ASBMB today

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REVIEWING THE BRAIN PROJECT

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COST-CUTTING IDEAS FOR RESEARCHERS

American Society for Biochemistry and Molecular Biology

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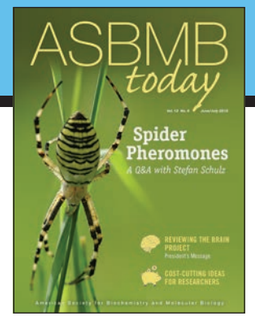

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Image courtesy of Vera Buhl, contributor to Wikimedia Commons

DERAILED *but* UNDETERRED

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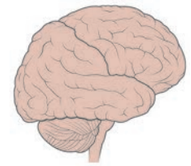

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ASBMB Today takes summer break

Please note that ASBMB Today will publish a combined June/July issue this summer. Monthly publication will resume in August.

ASBMB today

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Biochemistry and Molecular Biology

www.asbmb.org/asbmbtoday

president's message

Reviewing the BRAIN Project

BY JEREMY BERG

I was watching the State of the Union address with my family when I heard the following passage:

Now, if we want to make the best products, we also have to invest in the best ideas. Every dollar we invested to map the human genome returned $140 to our economy — every dollar. Today, our scientists are mapping the human brain to unlock the answers to Alzheimer's. They're developing drugs to regenerate damaged organs; devising new material to make batteries 10 times more powerful. Now is not the time to gut these job-creating investments in science and innovation. Now is the time to reach a level of research and development not seen since the height of the Space Race. We need to make those investments. (1)

I was delighted to hear President Obama acknowledge the tremendous potential impact of research.

Overnight, a friend pointed out a tweet sent by National Institutes of Health Director Francis S. Collins during the address:

@NIHDirector: Obama mentions the #NIH Brain Activity Map in #SOTU

I was puzzled and intrigued. NIH Brain Activity Map? A quick Internet search led to a 2012 paper in the journal Neuron (2). The authors of the paper proposed "launching a large-scale, international public effort, the Brain Activity Map Project, aimed at reconstructing the full record of neural activity across complete neural circuits." This put the president's remarks in a different context. Was the president referring to the tremendous progress that has been made in recent years on brain imaging? Or was he hinting at a new NIH project?

This point was clarified April 2 when Collins introduced President Obama in the East Room of the White House (3) to announce a new proposal: the BRAIN (Brain Research through Advancing Innovative Neurotechnologies) initiative (4). This proposal involves a first investment of approximately $100 million in fiscal 2014 from the NIH, the Defense Advanced Research Projects Agency and the National Science Foundation plus additional investments from private-sector partners. This announcement was followed by a public relations blitz, including an opinion piece by Collins and Microsoft co-founder and Allen Institute for Brain Science founder Paul G. Allen in the Wall Street Journal (5) and an appearance by Collins on "The Colbert Report" (6). Like many in the scientific community, I have been struggling to understand what is being proposed and how it relates to and affects ongoing NIH programs. In order to collect my thoughts, I turned to the format used for NIH grant-application reviews (7). Recall that the NIH is using a scoring system from 1 (best) to 9 (worst) in each of five criteria. My critique follows.

Description
(provided by applicants) (5):

In science there are moments when prior discoveries, advances in technology and visionary leadership align to create the opportunity for a great leap. It happened in 1961, when President Kennedy called for a new era of space exploration, which took Americans to the moon. It happened again in 1990, when the Department of Energy and the National Institutes of Health transformed the future of biomedical research by launching the Human Genome Project.

The timing is perfect now for a federally coordinated effort to unlock the secrets of the brain, in line with President Obama's call this month for an ambitious project to map the most complex organ in the known universe …

A new era of information technology allows us to build out super-data sets to track and organize these intercellular connections. With the aid of large-scale computer resources, we understand enough about the physics of the brain – in essence, a piece of highly excitable matter – to begin to simulate complete nervous systems …

Today we know that neurons fire, and we know that they are connected. We don't know how they act in concert to govern behavior, the essential question in treating neurological disease and mental-health disorders. Most of all, we have a limited understanding of how the brain translates its rich sensory experiences into complex mental states and behaviors, all at the speed of thought.

Big problems demand big solutions. The human brain contains nearly 100 billion neurons of at least a thousand distinct varieties. Those nerve cells make at least 100 trillion connections. No single discovery, no one researcher, will be able to crack the brain's code. The next generation of neuroscience breakthroughs will emerge from collaboration among a range of disciplines, from physics and biology to nanoscience, computer science and engineering. All hands must be on deck …

It is our view that tough fiscal times demand creative approaches and more innovation. As President Obama has noted, the Human Genome Project has returned $140 in economic growth and new industry for every government dollar invested. We are confident that the BRAIN initiative will pay comparable dividends over time and ultimately boost social productivity, reduce health-care costs and alleviate untold suffering. All humanity will benefit.

Critique 1:

Significance: 1
Investigator(s): 3
Innovation: 5
Approach: 7
Environment: 5

Overall Impact:

The proposal presents a self-described bold attempt to understand the human brain. This is, of course, a challenge of the greatest significance. The greatest strength of the proposal, which should be embraced, is the appreciation by those in the highest positions that fundamental knowledge of structure, function and mechanism is necessary to tackle problems related to human disease and the development of desired applications. However, this enthusiasm is dampened by some implications that the approach will be centered on large-scale data collection without any clear discussion of the conceptual bases for data analysis and by the relatively opaque manner in which the proposal was generated. In addition, the tremendous financial challenges currently facing the American biomedical research enterprise require that the bar be set very high for such large-scale projects, given the clear, destructive consequences of redirecting funds away from investigator-initiated research programs.

1. Significance

Strengths

- Understanding of the brain is one of the most fundamental challenges in human history.
- Such basic knowledge has tremendous potential to underpin understanding of the pathobiology of a range of neurological diseases that represent a substantial burden on individuals, families and society.
- Promoting collaborative approaches between a range of science and engineering disciplines spanning the basic-through-applied research continuum is essential for progress in many areas.

Weaknesses

- The significance of large "super data-sets" in addressing problems such as the basis of brain function is unclear.
- The justification that the human genome project provided a 140-fold return on investment is not compelling. The HGP represents an important accomplishment with tremendous economic impact, but the factor of 140 is based on a study (8) that undercounted the contributions of research not within the HGP budget and overcounted economic benefits. The applicants would be wise to view such economic

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studies with a critical approach similar to that they would use for other scientific studies. The expectation that any similar economic return will come from the present project is not justified.

2. Investigator(s)

Strengths

- The neuroscience research community is very strong, with many good connections between biological, engineering and computational fields.
- An advisory board of outstanding neuroscience investigators has been assembled.

Weaknesses

- Some of the spokespeople for the BRAIN initiative appear to have relatively little previous experience with neuroscience research.
- Some of the applicants have histories of promoting large-scale data collection projects without adequately recognizing the power of less directed and frequently more creative approaches.
- The engagement with leading investigators in the neuroscience community appears to have been relatively limited even when accounting for the early stage of this proposal.

3. Innovation

Strengths

- Support for technology development and interdisciplinary research has the potential to develop innovative tools and approaches.

Weaknesses

- The proposal does not recognize adequately the range of ongoing activities related to mapping brain connections and developing tools for neuroscience research and does not articulate how it is different from them.

4. Approach

Strengths

- Coordination of activities between research programs at different agencies has the potential to enhance brain research.

Weaknesses

- The approach is unclear, particularly with regard to the relationships between brain-activity mapping and other goals.
- The need for a large-scale, federally coordinated program rather than appropriately supported, investigator-initiated alternatives is not adequately justified.
- If the goal is to "crack the brain's code," the applicants would be wise to recall that "genetic code" was cracked not through large-scale data collection but rather through carefully conceived and incisive experiments designed and executed by individual investigators and small collaborative groups.
- The comparison with the program to put a man on the moon and the HGP is not apt, as those programs' ultimate goals were relatively unambiguous. In contrast, it is unclear how one would judge if an understanding of the brain or a brain-activity map had been achieved.
- The types of coordination of activities from different agencies in both new and ongoing activities are not described adequately.

5. Environment

Strengths

- There is a strong and vibrant neuroscience research community, including a range of interdisciplinary centers and programs that are well suited to contribute to this program.

Weaknesses

- Unprecedented financial challenges are gripping the American scientific community, and the laboratories of many investigators at both early and mid-career stages are downsizing or are in danger of closing down. In this context, it appears that directing resources away from the investigator-initiated grants programs has the potential to inflict additional damage and exacerbate the inefficiencies associated with investing time and financial resources in developing effective and productive laboratories only to underinvest in their continuing activities.

Budget and Period of Support

- There is little clarity about whether this program is intended to be supported with additional funds or by redirection or recounting funds that already are allocated to brain research. This is true both for the proposed federal support and for the listed contributions from nonfederal agencies. The intended duration of the program is unclear.

This completes my initial review. I hope that others in the scientific community will contribute their perspectives so that we can have an appropriate discussion of how the BRAIN initiative moves forward.

Jeremy Berg (jberg@pitt.edu) is the associate senior vice-chancellor for science strategy and planning in the health sciences and a professor in the computational and systems biology department at the University of Pittsburgh.

REFERENCES

1. http://www.whitehouse.gov/the-press-office/2013/02/12/remarks-president-state-union-address
2. http://arep.med.harvard.edu/pdf/Alivisatos_BAM_12.pdf or http://www.cell.com/neuron/abstract/S0896-6273(12)00518-1
3. http://www.whitehouse.gov/blog/2013/04/02/brain-initiative-challenges-researchers-unlock-mysteries-human-mind
4. http://www.nih.gov/science/brain/
5. http://online.wsj.com/article/SB10001424127887323646604578405073343715596.html
6. http://www.colbertnation.com/the-colbert-report-videos/425103/april-04-2013/francis-collins
7. http://grants.nih.gov/grants/peer/critiques/rpg.htm
8. http://battelle.org/docs/default-document-library/economic_impact_of_the_human_genome_project.pdf

Peer review at the National Science Foundation under threat

BY CHRIS PICKETT

Completing a grant application is a momentous event full of relief and apprehension, the latter of which is provoked by the next step of the process — peer review. What will a committee of scientific experts think about the work proposed in your application? How will your application rate relative to other applications? Will the application score well enough to be funded and support you and your lab?

Draft legislation circulating in the U.S. House could add another question to the mix: Will federal politicians find my work of high enough quality and important enough to society to warrant funding? Written by U.S. Rep. Lamar Smith, R-Texas, chairman of the U.S. House Committee on Science, Space and Technology, a draft bill would require the National Science Foundation director to certify that all grants awarded by the agency (1) have a foreseeable benefit to society, (2) solve important societal problems and (3) are not duplicative of other research. To be clear, this is a draft bill that has not yet been introduced to the full House and is not formally under consideration by the SST committee.

While it is doubtful this draft bill will become law, the thought processes behind it are concerning. The goal of scientific research is to broaden human knowledge, which requires discovering something previously unknown. Knowing the outcome and application of research before it has been conducted is impossible, in violation of the first two tenets of Smith's draft legislation. In fact, the benefits of scientific research may be realized only years or decades after it is conducted. This does not mean the research is unimportant or without benefit to society but merely that it is a step on an unknowable path toward discovery.

Peer review effectively provides a buffer against the politicization of scientific research by ensuring only the most scientifically meritorious grant proposals are funded. Smith's draft bill would implement an evaluation subsequent to peer review that would allow those outside the peer review process to disqualify grant applications based on nonexperts' opinions. At that point, the NSF would not be funding the highest-quality research but rather the highest-quality research that could survive political scrutiny. This could significantly slow or stop entire fields of research simply based on what Congress, not scientists, believes are important scientific questions.

This latest attack on peer-reviewed science won't be the last. We at the American Society for Biochemistry and Molecular Biology are particularly concerned about this proposal and the effect it would have on science funding, and we are working with our partners in Washington to do everything within our power to stop this proposal from becoming a bill, much less a law. That said, the community should not be surprised by this effort; nor should we be surprised by similar efforts that are sure to be on the horizon. As the scientific community makes passionate pleas to Congress for increases in funding in an environment where increases are less and less politically obtainable, increasing questions and criticism of the types of research that are funded should be expected. We must be vigilant and more vocal in defending our work and explaining the importance of our research to the public. If we are not, the questions that surround momentous events like submitting a grant application will be more about political perception than scientific excellence.

Chris Pickett (cpickett@asbmb.org) is the science policy fellow at the ASBMB.

Follow the ASBMB Policy Blotter blog for weekly updates by Chris Pickett on how across-the-board budget cuts are affecting U.S. scientists and institutions and other policy matters of concern to the research community.

New members of the National Academy of Sciences

The National Academy of Sciences announced in late April the election of 84 new members and 21 foreign associates from 14 countries in recognition of their distinguished and continuing achievements in research. ASBMB members who were elected include:

- James M. Berger, University of California, Berkeley
- Stephen M. Beverley, Washington University in St. Louis
- Vishva M. Dixit, Genentech
- Robert D. Schreiber, Washington University in St. Louis School of Medicine
- Gerhard Wagner, Harvard Medical School
- Graham C. Walker, Massachusetts Institute of Technology
- Wei Yang, National Institute of Diabetes and Digestive and Kidney Diseases
- Yigong Shi, Tsinghua University

New members of the American Academy of Arts and Sciences

The American Academy of Arts and Sciences announced in late April the election of 198 new members who will be inducted at a ceremony in October in Cambridge, Mass. ASBMB members who were elected include:

- Virginia Man-Yee Lee, University of Pennsylvania
- John T. Lis, Cornell University
- Joseph Loscalzo, Harvard Medical School and Brigham & Women's Hospital
- Suzanne Pfeffer, Stanford School of Medicine
- Charles J. Sherr, Howard Hughes Medical Institute and St. Jude Children's Research Hospital
- Yigong Shi, Tsinghua University

Three members win Melanoma Research Alliance awards


VARADARAJAN


GARRAWAY


APLIN

Three ASBMB members from Houston, Boston and Philadelphia were among the 49 scientists and clinicians who won awards for 2013 from the Melanoma Research Alliance, the largest private funder of melanoma research. The alliance issued 20 awards for a total of $9.61 million:

Navin Varadarajan of the University of Houston's Cullen College of Engineering won the Stewart Rahr-MRA Young Investigator Award, a three-year grant of $225,000 for his project titled "Quantitative single-cell biomarkers of melanoma immunotherapy."

Levi A. Garraway of the Dana–Farber Cancer Institute won the Christie's–MRA Team Science Award for a project titled "Chromatin-based therapeutic combinations for the treatment of melanoma" with collaborator Leonard Zon of Children's Hospital Boston.

Andrew E. Aplin of Thomas Jefferson University won one of five awards dedicated to academic–industry partnerships. Aplin's project, titled "Determinants of response to CDK4/6 inhibitors in melanoma," is in collaboration with Pfizer Inc.

AACR honors Levitzki with 2013 award for outstanding achievement


LEVITZKI

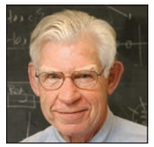
The American Association for Cancer Research recognized Alexander Levitzki for his work on signal-transduction therapy and development of tyrosine kinase inhibitors as effective agents against cancer with the 2013 Award for Outstanding Achievement in Chemistry in Cancer Research. Levitzki, professor of biochemistry at The Alexander Silberman Institute of Life Sciences at The Hebrew University of Jerusalem, gave an award lecture titled "Eradicating tumors by targeting nonviral vectors carrying polyIC" at the AACR's annual meeting in April in Washington, D.C. In 1988, Levitzki systematically screened low-molecular-weight protein tyrosine kinase inhibitors that had been synthesized in his lab and identified the compounds that inhibited potently the EGF-dependent proliferation of cancer cells. At the time, few believed such inhibitors would be specific enough for clinical use, but Levitzki went on to synthesize inhibitors of great specificity to other kinase targets, including the Bcr-Abl fusion protein, the PDGF receptor, the VEGF receptor and Jak2. His approach of doing large-scale screening of compounds against a large spectrum of protein kinases and then systematically testing in cell cultures and model animals is today the method used around the world, and over the years numerous targeted cancer therapies have emerged, including imatinib, crizotinib and lapatinib.

Raines wins Jeremy Knowles Award from Royal Society of Chemistry


RAINES

Ronald T. Raines, professor at the University of Wisconsin–Madison, won the 2013 Jeremy Knowles Award from the Royal Society of Chemistry. The award recognizes his work to illuminate the catalytic mechanism of ribonuclease A and then to transform this enzyme into a potent anticancer agent and his identification of n-to-π^* interactions as previously unrecognized forces that stabilize proteins. Raines is the third ASBMB member to win the award since it was established in 2008. Previous winners include Wildfred van der Donk of the University of Illinois at Urbana–Champaign (2010) and James Naismith of the University of St. Andrews (2009).

In memoriam: Francis "Frank" Ruddle, 83


RUDDLE

Francis "Frank" Ruddle, whose team announced in 1980 that it has created the first transgenic model organism, a mouse, died at age 83 in March in New Haven, Conn. Ruddle, a geneticist at Yale University, also is credited with helping to lay the foundation for the Human Genome Project, as he was one of the first researchers to map genes' locations on human chromosomes. *Image courtesy of Michael Marsland, Yale University*

Lively elected to become FASEB's next treasurer


LIVELY

Mark O. Lively of Wake Forest University School of Medicine has been elected the next treasurer of the Federation of American Societies for Experimental Biology. Lively, the immediate past president of FASEB, will begin his term as treasurer-elect July 1 and will take office as treasurer July 1, 2014. Lively is a professor of biochemistry and director of the Biomolecular Resource Laboratory, a core laboratory of the Comprehensive Cancer Center of Wake Forest University.

Beat the BioArt competition

The Federation of American Societies for Experimental Biology is holding its second annual BioArt Contest, and the deadline is approaching!

Each day, biomedical and life science investigators produce thousands of images and videos as a part of their research; however, only a few are ever seen outside of the laboratory. Sharing visually compelling research data with the public can create a sense of wonder and excitement about science.

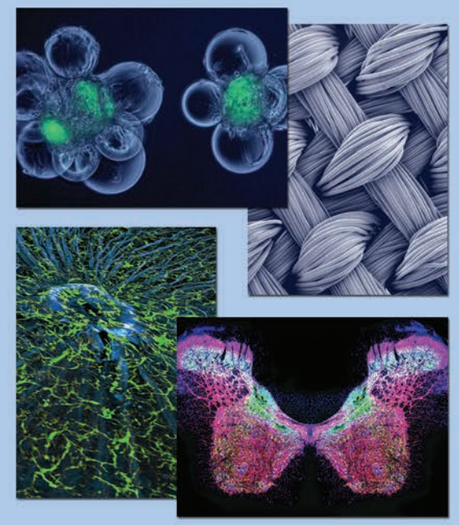
This year FASEB will select 10 winning images and two videos.

Last year's winning images were displayed at a Capitol Hill reception and at the National Institutes of Health's visitors center.

To participate, submit the following by July 11 to BioArt@faseb.org:

- *High-resolution, print-ready photograph, illustration or video*
- *100-word, nontechnical caption*
- *Names and institutional affiliations of all entrants*
- *Federal funding sources (e.g., agency and grant number)*

Visit www.faseb.org/bioart for more information.



CLARIFICATION: We reported in the May issue that Hudson Freeze was elected the next vice president of science policy for the Federation of American Societies for Experimental Biology and said his new term begins July 1. His term as VP-elect for science policy begins July 1, and his term as VP for science policy begins July 1, 2014.

IMPOSTER SYNDROME:
BEATING THE BLUE-EYED MONSTER

BY BETHANY BROOKSHIRE

I think it's all too good to be true. I have a Ph.D., scientific publications, interesting projects and awards for my scientific work. On the side, I have a successful career as a science writer and awards for that too. People tell me I'm smart and successful and that I'll be great some day. And I don't believe any of it. Why? Because I, like a lot of other scientists, have imposter syndrome.

Imposter syndrome is a psychological phenomenon that makes people unable to feel or internalize their own accomplishments. People with imposter syndrome, who often are mistaken for being exceedingly humble, can't believe they are as awesome as they really are, even though there is often very good evidence of their merits.

Imposter syndrome takes different forms. Sometimes you think the good stuff that happens to you is just luck. Sometimes you think people are just giving you accolades because they pity you or because they don't know that someone so much better is out there.

No matter what, it results in a feeling that you don't deserve what you have — your tenure-track job, your really good publications, your grant — and that the instant people realize or find you out, they're going to take it all away.

Oh, that award? They must not know what they're doing! If they knew what they were doing, they'd know I could never deserve it.

This job? I can't do this job! Who am I kidding? Soon they're going to realize I'm totally incompetent!

I like to call this phenomenon the blue-eyed monster. While jealousy is usually called the green-eyed monster, to my mind the blue-eyed monster is the one that colors everything a sad, unbelieving blue. All your bright accomplishments, constantly compared to the accomplishments of others, look duller. The blue-eyed monster is the one that stares out at the world unable to believe that anything is really as good as it is.

Imposter syndrome disproportionately affects women and minorities in science, preventing them from applying for awards, grants or raises, or from sending their papers to those high-impact journals.

After all, why try for it? You know you won't get it. If you did, well, it'd just be luck, right?

Wrong. Sometimes, you are a really good scientist. You really do great work. You have great ideas and are a great teacher. You really are a qualified candidate for that award, that grant, that raise and that job. But you won't get them if you don't apply. And, in order to apply, you need to battle back imposter syndrome. But how? How do we stop ourselves from denigrating our work? How do we internalize our own accomplishments?

HERE'S WHAT I RECOMMEND:

1. Go to your biggest fans. Trusting relationships with mentors can provide a lot of support. Good mentors have seen your successes and your struggles from the outside, and they know the successes for the great things that they are. When you see a grant or an award and think that it might fit but you couldn't possibly qualify, stop yourself. Ask your mentors. You might find that they are sure you qualify and that you should apply. I know that I would not have applied for any of the awards I have won had it not been for the support of my mentors, who, when I asked them, said I absolutely fit the criteria. If you have colleagues and friends who are relatively close to your work, they also can provide outside perspectives and much-needed encouragement. Share your doubts with people you trust.

2. Remind yourself of what you have done. When you're about to tell yourself that you can't do something, take a moment to look at something you are proud of. Have your degree(s) up on the wall. Update your CV. If you have them, read some nice letters of reference or support in which your mentors made you blush with their fulsome praise. Look at your work. See what you've accomplished. The more that you look at the positive messages, the harder they become to ignore. You've done a lot before. You can do more now. You can do this.

3. Think like a scientist. We scientists are pretty logically minded. Many of us pride ourselves on seeing the world for what it is and focusing on the facts. Well, focus on the facts! Especially when you evaluate your own work. Look at where you've published and at the other papers published there. They are pretty good! Look at the editorial board. Often it is full of well-established scientists: They can't be fools. Look at your citation index: Other people are reading and citing your work. The evidence is clear: You're pretty good!

4. Recognize that you are not alone. Because you're not. Imposter syndrome is incredibly widespread and very rarely talked about. Many of the people who look like they have it all together suffer from many of the same doubts that you and I have. And we can't all be incompetent!

Some people might say that imposter syndrome is just nonsense or that it's just another term for insecurity. It may very well be a type of insecurity, but it is certainly not nonsense when it prevents you from applying to jobs or for grants or submitting papers to the top-tier journals. When imposter syndrome is dragging down your career, it should not be dismissed.

Imposter syndrome, once recognized, can be fought. You don't have to let your doubts hinder you. By tapping your trusted mentors, colleagues and friends, by acknowledging all that you have done and by recognizing that doubt is difficult for all of us, you can fight it, and you can win. Sometimes, it's not luck or being an imposter. Sometimes, you really are that good.

Imposter syndrome still gets me down, especially in the face of rejection or in times of doubt or uncertainty. Unfortunately, those times are often the ones when you need to pick yourself up and move on the most. But talking with my mentors and friends has helped me to focus on the facts: I work very hard, and I need to be confident in what I do. I can't look at my career and let the blue-eyed monster dim my accomplishments. I have to see my work for what it is and use the confidence in myself to reach for the stars. And no blue-eyed monster is going to stop me.

Bethany Brookshire has a B.S. in biology and a B.A. in philosophy from The College of William and Mary and a Ph.D. in physiology and pharmacology from Wake Forest University School of Medicine. She recently finished a postdoctoral position at the University of Pennsylvania School of Medicine. She was guest editor of the Open Laboratory Anthology of Science Blogging (2009) and winner of the Society for Neuroscience Next Generation Award and Three Quarks Daily Science Writing Award, among others. She blogs at Scientific American at The Scicurious Brain (blogs.scientificamerican.com/scicurious-brain) and at Scientopia at Neurotic Physiology (scientopia.org/blogs/scicurious). Follow her at @scicurious.

Q&A with Stefan Schulz

BY RAJENDRANI MUKHOPADHYAY

For some spider species, love definitely is in the air. These arthropods emit sex pheromones, which are volatile compounds, to communicate with prospective mates, initiate courtship and accept partners. Stefan Schulz at the Technische Universität Braunschweig in Germany is an expert in spider pheromones. He spoke with science writer Rajendrani Mukhopadhyay about what is known about the pheromones that spiders emit for sex and other purposes. The interview has been edited for length and clarity.

Why is it important to study spider pheromones?

One important factor is to understand spider biology, because spiders are important in crop protection. A lot of pest insects are caught by spiders, so (the spiders) play an important role in crop protection. The other factor is to see whether there are mechanistic and chemical differences between spider and insect pheromones and understand more about pheromones as a communication system. The hope is to get some methods to trap poisonous spiders, such as the black widow spiders.

How did you become interested in spiders and their pheromones?

This was relatively early in my career, after I did my postdoc with Jerrold Meinwald at Cornell University (in 1988). I looked in the area of chemical ecology, a topic that was less explored at that time. No spider pheromone was known. I thought, "There must be chemical communication going on between spiders."

At that time, were there any hints that pheromones were involved?

There weren't any chemical characterizations of any spider pheromones. Many scientists at that time thought that spiders didn't have pheromones. In fact, a very important researcher at that time told me it was good that I was looking into the topic so I could show that spiders didn't have pheromones! But it turned out that was not the case.

What tools do you use to study pheromones?

I am an organic chemist, so we work in the lab. One problem we have is keeping the spiders. Unlike insects, you have to keep spiders separated. You need maybe 50 to 100 spiders, so you need 100 aquaria to house them. So there is a space issue. With insects, you can put them all in one aquarium.

We do extraction of silk and (spider) body parts. We also do headspace analysis, where we collect volatile material that a spider emits under hopefully

CREDIT: VINZENT SCHULZ

normal conditions onto small filters. We do extractions from the filters followed by (gas chromatography-mass spectrometry) analysis. From the mass spectra, we deduce a structure (of a pheromone). Then we synthesize the structure and compare its mass spectra to the natural compound to see if we got the structure correct. Another very important part is stereochemistry. We do stereochemical analysis by chiral gas chromatography.

There are 42,000 species of spiders. Do all of them use sex pheromones?

There are 50 to 100 species that have been shown to have pheromones. But there is a large number of spiders out there, and I doubt they all have pheromones. There are even some reports that definitely show that they use other forms of communication. It's certain that pheromones in spiders do not play as prominent a role as they do in many flying insects.

Are pheromones used simply for mating purposes?

No. There are other forms of chemical communication. An example is the bolas spider. They attract moths with a pheromone and then produce a glue droplet to attach onto a silk strand. When the moth approaches, the spider throws the strand with the glue droplet and catches the moth. Another example is that spiders can detect their prey based on their odor. It can go the other way around, so spiders that are preyed upon can perceive signals from approaching predatory spiders.

But sex pheromones are the easiest to study, because the spider behavior is so obvious.

Are there any common underlying biochemical mechanisms by which spiders make sex pheromones?

We think that spiders, more so than insects, generally use (sex) pheromones derived from primary metabolic pathways. Of course, we do not know many pheromones or much about them, so it's probably a bit premature to make such a statement. But (spiders) use relatively unique structures derived from citric acid metabolism or amino acid metabolism that you do not find in insects. Insects use more secondary metabolite pheromones.

One species of spider called linyphiids make their sex pheromones from fatty-acid metabolism.

Yes, they use a dimer of 3-hydoxybutyric acid as a sex pheromone. Another trait we see in spiders that is different from insects is that related spider species

Latrodectus hasselti. CREDIT: KEN JONES\COPYRIGHT MCB ANDRADE (2002)

use the same pheromone. You may think it's a bit strange because a spider probably would attract the wrong species. But species separation occurs at other levels. One could be on the type of silk used (to make webs) or by other biological mechanisms, such as activity periods and different habitats.

I find it fascinating that the male linyphiids cut up the webs of virgin females.

That is typical behavior. They arrive at the female's web and start to cut it up to reduce the evaporation rate of the pheromone that is on the silk. They cut the web and roll it up into a small ball so the surface-dependent evaporation (of the pheromone) is largely reduced. Then mating occurs. The mating can last up to several hours, so any subsequent arriving mate could potentially fight with the first one. So it's very important for the first male to cut up the web so that it's relatively undisturbed during courtship and copulation.

Do both males and females emit sex pheromones?

Mostly it's females. But there is one report that a male pheromone is present. It's not an attracting pheromone. It's more like a fitness marker. If they have (it) in relatively large amounts, these males are more readily accepted by the females than other males. It's a relatively simple hydrocarbon (emitted) from the surface of the male spider.

What do we know about the enzymes or the mechanisms involved in making pheromones?

There's nothing known about the biosynthesis except for hints from the structures. There's no enzyme reported that is involved in pheromone biosynthesis in spiders. Spiders are not as well investigated compared to insects. There is, of course, work on spider venoms and toxins but not on their signals.

In the next five years, what do you think are some of the big questions from a molecular or biochemical point of view?

The enzymes involved in the pheromone biosynthesis and the regulation of the biosynthesis are probably the big issues to tackle in the next few years.

Which is your favorite spider?

I like wasp spiders very much. They look like wasps. The tropical varieties are very shiny. The ones that live here in Germany and Eastern Europe are found in meadows, so they are easily seen by birds that are their predators. But their appearance may protect them against predation, because they have yellow and black striped abdomens.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer and blogger for ASBMB. Follow her on Twitter at twitter.com/rajmukhop.

Q&A with Steve Caplan

BY RAJENDRANI MUKHOPADHYAY

A molecular biologist by day, a writer by night. That pretty much sums up Steven Caplan, an associate professor at the University of Nebraska Medical Center. Caplan, an expert in vesicle trafficking, is an editorial board member of the Journal of Biological Chemistry, a blogger for The Guardian and the author of two novels, "Matter over Mind" and "Welcome Home, Sir." The novels fall into the category of "laboratory literature." His third novel (titled "A Degree of Betrayal") is about a highly successful graduate student whose young Ph.D. adviser is depressed and withdrawn and makes it difficult for the student to graduate. The book is slated to be out by the end of this year. ASBMB's science writer, Rajendrani Mukhopadhyay, spoke with Caplan. The interview has been edited for length and clarity.

IMAGE COURTESY OF STEVE CAPLAN

Q: What is your research focus?

My research is focused on understanding the basic mechanisms by which proteins and membranes are transported from place to place within the cell, in what we call membrane trafficking or vesicular transport. We've been looking at a family of proteins called the C-terminal EHD proteins, which are regulatory proteins. We've been studying them and a variety of interaction partners that we've identified. One of the most recent ones is called MICAL-L1, for MICAL-like 1 protein, and we've been trying to understand how these proteins work together to facilitate endocytic recycling or recycling of membranes and receptors back to the plasma membrane.

Q: How did you end up as a scientist?

It was a long route. I was born in the U.S., but I lived in Canada all of my childhood. I grew up in a city called Winnipeg. To make the story short, I would say I had various anti-Semitic experiences in Canada and other things. I felt like I really didn't belong very well. I ended up moving to Israel on my own. I had an adopted family in Israel, and I lived on a kibbutz, which is an agricultural type of community. I spent the next 18 years or so (in Israel). I served in the military, and afterward I did my undergraduate, master's and Ph.D. degrees all in Israel.

Q: What prompted you to join the Israeli military?

Reading and learning about the Holocaust, combined with my exposure to neo-Nazism and anti-Semitism, were probably driving forces in my decision to move to Israel at 18. Although I am definitely not militaristic by nature, I did feel it to be my duty to serve in the army, as does every other 18-year-old in the country. In retrospect, despite loathing all three years of military service, plus the active reserve duty during my undergraduate, master's and Ph.D. studies, I do think that the life lessons and experiences that I underwent in the military have greatly contributed to my academic success. It's prepared me well to meet goals, take and delegate responsibility, and show teamwork and leadership. Indeed, "Welcome Home, Sir" depicts a researcher whose military service is both the source of his academic success and his personal failures in dealing with his (post traumatic stress disorder).

Q: Why did you choose to pursue science in university?

I was starved for something intellectual when I finished the military. I really wanted something where I could engage my brain. I'd always loved science, in particular biomedical science. That's what I ended up going into, a three-year program in biology.

I had a greater problem deciding what to do after my bachelor's degree. I took a year off and backpacked through South America. During that time, I decided that I liked the biochemistry area, especially cell signaling and immunology. That's how I ended up in a laboratory that studied T-cell receptor signaling for my Ph.D.

IMAGE COURTESY OF STEVE CAPLAN

Q: How do you juggle science and novel writing?

I don't sleep much! I don't watch any television. I think I am reasonably efficient at what I do, so I guess with that combination of things I get things done!

Q: When do you do your fiction writing?

Late at night. Sometimes on weekends, if I have time. On a flight. Sitting in a coffee shop for half an hour, waiting for my daughter's voice lesson or my son's taekwondo lesson to end, I pull out my laptop and write. The fiction writing comes when I'm too tired to do any more scientific writing.

Q: Do you make a distinction between your scientific and fiction writing?

Oh yeah, they are completely compartmentalized. They better be! Just as a funny aside, I recall having a grant and a book rejected on the same day. I couldn't help wondering if I had the same reviewers for both!

But I do think the ideas (in fiction) of brevity and making sentences simple and easy to read have helped me put papers and grants together.

Q: How much of your novel writing is autobiographical?

I'll give you the standard author answer. When authors are writing good fiction, they are usually writing about something that matters and means something to them. In the case of "Matter over Mind," I can confirm that I did have a parent who was bipolar. My mother was bipolar. In the book, it's the father. My mother is no longer alive, so I don't have a problem talking about it. I found that there are a lot of books that deal with mental illnesses and mental health issues but not from the perspective of the family. It seemed to me that the impact such a disease can have on one's family was missing. I know (my mother's bipolar disorder) has impacted me greatly. You asked for the reasons for my moving to Israel. I am sure that also had something to do with it.

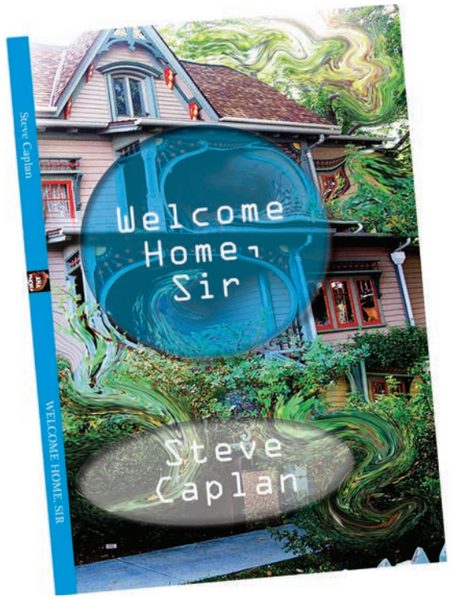
I think what's interesting about "Matter over Mind" is that I was a graduate student when I wrote the book. The hero of the book is an assistant professor who's trying to get tenure (in a Canadian university). I had never been in a U.S. or Canadian university at the time I wrote the book. All of what I wrote was based on my experience with my own mentor in an Israeli university in Jerusalem. I caught up with the age and situation of the protagonist in the book when I got here to the U.S. I promised myself that I would get the book published once I got tenure. That book sat around for a good 15 years or so.

Q: When did you start writing fiction?

I'd been writing short stories since I was young. I published a few along the way, not that many. I began writing short stories at a more regular pace over the course of my graduate work. When I started writing ("Matter over Mind"), it was a combination of things. I had an accident in the laboratory. I breathed in a chemical I shouldn't have! It was iodoacetamide. I was home for 10 days with that. I finished writing several manuscripts and reviews. I was fresh of out things I could do from home. Several other things converged at the same point, such as the death of my mother. I really felt this urge to write, and the book flowed out of me. Within a week, the skeleton of the book had been written. From that point on, it was mostly editing.

Q: Your novels fall into the laboratory literature, or lab lit, genre. What is lab lit?

Lab lit was defined by Jenny Rohn (at University College London), who coined the phrase. It's basically fiction with scientists in it. It has to have a realistic component. It's not science fiction. It's not about having an evil scientist who is out to destroy the world or the nerdy, geeky scientist who can barely tie his own shoelaces. It's more along the lines of what real scientists are like, what they go through, the stresses they have in their lives, their personal relationships. It's just like what you have with fiction about lawyers, doctors, policemen and other professions. These are stories that deal with people who



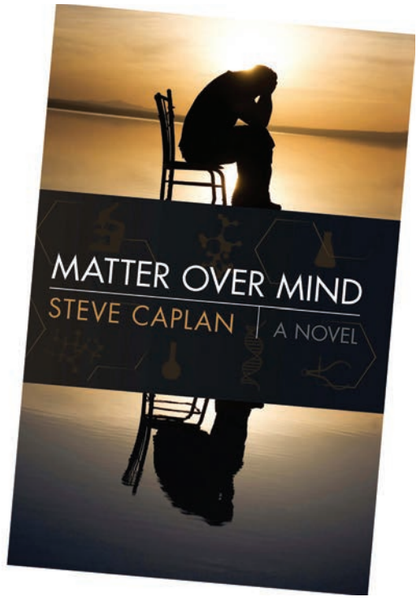


IMAGE COURTESY OF STEVE CAPLAN

have science as their profession.

Q: How did you become a blogger?

I met Jenny at an (American Society for Cell Biology) meeting in Philadelphia a couple of years ago. She said to me, "We have a group of bloggers called Occam's Typewriter. Would you be interested perhaps in sending us a piece about something?" I thought, "I can't do that! I'm a fiction writer, not a blogger." But I went online, and I saw what people were writing about. So I sent in a couple of pieces. They put them up, and they asked me, "Would you like to join as a regular contributor?" I did. After a while, we got an offer from The Guardian newspaper, saying (Occam's Typewriter) was one of the premier blogging sites, and they asked us to contribute to The Guardian articles that would be more globally relevant than the ones we write for our communities. About once a month or so, some of us send in a piece about something that we think is of importance to the scientific community.

Q: Do you tell fellow scientists that you blog and write novels?

I try to. When I give seminars, I always have my last couple of slides with the covers of my books. In my CV, I list that I write novels and blogs.

Somebody wrote me a request from England to see if I could send a couple of plasmids. I responded right away, and he wrote back saying, "Are you the same one who writes for The Guardian newspaper?" It was right after I wrote (the blog post) "Science as a Ponzi scheme." I thought that was funny. A while ago, I received another email from a high-school student in Kansas City who wrote to me to ask about the difference between basic and translational research and the importance of the two. I guess I'm starting to get recognition from people whom I don't know who see my name out there.

Q: Do you see your fiction writing and blogging as a form of outreach?

Yes, definitely. I try to reach other scientists but also people who are considering becoming scientists and let them know what the lifestyle is like as a scientist. It's a wonderful career, despite all the pressures today with funding and everything else. It's still a career that I would not switch with any other career. I can't help thinking I'm extremely fortunate that I've been able to choose this career.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer and blogger for ASBMB. Follow her on Twitter at twitter.com/rajmukhop.

Cost-cutting ideas for researchers

BY LOLA OLUFEMI

Do budget cuts have you asking your researchers how accurately they can mouth pipette 2 millimeters or how much serum they are willing to donate for research? Well, you are not alone. After years of belt-tightening, the sequester promises to bring even more devastating budget cuts. With the current funding climate, scientists are searching for ways to stretch every penny. Summarized are a few ideas that can be implemented in labs to save hundreds, and sometimes thousands, of research dollars.

NEED ANTIBODIES?

Purchasing antibodies can sometimes be a risky investment. Fortunately, suppliers are getting creative. For instance, Rockland Immunochemicals has teamed up with the University of Pennsylvania to provide its researchers with more than 200 free trial antibodies. In return, Rockland is asking researchers to send images demonstrating the utility of an antibody for the company's catalog. And Rockland is not alone. ThermoScientific offers an Innovators Program: When researchers provide data that demonstrate an antibody works for an application, ThermoScientific provides a free antibody of choice of equal or lesser value to the antibody tested. BioSource LifeSciences also offers a selection of GeneTex antibodies monthly. Registration in the program is required; upon registration, a list of that month's available antibodies includes a code that can be used to redeem free antibodies. Other reputable companies also are attempting to reduce the financial risk associated with trying antibodies. AbCam and Merck Millipore offer trial-size versions of certain antibodies, for instance.

REWARD PROGRAMS

Several biotech suppliers offer great reward programs. A conversation with your vendors can save hundreds to thousands of dollars. For example, Santa Cruz offers the Cruz Credit Program. For citation of Santa Cruz products in a publication, investigators receive 330 free Cruz Credits that can be used toward purchases. One Cruz Credit is equal to a dollar, so citation in a publication earns investigators $330. Once cited, the investigator also gets entered into the Investigator Awards Program, becoming eligible to receive 2,500 Cruz Credits. Meanwhile, AbCam offers an AbTrial program in which researchers use AbCam products for untested applications or in untested species and provide quality images of the experiments. In return, AbCam provides discount codes worth the full amount of the products tested.

REUSE, REDUCE AND RECYCLE

Instead of tossing high-dollar items, it might be a good idea to see how to get more bang for the buck out of products. A few items that are used routinely in the lab, such as certain types of resins and beads, can be used multiple times before being tossed. Some companies boast that their resins can be reused up to five times. After purifications, resins can be washed, stripped, equilibrated and stored in buffer containing sodium azide to protect them from fungal growth. Properly stored resins can be kept for months to years.

Nucleic acid extraction kits always seem to come with more reagents than extraction columns, forcing researchers into purchasing another kit or more columns. These columns typically account for the majority of the cost associated with purchasing the kit. Instead of tossing used columns, consider regenerating them by soaking them for 24 hours in 1M HCl. The next morning, wash the columns thoroughly with several column volumes of water and then equilibrate with equilibration buffer. Those who've used this method say the procedure does not alter the binding capacity of the column and does not change the properties of the nucleic acids purified, and there is no residual carryover that can contaminate downstream purifications. Remarkably, the columns can be reused multiple times — some suggest anywhere from four to 10 times.

HOMEGROWN ENZYMES

Commercial enzymes such as polymerases come with the convenience of aliquots of known concentration and standardized protocols but are not always the most cost-effective option. These seemingly tiny packages can cost close to a thousand dollars. For those with protein chemistry experience, weaning the group off some commercial enzymes can save money. This is not applicable to all enzymes; however, purification of recombinant PFU or Taq can be practically achieved. Purifying and standardizing enzymes can be a time-consuming endeavor initially, so determine if the amount of time spent on the effort outweighs the cost in cash. Some published protocols for purification and standardization of these enzymes can take a month or more; however, it comes with a big payoff. Once purified, high-concentration stocks can be stored stably at -80°C for years. Besides savings, purifying enzymes also will offer students an opportunity to learn a new technique.

DIY REAGENTS

Commercial kits, ready-made reagents like precast gels, and buffers are convenient but are not generally economical. There are experiments that require kits and ready-made products that offer higher quality results in a fraction of time. In other instances, such as DNA isolations, a kit can be swapped out easily for traditional methods. Skipping out on kits and ready-made reagents where possible is not only financially smart but also allows students to understand what they are doing. So allow the group as a whole to participate in making reagents and pouring gels, and forgo the kits.

DON'T DISPOSE OF THE "DISPOSABLES"

Research in a biological lab comes with the use of an enormous amount of disposables, including plastic consumables and glass product bottles. Just because they are disposable does not mean these items have to be tossed after use. Instead of tossing glass bottles, use them to bottle buffers. Also consider washing conical-bottom plastic tubes and old pipette-tips boxes for reuse. While these plastics cannot be used for experiments that require sterile plastics, they can be reused for buffer storage, staining dishes or blot preparation.

PURCHASE PRE-OWNED LAB EQUIPMENT

Refurbished equipment might come from a startup that goes out of business or from research institutions that opt for updated versions. Choosing to buy used can save investigators between 50 and 75 percent. Some companies offer everything from consumable glassware to incubators or imagers. These companies also have technicians who ensure the restoration of used equipment meets manufacturers' specifications. It is best to purchase items from well-established vendors with a warranty that is equivalent to the manufacturer's warranty.

GET TO KNOW YOUR VENDORS

Savings can come simply with having a conversation with your sales representative. Developing relationships with vendors can yield an insider's guide to deep discounts and specials on products used routinely. Vendors also will offer freebies and samples of newer products. Besides getting something for free, this offers researchers an opportunity to try the product before buying it. Also scope out your vendor's competition. Figure out how much can be saved by going with a competitor. Often suppliers will negotiate prices or even match prices if they know that they might lose business to a less expensive competitor.

MAKE A GROCERY LIST

Biotech suppliers boast of products made for the lab, but these items come at a price. These items can be swapped out for inexpensive alternatives found at a grocery or wholesale store. Items such as plastic wrap, foil, cleaning supplies and even dried milk for blocking Western blots can be found for cheaper. Before placing that purchase order, figure out how many of the products can be bought on a quick run down the street.

SAVE THE TREES

Ever notice how much paper gets wasted printing those lengthy manuscripts? What about all the space all those papers take up? Consider freeing up some space and saving on the costs of paper by having the group read articles on laptops, e-readers or smartphones. PubMed has an excellent app that gives easy access to research articles. Now readers on the go have access to publications from the convenience of smartphones.

MAKE FRIENDS AND PLAY NICE

Approaching research from a collaborative standpoint can save you time and money. Instead of purchasing or making some products, it might pay just to ask colleagues who have them. Also consider partnering with colleagues when making a purchase. Often buying products in bulk can reduce the per-item cost.

MORE ON THIS TOPIC

- "Save $29,000 this year" by M. L. Phillips in The Scientist Magazine in 2006.
- "Regeneration of commercial nucleic acid extraction columns without the risk of carryover contamination" by N. B. Siddappa in Biotechniques in 2007.
- "Cloning and expression in Escherichia coli of the recombinant His-tagged DNA polymerases from Pyrococcus furiosus and Pyrococcus woesei" by S. Dabrowski and colleagues in Protein Expression and Purification in 1998.

Lola Olufemi (olufemi_lola@yahoo.com) is an intern at the Office of Technology Transfer and a postdoctoral fellow at the Schol of Medicine at Emory University.

THE JOURNAL OF BIOLOGICAL CHEMISTRY

New insight into mechanism of rhomboid proteases

BY ANNA SHIPMAN

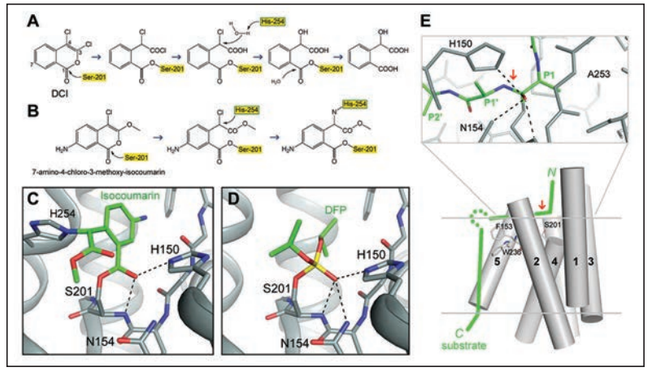
Rhomboid proteases are a family of enzymes, each with a common catalytic core made up of six transmembrane segments, that cleave membrane-protein substrates near the amino-terminus of the transmembrane domain. They were first identified from a genetic screen in Drosophila, where flies lacking this protein would express a pointy head skeleton phenotype. Homologs to the rhomboid protease from Drosophila have been discovered in many prokaryotes and other eukaryotes, and they are involved with a wide variety of biological functions. Rhomboid proteases are also members of a distinct class of proteases called intramembrane-cleaving proteases, or I-CLiPs, a term that emphasizes their ability to operate within the hydrophobic region of the lipid bilayer. E. coli rhomboid protease GlpG was the first I-CLiP to have its crystal structure solved; however, it remains unclear how it functions within the membrane.

In a minireview recently published in the Journal of Biological Chemistry, Ya Ha and Yi Xue of the Yale School of Medicine and Yoshinori Akiyama of Kyoto University discuss work done to determine the mechanism of rhomboid proteases. The minireview specifically focuses on research done on the catalytic mechanism and conformation changes in the catalytic core of the E. coli rhomboid protease GlpG.

One of the experiments reviewed showed that a serine residue from the catalytic center of GlpG is bonded covalently to a mechanism-based inhibitor, indicating that this protease may function via a classical mechanism. Other studies reviewed put forward a top-down model, suggesting that rhomboid proteases may cleave peptide bonds initially buried in transmembrane regions as well as those outside the transmembrane domains. One of the studies also identified a conserved motif specifically recognized by rhomboid proteases, suggesting that rhomboid proteases use a common and specific mechanism to recognize their substrates. However, not all rhomboid substrates share this motif, indicating that other specificity-determining mechanisms exist.

The authors of the minireview propose that further research should focus on interactions between rhomboid proteases and the lipid bilayer, generating additional crystal structures where they are in complex with peptide substrate analogs, and should examine their role in the life cycle on medically relevant parasites such as T. gondii and P. falciparum.

The authors write, "The biological functions of many related rhomboid proteins are now known, and there is optimism that the pace of such discoveries will only quicken in the near future. The crystal structures of E.coli and H. influenza GlpGs have provided a framework for in-depth probing of the membrane protein's mechanism of action."



The catalytic mechanism. (A) GlpG catalyzes the hydrolysis of DCI to form an α-hydroxy acid. The complex between 7-amino-4-chloro-3-methoxy isocoumarin and GlpG is stabilized by two covalent bonds. (B) The covalent adduct between DFP and GlpG mimics the tetrahedral transition state. (C and D) The crystal structures of GlpG in complex with isocoumarin and DFP, respectively. (E) A hypothetical model of substrate (green) bound to rhomboid protease. The protease's TM helices are shown as cylinders, and the loops are omitted for clarity. The substrate's extended cleavage site and helical TM segment are connected by a sharp turn (green dots). According to this model, Ala-253 is adjacent to the side chain of substrate's P1 residue (insert). The red arrows indicate the scissile bond.

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Revisiting metals in the fifth edition of the thematic minireview series

BY KYEORDA KEMP

The Journal of Biological Chemistry's thematic minireview series "Metals in Biology" is back for a fifth edition. While metals play crucial roles in many biological functions, our understanding of those roles is lacking. This series features metals in biochemistry and human health and is coordinated by F. Peter Guengerich of Vanderbilt University, a JBC associate editor. The first two editions of "Metals in Biology" discussed iron, copper, selenium, zinc, nickel, vanadium and arsenic, the third focused on iron homeostasis and eukaryotic cells, and the fourth concentrated on metal transport and homeostasis. The latest collection of minireviews covers the molybdenum prosthetic group, or pterin Moco; the biosynthesis of M-cluster molybdenum prosthetic group of nitrogenase; the biosynthesis of the nickel-based metallocenter of the enzyme urease; several of the processing, transport and medical aspects of cobalamins; and the growing roles of heme sensor proteins.

The first article begins with a review on the biological assembly of the molybdenum prosthetic group, or Moco. Molybdenum is an essential micronutrient for plants and animals and functions as a cofactor for enzymatic activity; however, it is catalytically inactive unless bound by a special scaffold, one of which is the molybdopterin or metal-containing pterin (MPT). The review by Ralf R. Mendel covers uptake of molybdenum by eukaryotes, the molybdenum prosthetic group Moco, the details and requirements for the biosynthesis of Moco, Moco storage and transfer, and Moco deficiency disorders and therapy in humans.

Moco forms part of the active centers of all molybdenum-containing enyzmes except bacterial nitrogenase, an enzyme vital in agriculture because it reduces atmospheric nitrogen to ammonia. Instead of Moco, nitrogenase contains an iron–sulfur cluster-based molybdenum group. In the second minireview, Yilin Hu and Markus W. Ribbe discuss the recent progress in understanding the biosynthesis and assembly of the iron–molybdenum cluster FeMoco.

According to the authors of the third minireview, "Biosynthesis of the Urease Metallocenter," "metallocenters serve essential biological functions such as transferring electrons, stabilizing biomolecules, binding substrates, and catalyzing desirable reactions." Furthermore, authors Mark A. Farrugia, Lee Macomber and Robert P. Hausinger explain that metallocenters are required for metal homeostasis and mediating conformational changes that result in enzyme activity. The authors focus on biosynthesis of the metallocenter of urease, a nickel-containing enzyme in bacteria and plants, to understand the mechanisms of the metallocenter assembly system. Their review introduces ureases, the urease activation pathway and variations in urease activation systems.

In the fourth minireview, "Navigating the B12 road: assimilation, delivery and disorders of cobalamin," Carmen Gherasim, Michael Lofgren and Ruma Banerjee discuss trafficking of the biochemistry of cobalamin in mammals and the human diseases that result from impairments in the pathway. The article covers vitamin B12 chemistry; absorption, transport, and storage of cobalamin; cobalamin processing; and incorporation of cobalamin into biological pathways.

In the final review, Hazel M. Girvan and Andrew W. Munro explore the role of the prosthetic group heme, which is best known for its role in oxygen transport as a biological sensor. They review recent discoveries on the role of heme in regulating circadian rhythms, ion channel activity and microRNA biogenesis, gas sensing and regulating microbial respiration and denitrification.

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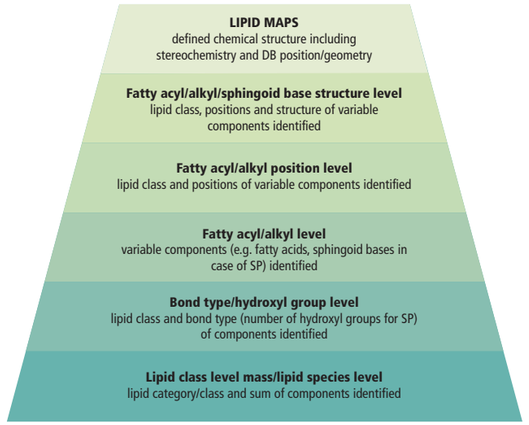
THE JOURNAL OF LIPID RESEARCH

Suggested shorthand for lipid structures ID'd through mass spectrometry

BY MARY L. CHANG



The June issue of the Journal of Lipid Research features a proposal for standardized terminology for lipid structures elucidated via mass spectrometry. The proposal by Gerhard Liebisch of the University of Regensburg and colleagues would complement the currently used comprehensive classification system for lipids on the LIPID MAPS website.

Mass spectrometry, the key methodology used in analyzing lipid species, often does not yield the structural details described by the LIPID MAPS nomenclature. As a result, scientists have taken to using a variety of different notations for lipid species, so a lack of consistency across the board has emerged.

In this special report, Liebisch et al. say that standardization would allow correct and concise reporting of research data and proper deposition of these structures in databases and that it would facilitate the exchange of data between labs.

The proposal covers major lipid categories and classes of mammalian lipids (fatty acyls, glycerolipids and glycerophospholipids, sphingolipids and sterols), but the authors suggest that future proposals could go beyond this and include minor lipid classes and lipid classes of other organisms.

Mary L. Chang (mchang@asbmb.org) is publications manager for the Journal of Lipid Research and Molecular & Cellular Proteomics.

Hens shift lipid metabolism away from egg-making when stressed

BY RAJENDRANI MUKHOPADHYAY

It's hard to make babies when you're stressed, even if you are a chicken. In a recent paper in the Journal of Lipid Research, a group of Chinese investigators looked into how stress can disrupt lipid metabolism, a source of reproductive energy, in egg-laying hens.

"Stress is a common problem that disrupts breeding in either birds or mammals," explains Hai Lin at Shandong Agricultural University in China, who led the team of investigators. "Glucocorticoids participate in the arousal of stress responses and trigger physiological adjustments that shift energy away from reproduction toward survival."

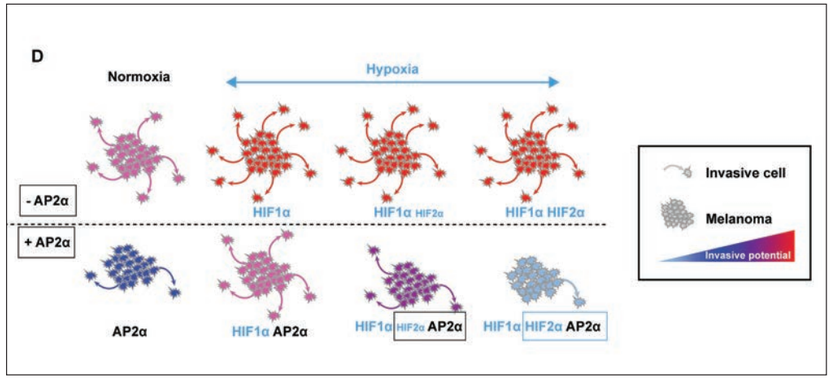
Glucocorticoids work to control whole-body homeostasis and trigger stress responses. Lin says the group's previous work on immature chickens showed that glucocorticoids enhanced hepatic lipogenesis and fat deposition in adipose tissues, indicating the redistribution of energy stores.

To see how energy sources got redistributed from reproduction to survival, Lin and colleagues tested the effects of corticosterone, a type of glucocorticoid, on egg-laying hens. They did two different experiments to see how corticosterone affected the development of ovarian follicles in hens. These follicles supply yolk precursors, which are very low-density lipoproteins, for eggs. In the first experiment, the investigators looked into how fasting and feeding affected ovarian follicular development and lipid production in the liver with or without corticosterone. In the second experiment, the investigators tested the effects of corticosterone on two groups of hens, each fed a diet with a different calorie count.

Lin says their results demonstrated that corticosterone "mimicked the endogenous glucocorticoids under stress to shift the energy expenditure away from reproduction to survival by suppressing ovarian follicular development, laying rate and egg production via multiple actions." The investigators concluded that the effects of stress on reproduction were energy-dependent.

The group will next look into the effects of stress on estrogen release. (Estrogen plays a role in triglyceride synthesis.) Lin explains that the investigators are interested in this direction of research because in their current study "the circulating concentration of estrogen was decreased by corticosterone, suggesting that the suppressive effect of corticosterone on ovarian follicular development is associated with a reduced estrogen release." They also would like to see if isoflavones, a class of plant-derived compounds with estrogenic activity such as those found in soy, has any potential to regulate the effects on stress-induced perturbation in reproduction.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer and blogger for ASBMB. Follow her on Twitter at twitter.com/rajmukhop.



Melanoma cell lines expressing both AP2α and HIF2α exhibit poor invasive properties. Schematic illustration of AP2α, HIF1α and HIF2α contributions to invasive capacities in melanoma cells growing under normoxic and hypoxic conditions.

MCP MOLECULAR & CELLULAR PROTEOMICS

The role of hypoxia-inducible factors in melanoma

BY RAJENDRANI MUKHOPADHYAY

Melanoma is the most aggressive form of skin cancer that metastasizes readily. In a recent paper in Molecular & Cellular Proteomics, a team led by Laurence Nieto at the Institute of Pharmacology and Structural Biology in France demonstrated that two hypoxia-inducible factors play a critical role in the progression of melanoma.

"The number of cases of melanoma worldwide is increasing more rapidly than any other type of cancer," says Nieto. "Indeed, the incidence of melanoma has more than tripled in the Caucasian population over the last 20 years." Standard cancer treatments, such as chemotherapy and radiation therapy, are unable to tackle the disease, so new therapeutic strategies are needed.

Invasive melanoma depends on the clonal selection of cells that have adapted to their microenvironment. One of the microenvironmental factors is hypoxia, a condition of oxygen shortage, which has an impact on cell transformation and tumor progression. Two hypoxia-inducible factors, HIF1 and HIF2, play a major role in the cellular adaptation to hypoxia and are overexpressed in most cancers. "In melanoma, several studies have demonstrated that HIF1 overexpression is correlated with all states of melanoma progression," explains Nieto. "However, how HIF2 influences melanoma initiation and progression remains poorly understood."

To better understand how HIFs affect melanoma progression, the investigators applied proteomics tools to a melanoma cell line and catalogued the binding partners of the HIF isoforms HIF1α and HIF2α. Nieto says their work is the first to describe "the whole repertoire of HIF interacting proteins. These data provide very useful material for HIF researchers by identifying new partners and demonstrating that some well-known partners are not universal." For example, the investigators found, with their binding assays, that the P300 transcriptional co-activators, thought to be binding partners of HIFs, were poorly detected.

Most importantly, the investigators established that HIF2α interacts with the microphthalmia-associated transcription factors SOX10 and AP2α, both of which play important roles in melanoma development. The investigators found that the melanoma cells became less invasive when HIF2α was present along with AP2α.

Nieto says, "Our work underlines that as HIF protein function could be specifically modulated by several protein partners which confer opposing properties, the function of HIF1 and HIF2 must be investigated specifically in each tumor type before envisaging the use of drugs targeting these factors for cancer treatments."

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer and blogger for ASBMB. Follow her on Twitter at twitter.com/rajmukhop.

Professional development at the annual meeting — and beyond

BY TAKITA F. SUMTER

This article provides synopses of sessions and special events at the Experimental Biology 2013 Conference sponsored by the American Society for Biochemistry and Molecular Biology Minority Affairs Committee. The well-attended sessions were aimed at expanding the knowledge base of scientists, particularly those from different backgrounds and at early or transitional career stages. While an introduction to our thematic programming on triple-negative breast cancer was featured in the April issue of ASBMB Today (1), other MAC sessions and events at the annual meeting included the following:

Professional development workshops for K – 12 teachers

At the Hands-on Opportunities to Promote Engagement in Science (HOPES) workshop for K – 12 teachers, Regina Stevens–Truss from Kalamazoo College directed a half-day experience for middle-school and high-school science teachers in the Boston area. The workshop attracted more than 70 teacher–participants who engaged in inquiry-based learning activities to be used ultimately in their classrooms. In addition to offering innovative pedagogies, the workshop provided a platform for college and university faculty members to collaborate and mentor the nation's secondary-school science teachers. Scientists from across the country helped make the workshop a meaningful experience for school teachers. The workshop was funded by a National Science Foundation grant to Stevens–Truss. Workshop participants and other ASBMB members are invited to submit proposals to receive up to $2,000 for classroom-centered activities. The grants issued during the first two years of the program have generated vibrant faculty–teacher partnerships across the country, and several of the models were presented to the 2013 cohort.

Ruth Kirschstein Diversity in Science Award lecture

The Ruth Kirschstein Diversity in Science Award is given to a prominent scientist whose work exemplifies a commitment to broadening the representation of biochemists and molecular biologists to include those who have not historically pursed careers in the sciences. This year's award went to Peter Blumberg from the Center for Cancer Research at the National Cancer Institute for his relentless commitment to providing significant research experiences to students with disabilities. Blumberg's lecture highlighted the low representation (less than 0.2 percent) of deaf employees in the science and engineering workforce. Through his extensive research endeavors to determine the mechanisms of phorbol esters and their derivatives in cell signaling, Blumberg has engaged 16 deaf students in using natural products as tools for drug discovery. In all ways, it was clear that Blumberg was worthy of this prestigious award.

The "professor rounds" mentoring network and the MAC welcome reception

Marion Sewer of the University of California, San Diego, coordinated a "professor rounds" experience that paired those who won minority travel awards from the Federation of American Societies for Experimental Biology's Minority Access to Research Careers program with established biochemists and molecular biologists from industry, academia and government. The mentor–protégé pairs spent one or two hours together during the meeting, often visiting posters and discussing vari-

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Protein carbonylation

Not just another -ation in the acylation nation

BY DAVID BERNLOHR

The advent of high-sensitivity mass spectrometers has allowed for the identification of numerous covalent additions to amino acid side chains and has heightened awareness of the role of intermediary metabolism and oxidative stress and major effects of protein structure and function. Indeed, protein propionylation, malonylation, butyrlation and succinylation are but a few of the most recent additions to the acylation nation (1, 2). Linking lipid metabolism and oxidative stress to the covalent modification spectrum is protein carbonylation.

Protein carbonylation is a generic term used to describe the covalent adduction of lipid aldehydes, often six, nine or 12 carbons, to the side chains of lysine, histidine and cysteine residues (3). Lipid aldehydes are produced from hydroperoxidation of polyunsaturated fatty acyl groups followed by nonenzymatic Hock cleavage. The resultant aldehydes can undergo Schiff-base formation with lysine residues but more commonly are subject to Michael addition reactions that produce a lipid acyl group containing a free carbonyl — hence the nomenclature. Such carbonyl groups are capable of secondary Schiff-base formation with an adjacent amine or cyclization, but in many cases the free aldehyde remains unmodified, thereby allowing for detection using a variety of hydrazide-based reagents or, in some cases, using antibodies directed to nine-carbon acyl derivatives such as 4-hydroxy 2,3 trans nonenal (4).

Protein carbonylation is studied most commonly in those systems where increased oxidative stress meets biological membranes or lipid droplets. As such, adipose tissue is a major site for protein carbonylation, and the loss of intrinsic antioxidant enzymes that occurs during the course of an obese inflammatory challenge produces a state of increased lipid aldehyde synthesis. Because lipid aldehydes are capable of diffusing across membranes, mass-spectrometry-based identification of carbonylated proteins reveals that they are widespread in the cell, including the nuclear, mitochondrial and cytoplasmic compartments. However, a major difficulty in carbonylation analysis is that modified peptides do not separate well in the mass spectrometer, and, as a consequence, the site and stoichiometry of modification often are not well defined. However, in some cases, such as the adipocyte fatty-acid binding protein, carbonylation modifies about 10 percent of the polypeptide and results in loss of lipid binding activity (5).

In the case of mitochondrial targets of carbonylation, such as enzymes of complex I of the electron transport chain (NDUFA2, NDUFA3), it is not clear if protein carbonylation is causative in the loss of NADH oxidation capacity associated with inflammation or simply correlative (6). However, it is tempting to speculate that protein carbonylation contributes to the mitochondrial dysfunction associated with obesity and insulin resistance. Intriguingly, protein carbonylation recently has been linked to epigenetic processes via carbonylation of lysine groups on histones and via carbonylation of class I and II histone deacetylases (7). Both types of modifications may affect gene expression and, as such, may provide a redox-based connectivity of lipid metabolism to epigenetics.

Interestingly, in adipocytes the loss of the major phase II enzyme controlling lipid aldehyde levels, glutathione S-transferase A4, is associated not only with increased protein carbonylation but also with increased superoxide anion production, suggesting protein carbonylation is a key determinant in reactive oxygen species synthesis (8). Superoxide anion synthesis leads to increased hydroxyl radical formation and, in turn, increased protein carbonylation, catalyzing a feed-forward process whereby increased protein carbonylation and reactive oxygen species formation go hand in hand. As reactive oxygen species can oxidize directly the side chains of many amino acids, such as cysteine and methionine, protein carbonylation may initiate an oxidative stress cascade and a change in the cellular redoxome, resulting in pleotropic effects on cellular structure and function. Within the context of diabetes and obesity, oxidative stress often leads to endoplas-

mic reticulum stress and the unfolded-protein response. As such, protein carbonylation by lipid aldehydes may not be simply another -ation to check but rather an important initiating event in a biological cascade affecting major components of cellular homeostatic control and gene expression.

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REFERENCES

1. Kluyver, A. J. and Donker, H. J. L. *Chem. Zelle Gewebe* **13**, 134 – 190 (1926).
1. Zhang, Z. et al. *Nat. Chem. Biol.* **7**, 58 – 63 (2011).
2. Peng, C. et al. *Mol. Cell. Proteomics.* doi: 10.12 M111.012658.
3. Esterbauer, H. et al. *Free Rad. Biol. Med.* **11**, 81 – 128, (1991).
4. Curtis, J. M., et al. *Trends in Endocrinology and Metabolism* **23**, 399 – 406 (2012).
5. Grimsrud, P. A. et al. *Mol. Cell. Proteomics* **6**, 624 – 637 (2007).
6. Curtis, J. M. et al. *J. Biol. Chem.* **39**, 32967 – 32980 (2012).
7. Doyle, K., and Fitzpatrick, F. A. *J. Biol. Chem.* **285**, 17417 – 17424 (2010).
8. Curtis J. M. et al. *Diabetes* **59**,1132 – 1142 (2010).

Continued from page 24

ous areas of research and career options to demystify the paths for awardees. Students also described their own projects to mentors, other awardees and ASBMB council members during the MAC welcome reception. This scholarly exchange provided an added opportunity for the students and postdoctoral fellows to discuss their work and further extend their professional networks.

Session on careers in industry

Meanwhile, Nestor Concha from GlaxoSmithKline, Garry D. Dotson from the University of Michigan and Lana Saleh of New England BioLabs discussed in the "Jobs in Industry" session those considerations to be made when deciding to enter the industrial arena, including the advantages and disadvantages. Truly capturing the essence of the discussion, Concha described an academic research career as one in which scientists makes long-term commitments to specific subdisciplines and noted that industrial careers allow periodic moves across a number of subfields. In addition, Dotson offered a first-hand account of his transitions from hospital pharmacist to industrial medicinal chemist and then to faculty member at the University of Michigan. Finally, Saleh discussed the value of completing an industrial postdoctoral fellowship. A panel discussion followed the three talks, allowing participants to ask the speakers additional questions. This led to an interesting discussion on ways to become competitive for positions in industry and the apparent lack of effort on the part of industry to hire racial and ethnic minorities for Ph.D.-level positions. It is important that government, academic and industrial agencies work to address the issue of underrepresentation. An excellent article for those interested in industrial careers was published in ASBMB Today in August 2010. (2)

What's next?

The MAC will host a mentoring and grant-writing workshop for biochemistry and molecular biology faculty in their first three years on the tenure track who have not received NSF or National Institutes of Health funding June 27 – 29 in Arlington, Va. Organizers hope the workshop will demystify the grant-application and funding systems at both agencies, promote skills in effective grantsmanship, provide networking opportunities for participants, and provide a platform upon which participants can present their proposal ideas and associated approaches and receive honest and expert feedback from successful faculty mentors and expert grant reviewers and program officers. A website describing the workshop and guidelines for submitting self-nominations can be found at http://www.asbmb.org/grantwriting2013/.

Takita F. Sumter (sumtert@winthrop.edu) is an associate professor of chemistry at Winthrop University.

REFERENCE

1. http://www.asbmb.org/asbmbtoday/asbmbtoday_article.aspx?id=33293
2. http://www.asbmb.org/asbmbtoday/asbmbtoday_article.aspx?id=8744

A new online resource for the outreach community

BY GEOFF HUNT

When it comes to science outreach, one barrier to participation is a lack of information about how to get involved. The irony of this perceived deficit is that there is in fact an (over-)abundance of information available online; however, lacking proper curation, the endless sea of search-engine results can make potential participants feel lost.

To ameliorate this problem, the American Society for Biochemistry and Molecular Biology Public Outreach Committee, which aims to enhance the ability of ASBMB members to participate in science outreach, has been working to develop an outreach website (www.asbmb.org/publicoutreach) that aggregates relevant information on existing outreach programs and resources for prospective and active participants. The website is intended to be an interactive domain — to be used, explored and maintained by anyone with an interest in outreach.

The site has several key features:

Informational resources

Ever wondered how to run your own science café? Curious about how to get financial support for your outreach program? The website has an ever-growing database of informational resources that serve to spread knowledge about all things outreach, such as ideas for outreach projects and how-to guides developed by the Public Outreach Committee. You also can find links to online outreach resources, such as Informal Commons (a massive compendium of outreach projects, materials and case studies), along with listings of other organizations that share ASBMB's dedication to outreach, including the Science Festival Alliance and the Coalition on the Public Understanding of Science. Also available is a list of funding sources from both the public and private sectors, which includes descriptions of outreach-oriented grant programs. Finally, the website homepage features a continually updated stream of outreach news.

Local outreach activities

Looking for outreach opportunities in your community? Go to our "Activities" page, which has a thorough, state-by-state listing of groups, institutions and outreach events complete with addresses and contact information, all gathered on an interactive map. You can zoom in on different locations, browse individual programs and jump from state to state, while the sidebar listing provides more in-depth details. Know of a program that is missing from the map? That is where the next section comes in.

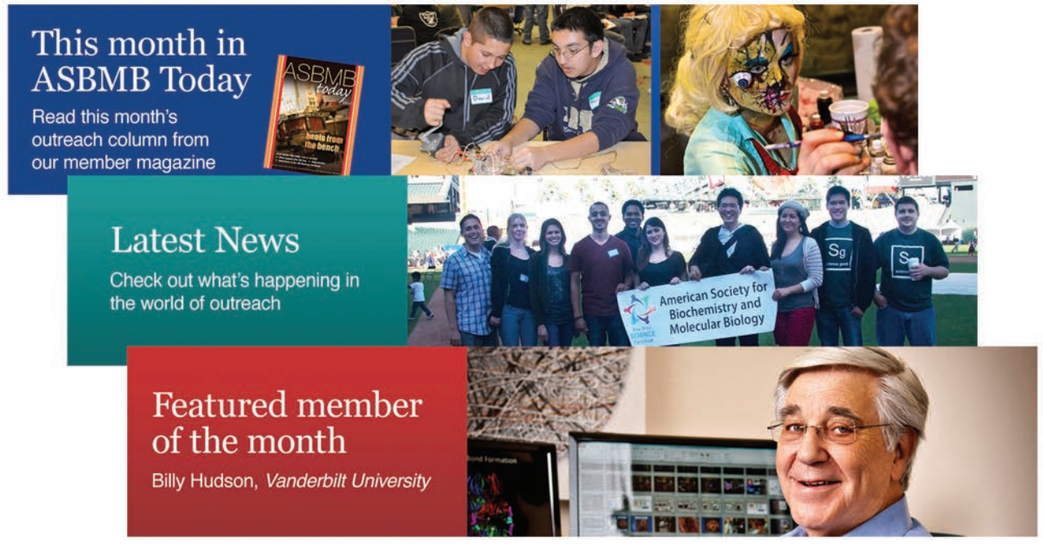
Community

The most important aspect of the entire outreach website is the "Community" page. There, registered users can share ideas, discuss best practices and contribute their knowledge and resources. The "Community" page is designed as a wiki, meaning that users can create editable content to be distributed and viewed by the entire community. The committee's goal for this section, and indeed the whole website, is to engender a dynamic, engaged community that provides educational resources and insightful feedback about all things outreach.

Additionally, users can upload their own outreach events, programs and activities, which will appear on both the "Activities" map and a sortable, state-by-state calendar available to registered users. This editing feature will ensure the website contains the most up-to-date information about ongoing outreach opportunities and permit interested individuals to identify and connect with peers in their communities. There is also a discussion forum that will keep the conversation going online.

Public Outreach Committee overview

To find out how the Public Outreach Committee works, take a look at the "About" pages, which provide overviews of the committee's aims, vision and organization.



There are also profiles of members of the Public Outreach Committee, including summaries of the outreach projects with which they are personally involved.

As the community grows, all these features will continue to improve. Moreover, as the Public Outreach Committee expands its programming, the website will serve as the central resource for members of the ASBMB community who are involved with outreach, connecting them to others in the field.

However, this website will reach its full potential only when there is full buy-in from the entire ASBMB community. The committee invites you to check out the features and let us know what you think. We welcome (and expect) feedback so that the site can be as useful and helpful as possible.

So go online, sign up and become part of the discussion!

Geoff Hunt (ghunt@asbmb.org) is ASBMB's outreach coordinator. Follow him on Twitter at www.twitter.com/goodbyeshoe.

Do you have a fledgling outreach program that needs help to get up and running? Check out our Outreach Seed Grant Program, proudly sponsored by the ASBMB Public Outreach Committee. Successful applicants receive up to $2,000 per year to establish innovative programs in local communities. Applications are due Sept. 1. Details and instructions can be found our website: **www.asbmb.org/publicoutreach.**

"Rap" and "PBS" are not usually terms that share the same sentence. So when the media outlet announced a science rap contest, ASBMB just had to participate. Taking inspiration from our Experimental Biology 2013 mascot, Muhammad Allele, ASBMB staffers put together a video paying homage to the knockout mouse. Check out our entry, "Knockout Mouse in Ya House," which won an honorable mention, on our YouTube channel: **www.youtube.com/asbmbio.**

Leaving the bench and finding the path less discussed but well-traveled

BY KRISTINA WASSON–BLADER

When I was in 10th grade, I fell in love with biology. I marveled at how biological systems worked: how a seemingly simple single cell could be so complex and communicate to other cells. By the end of high school, I knew studying biology was for me, and I sought an undergraduate program that allowed me to do just that.

I entered college in 1987 with a major in biology. In my senior year, I performed an independent research project, which further solidified my career choice. But I wasn't sure whether I wanted to spend another five years in school, so I decided to enroll in a master's program in biology. In addition to taking classes, I was required to perform independent research and write a thesis. My thesis adviser helped me choose a project and get started but then left for a six-month sabbatical in Australia. This was just before email communications began, so I was basically left alone in his lab during the data-generating stage of my project. This taught me self-sufficiency in the lab — no one was there to help troubleshoot problems or to ensure I had everything I needed for my experiments.

It was during this time — alone in the lab — that I realized that a long-term career in science was for me. I began to look into Ph.D. programs that would provide me with the scientific training that I needed to become an independent investigator. I acquired that training at the University of Alabama at Birmingham's biology department.

Realizing I needed molecular biology experience to be a successful scientist, I sought a postdoctoral fellowship in molecular biology; however, two years into my fellowship, I fell out of love with science, at least with the daily tasks of bench research.

During my doctoral studies, alternative careers in science were not discussed, and we definitely weren't trained for them: We were all supposed to be on the path to becoming independent scientists. Leaving academia, I found having a Ph.D. put me at a disadvantage; I had very little work experience, but I did have writing experience. I had written several papers and many abstracts during my graduate studies, and I understood how scientists think.

The more I learned about a career in science writing, the more I felt that love for science returning. I was a bit overwhelmed by the opportunities for science writing: science journalism, marketing writing, technical writing, writing for a pharmaceutical company and many more. But each of these niches also required experience.

I decided to start with a journalism course. During one of the classes, the reporter teaching the class explained how she was on deadline to get a story about an accident that had just occurred on the Bay Bridge in San Francisco. Because of where the accident was located on the bridge and where the traffic had stopped, she had to run across a portion of the bridge and jump the yellow crime-scene tape to interview a policeman working the accident. At this point, I realized I was too introverted to be a journalist.

Next, I found an entry-level job in the marketing department at a biotechnology company. This job gave me invaluable experience in the crafts of writing and editing. However, I found myself getting bored, and when I finally ran out of adjectives (at least those that could adequately explain the company's products) I knew it was time to move on.

Next up was technical writing. I found a job at a medical-device company where I would be helping the in-house scientists write manuscripts for publication. Unfortunately, I only stayed for a year at this job, because my family moved to Oklahoma.

The opportunities for a science-writing career in Oklahoma, however, looked bleak: No pharmaceutical companies were located in Oklahoma. Naively, I started freelancing with only one contact. After joining the American Medical Writers Association that same year, I learned from more established writers that freelance science writing was difficult, if next to impossible, to start doing with little experience, few nonproprietary writing samples and one business contact.

I decided I was up for the challenge. I attended as many continuing-education courses as I could, refreshing by basic grammar skills and learning effective communication skills. I became a certified editor in life sciences through the Board of Editors in the Life Sciences (BELS.org). I also learned how to run a business. I sought experts in accounting for small businesses, writing contracts and designing a website to make better use of my time for running my business.

Because I had little experience, I took any job that came to me. I enjoyed some, but I struggled with others. I liked the flexibility the freelancing offered me, but I worked based on my clients' schedules — often on weekends and evenings to get jobs done. I worked through many vacations because I didn't want to refuse a job.

However, I realized that to be a successful freelancer I would have to find more adjectives to use, but this time they would have be about my work, and that was even harder for me, as an introvert, to do. Marketing my business took as much time as, if not more than, the writing and editing work that I enjoyed doing. I relied heavily on recommendations from one client to another to expand my business. My client list and network grew slowly.

After freelancing for about five years, I finally found my science niche: helping scientists effectively communicate their science. Also during this time I established a professional relationship with a local university to edit their scientists' grant proposals and recently was hired through its Office of Research Administration as a science editor. I still continue to do the editing and writing work that I love but am looking forward to my first paid vacation, during which I will be shutting off my phone and email and leaving my laptop at home.

Through attending AMWA's annual conferences, I have met many individuals like myself who started on the path to become independent investigators but found their paths changing to writing about science and medicine.

Kristina Wasson-Blader is a science editor at The University of Oklahoma Health Sciences Center.

open channels

"With a lot of help from my friends," May 2013: Many thanks to Dr. (Christine) Guthrie for this honest and courageous article. It is very nice, as she discovered, to hear that others in the field face these challenges that so many of us face and will face and that they can still be successful in the midst of that. I appreciate hearing a very honest and open account of challenges that can arise during one's career (also kudos to this entire article series). Also great to hear there is a supportive community out there.

– ANGELA SCHLEGEL, UNIVERSITY OF ARIZONA

"The quiet creep of Alzheimer's disease," April 2013: A paper published in 2011 indicates that taking two 220 mg naproxen tablets every day after age 70 substantially diminishes the development of Alzheimer's disease, but only in asymptomatic individuals after two to three years on this regimen. By contrast, NSAIDs including naproxen had an adverse effect on patients with signs of AD pathogenesis, including those at the very early stages of cognitive impairment. Unfortunately, this trial (ADAPT) was not continued as long as it should have been because of health concerns about the cardiotoxic effects of one of the NSAIDs undergoing testing (celecoxib, Celebrex). However, clearly anyone with a family history of early-onset Alzheimer's disease or over the age of 60 should definitely consider taking daily naproxen as a preventive measure as long as no cognitive defects are already apparent, and they have the consent of their physician. Naproxen has a good overall safety profile and is available over the counter in the United States (Aleve). However, like all NSAIDs that block cyclooxygenase I (COX-1), there are known side effects, and it might not be possible for some individuals to tolerate this regimen.

CONFLICTS OF INTEREST: None. I do not work for any company that sells naproxen, nor do I own stock or give lectures for such companies. In summary, I do not derive any benefit whatsoever from the sale of naproxen. I am only concerned about those who are affected by this awful disease.

REFERENCE: Breitner, J.C. et al. Extended results of the Alzheimer's disease anti-inflammatory prevention trial. Alheimer's and Dementia 7, 402-411 (2011).

– GARY CLARK, UNIVERSITY OF MISSOURI SCHOOL OF MEDICINE

jbc Journal of Biological Chemistry podcasts

JBC podcasts allow readers to get to know the scientists behind the journal's Papers of the Week, thematic minireview series and more. To keep up with the podcasts, sign up for the RSS feed or iTunes feed.

Recent Podcasts

Vitamin C's potential role in epigentics

In this podcast, we hear an interview with Gaofeng Wang at the University of Miami. Wang talks about his Paper of the Week: Ascorbate Induces Ten-Eleven Translocation Methylcytosine Dioxygenase-mediated Generation of 5-Hydroxymethylcytosine. The paper delves into how vitamin C may play a role in epigenetics.

REFERENCE: J. Biol. Chem. 2013. 288 (19): 13669–13674.

Gedunin, Hsp90 and p23

In this podcast, we hear an interview with Ahmed Chadli at Georgia Regents University, who talks about his Paper of the Week, Gedunin Inactivates the Co-chaperone p23 Protein Causing Cancer Cell Death by Apoptosis. The paper delves into the molecular mechanism of action of a naturally occurring product that is found in the neem tree, an Indian medicinal plant.

REFERENCE: J. Biol. Chem. 2013. 288 (10): 7313–7325.

Sirtuins and JBC's Best of 2012

In this podcast, we hear a conversation between JBC Associate Editor Joel Gottesfeld and John Denu from the University of Wisconsin–Madison about JBC's Best of 2012 collection. The journal's associate editors chose 22 articles, one for each of the Journal's affinity categories, from more than 4,000 published throughout the year. Denu coauthored two articles selected for the Best of 2012 collection: Regulation of Glycolytic Enzyme Phyospho-glycerate Mutase-1 by Sirt1 Protein-mediated Deacetylation and Sirt3 Protein Deacetylates Isocitrate Dehydroge-nase 2 and Regulates Mitochondrial Redox Status.

REFERENCES: J. Biol. Chem. 2013. 287 (6): 3850–3858
J. Biol. Chem. 2013. 287 (17): 14078–14086.

Visit http://www.jbc.org/site/podcast/ for more information.

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