institute and then with Laurence Kedes back at USC. He began working on the actin-capping protein tropomodulin and found that the structural protein was expressed in specific subcellular locations in heart muscle, and, when it was over-expressed, it would prevent proper heart contraction and eventually led to heart failure as the organ tried unsuccessfully to remodel.

In the ricocheting world of science, that discovery soon led to a cardiovascular research fellowship, which, in turn, led to Sussman's development of the first mouse model of dilated cardiomyopathy and a long and fruitful career studying heart failure.

However, when the California native returned home to take up a position at San Diego State University, he decided a change of pace was in order. "I had sort of become an expert in making mouse hearts that failed, and I now wanted to see what I could do to keep a heart working properly," he says.

Sussman became intrigued with Akt/PKB kinase, a signaling protein that either helped protect heart cells or caused it to fail, depending who you asked. "It was a big paradox," he says. "Researchers found that if you activated Akt in heart cells, by adding agents like insulin like growth factor to the media, it made the cells resistant to death. But, when they induced Akt in mice by genetic manipulation, the heart responded by remodeling and eventually failed."

The reason for the paradox, as Sussman discovered, was that Akt goes through a specific set of localizations when activated and has specific targets, depending on where it is; in the case of cardioprotective stimulators, Akt ended up in the nucleus.

In 2006, Mark A. Sussman helped facilitate a National Institutes of Health program project grant for San Diego State University and the University of California, San Diego. It was the first such award for any school in the 23-campus California State University system.

"So it's not just activity level but where the activity occurs," he says. "Thus, the brute-force approach of simply inducing Akt in the heart was like drinking water from a fire hose: You'll quench your thirst, but a lot of bad stuff is going to happen as well." Once Sussman mimicked the process seen in cell culture and localized Akt to the nucleus, the mice exhibited the expected damage-resistant hearts.

Those studies did present one mystery, though. Many of the important cardioprotective targets where in the cytoplasm; so, how did Akt turn them on while trapped in the nucleus? The answer was that Akt turned on another activator protein called PIM-1, which mediates the protective effects.

And PIM-1, Sussman believes, is a key piece for regenerative medicine and stem-cell therapies for the heart. Early work in repairing hearts with stem cells was unsuccessful, because the stem cells did not graft well and died off; but combining stem cells with activation of PIM-1 and the survival pathway might make it work. Just recently, he had success in mouse models, and now he's hoping for similar results using human cells in immunized mice and then large-animal models.

And if all goes as planned, Sussman thinks we might soon see a future of genetically rebuilding hearts after acute stress or chronic injury. "We'll put the surgeons out of business, and I can spend my days on the beach, drinking cocktails with little umbrellas in them."

Journal of Biological Chemistry research highlight: Coordination of Growth and Endoplasmic Reticulum Stress Signaling by Regulator of Calcineurin 1 (RCAN1), a Novel ATF6-inducible Gene. *JBC* **283**, 14012-14021.

Nick Zagorski (nzagorski@asbmb.org) is a science writer at ASBMB.

National Lab Day: Get Involved

BY J. ELLIS BELL*

On Nov. 23, President Obama, in response to a letter from several scientific organizations, including the American Society for Biochemistry and Molecular Biology, announced the establishment of National Lab Day, a grassroots initiative designed to reinvigorate science and math education in the nation's schools and after-school programs and to lead to increased U.S. competitiveness in science. The goal of this "national barn-raising for hands-on learning" is to bring together millions of science, technology, engineering and mathematics professionals, volunteers and teachers from around the country to work on education projects focusing on experiential-learning opportunities for students.

National Lab Day is a project of Tides Center, a nonprofit public charity, and is a collaboration between government, educators, science and engineering associations, philanthropies and other organizations. There are several organizations that already have pledged support, including the National Institutes of Health, the National Science Foundation, the Jack D. Hidary Foundation, the John D. and Catherine T. MacArthur Foundation, the Bill and Melinda Gates Foundation and the National Science Teachers Association.

Although it's called National Lab Day, the goal is to develop a nationwide initiative to build local communities that will foster ongoing collaborations among volunteers from industry, students and educators. These volunteers will work together to improve labs and discovery-based science experiences for students in grades 6-12. During the first week of May, these collaborations will be celebrated with activities across the country.

Become a Part of National Lab Day

Biochemistry and molecular biology offer a rich source of interesting, educational laboratory activities, and ASBMB encourages you to develop a National Lab Day hub. This is a group of volunteers committed to improving labs and lab experiences for students. Hubs can support an individual teacher, a group of teachers, a school or school district, or a project. They form to match teachers' classroom needs with volunteer expertise, time and resources.

If you can't get a group together, the initiative also offers individual scientists the opportunity to be matched up with projects in the areas that need their expertise. Potential volunteer activities include assessing current labs, updating or refurbishing lab equipment, conducting equipment and materials inventory, cleaning and repairing equipment and providing technology support. To date, more than 3,000 teachers and educators have signed up on the National Lab Day Web site and have begun collaborating on more than 500 projects.

"Biochemistry and molecular biology offer a rich source of interesting, educational laboratory activities, and ASBMB encourages you to develop a National Lab Day hub."

To aid in tracking participation by ASBMB volunteers and teachers, a Web site is being set up by the National Lab Day organizers specifically for ASBMB members.

J. Ellis Bell (jbell2@richmond.edu) is professor of chemistry and chair of the biochemistry and molecular biology program at the University of Richmond. He is also chair of the ASBMB Education and Professional Development Committee.

* Many of the details in this article were taken from an e-mail from James Brown and Jodi Peterson, co-chairs of the STEM Education Coalition. I would like to thank them for all their efforts on this important initiative.

For more information:

- The National Lab Day Web site: www.nationallabday.org
- A video about National Lab Day: http://bit.ly/8Z4vCS
- The ASBMB-National Lab Day Web site: www.nationallabday.org/groups/asbmb

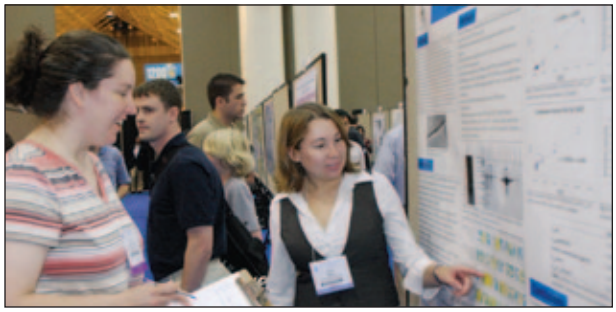
Get Engaged at the Annual Meeting

Volunteer as a Poster Competition Judge

BY JOAN GEILING

As part of its annual meeting, the American Society for Biochemistry and Molecular Biology will host the 14th Annual Undergraduate Student Research Poster Competition on Saturday, April 24, 2010, in Anaheim, Calif. The competition provides an excellent career-development experience for future biochemists through active networking and research presentation opportunities. The event continues to gain popularity, with more than 180 undergraduates signed up to compete this April, up from 150 in 2009.

After an initial judges' orientation conducted by the Poster Organizing Committee, each poster will be assigned to members of a volunteer team for judging. Judges are matched with posters in their areas of expertise, and volunteers are never assigned to judge their own students' presentations. The four judging groups are: systems biology, development, cell structure and fate; structural and functional analysis of proteins including enzymes; nucleic acid structure and function; and signaling.



Gina Troy (Hartwick College, Oneonta, N.Y.) presents her poster to judge Ann Kruchten (Linfield College, McMinnville, Ore.) at the 2009 ASBMB annual meeting in New Orleans.

At the conclusion of the competition, each team of judges selects a best poster award recipient and honorable mention citations to be presented at an awards ceremony Sunday, April 25.

Volunteering as a judge is a great way to actively engage in the annual meeting and support the growth of young scientists. If you are a principal investigator or a faculty member at an undergraduate institution and are available to volunteer on Saturday, April 24, please sign up to serve as a poster competition judge. To learn more about the poster competition or to sign up as a judge, please visit www.asbmb.org/postercompetition.

Joan Geiling (jgeiling@asbmb.org) is meetings manager at ASBMB.

ASBMB Looks to Grow Special Symposia

BY JLYNN J. FRAZIER

In the coming year, the American Society for Biochemistry and Molecular Biology plans to continue to expand its special symposia program, which offers scientists at all career levels the opportunity to attend a specialized meeting on a cutting-edge topic in biochemistry and molecular biology.

Special symposia meetings are usually held in the fall and have an average of 100 attendees, including investigators, industry professionals and graduate and postdoctoral students. One of the primary goals for the special symposia is to provide younger scientists, women and people from under-represented groups the opportunity to actively participant in the meeting. To facilitate this, each meeting organizer incorporates oral and poster presentations from abstracts submitted by scientists at various stages in their careers.

To complement the programming, each meeting is set in a unique location, usually with easy access to nature. These locations are intended to provide intimate settings for networking, including receptions and outdoor recreational activities.

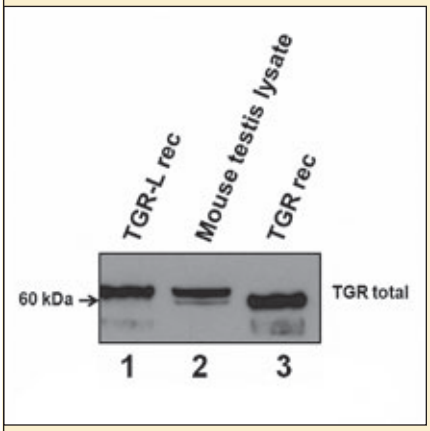
Meeting proposals for the 2011 Special Symposia are being accepted through March 1. To learn more about the ASBMB special symposia, please visit www.asbmb.org/specialsymposia.

Do you have a topic you would like to see become part of the special symposia program? To share your topics with us, please send an e-mail titled "Special Symposia Topics" to meetings@asbmb.org.

Jlynn J. Frazier (jfrazier@asbmb.org) is conference manager at ASBMB.

TGR: Two Isoforms Are Better than One

Thioredoxin/glutathione reductase is an important selenoenzyme in mammalian cells and is particularly abundant in testes. An interesting element of TGR and other mammalian thioredoxin reductases is that they generally lack AUG start codons for translation initiation, a feature common in viruses and bacteria but extremely rare in eukaryotes. In this study, the researchers combined immunoblot assays and proteomic techniques to identify a CUG codon as the start point of translation in mouse TGR. Mutational analysis revealed that the use of this codon occurs in an internal ribosome entry site-independent mechanism that likely relies on an upstream Kozak consensus sequence. As a result, the CUG start codon is quite inefficient and allows downstream translation from an internal AUG codon, thus generating two isoforms of the TGR protein. Because nonmammalian TGRs retain standard AUG start codons, the researchers believe the use of alternative start codons in mammals evolved to provide inefficient translation initiation so two forms of TGR could be produced from a single mRNA species.



Immunoblot analysis of mouse testis lysate (lane 2) reveals the presence of two forms of TGR.

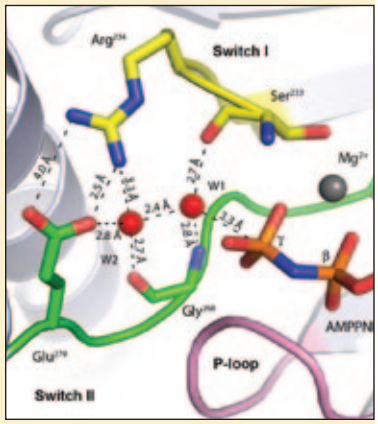
CUG Start Codon Generates Thioredoxin/ Glutathione Reductase Isoforms in Mouse Testes

Maxim V. Gerashchenko, Dan Su and Vadim N. Gladyshev

J. Biol. Chem., published online Dec. 14, 2009

jbc

Kinesin's Two-Water System



Binding pocket of Eg5 kinesin with AMPPNP.

Many motor proteins like kinesins generate force and movement by coupling large-scale conformational changes to ATP binding and hydrolysis. However, a direct cause-and-effect linkage between ATP catalysis and powered structural changes in such proteins has not been firmly established, partially because the catalytic base that extracts a proton from the water nucleophile is unknown. In this study, the researchers determined the crystal structure of the motor domain of human Eg5 kinesin bound with the nonhydrolyzable ATP analogue AMPPNP, thus trapping the motor in a prehydrolytic state. They observed that, in this closed state, the two switch regions are linked by a salt bridge, and an ordered two-water cluster spans the distance between the inter-switch salt bridge and the AMPPNP γ-phosphate. This arrangement suggests that the second water molecule serves as a general base and shares a proton with the lytic water; the sequential transfer of a proton across this water network would disrupt the inter-switch salt-bridge, thereby promoting conformational transitions. This study provides the first experimental detection of the catalytic base for an ATPase and provides a mechanism that may apply to other NTPases with conserved active sites.

ATP Hydrolysis in Eg5 Kinesin Involves a Catalytic Two-water Mechanism

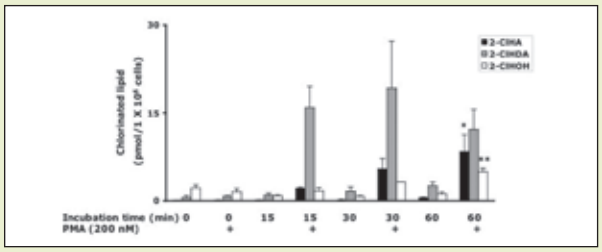
Courtney L. Parke, Edward J. Wojcik, Sunyoung Kim and David K. Worthylake

J. Biol. Chem., published online Dec. 15, 2009

jbc

Chlorine Keeps It Clean

Neutrophils are an abundant component of the innate immune system that attack pathogens by releasing chemical agents such as hydrogen peroxide and hypochlorous acid. However, these agents also can attack host macromolecules to form reactive species, such as chlorinated lipids. In this study, the authors traced the metabolic fate of two such metabolites: 2-chlorohexadecanoic acid and 2-chlorohexadecanol. Using isolated neutrophils, they demonstrated that both 2-ClHA and 2-ClHOH are produced and released in activated neutrophils in a time- and myeloperoxidase-dependent manner. (Myeloperoxidase catalyzes HOCl production.) Oxidation of 2-ClHDA to 2-ClHA also was dependent on the enzyme fatty aldehyde dehydrogenase. The authors confirmed these events in a physiological context, showing that mice exposed to intranasal Sendai virus experienced an increased recruitment of neutrophils to the lungs, followed by elevated ClHA levels in both plasma and bronchoalveolar lavage compared with control-treated mice. Thus, they demonstrated for the first time that chlorinated lipid metabolites are produced by neutrophils in vivo.



Temporal course of 2-ClHDA, 2-ClHOH and 2-ClHA production in stimulated human neutrophils.

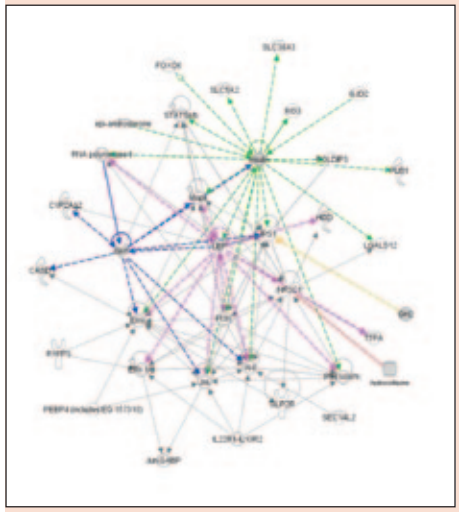
Chlorinated Lipid Species in Activated Human Neutrophils: Lipid Metabolites of 2-Chlorohexadecanal

Dhanalakshmi S. Anbukumar, Laurie P. Shornick, Carolyn J. Albert, Melissa M. Steward, Raphael A. Zoeller, William L. Neumann and David A. Ford

J. Lipid Res., published online Dec. 17, 2009

Cluster Analysis

The search for biomarkers that can help diagnose psychiatric disorders such as schizophrenia at very early stages has been going on for a long time. Most biomarker efforts have focused on identifying individual proteins that show significant expression differences between individuals with the disorder and the normal population. However, in this study, the authors searched for combinations of analytes that exhibited patterned changes in schizophrenia. They profiled 77 male schizophrenia patients and 66 matched controls and identified four sets of analytes, known as targeted clusters, which could discriminate schizophrenia in both human and rat models. These clusters were associated with specific molecular signaling pathways (insulin, cortisol, leptin and growth hormone signaling) and also were highly specific to disease. This study sheds new light into how complex psychiatric diseases behave at the molecular level and also holds great therapeutic promise, as it could aid in identifying disease-specific biomarkers.



In silico pathway mapping of the targeted analyte clusters.

Identification of Targeted Analyte Clusters for Studies of Schizophrenia

Tammy M. K. Cheng, Yu-En Lu, Paul C. Guest, Hassan Rahmoune, Laura W. Harris, Lan Wang, Dan Ma, Victoria Stelzhammer, Yagnesh Umrania, Matt T. Wayland, Pietro Lió and Sabine Bahn

Mol. Cell. Proteomics, published online Dec. 10, 2009

Note to Self: If I Network, the Jobs Will Come

BY SARAH EDWARDS

As a third-year chemistry graduate student at Stanford University, I wondered what life was like after graduate school. What were people out there doing, how were they meeting each other and how were they getting jobs? Admittedly, these questions relieved my brain from troubleshooting my repeated failure to turn my recalcitrant yeast cells green. However, I also recognized the utility of building a network – this is how I would discover what job I wanted and how I would obtain it.

The idea of networking, for most of us, incites fear. "People don't like networking," says Lance Choy, director of Stanford's Career Development Center. "There is 'stranger danger' and they don't know what to say." Very true, and, furthermore, networking requires skills not typically in a scientist's repertoire. So why bother? The statistics speak for themselves: I hear regularly that networking fills 80 percent of jobs. For four out of every five jobs, the person hiring is somehow connected to the person being hired. That's why you should bother.

I didn't do much networking while I was in graduate school. Instead, I used Stanford's Career Development Center to gather information that I knew I'd need one day. That day came six months ago. After finishing my graduate degree, I had taken a postdoctoral position at Harvard Medical School to work on finding a cure for Alzheimer's disease. However, I realized that bench research did not feel right, so I abandoned the laboratory in favor of finding another science-related career.

Thus, I found myself in a position I never would have imagined: I was unemployed. What has since ensued is a networking roadtrip. My goals: to discover what doors a doctorate in science can open and to land a job.

Networking 101

Networking is a numbers game: Connecting professionally with more people increases your likelihood of landing a job. As with any new task, start easy. I asked my parents if they knew anyone doing anything science-related I could contact. Then, I asked my next-door neighbor, my high school guidance counselor and math teacher, my mom's friend, my friend's mom. Before long, I was off to the races with several contacts.

I sent e-mails. It felt less invasive than cold-calling, especially with people I did not know well. The format is simple. In the subject line, write "referred by ____." This grabs the person's attention. Unsolicited e-mails are easily overlooked, so this tactic increases your chances of making the cut. Start with "Dear ____" and end with "Sincerely, ____." Use a four-paragraph approach with two sentences per paragraph. Begin with an introduction that includes a reference to your mutual contact, then describe your background and refer to your attached resume. Next, describe your area(s) of interest and intention to speak with this person, and end with an appreciative, enthusiastic exit. The goal is to be polite, concise and grateful. You are asking for a favor.

An effective tip is to ask for "insight and advice." This gem comes from a recent contact, Joan

Sarah Edwards received her bachelor's degree in chemistry from Wellesley College in 2002 and her doctorate in chemistry from Stanford University in 2008. Her dissertation research focused on developing biological tools to study proteins in the model organism Saccharomyces cerevisiae. This past year, she studied the mechanisms of Alzheimer's disease as a neurology postdoctoral fellow at Harvard Medical School. Sarah has recently begun a scientific coordinator role at Duke University's Center for Systems Biology, where she writes, edits, plans, presents, fosters interactions and collaborations and conducts outreach.

Plotnick, a writer and editor in Research Triangle Park, N.C.

A few people will not respond to your e-mails. A few more will reply but offer little help. The majority will happily oblige. They often explicitly tell you how they prefer to connect, so your job is to set up the phone or in-person meeting.

Before the interview, spend at least 15 minutes finding out who this person is and what he or she does. "This leads to more thoughtful questions," says Choy. "The unstated goal is building trust." Translation: Make a good impression.

Approach the meeting like an informational interview. Have a list of questions like: What is your role within the organization? How much travel is involved? What is the education or training necessary for this position? We may not know these people well (or at all), but these conversations encourage us to explore our interests, broaden our knowledge base and help us think outside the box. Most importantly, these people are our tickets to our next jobs.

Interviewees generally fall into three categories. One is awkward folks who answer questions with one or two words. Here, the responsibility falls on you to ask good questions. The second group of people answers your questions more thoroughly, and a back-and-forth ensues. The last group, my personal favorite, consists of contacts who are excited to share and connect. Listen well and write quickly, because the floodgates open with that first question.

The most important information you will gather in the meeting is two new contacts. If these are not offered, ask, "Do you know of anyone else within your field willing to share his or her career history with me?"

These two new contacts become the sources for your next two e-mails. Follow the same e-mail format. Set up your informational interviews. Rinse and repeat.

If at any point you lack contacts, fear not. LinkedIn is an excellent online professional networking community. Or, use the alumni services for your educational institutions. Go to conferences. Join the local chapter of your trade or professional society. Volunteer at your local science museum. Use recruiters and educators local to you. Google searches even have resulted in valuable contacts for me.

Do not ask your new contact for a job. If the information is not freely given, ask, "Do you know of any current or future opportunities for someone with my credentials?" or "How do you suggest I approach finding this type of job?" These questions have triggered job possibilities for me, leading to job postings I had not seen and new people to contact.

If you persevere with your networking project, your contact base will build quickly. Start a spreadsheet to record basic contact information: date, name, number, e-mail, company, job title. Include how you know the new contact, e.g. a "Referred by" column. This last column is crucial. When you call or meet with one of your contacts and hear, "So, how do you know Mark?" you had better be sure you know which Mark and what this Mark does.

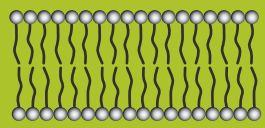
Give yourself a timeline for reinitiating contact. Three to four weeks after making your connection, send an e-mail to check back in. The e-mail should be personal. Refer to something you had previously discussed, what steps you have taken toward one of the suggestions from your contact, etc. This makes you pop back on the radar screen and gives your contact the chance to mention new job leads.

A follow-up thank-you note is crucial. Every single time you speak to or meet with someone in an informational interview, write "thank you for taking the time to [meet/speak] with me. I appreciate the advice you gave me concerning [something specific you learned]."

"Remember that the folks you are connecting with have lives, too," says Laura Dominguez Chan, a career counselor at Stanford's Career Development Center. "Be appreciative throughout the networking process and minimally send an e-mail message thanking them for their time." Based on a recent survey by Chan, most contacts had not received letters of thanks. The few written thank-you cards stood out like gold stars.

If, like me, you dislike asking for help from acquaintances or strangers when it isn't clear how to repay them, I have good news. People love talking about themselves! Three months and 90 contacts later, I can now give each new contact two of their very own new contacts. My networking adventure is still a work in progress, and I'm still out there searching for that tailor-made job. Along the way, however, I have gained much insight and advice.

The Stanford Career Development Center's motto is "Connect, Respect, Reflect." These three words make a world of difference between unemployment and employment. "Integrate [networking] into your goals," says Chan, "and if you are job searching, then by all means make it a priority. Look at networking as research." Scientists love research.



Looking Ahead…

BY DANIEL M. RABEN

As I mentioned in a blast e-mail to the American Society for Biochemistry and Molecular Biology Lipid Research Division members, we've come a long way since our inauguration last April. I would like to thank everyone involved in making this a real ASBMB division, especially ASBMB President Gregory A. Petsko, who was extremely supportive and helpful. There are many scientists who have been instrumental in making the division work, but none of it would have been remotely possible without help and insight from Barbara Gordon, executive director of ASBMB. Barbara, Hector Martinez (director of information technology), Nicole Kresge (ASBMB Today editor) and Steve Miller (director of finance) all have been truly invaluable at getting this division started. Amazingly, Barbara continues to keep us on the right path, which is no easy task indeed!

As we move into 2010, I'd like to summarize what we've accomplished in the past year:

- Thanks to the efforts of Membership Director Brian (Binks) Wattenberg, we now have slightly more than 400 members and still are growing.
- The division now is involved with the ASBMB Annual Meeting and will be participating in the lipid theme in Anaheim, Calif., in April.
- A steering committee was formed and consists of the following:

  Director Daniel M. Raben, *the Johns Hopkins University School of Medicine*

  Yusuf A. Hannun, *Medical University of South Carolina*

  Lina M. Obeid, *Medical University of South Carolina*

  Brian (Binks) Wattenberg, *University of Louisville School of Medicine*

  Timothy Hla, *Weill Cornell Medical College*

  John York, *Duke University Medical Center*

  Vytas Bankaitis, *University of North Carolina School of Medicine*
- Robert V. Stahelin, the division's financial director, obtained funding from Avanti to launch our Young Investigator Award. The first recipient, Sarah Keller of the University of Washington, will receive her award at the 2010 Annual Meeting.
- We have formed an advocacy committee chaired by Yusuf Hannun. The committee soon will begin its work to address funding issues in our community.
- We've begun stronger collaborations with our international colleagues. We have representatives in a number of countries, and Meetings Director Timothy Hla has begun discussions to initiate new international meetings. Our overseas representatives include:

  Gerrit van Meer, *Utrecht University, The Netherlands*

  Lucio Cocco, *University of Bologna, Italy*

  Pann-Ghill Suh, *Pohang University of Science and Technology, Republic of Korea*

  Hitoshi Yagisawa, *University of Hyogo, Japan*

  Rudi Zechner, *University of Graz, Austria*

  Isabel Merida, *Centro Nacional de Biotecnología, Spain*

  Stuart Pitson, *University of Adelaide, Australia*

  Tony Futerman, *Weizmann Institute of Science, Israel*
- Rosalind Coleman is chairwoman of the Research Highlights section on our Lipid Corner Web site (www.asbmb.org/lipidcorner) and continues to attract traffic to the site.
- We have launched a collaboration with Nature's Lipid Gateway.
- A job board has been created for employers and job seekers.
- We now have a calendar to let everyone know of upcoming meetings and events.

As this year begins, many of us are filled with the energy and enthusiasm needed to tackle our aspirations. The LRD is no different. We have many things to look forward to, and we plan to accomplish quite a bit. For example, a primary focus of the Advocacy Committee will be to define our goals, objectives and strategies to increase investigator-initiated funding for lipid scientists. This is one of the more important endeavors of the LRD, and it will receive the attention it needs. Additionally, while we maintain our current trajectory and enhance our Lipid Corner Web site, we hope to continue our efforts to grow the Lipid Division, continue our Young Investigator Award, strengthen our growing international collaborations and institute a mechanism for electing officers at regular intervals.

So, we're off to another great start, and we hope this year will be as productive as the last. XXXX

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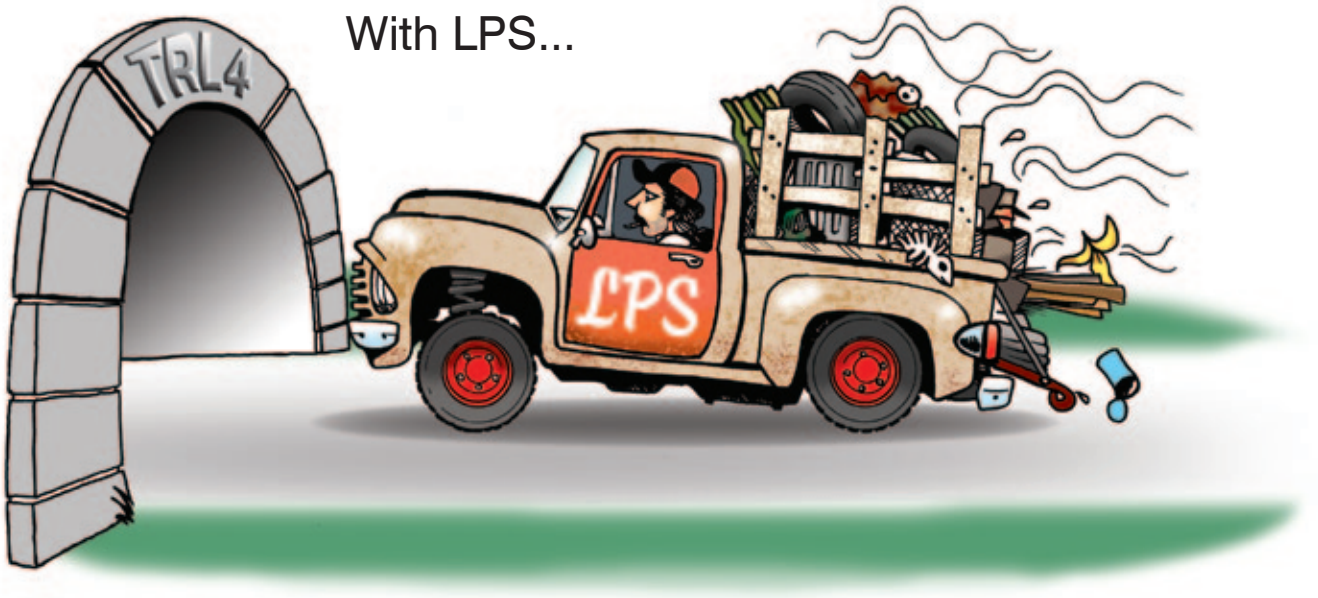
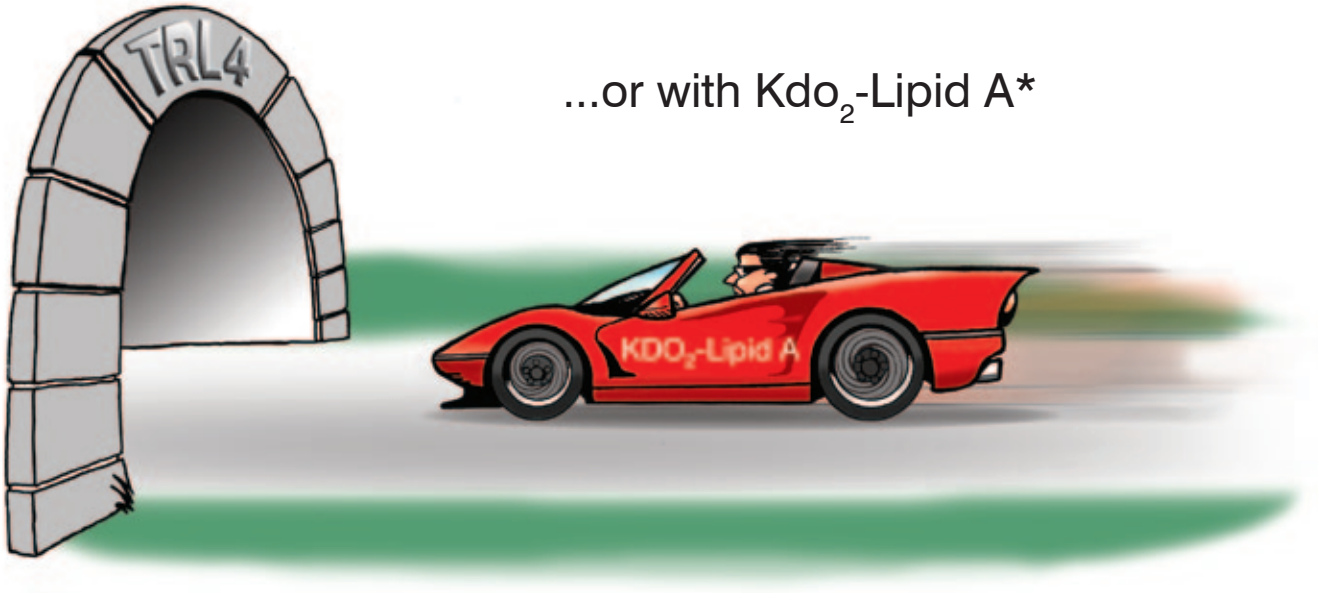


...or with Kdo_2-Lipid A*



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