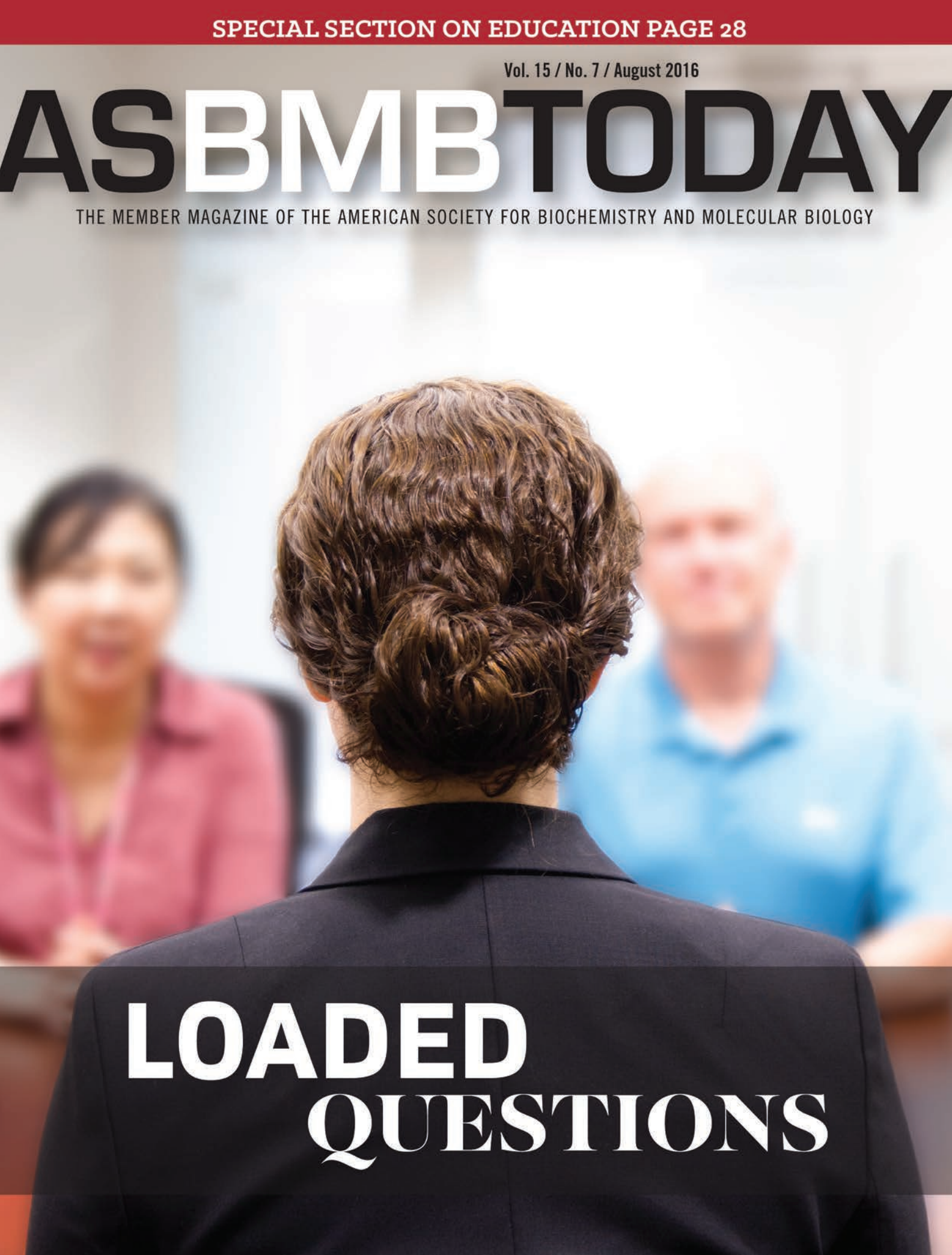
SPECIAL SECTION ON EDUCATION PAGE 28

Vol. 15 / No. 7 / August 2016

ASBMB TODAY

THE MEMBER MAGAZINE OF THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY



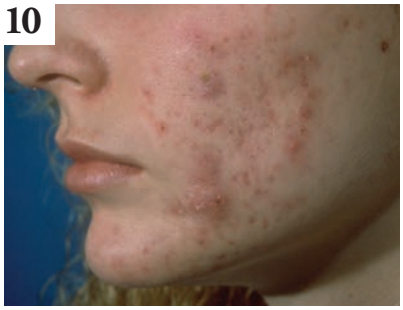
LOADED QUESTIONS

CONTENTS

NEWS

9

10



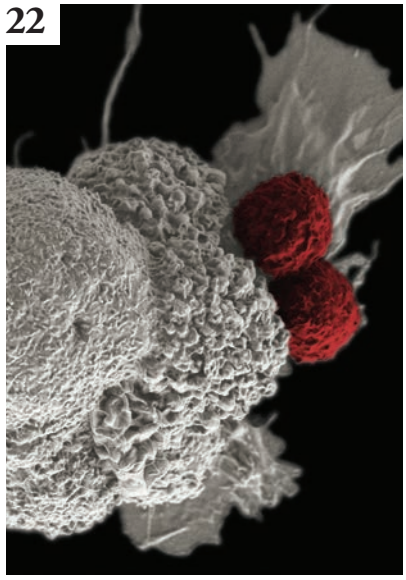
FEATURES

12

Illegal questions during interviews derail recuitment of women in academia.

Photo by Emily Huff.

22



PERSPECTIVES

52

TRANSITION STATES

ASBMBTODAY
THE MEMBER MAGAZINE OF THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

ASBMB
American Society for Biochemistry and Molecular Biology
www.asbmb.org/asbmbtoday
PRINT ISSN 2372-0409

Hanging out with friends

The two stories I wrote for this month's issue of ASBMB Today were born out of tips from scientist friends.

The Q&A I did with Christine Pfund at the University of Wisconsin-Madison on mentoring came out of a lunchtime break with a friend at a nail salon. As we settled into pedicure chairs, my friend, who is an investigator at the National Institutes of Health, and I started to chat about recent conferences and talks we had attended.

My friend mentioned a talk she had heard by Pfund in which Pfund described the interesting work she and her colleagues were doing in making mentoring in the sciences more effective. I sensed Pfund would make a great person to interview and learn more about a critical aspect of the scientific enterprise.

The second story is the magazine's cover story. It's about the inappropriate and illegal questions that get asked of female job candidates during hiring for tenure-track faculty positions. That story came to me during a happy hour with two other girlfriends who, like my NIH friend, are scientists. As we downed a bottle of sparkling wine at a French bistro, one of my friends started to tell us about her experiences of going on interviews for tenure-track faculty positions. While she had enjoyed visiting most of the places where she was invited to interview, one place stuck out because she had been asked a blatantly illegal question right off the bat. I began to wonder how many women on the academic job market had similar experiences. So I asked around, and others affirmed that the issue deserves attention.

I am telling you this because I want to drive home the point that this magazine is at its best when you share with me and the rest of the ASBMB Today team your experiences. The executive editor of ASBMB Today, Angela Hopp, and I believe that everyone in science — be it an undergraduate student from India attending a small-town American college or a retired scientist in the San Francisco Bay Area — has a story worth telling. By telling us your stories, you help us give voice to the excitement of science, the perseverance needed to chip away at a vexing problem, and the awe and thrill that come when you realize you've observed something for the first time. You also help us highlight the issues that are part and parcel of life as a scientist.

So go on and drop us a line. You can get a hold of me and the rest of the ASBMB Today team by email (asbmbtoday@asbmb.org) or find us on Facebook or Twitter. Tell us about the scientific adventures that you embark on and the directions in which they take you, the notable accomplishments of your colleagues (and your own), and tangle of challenges you face in your profession. Even if you don't have a full-fledged story to share, we love hearing from you, because we never know from where the inspiration for the next ASBMB Today story will come.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the chief science correspondent for the American Society for Biochemistry and Molecular Biology. Follow her on Twitter at twitter.com/rajmukhop.

We're excited, sort of

By Benjamin Corb

The annual appropriations process, through which Congress provides funding for all federal programs, has reached its predictable summertime stall. On paper, the appropriations process is predictable and easy to navigate. The U.S. House and Senate appropriations committees draft spending bills in which they establish the funding levels for the next fiscal year for agencies like the National Institutes of Health and the National Science Foundation. Each chamber of Congress establishes its own funding priorities and levels and approves the spending bills. Then the House and Senate committees work together to negotiate the differences between the two proposals before settling on one final proposal, which is sent to President Barack Obama. The process is called regular order here in Washington. But it is anything but regular.

As you certainly have experienced recently, regular order has not been the standard operating procedure. Congress, over the past decade, has stumbled during the appropriations process, which has resulted in the need for continuing resolutions. The continuing resolutions forgo annual spending plans in favor of simply continuing into the next year with the same funding levels as the previous year. Sometimes those continuing resolutions last a few weeks, long enough to allow Congress to pass one massive spending bill that funds all government programs.

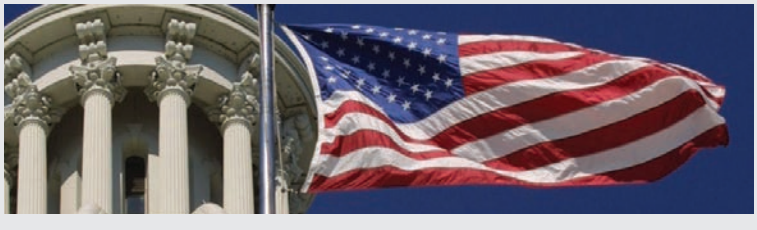
Last year, Congress passed an omnibus spending bill. The NSF saw a modest $120 million increase in fiscal year 2016, and the NIH saw a robust $2 billion increase. A continuing resolution would have rendered those increases impossible, thus reminding us that an omnibus spending bill is better than a continuing resolution.

This year started with promises from Congress that regular order would be followed. Both the House and Senate appropriations committees passed spending bills. The House proposal cuts $57 million from the NSF's budget, while the Senate increases the NSF's budget by $46 million. While the overall proposed budget for the NSF is cut by the House, the research budget actually is proposed to increase by $46 million. For the NIH, the House proposal increases the budget by $1 billion, and the Senate increases it by $2 billion.

If regular order does occur, we have reason to believe the NSF and NIH will fare well. The 114th Congress has been opposed to increases in federal spending, but they have been swayed by advocacy efforts expressing the needs for investments in basic research. The NSF has received modest growth to its research portfolio. On a bipartisan basis, Congress has favored investments in biomedical research at the NIH as exemplified by the proposed increase of upward of a billion dollars. We're excited, because our advocacy efforts are beginning to bear fruit in the form of sustained increases in funding levels.

Our excitement is tempered, though, by the understanding that this is still Washington, and it's an election year. With Congress in recess now, the appropriations process is stalled. With a compressed legislative calendar in the fall resulting from presidential campaigns and the November election, a continuing resolution is probably the only way to avoid a government shutdown in September. Keeping spending levels flat for a portion of fiscal year 2017 will cost our community, because every day, week and month of delay in passage of spending bills for FY17 is a delay in the much-needed proposed increases to our research portfolios. We are optimistic that Congress eventually will pass a spending bill that sets funding levels for FY17 that will increase research dollars at the NIH and the NSF. We just want to see that bill pass sooner rather than later.

Benjamin Corb (bcorb@asbmb.org) is the director of public affairs at the American Society for Biochemistry and Molecular Biology.



Interested in science policy?

Follow our blog for news, analysis and commentary on policy issues affecting scientists, research funding and society. Visit policy.asbmb.org.

2017 annual award winners

ALICE AND C. C. WANG AWARD IN MOLECULAR PARASITOLOGY
David L. Sibley, Washington University School of Medicine in St. Louis

ASBMB AWARD FOR EXEMPLARY CONTRIBUTIONS TO EDUCATION
Erin Dolan, The University of Texas at Austin

ASBMB YOUNG INVESTIGATOR AWARD
Sinisa Urban, Johns Hopkins University School of Medicine

ASBMB–MERCK AWARD
Judith Frydman, Stanford University

AVANTI AWARD IN LIPIDS
Volker Haucke, Leibniz–Institut für Molekulare Pharmakologie

BERT AND NATALIE VALLEE AWARD IN BIOMEDICAL SCIENCE
Ronald Evans, The Salk Institute for Biological Sciences and Howard Hughes Medical Institute

DELANO AWARD FOR COMPUTATIONAL BIOSCIENCES
Brian K. Shoichet, University of California, San Francisco

EARL AND THRESSA STADTMAN DISTINGUISHED SCIENTIST AWARD
Susan S. Taylor, University of California, San Diego

HERBERT TABOR RESEARCH AWARD
Susan Gottesman, National Cancer Institute

MILDRED COHN AWARD IN BIOLOGICAL CHEMISTRY
Wei Yang, National Institute of Diabetes and Digestive and Kidney Diseases

RUTH KIRSCHSTEIN DIVERSITY IN SCIENCE AWARD
Douglas Robinson, Johns Hopkins University School of Medicine

WALTER A. SHAW YOUNG INVESTIGATOR AWARD IN LIPID RESEARCH
Gregory D. Fairn, St. Michael's Hospital

WILLIAM C. ROSE AWARD
William T. Wickner, Dartmouth Medical School

Zeitlinger receives Neaves Award

ZEITLINGER

Julia Zeitlinger, associate investigator at the Stowers Institute for Medical Research in Kansas City, Mo., received the 2015 Neaves Award for her innovative approach to studying genome regulation.

The Neaves Award comes with a two-year, $150,000 prize and supports Stowers researchers who are pursuing high-risk research projects that have the potential to make a broad impact.

Zeitlinger will use the award to refine a technique that gives an accurate picture of how protein factors bind to the genome. She hopes that further work on the technique, called ChIP-nexus, will result in researchers being able to analyze binding in populations of cells too small for other technologies to characterize.

Zeitlinger has been a Pew scholar and a recipient of the National Institutes of Health New Innovator Award.

Pieter Dorrestein named Blavatnik award finalist

DORRESTEIN

Pieter Dorrestein at the University of California, San Diego, was chosen as a 2016 Blavatnik National Award finalist in chemistry.

The Blavatnik National Awards, administered by the New York Academy of Sciences, celebrate young researchers who are driving scientific innovation and investigating complex scientific questions. Finalists are selected from more than 300 nominees representing the three disciplines of chemistry, physical sciences and engineering, and life sciences. Finalists compete for three national laureate

spots, one for each discipline, worth $250,000.

Dorrestein uses mass spectrometry techniques to study microbes and microbial communities. A recipient of the Beckman, Hearst Foundation, PhRMA Foundation Research and Abel Pharmacology awards, Dorrestein is the director of the Collaborative Mass Spectrometry Innovation Center. He was named a scientist to watch by the magazine The Scientist while Nature defined him as "the man who can map the chemicals all over your body."

Written by Courtney Chandler

Cohen named Weill division chief

COHEN

David E. Cohen has been named Vincent Astor distinguished professor of medicine and chief of the division of gastroenterology and hepatology at the Weill Cornell Medical College.

Cohen, whose appointment began in July, will support the division of gastroenterology and hepatology's mission to provide excellence in clinical care and education and grow the research programs of the department. Formerly director of hepatology at Brigham and Women's Hospital, Robert H. Ebert professor of medicine at Harvard Medical School and director of the Harvard–MIT division of health sciences and technology, Cohen is a physician-scientist whose research examines the molecular regulation of hepatic lipid and glucose metabolism.

Greider and Marletta elected to APS

Carol W. Greider and Michael A. Marletta have been elected to the American Philosophical Society. Founded in 1743 by Benjamin Franklin, the American Philosophical Society is a scholarly organization that promotes useful knowledge in the sciences and humanities. The organization supports research and discovery through grants, fellowships and prizes and encourages fellowship among scientists, humanists and civic leaders.

Each year, the APS nominates new members from a wide variety of scholarly and academic disciplines who have distinguished themselves through their intellectual achievements.

GREIDER

Greider is a Daniel Nathans Professor, Bloomberg Distinguished Professor, and director of molecular biology and genetics at John Hopkins University School of Medicine. A renowned researcher in the field of genetics, Greider won a Nobel Prize in 2009 for discovering how chromosomes are protected by telomeres and the enzyme telomerase.

MARLETTA

Marletta is a professor of chemistry and molecular and cell biology and holds the CH and Annie Li Chair in the molecular biology of diseases at the University of California, Berkeley. Marletta's lab studies protein function and enzyme reaction mechanisms. Last year he was awarded the Alfred Bader Award in Bioinorganic or Bioorganic Chemistry for his research accomplishments.

Steven co-authors textbook

STEVEN

Alasdair Steven is co-author of the new book "Molecular Biology of Assemblies and Machines."

Published by Garland Science and intended for advanced undergraduates, graduate students and researchers in biochemistry, structural biology, molecular biology, biophysics, cell biology and microbiology, the textbook explores the structures of macromolecular complexes and how they assemble and interact. Steven and his co-author examine molecular mechanisms involving individual macromolecules such as proteins, RNA and DNA, and cells and organelles.

The current editor-in-chief of the Journal of Structural Biology, Steven is a senior investigator in the Laboratory of Structural Biology Research at the National Institute of Arthritis, Musculoskeletal and Skin Diseases, where he leads a team that explores the structure–function–assembly relationships of macromolecular complexes by cryo-electron microscopy.

Huganir named president of Society of Neuroscience

HUGANIR

Richard Huganir, professor and director for the department of neuroscience and professor of biological chemistry and pharmacology and molecular sciences at the Johns Hopkins University School of Medicine, has been elected president of the Society for Neuroscience. The SfN is the world's largest organization of scientists and physicians who study the brain and nervous system.

Huganir heads a lab at Hopkins focused on the mechanisms that regulate synaptic transmission and synaptic plasticity. As director of the Kavli Neuroscience Discovery Institute at Johns Hopkins and co-director of the Johns Hopkins Brain Science Institute, Huganir will use his leadership experience to further the society's mission to promote and advance neuroscience. His term begins in November.

Written by Erik Chaulk

Please congratulate and welcome new ASBMB officials and committee members!

Council:

Victoria DeRose
University of Oregon

Jennifer DuBois
Montana State University

Celia Schiffer
University of Massachusetts Medical School

Finance Committee:

Joan Conaway
Stowers Institute for Medical Research

James Stull
University of Texas Southwestern Medical Center

Nominating Committee:

Alexandra Newton
University of California San Diego

Publications Committee:

Andrew Emili
University of Toronto

Tanya Paull
The University of Texas at Austin

Sandra Weller
University of Connecticut Health Center

Public Affairs Advisory Committee:

Susan J, Baserga
Yale University

Susan L. Forsburg
University of Southern California

Katherine L. Friedman
Vanderbilt University

Marina Ramirez–Alvarado
Mayo Clinic

Education and Professional Development Committee:

Kathleen H. Goss
University of Chicago Medicine Comprehensive Cancer Center

Rita-Marie T. McFadden
University of Kansas

Tomi Sawyer
Merck Research Laboratories

Public Outreach Committee:

Edwin Li
Saint Joseph's University

Stuart Ravnik
University of Texas Southwestern Medical Center

Richard J. Havel (1925 – 2016)

Richard "Dick" J. Havel, former director of the Cardiovascular Research Institute at the University of California, San Francisco, died in April in Greenbrae, Calif. He was 91.

Havel contributed to the emergence of the field of lipid metabolism both as an institute director and head of the Specialized Center for Research in Arteriosclerosis, a National Institutes of Health-supported group of laboratories that brought an array of technical approaches to lipid research.

Born in Seattle, Wash., Havel attended Reed College and went on to obtain his M.S. and M.D. from the University of Oregon Medical School in 1949. He completed his residency in medicine at Cornell University, serving as chief resident from 1952 to 1953. He then worked at the National Institutes of Health until 1956 before moving to UCSF to join the founding faculty of the Cardiovascular Research Institute.

While at the NIH, Havel developed the technique of quantitative ultracentrifugation, which remains a standard technique in the field to this day. It allowed the discrimination of clinical phenotypes and provided a basis for understanding lipid transport in health and disease. As a result of this work, Havel became the first to define the genetic disorder of lipoprotein lipase deficiency.

Richard J. Havel

Havel succeeded Julius Comroe as director of the Cardiovascular Research Institute and later become interim director until his retirement in 1996. From 1971 until 1996, he also served as director of the NIH's Specialized Center for Research in Arteriosclerosis, or SCOR.

Under his direction, SCOR investigators created a large body of integrated discovery on lipoprotein biology and its clinical significance, including the multistaged formation of triglyceride-rich lipoproteins, cholesterol efflux, structural and functional studies of HDL, and one of the first demonstrations that reducing the levels of atherogenic lipoproteins would result in diminution of the volume of arterial plaques.

Havel was elected to the National Academy of Sciences in 1983 and the Institute of Medicine in 1989. He won the Bristol Myers Squibb/Mead Johnson Award for Distinguished Achievement in Nutrition Research and a Distinguished Achievement Award from the American Heart Association Council on Arteriosclerosis. He served as editor-in-chief of the Journal of Lipid Research from 1972 to 1975 and as chair of its advisory board from 1982 to 1992.

Part of Havel's legacy will be the careers of a large number of investigators who trained in his laboratory and with the SCOR group, who are now distinguished academicians in many countries. Havel leaves behind his wife, four children and three grandchildren.

This is a condensed version of an obituary that first appeared in the Journal of Lipid Research. It was written by John P. Kane and Mary J. Malloy at the University of California, San Francisco.

Never a rest for arrestins

By Caitlin Hanlon

Much like actors, proteins can be underestimated and their complexity ignored once they've been pigeonholed into a role. Such was the case for the beta-arrestin family. Concisely named for their function, beta-arrestins were long thought to only have one purpose: to arrest G–protein–coupled receptor, or GPCR, signaling. But recent research has widened their range of roles and shown that this widely expressed protein family does much more than its name suggests.

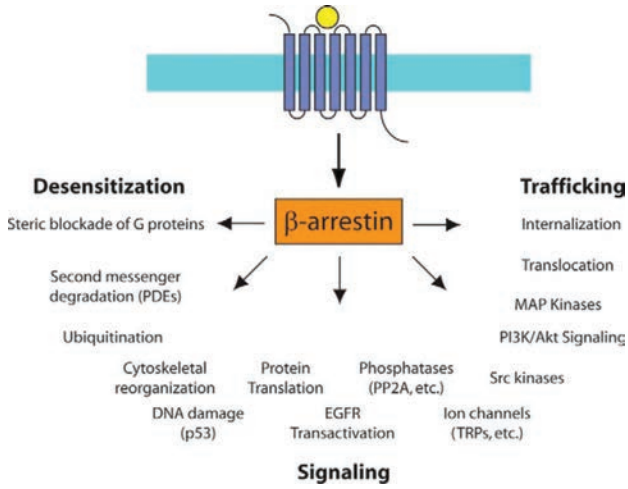
In the recent **Journal of Biological Chemistry** minireview "The β-arrestins: multifunctional regulators of G protein-coupled receptors," Jeffrey Smith and Sudarshan Rajagopal at Duke University Medical Center discuss beta-arrestins' newly identified roles as hubs of complex cellular signaling.

After a GPCR is activated through ligand binding, the receptor adopts an "on" position and begins to signal to downstream pathways through G proteins. This signaling continues until the receptor is desensitized and removed from the membrane through the active transport process of endocytosis. To facilitate receptor endocytosis, active GPCRs first are phosphorylated by G–protein receptor kinases. Beta-arrestins then bind to the phosphorylated GPCRs and mitigate receptor signaling in two ways. First, beta-arrestin desensitizes the receptor by physically blocking it from activating more downstream effectors. Then beta-arrestin acts as a scaffold for the protein coat of clathrin, which drives the internalization of the receptor. Most GPCRs require beta-arrestins for internalization.

For many years, this curtailing of GPCR signaling was thought to be beta-arrestins' sole role. But we now know that the beta-arrestins are more than adapters between phosphorylated receptors and clathrin. Over the past decade, beta-arrestins have been discovered to interact with many different types of proteins and consequently several different signaling pathways. For example, beta-arrestins can bind both ubiquitin ligases and deubiquitinating enzymes, thereby promoting ubiquitin signaling pathways, receptor degradation or receptor recycling. In fact, some ligands preferentially signal through beta-arrestin-related pathways, a process known as beta-arrestin biased agonism. Certain ligands specifically promote GPCR phosphorylation and beta-arrestin binding, regardless of G–protein activation. These ligands cause the receptor to select beta-arrestin-based signaling instead of conventional G–protein signaling. In this way, beta-arrestins greatly expand the world of GPCR signaling instead of diminishing it.

Compared with the hundreds of GPCRs in a cell, there are only two beta-arrestins in humans. So how are beta-arrestins able to choose which pathway to activate for a specific receptor? Smith and Rajagopal describe how beta-arrestins are able to act as interpreters for distinct patterns of receptor phosphorylation. Different ligands cause different phosphorylation patterns (barcodes) on the receptor. By "reading" this phosphorylation barcode, beta-arrestins then activate different downstream signaling pathways.

Many specifics about this barcode are not yet fully understood, but this unique role of beta-arrestins potentially positions them to play a major new role in the area of drug development. GPCRs already are widely targeted by various pharmaceuticals, and identifying new ligands or small molecules that can influence how beta-arrestins interact with receptors will be crucial for understanding signaling in disease states.



The spectrum of beta-arrestin-mediated signaling. Beta-arrestins regulate a wide array of pathways downstream of GPCRs. PDEs, phosphodiesterases; EGFR, EGF receptor; PP2A, protein phosphatase 2A; TRP, transient receptor potential.

Caitlin Hanlon (chanlon3@jhmi.edu) earned a B.S. from Ursinus College and a Ph.D. from the department of cell biology at the Johns Hopkins School of Medicine.

The most complete catalog of proteins in king cobra venom yet

By Rajendrani Mukhopadhyay

Seven milliliters of a king cobra's venom can kill 20 people. But what exactly is in the snake's venom? Researchers have pursued that question for decades.

Now, in a paper published in the journal **Molecular & Cellular Proteomics**, a team of researchers reveals a detailed account of the proteins in the venom of king cobras. "I believe this study to be one of the most complete and precise catalogues of proteins in a venom yet obtained," states Neil Kelleher at Northwestern University, one of the study's senior investigators.

Snake venoms always have intrigued scientists, because they "have a rich diversity of biological activities," says Kelleher's collaborator Gilberto Domont at Universidade Federal do Rio de Janeiro in Brazil. Among other things, venoms contain various proteases, lipases, nerve-growth factors and enzyme inhibitors. Besides understanding how venoms function, researchers want to develop better antidotes to snake venom and identify molecules from venom that can be exploited as drugs, such as painkillers, anticlotting medications and blood pressure treatments. Domont points to captopril, a drug now commonly used to treat high blood pressure and heart failure. It was derived from a molecule found in the venom of a poisonous Brazilian viper.

Although the venom of the king cobra, the largest venomous snake in the world, which can stretch up to 13 feet, has been analyzed previously, questions persist about the venom. How do the sequences of the toxins evolutionarily vary? How do some post-translational modifications on proteins make the venom lethal? But to answer these questions, researchers need a proper count of the proteins in king cobra venom.

THAI NATIONAL PARKS

King cobra at Kaeng Krachan National Park in Thailand.

The advent of proteomics has allowed scientists to survey the rich diversity of proteins in a given sample. There are different approaches that rely on mass spectrometry to carry out proteomic analyses. One approach is called top-down proteomics. It allows researchers to look at proteins as whole, intact entities. In the more conventional approach, called bottom-up proteomics, proteins are cut into bite-sized fragments for analysis.

In bottom-up proteomics, researchers have to use computer algorithms to stitch back together protein fragments identified by mass spectrometry. Top-down proteomics avoids this problem. Its biggest advantage is that it can capture variations within the proteins as well as post-translational modifications.

Kelleher's group is one of the leaders in developing top-down proteomics, so that's what the investigators decided to use to analyze king cobra venom. Domont, Kelleher, Domont's graduate student, Rafael Melani, and colleagues obtained venom from two Malaysian king cobras held at the Kentucky Reptile Zoo. They analyzed the venom by top-down proteomics in two modes, denatured and native. In the denatured mode, the protein complexes were taken apart; in the native mode, the venom was kept as is so the protein complexes remained intact.

The investigators identified 113 proteins in king cobra venom as well as their post-translational modifications. Only 17 proteins had been known in king cobra venom.

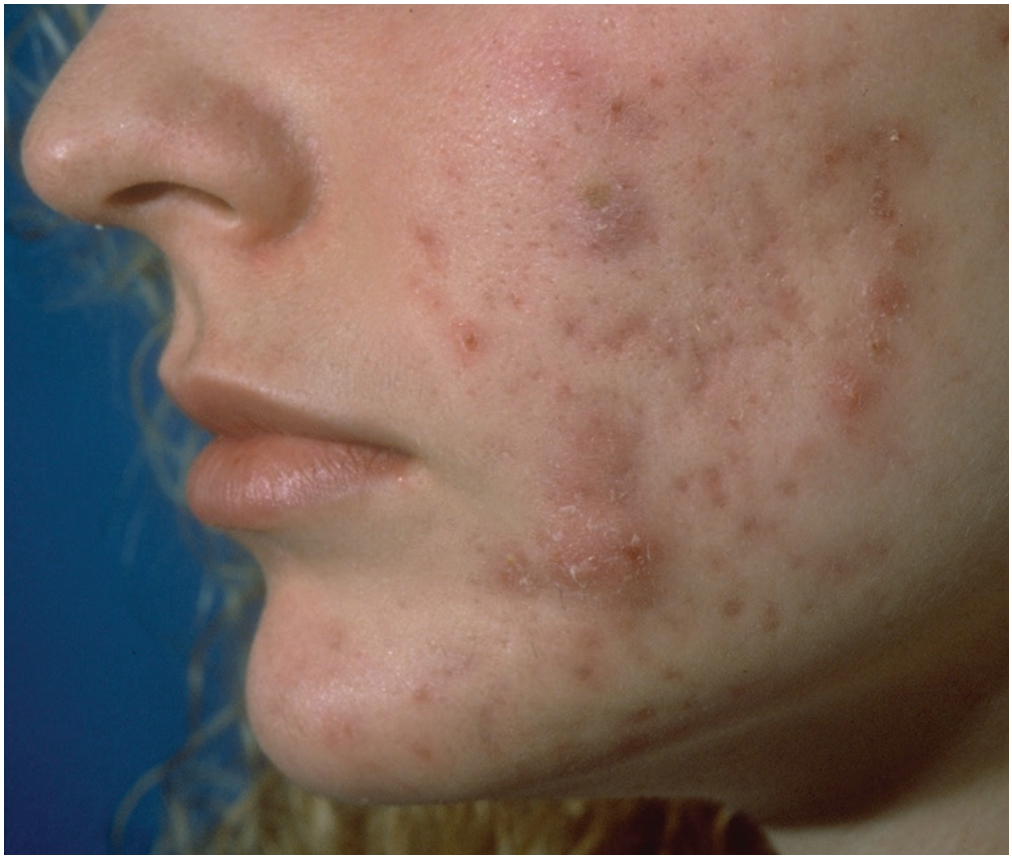
Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the chief science correspondent for the American Society for Biochemistry and Molecular Biology. Follow her on Twitter at twitter.com/rajmukhop.

Figuring out fats in zits

By Rajendrani Mukhopadhyay

One of the many insults of adolescence is pimple-speckled skin. Sebum, an oily skin secretion, plays a major role in causing zits. But "the knowledge of what exactly in sebum is responsible for the occurrence of acne is rather limited," says Emanuela Camera at the San Gallicano Dermatologic Institute in Italy.

In a paper recently published in the **Journal of Lipid Research**, Camera and colleagues describe their analysis of the lipids in sebum and report a clue as to how sebum composition might correlate with the severity of acne.



AMERICAN ACADEMY OF DERMATOLOGY

Researchers analyzed some of the fat molecules in acne.

The lipids in sebum "are highly complex and unique," notes Camera. The lipids in human sebum are so diverse that some aren't found in other oily substances in the body or even in other species. The complexity of sebum lipids make them hard to analyze. Researchers are unsure of what they are and how they contribute to skin disorders, such as acne.

For their study, Camera and colleagues, with the help of dermatologists, recruited 61 teenagers. They grouped adolescents, who were almost evenly split between male and female, into those who had acne and those who didn't. The acne group was further subdivided into mild, moderate and severe groups. They asked all the teenagers to stick a special tape onto their foreheads to absorb sebum.

Camera and colleagues then took those tapes and analyzed them by mass spectrometry to see which lipids collected on them. To avoid going on a fishing expedition, the investigators focused on the neutral lipids in sebum. Their data suggested that diacylglycerols were the predominant species among the lipids in acne sebum. There also were fatty acyls, sterols and prenols. Notably, the investigators discovered that higher amounts of diacylglycerols correlated with the more acute cases of acne.

Given that more severe forms of acne can be disfiguring, it's important to understand what causes the skin disorder. Acne can look different from person to person, such as in "white and black heads, papules, pustules, or as a miscellany of them," says Camera, adding that the different ways acne can manifest itself and its varying severity require "a personalized approach. Thus, biomarkers of acne and acne severity can be instrumental in the definition of acne pathogenic mechanisms and indicate novel drug targets."

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the chief science correspondent for the American Society for Biochemistry and Molecular Biology. Follow her on Twitter at twitter.com/rajmukhop.

American Society for Biochemistry and Molecular Biology

ACCREDITATION & ASSESSMENT *for* B.S./B.A. PROGRAMS IN BIOCHEMISTRY & MOLECULAR BIOLOGY

The ASBMB accredits departments and programs offering baccalaureate degrees in biochemistry, molecular biology and other related degrees. Accredited programs gain access to an independently developed and scored examination that leads to the conferral of an ASBMB-certified degree.

There are now more than 50 ASBMB-accredited programs across the US. Recently accredited programs include:

- Presbyterian College
- University of Virginia
- Hunter College of the City University of New York
- Boston University
- Texas A&M University
- University of Arizona
- University of New Mexico
- University of Montana

ASBMB ACCREDITED

Updated application guide now available.

Next application deadline: Oct. 15

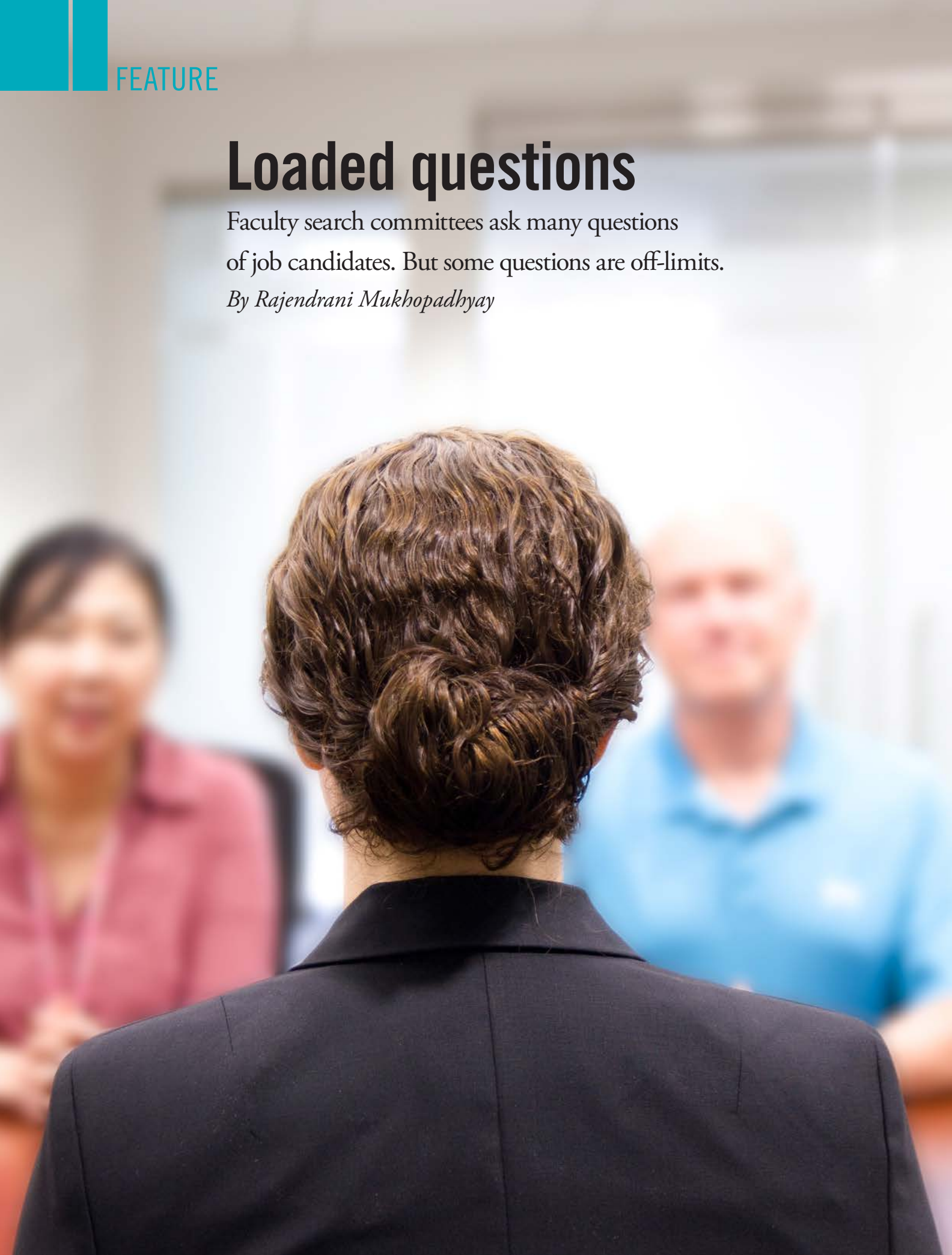
For more information, visit
www.asbmb.org/accreditation

ASBMB
American Society for Biochemistry and Molecular Biology

Loaded questions

Faculty search committees ask many questions of job candidates. But some questions are off-limits.

By Rajendrani Mukhopadhyay



In January, Deborah went on an interview for a tenure-track faculty position at a large, state-run research institution. The two-day interview kicked off with dinner at a restaurant with the department chairman.

As Deborah, a cell biologist who asked that her real name not be used, and the chairman were settling down at the table, the chairman asked her a question. "He asked me whether or not I was in a relationship," says Deborah, who at the time was a postdoctoral fellow with a career-transition grant from the National Institutes of Health.

Taken aback, Deborah revealed that she was married. Then the chairman asked what her husband did for a living. "I gave a very generic answer that my husband's career wasn't really a factor and (that) he was very supportive of me in this important time of my career," she says. "But (the chairman) didn't get my attempt to lay off the conversation. He just persisted with 'No, no, no. What does he do?' It seemed very odd for that to be our first conversation" of the interview.

In May, a paper in the Journal of the American Medical Association reported results from a survey of people who had received NIH career-transition awards between 2006 and 2009. Of the 1,066 respondents, 22 percent of the men reported perceiving or experiencing gender bias in their careers. In contrast, 70 percent of the women did.

According to the Equal Employment Opportunity Commission, Title VII of the Civil Rights Act of 1964 makes it illegal to discriminate against a person on the basis of race, color, religion, national origin or sex (the last one includes pregnancy, gender identity and sexual orientation).

As questions about marital status, as well as the number and ages of children, are frequently used to discriminate against women, they can violate Title VII. Even asking about a spouse's name or employment status and child-care arrangements during an interview could be presented in court as evidence of intent to discriminate.

During a recruiting visit at another university, Deborah attended a dinner with several people, including the chairman of the search committee and a woman from the department head's laboratory. Deborah recalls quietly listening to the conversation about their families. When there was a pause, "the woman turned to me and said, 'Based on our conversation, I take it you don't have children,'" Deborah says. "I looked around, expecting someone to change the subject, but everyone was staring and waiting for my answer."

Put on the spot, Deborah says, she felt obligated to reveal that she didn't have children. "It was very awkward," she says. "I was hoping someone was going to fish me out of that situation, but that never happened."

At times, the questions to female job candidates are outright in their biases. "My first interview for a tenure-track position was at a top-10 university," says Talia, a biochemist with tenure at a state university who requested her real name not be used. "The first day went really well."

However, on the second day, a faculty member pulled out Talia's CV and noted that she had attended a women's college. Talia recounts, "He said, 'Do we have to worry that you are going to be some bra-burning feminist who will make trouble in faculty meetings?'"

And sometimes the questions are insensitive. In February, the story of molecular biologist Jason Lieb's resignation from the University of Chicago broke. Lieb resigned after the university recommended he be fired for sexual misconduct with female graduate students.

Catherine is a postdoctoral fellow with an NIH career-transition award who asked that her real name not to be used. She earned her Ph.D. at the

CONTINUED ON PAGE 14

CONTINUED FROM PAGE 13

University of Chicago in the same department as Lieb but under a different adviser.

During a job interview shortly after the story broke, a male faculty member at the recruiting institution "asked me if I knew Jason Lieb," she says. "I said that he was in the department while I was there or something like that. It was obvious I didn't want to talk about it. The person continued to press for details and really wanted to know about this guy. I felt it was an inappropriate conversation to have with anyone (during an interview), but especially with a woman when the man was found to be having inappropriate sexual conduct with female graduate students."

Deborah, Catherine and Talia say their experiences with illegal and inappropriate questions make the institutions stick in their minds and not in a pleasant way. It's not surprising. For some women, such an experience can be the final straw.

"We asked people who withdrew from (job) searches before or after an offer was made and found that women were likely to do so because they had been asked these questions," says Abigail Stewart, a professor of psychology and women's studies at the University of Michigan. She was the senior author on the JAMA paper and the director of the university's ADVANCE program.

The goals of the ADVANCE program, established in 2001 by the National Science Foundation, are to retain women in academic science and engineering careers and make academic institutions more gender-equitable. While more and more women are obtaining doctoral degrees in science, technology, mathematics

and engineering, they remain significantly underrepresented in almost all positions at academic institutions.

Stewart and others involved with ADVANCE say they aren't aware of any studies of candidates being asked illegal questions during job interviews. But, Stewart says, "We all know of these questions, from having been asked them, having colleagues ask them in our presence, and from students coming back from interviews telling us they were asked them."

Beth Mitchneck agrees that these incidents, although not rigorously tracked, happen frequently. Mitchneck, a faculty member in the University of Arizona's geography department, worked at the NSF for several years to spearhead ADVANCE. She says, "For the people who say, 'I can't believe this is still happening,' their heads are still in the sand."

Caught in an uncomfortable position

Many candidates know what can and cannot be asked of them during interviews. But no matter how aware candidates are, they often feel trapped when asked illegal questions.

"You have the right to call that person out and say, 'That's an illegal question. I don't want to answer that.' But, realistically, how you answer that question determines what happens next," says Alexandra Tracy–Ramirez, an attorney with the law firm HopkinsWay who works with individuals who have experienced harassment or discrimination.

"If you point out that this person is potentially engaged in illegal behavior, that could signal that you're some sort of troublemaker, because you know your rights and responsibilities and may next want to know how much people make so you can fight for pay equity," says Tracy–Ramirez. "But if you do answer, you don't know where that information is going to go or how it's going to be used."

Deborah says objecting to illegal questions was not feasible for her. "It's such a competitive job market," she says. "In my head, I wanted to tell them I wasn't comfortable talking about something personal, but I ran the risk of sounding cold, unapproachable or not willing to play ball."

Departmental culture and due diligence

Academia doesn't have a common set of guidelines or training on hiring best practices and how to avoid biased or discriminatory questions.

"There's a lot of flexibility in how the whole (hiring) process gets structured from department to department and from institution to institution," says Heather Metcalf, director of research and analysis at the Association for Women in Science. "I've seen departments that have really great written policies and guidance documents … I've seen the 'we have no written policy at all, no kind of guidance, it just happens' (approach)."

Often, it's the head of a department who decides how much effort a department will put into learning about recruiting best practices. The department head might, at minimum, require members of the search committee to attend a training session. However, not placing more attention carries the risk that the department isn't fully aware of how discriminatory questions and biases can crop up during recruitment.

Plus, discrimination laws are complicated. The EEO rules are just the beginning. There's the American Disabilities Act and equal pay laws at the federal level. States and institutions have their own policies regarding what constitutes discrimination against a member of a protected class.

Besides overt discrimination, there are implicit biases that stack against certain candidates. "Everyone has biases, whether they like it or not,"

CONTINUED ON PAGE 16

CONTINUED FROM PAGE 15

says structural biologist Karen Allen at Boston University's chemistry department.

The culture of the department determines how much attention is paid to biases and whether department members are actively creating an environment to mitigate biases over the long run. Everyone interviewed for this story agrees that mitigating people's biases is extremely difficult.

"I'm chairing a high-level, important search committee for my department. Even though I have tried very hard from the very beginning to make it as little of a gendered process as it possibly can be, people are people," says Mitchneck. "When it came down to the actual interviews, the way the people were talking about the candidates was still based on gender. It's so intransigent."

One way to reduce the creep of biases and discrimination is to make sure that the people on a search committee have different backgrounds and perspectives. Allen says, "The best way to avoid bias is to have a mixed group of people on the committee."

She also urges people to think deeply about why they like a particular candidate and to make sure they are not resorting to assumptions and stereotypes.

"You have to make your decisions based on facts. That's a really important thing," says Allen. "When someone on my committee says, 'This guy is great!' I ask, 'Can you please explain why he is great? What makes him great? Is it the number of publications? Is it the proposal? Is it the area that he is suggesting working in?'"

It's not all casual

In the winter of 2014, Alexis Webb went to a small liberal arts college to interview for a science faculty position. Webb, who has a Ph.D. in neuroscience and has completed a postdoctoral fellowship, was looking forward to learning more about the department during a dinner with several female faculty members. Instead, the faculty members "all sat around talking about what their experiences were like, whether they were married and had family, whether they were single at the time they joined the faculty and what dating in the small college town was like," she says. "I felt, to engage in the conversation, I had to talk about very personal aspects of my life with people who were also evaluating whether or not they wanted to hire me for the position."

This incident drives home the point that women as much as men can be part of the problem. "I find a lot of times that women automatically think they cannot be sexist, that they can do no wrong when interacting with other women," says Jennifer Ross, a biophysicist at University of Massachusetts, Amherst, who writes the blog Woman of Science. "That's absolutely not true."

Candidates and hiring managers interviewed for this article report that the illegal and inappropriate questions tend to come up during the social moments of campus interviews, such as meals and receptions. Candidates know that anything they say at any time could get noted in their applications. But social events during recruitment visits are intentionally more casual than sit-down interviews, and faculty members often ask personal questions as they might at gatherings without job candidates.

"Even the people who would never say anything related to personal lives in the interview context can slip up because we convolute social interactions with the interview," says enzymologist Carol Fierke at the University of Michigan, Ann Arbor, who is also a graduate school dean and a vice provost for academic affairs.

And, yet, the more casual moments of an interview are critical. After all, faculty hiring is different from most

CONTINUED ON PAGE 18

Five don't's for introducing a female speaker (and why this matters)

Janina Dill recently wrote a blog post on why it's important to pay attention to how female speakers are introduced. Dill is an assistant professor at the London School of Economics and a research fellow at the Center for Ethics, Law and Armed Conflict at the University of Oxford in the U.K. The post originally appeared in May on the world politics blog "Duck of Minerva." The post has been excerpted here and edited for length:

"She may be a small person, but she has big ideas," states the panel chair by way of introducing one of the most impressive senior scholars in security studies. At a recent conference, a more junior panelist's contribution is prefaced with the chair's observation: "It is hard to believe that such a fragile woman should be an expert in this topic!"

Avoiding gender discrimination when introducing speakers/lecturers/panelists should be as easy as a wink. Why then is the unequal treatment of women in just that situation about as likely as a flood of anxious emails from students the week before an exam?

Panel chairs often fail to paint the picture of a competent professional, instead lingering much longer than in the case of male speakers on the women's physical attributes, age, country of upbringing, family situation and so on. Even well-meaning, jovial endorsements of a woman's nonprofessional attributes — "how nice to see X, Y, Z in a discussion of such a serious topic" — can be distracting at best. At worst, such comments outright undermine the speaker.

So here are five don'ts when introducing a female speaker:

1. Don't mention her looks. That includes her stature. It doesn't matter whether it is a compliment or not. Just don't do it! Really, please don't!

2. Don't mention her age or gender. It is quite possibly obvious and definitely irrelevant.

3. Don't mention other pieces of information that would be useless in determining whether listening to her will be more or less intellectually rewarding than scanning Twitter for the latest celebrity feud. Those irrelevant pieces of information include, but are not limited to where she grew up and how much you like that country, what profession her father had and how that may have sparked her interest in the topic, or that you think her alma mater has a great sports team. It distracts from her professional standing, and you will almost certainly mention those things at the expense of passing on more relevant information to the audience, the kind that you will likely convey about the male speakers on the panel.

4. Don't use double standards. If you call every other speaker by their academic title, it is probably a bad idea to leave out hers. If you call every other speaker by their first and last name (or just last name), you can safely assume that reducing her to her first name will sound odd.

5. Don't call her "Miss." If she does not have an academic title, the go-to alternative is obviously "Ms." For pertinence of information given the context, her marital status is in a category with her shoe size and her favorite Muppet.

The reason this issue deserves attention is not that this is the only/worst form of gender (or other) discrimination out there (obviously not by a long shot) or because everyone who ever called a female speaker "Miss" is a despicable misogynist. If they were, it would be easier to snark back right there and then. Not introducing female scholars as if they were either slightly suspicious anomalies or much appreciated diversions to lighten the mood and improve the decor is crucial because it is one among few steps on an otherwise extraordinarily difficult path to gender equality that is easy to take.

CONTINUED FROM PAGE 16

other types of hiring in that a department is hiring a person potentially for life. So, Fierke says, the more casual parts of an interview are important for gauging if a long-term partnership might be possible. This is also why having a conversation with all of the faculty members about "the questions that derail the recruitment process" is an important one, she says.

Even someone who is not on the search committee but who has a chance to chat with a candidate has to be mindful. Everyone at an institution involved in a campus interview, directly or indirectly, is "acting as a representative for the institution," says Tracy–Ramirez. "If they have engaged, even unwittingly, in discrimination, and someone does find that it was highly offensive and wants to seek some sort of remedy for it, then it's the institution that's responding, not the individual."

One way those who ask illegal or inappropriate questions defend their behavior, Tracy–Ramirez says, is by saying something along the lines of "I just wanted to get some information and make sure the person was a good fit."

But the notion of "good fit" itself is problematic.

As Ron Friedman, author of "The Best Place to Work: The Art and Science of Creating an Extraordinary Workplace," explained in an article in the Harvard Business Review last year: "The idea holds intuitive appeal: When employees share similar attitudes, they're more likely to get along, and more likely they are to produce. Right? Not necessarily. There's a point at which too much similarity can stifle performance. For one, similarity fosters complacency. We get stuck doing things the way we've always done them because no one is challenging us to think differently. Similarity also breeds overconfidence. We overestimate the accuracy of our opinions and invest less effort in our decisions, making errors more common."

Just don't ask

Getting faculty members to stay away from prying personal questions is difficult.

A decade ago, Fierke, Stewart and others, funded on an ADVANCE grant to the University of Michigan, began to raise awareness of how personal questions or even casual conversations about personal lives affect female candidates. For example, a female candidate might interpret questions about her family life as a surreptitious investigation into her true dedication to the job.

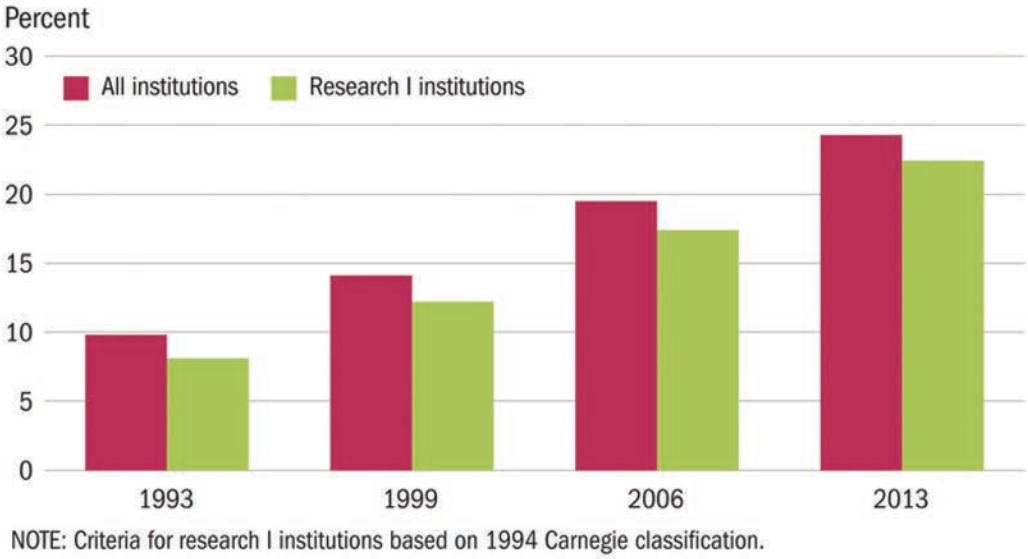
Fierke and colleagues first tried listing the topics that should be off limits during job interviews, such as marital and family statuses. "We got a lot of pushback from the faculty," says Fierke. "For instance, in a place like Ann Arbor, faculty feel that one of our selling points is that we are a great place to live and to raise a family." When people bring this up with candidates, she says, "They feel this is being social and being friendly." Fierke and her colleagues have been trying to convince colleagues that those conversations, no matter how well-intended, can backfire.

Importantly, revealing personal details can hurt women more than men in terms of competitiveness.

"We know men who have families are valued" for having families, says political scientist Sara Rushing at Montana State University, who is a co-director of the university's ADVANCE program. "For women who have families, people worry that their attention will be divided."

Discrimination against mothers has been well-documented. For example, in a 2014 paper in the American Journal of Sociology, researchers at Cornell University found that applications from mothers were evaluated less favorably than applications from

Women as a percentage of full-time, full professors with science, engineering and health doctorates, by employing institutions: 1993-2013



NOTE: Criteria for research I institutions based on 1994 Carnegie classification.

IMAGE COURTESY OF NSF
WOMEN, MINORITIES, AND PERSONS WITH DISABILITIES IN SCIENCE AND ENGINEERING: 2015 (WWW.NSF.GOV.STATISTICS/WMPD/)

women without children as well as men with and without children. The authors noted, "To the extent that mothers are believed to be less committed to the workplace, we argue that employers will subtly discriminate against mothers when making evaluations that affect hiring, promotion and salary decisions. We do not expect that fathers will experience these types of workplace disadvantages since understandings of what it means to be a good father are not seen in our culture as incompatible with understandings of what it means to be a good worker."

The other extreme isn't helpful either. "We've had job candidates say things like, 'My partner is a doctor, so is there a good hospital in town?' And people go, 'I can't answer that!'" says Rushing. "You have to explain that, no, you actually can answer that question if a candidate brings it up."

This is a point that both candidates and hiring committees need to know: If a candidate volunteers personal details, those personal details can be used as discussion points during an interview.

One tactic that people at the University of Michigan's ADVANCE program have found to work is to build an understanding among faculty members of what a candidate thinks and feels when posed with a supposedly innocuous personal question.

The ADVANCE team takes images of a male interviewer and a female candidate. They place speech and thought bubbles to describe what the interviewer is asking and thinking when posing a personal question, such as whether the candidate has children, and thinking about what child-care arrangements can be made to accommodate the candidate. Then they use speech and thought bubbles on the female candidate to show how differently the candidate is interpreting the question and feeling that her professional passion is being judged to take

CONTINUED ON PAGE 20

CONTINUED FROM PAGE 19

a back seat to parenthood.

The speech-and-thought-bubble approach "seems to be much more successful," notes Fierke. She says the approach allows people to understand that the questions about marital status or children, no matter how they are presented, aren't perceived the same way by the candidate. Those questions tend to mar the candidate's experience with the department, and the result can be "a de-recruitment," says Fierke.

Another way to help candidates figure out if an institution and a town will meet their needs is to bring in a third party. Rushing says MSU has had success with its family advocate program. The advocate "meets with all the on-campus job interview candidates. We email the candidates in advance, and we let them know that they'll be having a meeting with a family advocate that is confidential and completely independent from the search," she explains.

Candidates use this 30-minute segment of their interview to learn about how the university supports work–life balance and ask all the questions that they can't ask members of the search committee. "The family advocate has no interest in who's getting hired in this search. Often we don't even remember what search they are part of!" says Rushing, who is one of two family advocates on campus. "We can tell them about dual hiring in Montana State. We can tell them about our modified duties for faculty for family caregiving. We can tell them about our tenure extension policies. They can ask all the questions that they are perhaps not inclined to ask members of the search committee: What are the real estate prices like? What's it like to be gay in Montana?"

Rushing says the family advocate position helps search committees as well. "If they are at all uncomfortable, they can just say, 'This is a great place to work. We have all these great work-life supports, and when you talk to the family advocate, you'll get to learn about what they are,'" she says. "They know that information is getting through, but they don't have to be in charge of conveying it."

The spouse issue

Without fail, everyone who was interviewed for this story brought up the issue of a candidate's spouse. Figuring out if a candidate has a spouse who also requires a job at the institution is one of the biggest hurdles faced during hiring. After all, "83 percent of women in STEM have partners who are academic scientists," notes Rushing.

But in trying to find out if there's a spouse involved, hiring committees can end up asking an illegal question. Unfortunately, there is no way for a candidate to gauge whether having a spouse is a help or hindrance to the hiring process. For example, Ross is certain that when she and her husband were interviewing for faculty positions 10 years ago, one institution bypassed her for another woman who didn't have a spouse who needed a job. So broaching the topic of a spouse is an awkward dance between the candidate and head of the department.

Heads of departments who were interviewed for this story do not condone any personal questions on the first campus interview. However, "the tables turn for one or more top candidates when they are brought back a second or third time and it's made clear to them that the department is really trying to evaluate them for fit and meet their needs," says Charles Brenner, who chairs the biochemistry department at the University of Iowa Carver College of Medicine.

Brenner and William Guggino, the chairman of the physiology department at Johns Hopkins University School of Medicine say that at the subsequent stages of the interview process, if the candidate is still in the running, they shift into courting

mode and try to woo the candidate. The heads of departments need to know if there is anything they need to do to make potential new hires feel welcome. To find out what a new recruit needs, say the department heads, the most logical thing to do is to ask an open-ended question.

"I'll often ask candidates, 'Is there anything that's unusual about your situation that I need to know and that will take me time to put together?'" says Tricia Serio, who chairs the molecular and cellular biology department at the University of Arizona. "Some people will tell me, 'I need this large piece of equipment.' That will require me to try to get resources from the university. Some people tell me, 'I need a job for my spouse.'"

Although Brenner, Guggino and Serio say they prefer to find out sooner if they need to wrangle with another department to accommodate a spouse, it is wrong to ask the candidate about a spouse during the first interview.

However, a candidate can voluntarily bring up the need for a job for a spouse during the first interview. Heads of departments interviewed for this story say they appreciate being told early in the process if they need to find a position for a spouse. "By waiting to reveal that information, it makes it harder for the chair to actually try to do something," says Serio. "A lot of people are hesitant to mention their spouse because they think they won't get the offer because their situation is more complicated. I always tell people if that's the case then it's better for you as well to know that early on."

More aware

Biases and discriminatory moves aren't limited to the campus interviews. (See box on "Five don't's for introducing a female speaker (and why this matters).") Biases and discrimination can pervade the entire hiring process.

Rushing uses the job ad as an example, noting that there is a craft to writing a job description so that it doesn't favor one gender over another. "Women apply when they are 90 percent qualified for a job. Men apply when they are 60 percent qualified," says Rushing. "If you pack your job ad with qualifications, you're not going to get a lot of women."

Then there is the art of interpreting job applications. Rushing says, "You have to understand that women may not toot their own horns in the same way as men. When you read letters of recommendation, you have to understand that the language used to assess a woman may be different from the language used to assess a man. That's the problem with the letter writer, but it's something for which the committee can control."

Experts interviewed for this story do say that with a bit of effort, inappropriate and illegal questions can be prevented. That way, people like Deborah won't encounter such questions at three different institutions out of 10 campus interviews.

The third time, Deborah had gone to the restroom. When she was at the sinks, she was joined by a female member of the search committee, who began to ask her if she had a boyfriend or a husband and what he did for a living. Deborah was unsure if the woman was being friendly or interrogating her to figure out what kind of package the committee would need to put together to hire her.

But Deborah is putting all that behind her. Starting in the fall, she will set up her own research group at a large, private academic institution. And no, it isn't one of the institutions where she was asked about a husband and children.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the chief science correspondent for the American Society for Biochemistry and Molecular Biology. Follow her on Twitter at twitter.com/rajmukhop.

Great hope for immunotherapy

Heavy hitters pony up big bucks on the promise that the approach will be a serious blow to cancer

By Bree Yanagisawa

In the late 1800s, William B. Coley created a concoction out of bacteria and injected it into cancer patients. The first patient treated with what became known as "Coley's Toxins" — a 21-year-old man with an inoperable tumor — was cured of his cancer. Though that might not have been the very first foray into immunotherapy as cancer treatment, it certainly was one of the earliest. Coley spent decades studying how bacterial infections affected cancers, earning him the moniker of the "father of immunotherapy." Since then, the field has come a long way.

Immunotherapy is a means of encouraging a patient's own immune defense mechanisms to do what they're already supposed to — protect the body against bad stuff. Immunotherapy researchers and practitioners have had a recent spate of dramatic successes in the area of cancer treatment. Some members of the public have taken note, and the recent announcements of two new immunotherapy centers focused on cancer research and treatment — the Parker Institute for Cancer Immunotherapy and the Bloomberg–Kimmel Institute for Cancer Immunotherapy — highlight a newfound, popular appreciation for the field.

But why has immunotherapy suddenly become such a darling of cancer research and its funders?

The answer lies in its potential to be a broadly used and durable treatment.

Evasive maneuvers

Almost all cells in the body carry the same DNA and are capable of performing every cellular function. But they don't. Intricate mechanisms regulate cells to ensure each performs only its assigned function.

But cancer cells are shifty. Tough to target, they can activate mechanisms beyond their original function. This way, they can avoid the processes that normally keep them in check.

In a process called immune evasion, cancer cells can hijack the cellular mechanisms of immune tolerance and immune exhaustion. In these mechanisms, the body's T cells learn to recognize the types of signals they should respond to and those they should overlook. Inhibitory receptors on the surface of T cells are a part of immune tolerance and exhaustion. When one T cell wants to let another know it shouldn't be attacked, it displays ligands on its surface that are recognized by the inhibitory receptors of the T cell. When they see these ligands, the T cells put on the brakes.

When this target is on a cancer cell, the cancer is free to continue living and growing inside the body, avoiding the surveillance of the immune system and achieving immune evasion.

Unbraking the system

Immunotherapy aims to counter the tricks cancers use to persist in the body. For example, Herceptin, an antibody that targets a disease-specific pathway in certain breast cancers, is a form of immunotherapy.

Other cell-based immunotherapies, like engineered T cells, allow scientists manually to construct cells that can target each patient's specific cancer. These types of therapies have the potential to treat many patients but are limited by current technologies and the cost.

Enter a focus on therapies that work against immune checkpoint molecules. These agents, which could have treatment potential for a number of diseases, are antibodies designed to release the brakes on the broken immune-tolerance system of which cancer cells often take advantage. The antibodies interfere with the interactions of inhibitory receptors on T cells and their corresponding ligands, effectively alleviating the block that keeps the T cells from responding.

These antibodies work against

CONTINUED ON PAGE 24

Research topics go in and out of fashion. One day everyone is shouting about stem cells, and the next they are excited about the microbiome. Some believe that immunotherapy has the potential to stay in the spotlight.

CONTINUED FROM PAGE 23

specific inhibitory receptors on T cells called PD-1 (or its associated binding partner, PDL-1) and CTLA-4. First made popular in clinical trials for the treatment of melanoma, these antibodies over the past few years have been used to treat many other cancer types, and the patient recovery data have been striking. Patients have responded with long-lasting results in some cancers, including those cancers resistant to other treatments, such as Merkel cell carcinoma, melanoma and non-small cell lung cancer.

The reason for the antibodies' generalizability is simple: PD-1 and CTLA-4 are molecules every person has within his or her body. They aren't individualized therapies like many of the cell-based vaccine strategies that require tailoring in the lab.

"What's exciting about this is it doesn't involve cell therapies," says Melody Swartz at the University of Chicago. "It's just something you inject; it's just an antibody."

Which brings up a critical point with these types of treatments: Researchers are unleashing the body's own exquisitely specific response against cancer.

Unfortunately, though they are potentially generalizable, the strategies currently work in only a subset of patients. Paul Nghiem at the University of Washington Medical School and the Fred Hutchison Cancer Research Center points out that while early results may be encouraging, the therapies targeting PD-1 and CTLA-4 are "dumb." He explains, "We're really just releasing the brakes on this smart system, and we're not smart enough to understand what the system is seeing yet."

In cases where patients don't see lasting improvements with PD-1 and CTLA-4-based treatments, researchers believe it's likely that they haven't formed a significant response to their own cancer before the treatments are administered or their cancer has found an alternate method of side-stepping immune regulation. Determining which patients will respond to these therapies and which will not is an ongoing area of investigation.

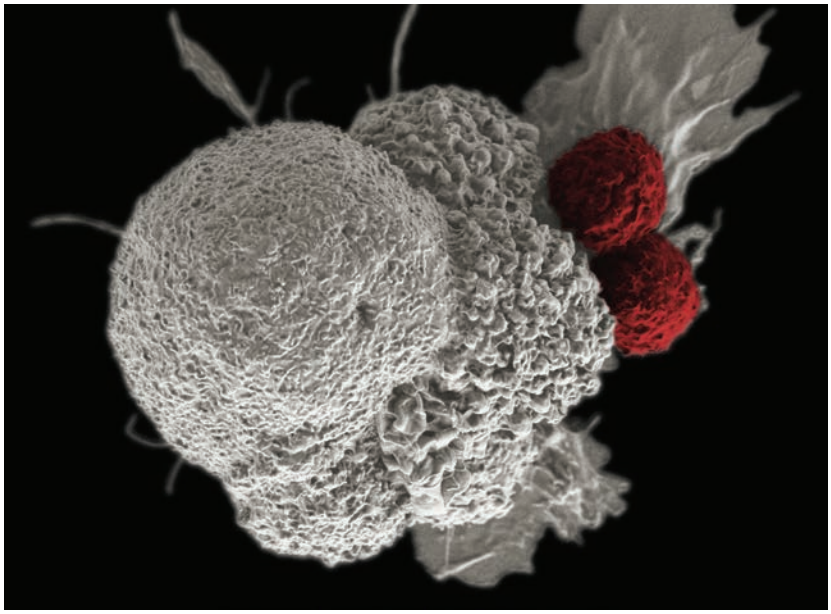
Holding the spotlight

Research topics go in and out of fashion. One day everyone is shouting about stem cells, and the next they are excited about the microbiome. Some believe that immunotherapy has the potential to stay in the spotlight.

To Nghiem, immunotherapy's staying power can be found in the results of numerous clinical trials. Like the important cancer strategies that came before it — surgery, radiation and chemotherapy — it will stick around in an oncologist's treatment repertoire because it does work for many people. "I believe — and I'm certainly not alone — that this is now absolutely clearly planted as one of our pillars of therapy for cancer," says Nghiem.

David Kaufman, executive director of oncology clinical research for Merck Research Laboratories, agrees. "For patients who do have a response to immunotherapy, the benefit is extremely durable," he says. "We haven't seen that kind of durability of response with the vast majority of other anti-cancer agents out there."

Indeed, immunotherapies — and especially those targeting the immune checkpoint blockades — offer some of the most generally applicable treatments seen in cancer therapy in a while. Cancer types in which the immunotherapy Merck drug Keytruda (an anti-PD-1 antibody) has shown clinical promise are in the double digits, says Kaufman. That number



NATIONAL INSTITUTES OF HEALTH

Two T cells attack a cancer cell.

likely will increase as more clinical trials emerge.

More to learn

Though the field of immunotherapy is booming, researchers have a lot to learn. Most of the current clinical trials, though promising, still work in only a few patients. Moreover, the trials are still too new to observe long-term consequences.

There also may be reasons to be cautious about the potential long-term effects of checkpoint inhibitors. Their action is broad, taking the brakes off all immune cells, not just those that target cancer cells. This could lead to autoimmune side effects, as were seen in early clinical trials of anti-CTLA-4 agents. Beyond that, these checkpoint inhibitors likely serve other functions within the body that scientists don't fully understand yet, like their involvement with developing immune memory.

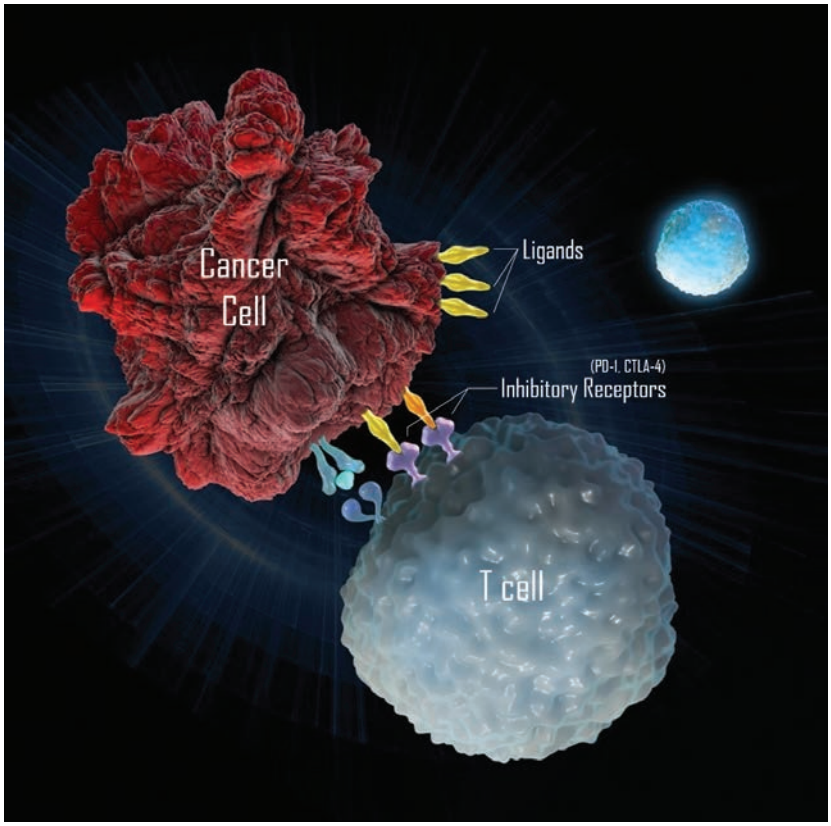
"The immune system is really complicated and highly regulated," warns Swartz, who also is interested in the process of immune regulation and memory. "Checkpoint inhibitors have a lot of promise, but only if we really understand the broader consequences."

The unknown intricacies of the immune system were highlighted in a big way with the closing of a recent clinical trial targeting acute lymphoblastic leukemia. The trial was using engineered T cells as a therapeutic against the disease but had to close after three patients died of excess fluid in their brains. The company responsible for the trial, Juno Therapeutics, is known for their work using immunotherapies to treat cancer. Though these devastating side effects might have been a result of the T cell therapy itself, Juno suspects the problems had more to do with the addition of another drug to the trial, which hadn't been used previously. Clearly, more research is needed to thoroughly understand how these treatments work. And that's where recent large-scale donations can have a big impact.

The future of immunotherapy

Sean Parker, former Facebook president and co-founder of the music sharing site Napster, has promised

CONTINUED ON PAGE 26



MERCK

Immunotherapies can use antibodies against inhibitory receptors on T cells.

CONTINUED FROM PAGE 25

$250 million to create the Parker Institute for Cancer Immunotherapy. Philanthropist Sidney Kimmel and former New York City mayor Michael Bloomberg, along with more than a dozen other supporters, will donate $125 million to fund the new Bloomberg–Kimmel Institute for Cancer Immunotherapy. And both the centers have touted collaboration and streamlining clinical research as major facets of their research plans.

Scientists certainly were collaborating before these large centers started appearing. However, the process of making agreements between pharmaceutical companies, research institutions and clinical centers from a diverse range of locations was tedious, to say the least.

Nghiem, who led clinical trials using Keytruda in Merkel cell carcinoma patients, knows the difficulties of cooperating firsthand and understands how meaningful streamlining the collaborative process in research can be. He says, "If these centers can facilitate those communications and break down those barriers and silos, that's really a key role they can play."

Past is prologue

The immunotherapies of today are nothing like "Coley's Toxins," which, by the way, received their fair share of criticism over the years. But there is one parallel worth noting, and that is the promise of philanthropy.

In October 1890, a year before he reported the first results from his bacterial vaccine experiments, the then-28-year-old surgeon Coley took on a new patient. Bessie Dashiell had a bump on her hand after pinching it between the seats of a Pullman car.

Coley at first suspected Dashiell just had a serious bruise, but her pain worsened. Ultimately, after consulting other experts, he determined that

Dashiell had sarcoma. She agreed to an amputation at the elbow. But the cancer had spread, and she died a few months later.

One of Dashiell's very good friends was John D. Rockefeller Jr., son of the founder of Standard Oil. In his 1998 book "A Commotion in the Blood: Life, Death and the Immune System," Stephen S. Hall described how Dashiell's death influenced Rockefeller's giving philosophy:

"As a young adult, he dedicated much of his philanthropic effort to the conquest of cancer; those efforts began five years after Dashiell's death, in 1896, with dabbling support for William Coley's research …, grew prodigiously with his family's creation of the Rockefeller Institute for Medical Research (now Rockefeller University), and led ultimately to a multimillion-dollar gift that allowed creation of Memorial Hospital (now Memorial Sloan-Kettering Cancer Center) at its present site in New York City. Asked many years later how he became interested in cancer research, Rockefeller replied, 'I think it goes back to Bessie Dashiell … Her death came to me as a great shock.'"

According to a brief biography of Coley written by Edward F. McCarthy in 2006 in the Iowa Orthopaedic Journal, Coley also received in 1902 part of a large grant from the Huntington family for cancer researchers. "This endowment was the first in the United States designated specifically to study cancer," McCarthy wrote.

Relatively speaking, these recent donations aren't huge. When you take into account the billions of dollars spent in any given year on scientific research, these donations can feel like a drop in the bucket.

But some researchers believe focusing on the most clinically relevant research is a smart move. "These initiatives have very thoughtfully targeted this money to the translational research interface, which is where I think donations of that size can really make a significant impact," says Kaufman.

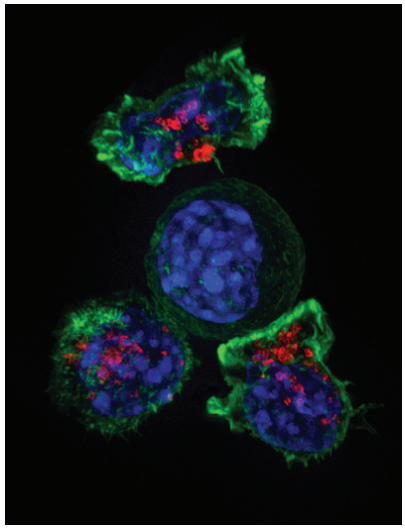


IMAGE BY ALEX RITTER, JENNIFER LIPPINCOTT SCHWARTZ AND GILLIAN GRIFFITHS, NATIONAL INSTITUTES OF HEALTH

A group of T cells (green and red) surround a cancer cell (blue, center).

The centers also draw public attention to the immunotherapy research arena. While some might worry that these high-profile funds might put too much pressure on scientists to find a cure quickly, others remain cautiously optimistic. Even small donations can make big differences when they're used efficiently, and big-name donations might encourage nonscientists to lend their support. As Nghiem says, "Success and attention and giving from big donors will probably even raise all the boats, rather than deflate people's enthusiasm and willingness to support cancer research."

Though Coley's concoctions went in and out of vogue, it's clear that he was a man ahead of his time. And even if the investments by Parker, Kimmel and Bloomberg don't deliver results as striking as are hoped, perhaps one day a future generation will look back and appreciate that they helped get the ball rolling — again.

Bree Yanagisawa was an intern at ASBMB Today when she wrote this story. She is a Ph.D. candidate in pathobiology at the Johns Hopkins School of Medicine. Follow her on Twitter at twitter.com/BreeTalksSci.

Enabling effective mentorship

By Rajendrani Mukhopadhyay

What makes mentorship successful? That's what Christine Pfund studies at the University of Wisconsin–Madison. Pfund is interested in understanding, developing and implementing effective mentor training in science, engineering and medicine.

"We're putting our precious trainees in the hands of folks who are well-intentioned but have had no professional development in the arena (of mentoring). It leaves a lot to chance," she says. "No matter how well-intended someone is and no matter how good they are, there is always room" to improve.

After earning a Ph.D. in cell and molecular biology, Pfund did a postdoctoral stint in the early 2000s in the department of plant pathology. She then switched her focus to improving classroom teaching and research mentoring.

These days, Pfund is one of the principal investigators of the National Research Mentoring Network that was established recently by the National Institutes of Health. She is also director of the new Center for the Improvement of Mentored Experience in Research.

Rajendrani Mukhopadhyay, the chief science correspondent for the American Society for Biochemistry and Molecular Biology, spoke with Pfund to find out more about her research in effective mentoring practices. The interview has been edited for length and clarity.

How did you become interested in mentoring?

I'd always been interested in

PHOTOS PROVIDED BY PFUND

Christine Pfund

improving teaching in the classroom and had been doing a lot of work on the side at UW Madison. About halfway through my postdoc, I started to think about what I really could do in that arena. (At the same time,) UW Madison got two big grants. One was a (National Science Foundation) grant to Robert Mathieu to establish a Center for the Integration of Research, Teaching and Learning, CIRTL, and the other was the (Howard Hughes Medical Institution) professor grant to Jo Handelsman.

I spent the next eight years working for both programs. I was an associate director of the CIRTL program at UW Madison, working primarily on professional development for future faculty in STEM. I was also a co-director of the Wisconsin Program for Scientific Teaching, which came out of Jo Handelsman's HHMI grant. (Author's note: Handelsman currently is the associate director for science at the White House Office of Science and Technology Policy.) The program was on improving teaching in biological sciences, faculty professional development and establishing national summer institutes. A part of that project also was to develop research mentor training.

The research mentor and mentee training continued to grow. We were able to take successes from the original HHMI grant and work with CIRTL and get an NSF grant. Then I moved over to the medical school and started working on adaptations of our approaches for clinical and translational research. I started to get some research grants and worked with social scientists and others to study interventions and start to understand mentoring relationships.

Most recently, I used all of that to become part of the leadership for the National Research Mentoring Network. It allows us to continue the work to understand interventions on a much more national scale and scale up training from evidence-based approaches.

How do you define mentoring?

The across-the-board generic definition of mentoring focuses on it being a collaborative learning relationship that proceeds through purposeful stages over time and has the primary goal of helping the mentees gain the skills and knowledge they need to move on in their chosen careers. That applies to many different kinds of mentoring relationships. It could be a classic research mentoring relationship like we know in the sciences. It can have elements of career coaching. It could be peer mentoring. It could be virtual mentoring with someone who doesn't even have a research relationship with you.

Pfund says people need to reflect on their motivations to mentor.

Are there differences in mentoring between science and other fields?

When we did our adaptation work for some of our mentor–training interventions, we expected, across the STEM disciplines, for things to be very similar. What we found out was that the differences that were most salient were not between, for example, chemistry, physics and math. The differences were in projects. The kind that were theoretically based, where there was a lot of thinking, had a different nature (of mentoring) because you were working together on an idea. It was different than the "we're doing something hands-on together." We found the nature of the work had implications on the relationship.

Imagine when you're in a meeting (with a mentee). You're saying, "You need to have your own idea, and I'll bounce off whether it's a good theoretical idea." Even the nature of those conversations is different from "Here, you need to master these skills, come up with an idea and implement it."

The nature of the work influences the nature of the conversation that happens between mentor and mentee.

How do you make sure you're not creating "mini-mes" (clones of professors) and are paying attention to diversity?

There needs to be, both at the individual mentor–mentee level as well as at a systems level, the recognition to address diversity within these relationships and acknowledge that culture plays a role. How people work, what they think is important, the motivation to do it, the vision they have for what is possible and why it matters — those are all culturally informed. If we don't pay attention to those things within mentoring relationships, research programs and training programs, it's going to continue to privilege the dominant cultural norms. There will not be an acceptance and a benefit from embracing different value orientations (as well as) an allowance for diversification of the workforce.

Diversification of the workforce isn't just about embracing people who have different backgrounds. It's about embracing that they bring different values and orientations to the table. That happens at the individual level and at the organizational level. Mentoring is the place where this needs to be addressed. If individual mentors believe that their role is to create "mini-me's," then who they accept, how they train, what they see as success and what ideas they accept become enormously limited.

How do you get mentors to think about what they are doing?

Mentors need to reflect on what is their motivation for taking on mentees. If their motivation for doing it is so that people can be just like them, then that has a huge influence on who they should be taking. If their idea is to inspire the next generation to do amazing things, then they need to really think about if they have set up the relationship and the environment to empower those successes.

We are putting forth this idea of culturally responsive mentoring. Cultural context matters. We are creating

CONTINUED ON PAGE 30

CONTINUED FROM PAGE 29

training to get mentors to start to work through their own assumptions — not just their biases but their own assumptions about the role that culture plays, how they can create space for that and acknowledge the impact it has. If we continue to force folks to check their culture at the door when they enter the lab, then we also choose to check all the benefits that come with it at the door.

Do you think mentorship in science has changed over time?

It may feel like there's not been a lot of change, but there has been. The conversation alone has changed. The fact that federal agencies are calling for evidence-based mentoring to be part of the training programs — it's a huge change. While it's going to take a long, long time, and we certainly aren't anywhere near where we need to be in order to capitalize on the investment, the needle has moved. I want to respect the people who feel like it hasn't moved enough and that there is an enormous amount of work to do. (But) there has been a lot of movement in the last decade.

I should have asked this earlier: What is the payoff of mentorship?

There is a lot of research out there that has linked strong mentorship to things like enhanced scientific identity, a sense of belonging, persistence, productivity, career satisfaction and definitely enhanced recruitment of folks from traditionally underrepresented groups.

The issue is that the evaluation (of mentorship) has not been methodically rigorous. Also, often, because the definition of mentoring and the context in which it occurs is so ubiquitous, we don't know what we're studying or what the results are linked to. If we really want to understand the critical elements of mentoring and the roles that mentoring plays in the elements of success we want to see in diversifying the workforce, then the community has to get on board with describing what they are studying and using common metrics.

Who were your mentors?

A part of why I'm so passionate about this work is because I've had the privilege of having some amazing mentors! Without a doubt, Jo Handelsman has been an amazing mentor to me. My graduate adviser and folks with whom I've worked along the way all played different roles. One of my current mentors, Christine Sorkniss, whom I work with on the NRMN, has the amazing ability to push me beyond my comfort level and make me believe that I can do it but also to say, "I'll be here if you stumble."

That has been a common theme — my mentors strongly believe in my potential and push me, but they also let me know that they'll be there to help.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the chief science correspondent for the American Society for Biochemistry and Molecular Biology. Follow her on Twitter at twitter.com/rajmukhop.

Upcoming ASBMB events and deadlines

AUG

Aug. 17: ASBMB webinar: "Building professional relationships: pragmatic advice for the human scientist"
Aug. The Journal of Biological Chemistry exhibits at the American Chemical Society annual meeting, booth #504, Philadelphia.

SEPT

Sept. 1: Registration deadline for ASBMB Special Symposium: Transcriptional Regulation by Chromatin and RNA Polymerase II, Snowbird, Utah

OCT

Oct. 6–9: ASBMB Special Symposium: Transcriptional Regulation by Chromatin and RNA Polymerase II, Snowbird, Utah
Oct. 13–15: Society for Advancement of Hispanics/Chicanos and Native Americans in Science National Conference, Long Beach Convention Center, booth #226, Long Beach, CA.

NOV

Nov. 17: Abstract submission deadline for ASBMB 2017 Annual Meeting, Chicago
Nov. 9–12: Annual Biomedical Research Conference for Minority Students, booth #701, Tampa, Fl.

ASBMB
American Society for Biochemistry and Molecular Biology

Teaching undergraduates professional skills

By Pamela Mertz & Craig Streu

As educators who spend most of our time teaching biochemistry to undergraduate students, we can become mired in developing subject-specific proficiencies. Developing our students' writing and other professional skills is not always a priority. But surveys have shown repeatedly that employers place tremendous value on the ability to work effectively in a team as well as verbal, critical thinking and written skills.

To help our students acquire the skills necessary to be successful in their scientific careers, we have designed and implemented writing projects in two sequential courses in our biochemistry curriculum that work synergistically. The first semester is designed around a putative protein that students research using bioinformatics tools and write up as a paper. The second semester is a grant writing project that builds upon the skills gained in the first semester.

Like most things, we arrived at the current version of the project after several rounds of trial and error. The first semester already had a writing project, so we started by adding a grant writing project into the second semester of a biochemistry course. A grant writing project had the potential to meet our desired outcome of teaching critical thinking, verbal communication, writing and teamwork. However, we found that while students could propose ways to test novel hypotheses, they struggled with the initial novel hypothesis generation.

To address this problem and increase student exposure to bioinformatics methods, we next replaced the first-semester writing project with what we now call the Putative Protein Project. At the time, the first semester had a literature-based project in which students were asked to choose a well-characterized enzyme and write a review paper about its structure and function. While this assignment did give students experience with scientific writing and searching the primary literature, it did not give students the experience of generating novel hypotheses or results. In the new version of the writing project, students now choose a putative protein and use bioinformatics resources and the primary literature to generate a hypothesis for that protein's biological role.

By all accounts, this new sequence of projects improved the ability and confidence of our students to develop novel hypotheses, which they could then put into practice during their grant writing project in the following semester. Some groups even used their putative protein as the springboard for their grant proposal.

Of course, over time, both projects went through further rounds of revision. It became clear that the most interesting putative protein projects tended to come from putative proteins of non-mammalian origin since there often are very close homologs of mammalian proteins that have been studied extensively. In fact, the best putative proteins most often come from interesting bacteria or fungi. For example, students have identified previously uncharacterized drug-resistance transporters from pathogenic strains of bacteria and novel proton pumps in halophiles. For the grant proposal project, we introduced additional assignments, such as turning in a draft of the research methods section, to allow the instructor to give feedback

Student reflections

I learned how to write a grant proposal according to standards of the National Institutes of Health (and gained an appreciation for researchers that have to do this all the time). It was tough to keep certain sections — like the specific aims — down to one page but it was a good lesson in being concise and to the point in our writing.

– Alex Rogalski at St. Mary's College of Maryland

Although we didn't continue with our bioinformatics project from last semester, we were able to apply our skills at finding and reading through appropriate scientific journals and working together as a team (splitting the work/sections) to the grant proposal this semester.

I learned the exact components that make up a grant proposal and the importance of making sure that your research will be novel and significant. I also learned about the significance of the peer review process.

– Sarah Lock at St. Mary's College of Maryland

The grant proposal project allowed us to research cutting-edge (science) which is always really awesome. When I was researching internships for the summer, I actually knew a lot about the different projects based on the research I had conducted while doing this (course).

I think one of the most challenging aspects was trying to come up with novel ideas. It took a lot of research into figuring out what we currently know about a particular topic, and then determining the gaps in our current knowledge and how we can address this.

Learning how to use all of the bioinformatics sites was really useful because we all had tons of tools at our disposal for preliminary research. For example, if we wished to look at a particular drug's interaction with an active site we could model it in Chimera and see exactly how it worked.

– Taylor Engdahl at St. Mary's College of Maryland

One of the most challenging aspects of this project was learning how to do deal with differences in opinion and learning how to compromise in order to work as a cohesive team. This is a life skill (that) will be necessary in professional environments.

– Megan LaSavage at St. Mary's College of Maryland

I learned that it is OK to completely drop your original grant idea and work on something else with more potential.

– Stephen Swanson at St. Mary's College of Maryland

The grant project allowed us to integrate what we had learned in class with our interests and apply it in a real-world situation. It made us think critically about which techniques would be the most useful in a given situation and how we could use them to further the research in that particular area. It also gave us a chance to better our scientific writing, which we can normally do only on lab reports. I think working in partners also helped prepare us for our careers, where we will often be working with a partner or team and need to produce a single, cohesive document, such as a report, grant or paper.

– Autumn Bernicky at Albion College

earlier in the semester and to help keep students on task.

Based upon student feedback and our general observations, we made a concerted effort to increase the peer review portions of the grant writing exercises. The first full draft is carefully peer-reviewed by multiple groups of students. Students report that reading the drafts of other grant projects helps them present and refine their own ideas and helps them understand how the grant-review process works. In addition, the students critique the presentations of the proposals so students can receive feedback on their oral communication skills and content.

Although the two-semester sequence of writing projects was designed to allow students to develop the skills necessary to generate high quality original written grant proposals, we have found that one of the most important outcomes is that the projects give students practice with critical thinking, oral communication and teamwork skills. The writing assignments work well for two semesters of biochemistry, but the assignments could be adapted to other life science courses that are taken in sequence. We believe that the progressive building of skills — beginning with the experience in the first semester of generating and interpreting data and following it with the practice of hypothesis generation and experimental design in the second semester — is more important than the specific content of the courses.

Pamela Mertz (psmertz@smcm.edu) is an associate professor of chemistry and biochemistry at St. Mary's College of Maryland. Craig Streu (cstreu@albion.edu) is an assistant professor of chemistry and biochemistry at Albion College.

When 'I don't know' is the right answer

By Ana Maria Barral

"Professor, you have to see this!" Kim exclaimed, visibly excited. "My producer changed from Gram positive to negative and has this pretty green color to it!"

Oh, the joys of teachable moments! This was my opening to introduce Kim to things learned through years of grad school and postdoctoral training: the scientist's discipline not to believe in anything exciting until proven again and again, to double-check everything, and to assume errors before breakthroughs.

Except that I was standing in an undergraduate classroom, in a microbiology laboratory course with students heading to popular allied health careers, such as nursing. Students in such courses seldom think about research, especially not at colleges like mine, where most students are nontraditional like Kim (not her name), who worked during the day as a licensed vocational nurse and was planning to apply to a nursing program to get her bachelor's degree. Most of the students in my class were in their late 20s or early 30s, worked and had families, and many were veterans.

They are, in many ways, dream students: mature, focused and disciplined. On the other hand, they know what they want (good grades) and do not have a lot of patience with uncertainty in the classroom.

But uncertainty was what I offered them the first day of class when I announced that, besides learning the basic techniques of a microbiology laboratory, they would also do their own research: trying to find antibiotic-producing bacteria in the soil from their backyard or neighborhood.

"Go and find some dirt!" I exclaimed, handing them 50-milliliter tubes and spatulas.

They returned the next period with soil in their tubes sampled from a variety of locations, ranging from a basil plant pot to the soil near a cactus in Camp Pendleton Marine Base.

They did not know what to expect. In all honesty, I did not know what to expect.

This course, the Small World Initiative, is a brainchild of Howard Hughes Medical Institute Professor Jo Handelsman and her close collaborators at Yale University. It combines the urgency of the antibiotic crisis (acutely felt as I write this due to the appearance on American soil of the dreaded colistin-resistant E.coli) with a new way to engage students in scientific research (see box).

I learned about the SWI in 2013 through a call for applicants to participate in the training workshop at Yale only days before the deadline. My colleague Huda Makhluf and I scrambled to make the deadline, and a few weeks later we learned that the National University team had been selected as one of the pilot partners to come to New Haven.

In July 2013 I spent a crazy and inspiring week at Yale with 23 other instructors, learning not only the lab protocols and techniques but also the pedagogic foundations of scientific teaching. We picked and patched colonies from smelly plates, got excited about inhibition zones, eagerly anticipated the PCR results, and returned to our home institutions with the mission to implement the SWI.

Most (if not all) institutions that implemented the SWI in that first round were very different from Yale: small colleges, nontraditional universities and community colleges whose material resources and student populations do not compare to those of Yale. Upon returning to our home institutions, we worked to adapt the SWI's framework to our courses and school styles, to pass the hurdles of institutional review board applications, and to figure out the logistics of lab activities.

Originally a biochemist who over the years has moved toward cell and molecular biology, I picked up microbiology first through basic techniques in the lab and then as I taught classes. By 2013, I was fairly comfortable handling the usual suspects from E.coli to P. aeruginosa (and its characteristic green sheen, which was invading Kim's plate), but soil microbiology was a different monster. When students asked me what was this or that colony sprouting up on their plates, it was liberating to answer, "I don't know," followed by "Let's find out!"

As the SWI has expanded (currently there are more than 135 pilot partners at 108 schools, from R1 research universities to community colleges, home and abroad), one aspect remains the same: the SWI improves the class environment.

We can talk about "student project ownership" and "engagement," but in plain English, teaching and learning using the SWI is just more fun. With

the SWI, there are no right or wrong results, reflecting what research is like.

Instead of the professor handing out good and bad verdicts (in the form of grades), I became more like a PI advising students. If I do not know the answer to their question, I tell them and share my ideas about how to move forward. Often students surprise me with their immaculate lab techniques and unconventional ideas.

Errors are handled as learning experiences, not a reason for a failing grade. When Kim showed me her green plate, I advised her to go back to a previous plate and compare morphology and Gram stain results. She arrived at the conclusion that she had a contamination issue and, as a result, probably learned the importance of aseptic technique and research discipline.

Looking for antibiotic producers in the soil as a classroom project is not unique to the SWI. Unique aspects of the SWI include its modular and flexible nature as well as its emphasis on the research experience and assessment.

The SWI has been adapted to microbiology, general biology, and cellular and molecular biology courses. While 16S rRNA PCR amplification and sequencing of isolates are part of the SWI curriculum, instructors have the option to add more molecular biology. Likewise, the organic extraction of the isolated antibiotic producer and extract activity testing can be expanded to include more advanced chemical and biochemical analysis. In fact, the SWI is establishing a chemical discovery hub to screen and characterize the extracts coming from SWI classes.

At the 2014 American Society of Microbiology General Meeting in Boston, a group of SWI students proudly exhibited their results as part of the Presidential Forum. Kim was there, beaming as she explained the characteristics of her Bacillus, which she had narrowed down to three possible candidates based on PCR and biochemical techniques.

PHOTO PROVIDED BY BARRAL

Nursing students get exposure to microbiology through the Small World Initiative's projects.

Since that inaugural poster symposium, SWI students have been presenting their results at many national and international events, including the 2016 American Society for Biochemistry and Molecular Biology meeting.

SWI instructors, in turn, have been researching the effectiveness of the course, showing that the SWI's approach improves critical thinking and student test scores (see box). The possibility of doing research even at teaching-oriented institutions is yet another reward of adopting the SWI.

While one of the goals of the SWI is to increase the number of graduates in science, technology, engineering and mathematics, I have come to appreciate its broader impact on education. Through the SWI, whether they pursue STEM degrees or not, students have an invaluable opportunity to learn firsthand the challenges and excitement of science at every stage of the process, from sample gathering to the public presentation of research.

Our society needs citizens who know and appreciate science, and the world needs more awareness of the antibiotic crisis.

Everybody wins!

Resources

Visit **www.smallworldinitiative.org** to learn more about the program. See this article by Joseph P. Caruso and co-authors to learn more about student outcomes: **www.ncbi.nlm.nih.gov/pmc/articles/PMC4798800**.

Ana Maria Barral (abarral@nu.edu) is an assistant professor at National University's Costa Mesa, California, campus. Follow her on Twitter at www.twitter.com/Bio_prof.

Teaching challenging concepts to transform learning

By Jennifer Loertscher

Most of us teaching biochemistry and molecular biology at colleges and universities are motivated by love of the discipline and relish the opportunities we have to share our excitement with our students. Yet few of us have received formal training related to teaching, and we may struggle to engage students with the material in deep and meaningful ways.

Recently, the American Society for Biochemistry and Molecular Biology brought communities of faculty together to learn about best practices in teaching and to share expertise. This work, funded by a grant from the National Science Foundation, resulted in the publication of foundational concepts and skills for BMB.

A growing body of research reveals that many students exhibit incomplete or incorrect understanding of essential or "foundational" knowledge in BMB (1, 2, 3). Foundational concepts include such ideas as energy in biological systems, macromolecular structure and function, genomic information storage, and the variety of scientific skills necessary for discovery (see http://www.asbmb.org/education/teachingstrategies/foundationalconcepts/).

Now that foundational concepts have been defined, an important question arises. Can undergraduate BMB curricula be reimagined to emphasize and clarify those concepts that are most important and most challenging to master? With the help of something called threshold concepts, the answer may just be yes.

Foundational concepts encompass the breadth of a discipline and describe all of the basics that an expert would know. Threshold concepts are those ideas that are most difficult and central to understanding a discipline. Although there is often overlap, identification of threshold concepts allows teachers to tailor instruction to emphasize pivotal concepts with the hope that once students understand threshold concepts deeply, proficiency with other concepts will follow more easily.

In box 1, I've described the five threshold concepts of steady state, biochemical pathway dynamics and regulation, the physical basis of interactions, thermodynamics of macromolecular structure formation, and free energy. The chart shows how once students understand a threshold concept, a ripple effect of unlocking other biochemical ideas takes place and connections to additional processes become apparent. If students don't experience these insights, they may become stuck and be unable to progress as learners.

Threshold concepts also provide a starting point for focused curricular redesign, since an intentional approach to teaching threshold concepts is likely to result in the greatest improvement in student learning (4). In their book "Overcoming Barriers to Student Understanding: Threshold Concepts and Troublesome Knowledge," Jan Meyer, Ray Land and colleagues suggest that threshold concepts "be viewed as 'jewels in the curriculum' insomuch as they provide opportunities for students to gain important conceptual understanding" (5).

Meyer and Land also suggest that threshold concepts can be identified for any discipline and have four defining characteristics (6):

- **Transformative:** Once a threshold concept is understood, a student's perception and comprehension of a subject radically alter. In addition to cognitive development, learning of threshold concepts can alter a student's self-perception or sense of identity. For example, students may shift from viewing themselves as students of biochemistry to recognizing that they have begun to think like biochemists.
- **Irreversible:** Once a threshold concept has been understood deeply, students are unlikely to forget it. The concept becomes central to how students think about everything else in the field. Experts have difficulty remembering how they understood the discipline prior to understanding threshold concepts.
- **Integrative:** Threshold concepts bridge concepts within a discipline and among disciplines. Once understood, previously hidden connections within a discipline, and perhaps even across disciplines, are apparent.
- **Troublesome:** Most (but not all) threshold concepts are troublesome for students and can be difficult for a number of reasons. However, although threshold concepts tend to be troublesome, not all "troublesome knowledge" has a threshold concept at its source.

We worked with a national com-

CONTINUED ON PAGE 39

Box 1

Name	Knowledge statement(s)	Biochemical ideas that are unlocked once this concept is understood	Connections that were invisible prior to deep understanding of the concept
Steady State	• living organisms constitute open systems, which constantly exchange matter and energy with their surroundings, yet net concentrations remain relatively constant over time. This dynamic, yet outwardly stable condition is referred to as a steady state. • "Steady" is not synonymous with chemically "stable." Concentrations are determined by kinetic, rather than thermodynamic factors. Hence, biological systems do not exist in a state of chemical equilibrium. • If an organism reaches chemical equilibrium, its life ceases. Consequently, organisms have evolved extensive regulatory systems for maintaining steady	• Steady state is an emergent process that results from regulation of numerous biological reactions. • Steady state is a metastable condition that can be maintained only because of constant input of energy from the environment. • Steady state defines the conditions of life under which chemical reactions take place in cells and organisms. Therefore an understanding of steady state is necessary in order to correctly contextualize all of biochemistry.	• Once the condition of steady state is recognized, the purpose of complex regulatory systems in maintaining steady state and their connections to each other become apparent. • Once the metastable nature of steady state is recognized, the importance of multi-tiered energy storage systems (starch, glycogen, triglycerides, etc) becomes apparent
Biochemical pathway dynamics and regulation	• Reactions and interactions in biological systems are dynamic and reversible. • Directionality of processes depends on the free energy and relative concentrations of reactants and products available. • Observable flux is the net result of forward and reverse processes. • Enzymes control rates of forward and reverse reactions. • Enzyme activity is highly regulated.	• Chemical drivers result in bulk (emergent) properties observed in biological systems. • Enzyme-mediated regulatory mechanisms allow pathways to be sensitive and responsive to the needs of the organism. • Enzymes act as gatekeepers rather than drivers of chemical change.	• Once these concepts are understood, predictions can be made about 1) how biochemical pathways are likely to respond to changes environmental conditions and 2) cause and effect of fluctuations in biochemical pathways.

Name	Knowledge statement(s)	Biochemical ideas that are unlocked once this concept is understood	Connections that were invisible prior to deep understanding of the concept
The physical basis of interactions	• Interactions occur because of the electrostatic properties of molecules. These properties can involve full, partial, and/or momentary charges.	• Once this concept is understood, similarities between different types of interactions become clear. Although interactions are given different names, they are all based on the same electrostatic principles.	• A core biochemical principle is that structure governs function. Correct understanding of non-covalent interactions is essential in integrating structure and function.
Thermodynamics of macromolecular structure formation	• Interactions in biological systems almost always take place in aqueous solution. • Bulk interactions in an aqueous system have an entropic component. • Enthalpic and entropic contributions are responsible for biological structure.	• Protein folding, the assembly of lipids into micelles and bilayers, the association of polypeptide subunits to form oligomeric proteins, base pairing of DNA and RNA molecules, and all other biological interactions are driven by a common set of thermodynamic forces. • The aqueous environment of the cell plays an active and essential role in biochemical structure formation.	• When the entropic and enthalpic forces that drive processes like protein folding and binding are understood, predictions can be made about the conditions under which these events will occur and what effect perturbations, like mutations, will have.
Free Energy	• The tendency towards equilibrium drives biological processes. • Differences in free energy drive the chemical transformations underlying biological function. • By providing a direct link between a thermodynamically favorable reaction with a thermodynamically unfavorable one, enzymes enable biological systems to drive a normally unfavorable reaction by coupling it to one with a large and favorable free energy change. • Enzymes affect reaction rate yet do not affect equilibrium position.	• Biological systems use favorable processes to drive less favorable processes, which allows for maintenance of steady state.	• Once this concept is understood, the relationship among free energy, equilibrium, and steady state becomes apparent.

Faculty experiences with threshold concepts

JAKUBOWSKI

I describe myself to students as a protein chemist and biophysicist as I evolved from my first undergraduate research project and an initial major in physics over 40 years ago. Both of these backgrounds led to a deepening insecurity as I attempted to help my students understand the hydrophobic effect in protein folding. An unease arose one day when I knew that I had given a student an inadequate explanation for its role in protein structure and stability because I never fully understood it myself. This unease exploded when I attended a two-day workshop at the University of Minnesota on the hydrophobic effect presented by Ken Dill. Driving home after the first day, my understanding of the hydrophobic effect seemed to have collapsed. I questioned whether I ever understood it. On the second day, I became aware that I had achieved a much deeper understanding of this threshold concept. Previously unappreciated and misunderstood differences in plots of heat capacity vs. temperature for protein denaturation suddenly became clear as I internalized a more nuanced understanding of the hydrophobic effect based on characteristic heat capacity changes with changes in local environments of nonpolar groups. Compensatory enthalpic and entropic changes relating to changes in water structure made sense. I relate this story to my students as they struggle with the topic and tell them that we all struggle as we seek to understand our internal and external worlds.

Henry Jakubowski, professor of chemistry, College of Saint Benedict Saint John's University

MURRAY

The idea of threshold concepts seems very straightforward until you find yourself in a room of experts contemplating the threshold concepts of your discipline. In the midst of a discussion of steady state and why this should be a threshold concept in biochemistry, I realized that I did not truly understand the difference between equilibrium and steady state and therefore had not yet fully crossed that threshold myself. I used the words interchangeably, and because equilibrium was the concept with which I was most familiar, I taught students many aspects of what I now recognize as steady state as equilibrium. At first glance, whether the system is opened or closed seemed like a minor issue, but like a threshold concept should, understanding this difference at a deeper level has changed my understanding of the chemistry of living organisms and why it needs to be addressed differently than chemistry in a test tube. This change in my perception of the concept of steady state and its importance in developing a deep understanding of biochemistry has definitely influenced the way I teach protein-ligand and enzyme-substrate interactions, inhibition, regulation, and metabolic flux.

Tracey Murray, associate professor and chair of chemistry and biochemistry, Capital University

CONTINUED FROM PAGE 36

munity of more than 50 students and 75 faculty members to identify threshold concepts for the field and currently are collaborating with biochemistry colleagues to design instructional and assessment materials targeting these concepts. Reference 7 has a complete description of the concepts and the process used to identify them.

Although the goal of our project was to transform student understanding of BMB, faculty have benefitted unexpectedly from transformative experiences as well as their understanding of biochemistry continues to evolve (see "Faculty experiences with threshold concepts"). We continue to expand the community of people engaged in improving learning and teaching in BMB using threshold concepts. If you are interested in joining us, please get in touch!

REFERENCES

1. Sears, D.W. *et al. Biochem. Mol. Bio. Edu.* **35**, 105 – 118 (2007).
2. Villafañe, S.M. *et al. Chem Educ. Res. Pract.* **12**, 210 – 218 (2011).
3 Linenberger, K.J., & Bretz, S.L, *Biochem. Mol. Bio. Edu.* **43**, 213 – 222 (2015).
4. Entwistle, N. *Threshold concepts and transformative ways of thinking within research into higher education* in "Threshold concepts within the disciplines" Land, R.; Meyer, J.H.F., and Smith, J., eds., Sense Publishers, Rotterdam, 21 – 35 (2008).
5. Land, R. *et al. Conclusions: implications of threshold concepts for course design and evaluation* in "Overcoming barriers to student understanding: threshold concepts and troublesome knowledge" Meyer J.H.F. & Land, R., eds.; Routledge, London, 195 – 206 (2006).
6. Meyer, J.H.F. & Land, R. *Threshold concepts and troublesome knowledge. In Improving student learning — ten years on* Rust, C., ed. Oxford, 412 – 424 (2003).
7. Loertscher, J.L. *et al. CBE Life Sci. Educ.* **13**, 518 – 528 (2014).

Jennifer Loertscher (loertscher@seattleu.edu) is a professor of chemistry at Seattle University.

Giving resources to graduate students and postdocs

By Erica Siebrasse & Jenna Hendershot

Graduate students and postdoctoral fellows constitute 10 percent of the American Society for Biochemistry and Molecular Biology membership. To support these members and discover which professional society resources are most useful to them, the ASBMB Education and Professional Development committee recently conducted a survey of member and nonmember life science graduate students and postdoctoral fellows working in the U.S.

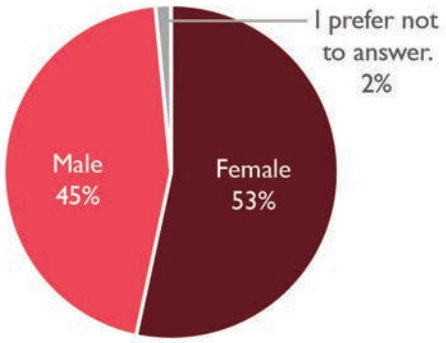
The infographic below summarizes the survey results. Surveyed graduate students and postdoctoral fellows say they are most interested in research careers — in academia or industry — and want to be supported in multiple aspects of their career development.

Using this survey data, the committee has developed a multifaceted plan to improve the career resources that the ASBMB offers to all of its members (www.asbmb.org/careers). The infographic on the following page highlights a few of the new resources, which will be assessed and refined over the next few months. Members can expect new videos or webinars monthly.

EPD members serving on the graduate student and postdoctoral fellow subcommittee are committee chair Jenna Hendershot at Cayman Chemical Company; Suzanne Barbour at University of Georgia; José Barral at the University of Texas Medical Branch; Shea Feeney at the University of California, Davis; Chloe Poston at the Genetics Society of America; Martin Rosenberg at Promega, Walter Shaffer at the National Institutes of Health; and Ray Sweet, an independent consultant.

Erica Siebrasse (esiebrasse@asbmb.org) is an education and professional development manager at ASBMB. Jenna Hendershot (jenna.m.hendershot@gmail.com) is at Cayman Chemical Company and a member of the ASBMB EDP committee.

Respondent demographics



1,300 responses
53% graduate students
47% postdocs

32% ASBMB members

92% 23–39 years old

Most valued society resources

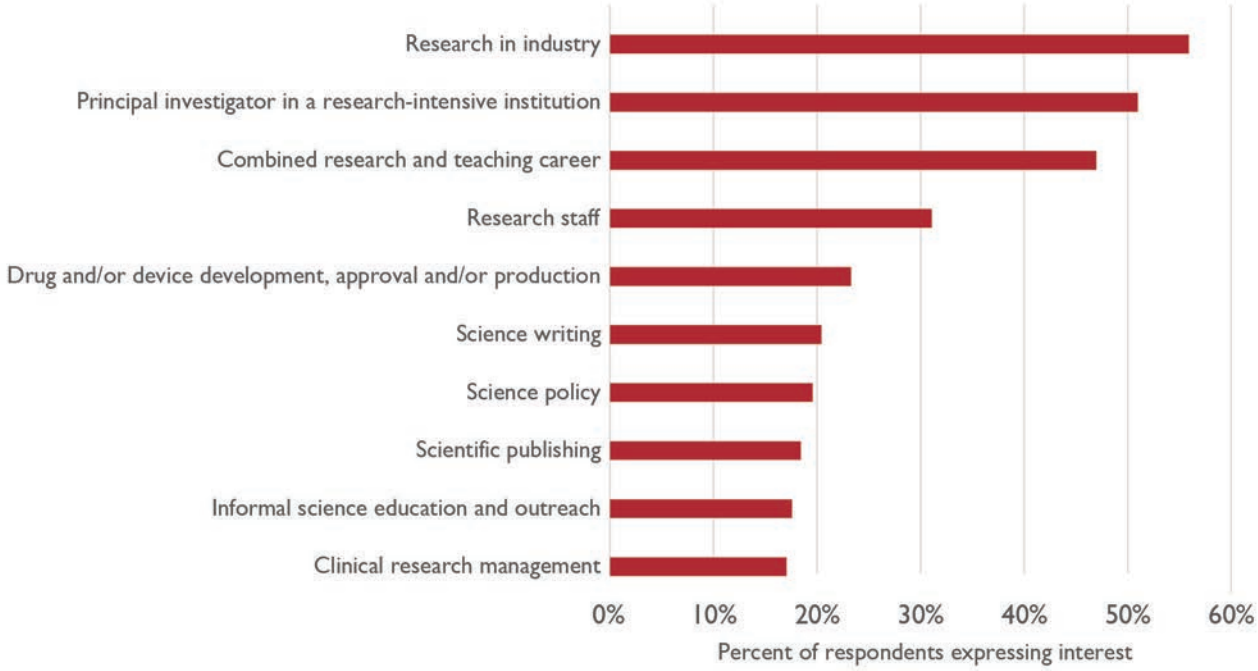
1. Travel awards, grants and scholarships
2. Networking with other members
3. Job board
4. Skill development resources
5. Discounted registration for meetings

Most needed career resources

1. Identifying career options
2. Maintaining a professional network
3. Interviewing and negotiating
4. Developing and communicating a career plan
5. Preparing application materials

Career paths of interest

(Respondents could select multiple paths)



The ASBMB plan for supporting graduate students and postdoctoral fellows

ASBMB website

The education and career sections now include career–stage–specific information and new career–development resources.

Workshops

New career workshops support career–path exploration and provide training on communication, networking and applying and interviewing for positions.

Video tutorials

This new series has short videos on career topics such as networking and dressing professionally.

Member e-news

The monthly e–newsletter now includes a section for graduate students and postdoctoral fellows that highlights events and resources of interest.

Webinars

A new career webinar series began in June in partnership with the National Institutes of Health. The next webinar is Aug. 17 and covers building professional relationships.

Career path exploration

New videos highlighting different careers and updated Web resources support a better understanding of career options.

Learn more about ASBMB career–development resources at www.asbmb.org/careers!

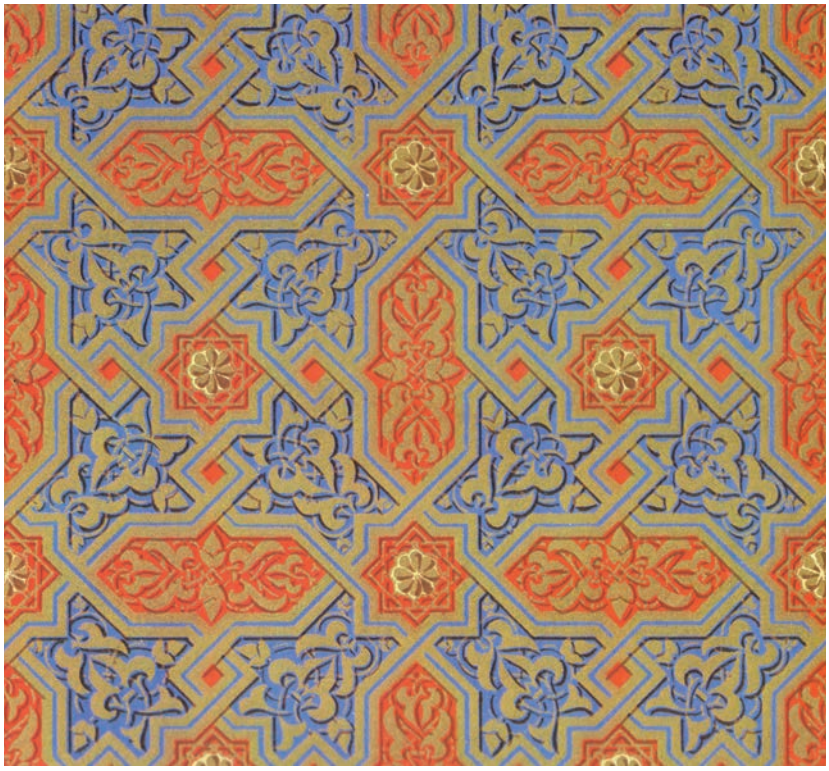
Mastering science through games and everyday art

By Yan Jessie Zhang & Tyler Stack

In Chinese martial arts doctrine, there are three levels of supremacy. At the first level, the level of physicality, martial arts masters hold swords in their hands and exhibit command over their weapons through unassailable technique. At the second, conceptual level, the masters no longer carry the swords and have developed a keen sense of all weapons surrounding them. At the ultimate level, the understanding of how an object like a sword functions as a weapon is so deep in the masters' hearts that nearly anything can take the place of a sword. A thin tree branch or a roll of ribbons can be transformed instantly into something dangerous.

A passionate scientist is not unlike a third-level martial arts master. With a heart full of love for science, she sees the world though a scientific lens that allows her to appreciate the inherent complexity in her world and apply abstract science concepts to an endless array of concrete materials. Just like the twig in the hands of a martial arts master, anything she sees or holds can become a medium for conveying the magic of science.

In the molecular biosciences department of the College of Natural Science at the University of Texas at Austin, we are passionate scientists hoping to instill passion and mastery in our students. One way we do this is by using unexpected mediums in the classroom.



Everyday objects and art, like this frieze on the Alhambra in Spain, can be used to teach symmetry.

Smartphone purification

Take a walk around any undergraduate campus these days, and you will note that most students are on their smartphones. Some are doing actual work, but a good number are playing games. Those games can be quite addictive.

Student addiction to smartphones can be a huge headache for teachers, but we have discovered an upside. When we designed an upper-level undergraduate biochemistry course meant to encourage problem solving, we needed to provide large numbers of students with hands-on experience. These students had to master protein purification, a core technique for biochemists. The only time most undergraduate students attempt protein purification is in a well-structured biochemistry lab class, during which they follow an established purification procedure like a cooking recipe. This teaching method doesn't prepare students for real lab life, in which protein targets are often elusive despite adherence to procedural protocol.

To include interactive experimental design, iterative troubleshooting and problem solving in our teaching of protein purification, we asked our students to put their smartphones to use by playing a free video game during class called "Protein Purification."

It turns out the game, created by

Andrew Booth and be downloaded for free from the app store on smartphones, is an effective way to teach students the intricacies of various forms of chromatography. It allows them to simulate the purification of a protein from lysate to a single band on a gel in 10 minutes. Students can design the first purification step, and the experiment is run virtually with the results of this step shown in 1D or 2D electrophoresis gels, Western blots or chromatography spectra, which the students can then use as a basis for designing their next purification steps.

Student responses to the exercise have been overwhelmingly positive, and they've described the app as being "as addictive as a video game." During the last semester, we held an optional grand challenge and asked students to completely purify one protein from a mixture of 60 proteins. One hundred of our 125 students participated in the challenge and proposed more than 10 different ways to purify the sample. The final winner of the challenge designed a strategy that was better than the one that we ourselves had designed. It had the fewest purification steps and maintained the highest yield and purity.

Exam scores related to protein purification questions have been consistently higher since we began using the game, and students report feeling confident about designing purification protocols for unknown proteins in future research.

Molecule "Survivor"

When teaching graduate students, we like to encourage individual thinking. Taking a cue from a 2009 Nature magazine poll, we recently asked each of the students in the class to make a case for the best, most desired molecule in the field. We then hosted a game of "Molecular Survivor", adapting the voting format of the popular television show "Survivor" — including the torch and tribe gathering fanfare — to arrive at a winning potential molecule. Students in class were grouped and challenged to nominate a dream molecule whose structure and mechanism would change our world.

The students made passionate cases for their molecules, explaining why knowing each molecule's structure would answer many important scientific questions and cure diseases. The tribe then spoke and narrowed the choices. In the end, their final choices closely matched those of the field at large as published in Nature. They were the eukaryotic ribosome, spliceosome, nuclear pore complex, HIV trimer and the epidermal growth factor receptor (1).

Not only did students deepen their knowledge of molecular function, but they also laughed and bickered while defending their choice of molecules — helping them to explore further the depths and nuances of learning and communicating science.

The art of symmetry

Scientists and science students are often joyfully curious. We like to encourage this happy curiosity in all of our students by urging them to look for scientific concepts playing out in daily life. These "I spy" games bring out the inner child in us all.

One example is our teaching of crystals and crystallography. Part of this teaching involves getting the students to understand the element of symmetry. On paper, symmetry is a mathematical operation where the result is identical to the starting state. An innately complex, visual problem, symmetry easily lends itself to real-life examples. Ballroom dancing can explain rotational and translational functions. The world around our students and under their feet contains numerous examples of symmetry. One way to grasp this is through the use of an online program called Escher-sketch (https://levskaya.github.io/eschersketch/), which helps students visualize symmetry and feel like artists at the same time.

As an extra credit assignment, we provide a worksheet with examples of symmetry possible in two dimensions and challenge students to find the symmetry operators. The images aren't scientific illustrations but samples of tile and wallpaper like those found in popular home stores like Home Depot. After this section, students end up finding the symmetry in the common objects everywhere around them, pointing out the symmetry used in buildings or even each other's clothing.

When we introduce these real-world examples of symmetry, the conceptualization of crystal symmetry — the arrangement to biological molecules in protein crystals, which we cannot visualize even under the most powerful microscopes — doesn't seem so intangible.

Smartphone apps, reality television shows and design art are just a few of the ways we've found to help students conceptualize complex issues and have fun while talking about abstract scientific topics. Turning science from something that students memorize into something that, like martial arts masters, they innately see and feel in their hearts is our ultimate goal. We hope that for our students, loving science will become a lifestyle that adds magic and joy to their lives.

REFERENCES

1. Bhattacharya, A. *Nature* **459**, 24-27 (2009).

Yan Jessie Zhang (jzhang@cm.utexas.edu) is an associate professor in department of molecular biosciences at University of Texas, Austin. Tyler Stack (tmmstack@gmail.com) is a biochemistry graduate student in the department of molecular biosciences at the University of Texas at Austin.

Gap years

We wondered how stepping off the road of higher education influenced people's careers and outlook on life. Here is what some of our members and affiliates had to say about gap years.

STEM-focused gap years

Gap years are a growing trend in the U. S. They're not the exclusive territory of high schoolers in search of direction before diving into university studies. At the American Gap Association, the official standards and accreditation agency for gap years, we define a gap year as an experiential semester or year "on" taken in order to deepen personal, practical and professional awareness. Increasingly, students completing their baccalaureate studies are taking a year before beginning their graduate work to refresh their zeal for academic studies and nibble around the edges of career possibilities before committing to the long haul of advanced degrees.

According to the 2015 American Gap Association National Alumni Survey, the number of science, technology, engineering and math students who have taken a gap year before beginning their studies is on the low side. Although we don't have the latest numbers on post-baccalaureate gap years for this population, we do know that only 14 percent of those who take one or more gap years before undergrad are pursuing degrees in STEM.

However, David Verrier, director of the Office of Pre-Professional Programs and Advising at Johns Hopkins University in Baltimore, told Science magazine in 2013 that more pre-med college graduates are interrupting the traditional path from undergrad to graduate or medical school and taking at least one gap year. He cites statistics that put that number at 50 percent of medical school-minded students overall and around 60 percent of undergrads from high-powered research institutions like Johns Hopkins.

STEM-focused gap year programs can provide students with an opportunity to explore career possibilities and build experience in relevant fields by participating in internships or volunteer work related to their academic plans. For now, most STEM students are seeking to round out their academic experience with more tangential skills and citing the need to differentiate themselves from an increasingly competitive field. But a few STEM-focused gap year programs are popping up to meet a growing demand for research-related practice. One example is the Year in Industry, a U.K.-based organization that specializes in high quality, paid placements for students in related fields. In the U.S., the National Institutes of Health offers a competitive post-baccalaureate training award that grants recent graduates one or two years of full-time research experience at an NIH lab.

As students complete their baccalaureate studies and consider whether to head down a path of graduate studies or immediately begin a career, there is evidence that encouraging students to do a year of hands-on exploration based on their academic interests could bear career fruit over the long haul. According to the 2015 American Gap Association National Alumni Survey, 86 percent of students who took gap years reported that they were satisfied or very satisfied with their jobs. The survey also found an association between gap years and high levels of civic engagement and community service. The evidence is clear that participating in a gap year has long-lasting positive implications.

Ethan Knight (ethan@american-gap.org) is executive director of the American Gap Association.

What's your re-entry plan?

One of the strong attractions of a gap year experience is the chance to take a year off, to step out of the familiar herd and take an opportunity to reflect, refresh and recharge. However, it is important to remember that your gap year constitutes a step in a longer journey. You will need to keep your long-term goals in mind when planning a gap–year experience, to map out not just your plan of escape but a strategy for your eventual re-entry.

Whether simple or detailed, linear or flexible, the hallmark of an effective re-entry plan is the establishment of a concrete timeline that specifies when key decisions must be made or specific tasks completed. A graduate who starts a gap year experience in May must be cognizant of the fact that, to enter graduate school in the fall of the following year, the application deadlines for most Ph.D. programs fall in January or February, when the gap year only has reached its halfway point.

As the old saying goes, "Not to decide is to decide." Putting together a re-entry plan that keeps you ahead of the calendar rather than reacting to it will enable you to maximize your options and make decisions that are informed by investigation and reflection.

Peter J. Kennelly (pjkennel@vt.edu) is a professor of biochemistry at Virginia Tech.

Gap years with kids

I was fortunate to have had the opportunity to take a few gap years when my children were young. These years challenged my working lifestyle and mentality and exposed several flaws in my character and habits, but I wouldn't trade them for anything. They provided me precious time with the amazing young persons I still sometimes can't believe I'm actually related to.

My gap years also brought perspective on work–life balance, coerced maturity, improved — if only slightly — my organizational skills, and gave me a break from what can feel like the hamster wheel of science. When I came back to the field, I came back fresh, ready, focused and even more enthusiastic than when I left.

My gap year has convinced me that maybe we all need a sabbatical, even if we're not faculty.

Susan Yeyeodu (syeyeodu@nccu.edu) is a research associate at North Carolina Central University.

Was I suited for graduate school?

Ah, that dreadful time of deciding what to do with your life when you finish college! When I was finishing my masters degree, I was inclined to go right on to graduate school for research, but I had some concerns. I knew I liked the hands-on training of techniques as a master's student, but, at the same time, I had no idea what to expect during the four or five years it would take me to finish a Ph.D.

All the faculty members who taught me during my master's shared the same advice about the Ph.D.: that it would be tough but rewarding. They shared stories about alumni who were successful principal investigators at various universities and stories about numerous alumni who had quit midway through their doctoral training and were doing nonresearch–based jobs.

As I weighed these potential outcomes for myself, there was one thought I couldn't shake: Was I even suited for graduate school? When I performed techniques as laboratory practice during my master's, the graduate students in my department always gave me tried and true protocols. I had no idea if I was any good at troubleshooting techniques by myself.

I was skeptical enough about my abilities and devotion that I decided to take a year off after my master's degree

CONTINUED ON PAGE 46

CONTINUED FROM PAGE 45

to figure out if I really could survive in a laboratory environment. I took that year to volunteer for one of the labs in my department. The principal project of the lab was something I knew nothing about: studying the regulation of the cell cycle in fission yeast by a specific transcription factor. I had learned some basic theory about the cell cycle in class, but that was all the background knowledge I had.

I spent the first few weeks learning basic techniques and reading a few papers to gain an understanding of the project. After that, the real work began. I was asked to make some mutant strains in order to begin my studies. For the first couple of months, I was pretty much under the direct guidance of my principal investigator and would do the experiments she asked me to do. I would show her the density of my cells before transforming them, have her oversee me when I performed experiments, and sometimes even show her my cast gels before performing Western blots. I was that scared of making a mistake and ruining the entire experiment!

Then my adviser explained to me that it is only by making mistakes that I would learn to troubleshoot. Slowly, I started to understand my project and come up with my own experimental suggestions. I was still under my PI's guidance, but I felt a lot more independent when it came to doing experiments and troubleshooting them.

Within a few months, I felt like I had full control over my project, and that feeling motivated me to work harder. I started to enjoy repeating the same experiments. I learned to look beyond experimental failures and to think critically, and I developed an eagerness to learn new techniques. I started to enjoy research. I was not sure about a lifetime commitment to research, but I was definitely sure I wanted to go to graduate school.

I am now a fourth-year graduate student. I face experimental failures every now and then, and I consider them part of the learning process. I've realized that it is through these failures that I learn new things.

Yes, at times graduate life is frustrating. It can make you feel regularly that something somewhere is going terribly wrong. But you have to be prepared to go through those feelings. The year-long gap between my master's and the start of my graduate school prepared me for this. I can say I joined graduate school knowing what would be coming my way. The prelude that the gap year provided helped me to realize that the journey to a Ph.D. was not going to be easy. But it also helped me to believe that it would be OK and that, at least in my case, when the going gets tough, the tough get going.

Isha Dey (ishaadey@gmail.com) is a graduate student at Rosalind Franklin University of Medicine and Science.

Gap year or personal year?

When speaking with my students who know they will be taking a break before graduate or medical school, I distinguish between a gap year and a personal year. The distinction makes the conversation more productive and frames it with the student's needs in mind.

A gap year, as I explain it, is when students need a Plan B — typically because they didn't get into medical or graduate or professional school and need additional professional development to become a more competitive applicant.

A personal year, as I define it, is purposely planned to enhance personal development, explore opportunities or take time to consider what the graduate's next step should be. Typically, the student has already been accepted into a program for graduate, medical or professional school and defers for a year to pursue meaningful experiences or chooses to put off applying for another academic program until he or she has had experiences beyond undergrad.

An important strategy for a graduate considering either type of year is to give serious thought to what she or he wants to accomplish, set goals, and put a plan in place to pursue and accomplish those goals.

The vast majority of my students have been premed, and so far only five have taken either a gap or personal year. One former student spent her personal year at the National Institutes of Health in a research position. Her main goal was to focus on research for one year to help determine if she wanted to pursue an M.D./Ph.D. or simply an M.D. before attending medical school. Another former undergrad began a position as a research scientist during a gap year while he decided if he wanted to reapply to medical school or choose nursing school.

Thus far, I've only had five former undergrads who attended grad school, and none of them took a gap or a personal year before doing so.

I never overtly recommend that students take a gap or personal year. Nor do I try to dissuade them from

doing so. I firmly believe that it is a decision that should be made by the student. My key responsibility as a mentor is not to influence their decision unduly but to ask open-ended questions and to encourage them to determine and subsequently follow the path that is right for them. My standard first question is "What do you want to have accomplished by the end of the year?"

I find that students who thoughtfully consider the question and give solid answers — even if they need to think it over for a couple of weeks before answering — have well-planned gap or personal years, gain the most benefits and are more satisfied with the experience overall. It is easy to write a recommendation letter for these students when they apply to internships, jobs or postbac programs for their gap years and once again when they return for a letter to pursue their next career step.

As far as whether a graduating student should consider taking a gap or personal year in the first place, I've never had that conversation. The students who come to me already have decided that they will be taking a gap or personal year. So I asked David Oppenheimer, the principal investigator I work with, to write a summary of what he shares with those who come to him with this question.

He said, "Don't choose grad school because you don't know what else to do after undergrad or because being recruited by a lab makes you feel special. For many students, it will be much harder to quit grad school even if they are unhappy and it's not where they want to be than it is to apply to grad school after a gap year. But if you decide to take a gap year, use it to your full advantage. Explore opportunities that will help you choose grad school or rule it out, and make sure to gain skills and build professional relationships that will help you succeed regardless of what you ultimately decide to do."

Paris Grey (phgrey@ufl.edu) works as a molecular biologist and is co-creator of the blog Undergrad in the Lab. She is also co-author of the book "Getting In: The Insider's Guide to Finding the Perfect Undergraduate Research Experience."

Learning what you don't want

The gravel churned under my tires as I made my way down a series of unmarked roads. I tried to pace myself: going slowly enough to not spin out on the dry, dusty roads and fast enough to keep air flowing through the windows of my AC-deficient car.

Cornfields spread out on either side of me like an endless sea. Finally, on a turn down another dirt road, I started to see some potential. A large, red, barnlike building materialized in the distance.

I closed in on the building and parked next to a group of dust-coated, haphazardly arranged vehicles in what passed for a parking lot. As I turned off the engine and surveyed the surroundings, my chin dropped.

This couldn't be the place, could it? Standing mere yards from my bumper were goats. Goats.

Notwithstanding the combination of farm animals and an absence of signs on the building, I straightened my interview clothes and headed for the only door I saw.

So began the first of the so-called gap years between my undergraduate and graduate training. Taking that time off felt more like a necessity than a choice back then. When I graduated from college, I didn't really know what I wanted to do. So I did one of the few things I knew I could do with a degree in biology: I became a lab tech.

Some may feel gap years are reserved for people who are too afraid or soft to commit to a challenging future. The phrase itself can conjure inadequacy. Gap: a lack of something, something that needs to be filled, something missing.

In reality, I found those two years enlightening and critical. Not because I discovered my calling or identified a vocation and, suddenly possessed of a sense of purpose, dove headfirst into graduate school. My experience was quite the opposite, really.

I spent my first gap year as a lab tech at a tiny private lab in rural Wisconsin that happened to abut a small hobby farm for the owners (hence the goats). In addition to the unexpected element of goats, the lab itself was strange. It was so open. All the labs I had been in before were cluttered, stuffy and full of people. Given all the windows and light pouring in, my first moments in my new workspace felt like arriving in an aviary. It was also nearly empty of people. For the year I was there, I had just two direct co–workers.

Every day, I punched in my arrival on a time card and punched out on my way home. Every day, I processed the incoming patient urine samples on the same automated machine — unscrewing the caps, running the samples on the machine, pouring their contents into a smaller vial so they'd

CONTINUED ON PAGE 48

CONTINUED FROM PAGE 47

fit in storage and screwing the caps back in place. Luckily, I only spilled a few vials, and yes, it smelled as awful as you'd imagine.

It took just a few months at my new 9-5 job for me to realize this type of work was not what I wanted.

Making the nearly 140-mile commute there and back from Minnesota each day showed me that I didn't like driving hours to get to work. The small company workspace taught me I didn't like cliquey environments. Running the repetitive assays proved to me that I hated doing the same thing every day.

So I decided to try something new. My first gap year helped me realize that I wanted to think critically in my work and was interested in human disease. So I enrolled in a one-year training program in medical laboratory science. I loved the coursework, but the actual practice was less than desirable. I didn't like drawing blood. Nor was I fond of waking up for clinical rotations at 5 a.m. And engaging in clinical-machine babysitting for hours on end again only exacerbated my hatred for monotony.

With all of the negatives I experienced in those two years, you'd think it might be hard for me to endorse gap years. It is certainly true that at the time I felt like I was stuck in a perpetual vortex of trying one thing only to hate it the next week.

But it's because of those experiences that I was able to hone in on what I did and did not want in a job. What both years also made blatantly clear to me was that I wasn't going to find jobs that were intellectually stimulating enough for me without going to graduate school. So graduate school became the next step.

Even now, as a graduate student at Johns Hopkins University, I find myself wading through daily activities and gauging which ones I find enjoyable and which I'd rather avoid. I am simultaneously narrowing in on what my ideal job is and realizing the perfect job might not exist.

But that's OK. Knowing what you do and don't want in a job is important, and, as I learned in my gap years, each step it takes to get you closer to a good work fit can be its own informative experience.

Bree Yanagisawa (breannwoelfel@gmail.com) was an intern at ASBMB Today when she wrote this story. She is a Ph.D. candidate at the Johns Hopkins School of Medicine. Follow her on Twitter at twitter.com/BreeTalksSci.

Science interrupted

Undergraduates face a critical choice as graduation nears: enter a graduate program immediately or postpone. Graduate school in the biomedical sciences can be an intimidating prospect. In order to solve graduate-level research problems, students are asked to apply creatively concepts and principles that they were asked only to absorb during college. Other factors, including financial, familial and professional, influence the decision to go to graduate school. Often these factors prompt students to take gap years, or time off between undergraduate and graduate studies, to better decide what to do. Occasionally, however, gap years are forced upon the student, such as for health considerations. Gap years may even occur once graduate school is already underway. That was my situation.

Culminating accomplishment

I completed my four years of college at the University of Maine in May 2006. I decided to pursue a Ph.D. in biochemistry the next semester. I had been working in my thesis adviser's lab for a couple of years and enjoyed research immensely, despite the failed experiments and negative results! The biological and biomedical sciences Ph.D. program at Harvard Medical School accepted me. I remember vividly the elation I felt upon receiving the substantial admissions package in the mail at my tiny dormitory in Maine. Few feelings have come close to the satisfaction and sense of accomplishment I experienced at that moment. I felt ready to tackle any challenge come autumn.

The onset

I began graduate studies at Harvard in September 2006. My first-year classmates and I were wide-eyed and enthusiastic, imagining that we could conquer the world and any scientific problem in it. I began my first lab rotation in a yeast biochemistry lab that studied scaffold proteins, the molecular platforms that help organize the cell and direct other proteins. I had three introductory courses: molecular biology, genetics and literature review. Brilliant professors taught each class, endlessly inspiring and intellectually stimulating us students. I was overjoyed to be in what I considered the biomedical center of the universe.

I was progressing smoothly through my first semester in both my rotation and courses. I thought nothing stood between success and me. That illusion

crashed to Earth in mid-November, the day after watching the Harvard–Yale football game in Cambridge, Mass, with my parents. I suddenly felt a great general anxiety, and my emotions flew out of control. Gentle, normal waves of different moods were replaced by staggering highs and precipitous lows. The worst part was my ignorance of what was happening to my mind.

Lost focus

These experiences persisted and were an enormous disruption to my graduate studies. Concentration was nearly impossible since I had no internal regulation of my moods. I failed tests, dropped out of rotations and withdrew from my peers. I was able to join a thesis lab, studying Drosophila neurodevelopment, and pass my qualifying exam only out of sheer determination. I managed to remain a full-time student until May 2008. At that point, I lost my self-direction and decisive powers, quit my thesis lab, and took a leave of absence.

I met with an endless stream of professors during the leave but couldn't gain any professional traction. Everything felt boring, empty and pointless. My leave lasted a year and a half, and in consultation with my program administration, I eventually decided to leave the Ph.D. program. My situation worsened after losing what professional structure I had left.

The bottom and recovery

My mental health continued to deteriorate after leaving Harvard, to the point that I was hospitalized in psychiatric units twice, in January and March 2010. That was the darkest and most frightening experience of my life. I did not know whether I would live or die by my own hand.

After my second hospitalization at McLean Hospital in Belmont, Massachusetts, a psychiatrist there offered to work with me. She diagnosed me with bipolar disorder, and over the next few months we found stabilizing medication that helped me function. The next five years, from the summer of 2010 to spring of 2015, were difficult. I drifted in and out of jobs and relationships as my medication was adjusted and I tried to find mental balance. In April 2015, I began working as a research assistant in a lab at Boston Children's Hospital with a professor who understood my predicament and gave me a chance. I improved significantly over the next year thanks to my work, family support and finding the right combination of medications.

Unexpected return

In October 2015, my principal investigator suggested that I apply for readmission to my former Ph.D. program at Harvard Medical School. She thought I was having great success in her lab, and she believed in me. I discovered that there is a readmission process separate from the standard application, so I submitted the required documentation. I was accepted back into the biological and biomedical sciences Ph.D. program at Harvard Medical School in February, in time for my 32nd birthday. It had been almost 10 years since I first entered the program in 2006. We planned that I would resume working in my current PI's lab on Aug 1 of this year.

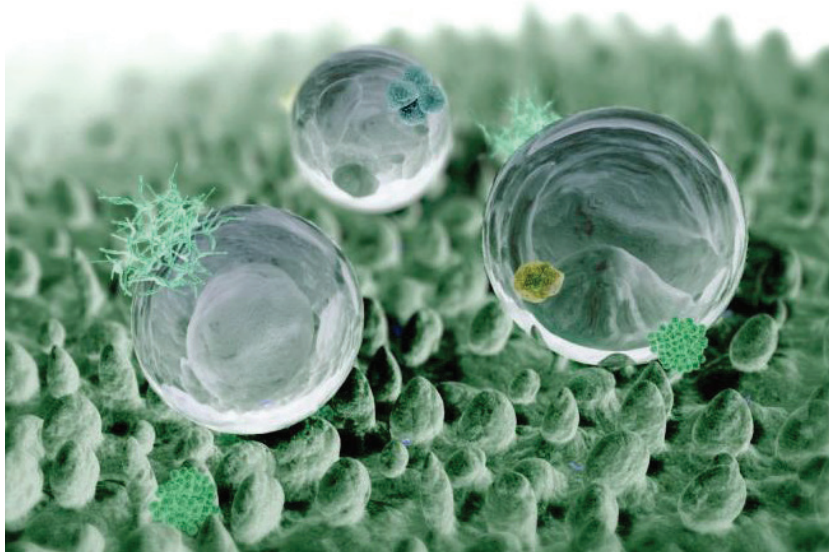
I cannot express how grateful I am to all involved in my readmission. It is a triumph I never expected to happen and testifies to what can be accomplished through modern medicine, support, faith and willpower. I feel prepared to succeed this time, tackling eagerly any challenge or obstacle. My plan is to finish in two years, as my qualifying exam, my teaching requirement and the majority of my coursework are finished. I am now confident that my future is bright and limitless. My involuntary gap years have come to a close.

Stefan Lukianov (stefanlukianov@gmail.com) was a research assistant in the urology department at Boston Children's Hospital. He has recently re-entered the biological and biomedical sciences program at Harvard Medical School.

NISE Net: Making a macro impact with nanoscience

By Geoff Hunt

Larry Bell is the senior vice president for strategic initiatives at the Museum of Science in Boston. Geoff Hunt, the American Society for Biochemistry and Molecular Biology's outreach manager, talked with Bell about the National Informal STEM Education Network, or NISE Net, a National Science Foundation-funded initiative that Bell has directed since its inception in 2005. This interview has been edited for style and content.



WILLIAM THIELICKE

Water droplets bead on nano-coated fabric.

How did the NISE Net get started?

The NSF was investing about $1 billion a year in nanotechnology research, and all of the surveys said that the public didn't know anything about nanotechnology. I think folks at the NSF were worried that the public was going to learn about nanotechnology from Michael Crichton's novel "Prey." They wanted people to learn about it some other way.

The NSF put out a solicitation looking for a science museum to take on the job of building a network of informal science education organizations and university research organizations to raise the public's level of awareness, knowledge and engagement with nanoscale science, engineering and technology. We partnered with the Science Museum of Minnesota and the Exploratorium in San Francisco to put together a proposal.

Larry Bell

What is the main function of the NISE Net?

The original idea was that we would work through science museums and their university partners to reach the public. It was uilt on the idea of, "Who are the audiences at science museums?" Because science museums have so many young visitors, if you wanted to reach the adults, the parents, who were visiting the museum with their children, you had to have something for the children to do too. So the NISE Net developed activities that would work for young children, older children as well as adults, so that the whole family could be engaged.

Give me an example of an activity

We made these pants that were about big enough for a doll to wear, one with nano-coated fabric and one without nano-coated fabric. There's a little squirt bottle with a little bit of water. You put a couple of drops of water on one of the pants, and the water soaks in. You put a couple of

EMILY MALETZ FOR NISE NET

The nano-fabric kit is one of several activities designed by NISE Net.

drops of water on the other pants and they roll right up; they bead up and roll right off.

It's clearly an activity that a little kid can do: give them the squirt bottle, let them squirt a little bit of water, and they see that it rolls off. At the 2015 Coalition for National Science Funding Annual Exhibition on Capitol Hill, the director of the NSF (France A. Córdova) came over to our table, and the first thing she went over to was those little nanopants and squirted water on them. It's an activity that works for people of all ages.

Who designs the activities?

Some of the very first activities had been developed by the education and outreach folks at University of Wisconsin-Madison. Some of their activities that were designed for classrooms got redesigned by the folks in the NISE Net to use in this kind of informal environment. But then we had a team (that) would work on developing different kinds of activities in sort of prototype form. They were balancing subject matter and how complicated the activities were and how expensive they were. Could they make 250 copies of them? Were the parts easy to get?

How do the activities go from idea to reality?

(The design team) would show (activities) off to their peers in meetings. People would bring their activities and get feedback from each other. They were responsible for getting review by scientists to make sure the science was accurate. Then they would have to take them out on the floor of the museum (or some other place where they had access to a public audience) and test them with the audience and make modifications to improve them. When they had gone through all of those steps, they could add them to the NISE Net online catalog. And then the team would perfect the activities for inclusion in kits.

How can ASBMB members get involved with the NISE Net?

Digital versions of the kits are online at www.nisenet.org. If there's a science museum in your neighborhood not too far away, it's possible that that science museum has gotten (an activity kit) and by connecting with them you could get your hands on the physical materials. Even though we, the Museum of Science, may be coordinating an event, it's grad students and undergraduate students who actually are using the activities to interact with the public. And the public gets a kick out of that, because they're talking to people who are actually working in the field.

What can we expect from the NISE Net going forward?

The NISE Net is continuing on to developing more materials. We've just sent out a bunch of kits about synthetic biology as part of the Building with Biology project. Those kits are being used this summer by a bunch of organizations around the U.S. We're just about to start a new project on chemistry. We're going to go through about a year's time in a design-based research project. Then we'll make 250 kits, and we'll put those out into the field.

Can you give me an example of the kind of impact these activity kits can make?

A representative from a children's museum (later revealed to be the Port Discovery Children's Museum in Baltimore) said, "Initially, to bring nano to the museum after I went to my very first workshop, I didn't get a lot of support. There was a lot of, 'We're not a science center,' and, 'That's not what we do.' … But now, it's a very different thing. Nobody wants nano to stop. It has become embedded in our museum. It is our niche. It is what we do." So totally transformative!

Geoff Hunt (ghunt@asbmb.org) is the ASBMB's public outreach manager. Follow him on twitter at twitter.com/thegeoffhunt.

Designing a career in science and art

By Dhruba Deb

Something was missing. Several years ago, I felt its absence growing. It was beginning to drive me insane.

After getting a M.Sc. in bioinformatics, I worked as a research fellow for a year and then became a joint Ph.D. student of math and medical oncology before landing a postdoc doing cancer research. I was living a conventional life of science — becoming a character straight out of the show "The Big Bang Theory."

But there was another part of me, an artistic side. I'd practiced studio-based art throughout my childhood and loved it. But during my scientific journey, the artist in me had become stifled by the solid bars of reproducibility, statistical significance and peer-reviewed publications. Over time, my vital connection to art had been reduced to a hobby.

PHOTOS PROVIDED BY DEB

Early example of Deb's art.

In 2011, I lost my mother to an aggressive brain cancer. The pain and anguish of that loss made me think hard about the purpose of my life. It was then that it came to me that I love science and want to keep working on cancer research. But I also love art. Could there be a way to combine these passions?

Would it be possible to put scientific methodologies together with artistic practices and still advance prevention, diagnosis or a cure for cancer?

Maybe, I thought, I could pursue the "how" of cancer in the lab during the day and the "why" of cancer in the studio during the night. But how?

Finding cancer scientist-artists

I started looking into existing art-science collaborative projects and searching for people trained in both scientific research and artistic practices. Although I found that there were many scientists and artists involved in various types of collaborations, there were few cancer scientist-artists like me interested in using artistic processes to do better cancer research in addition to simply making art about cancer.

"Hallmarks of cancer" created by Deb.

There was a plethora of work on art therapy and science outreach related to cancer. There were many examples of cancer data visualization too. But back then none of them rigorously combined scientific methodologies with artistic practices to generate novel research ideas or propose solutions for the crucial problems faced by cancer researchers when real-life data were not available.

One such problem is the variability of cancer cells. Even within one tumor, there can be cells with different biological properties and therapeutic implications. When I apply techniques of visual art, such as divergent thinking, to this problem, I can come up with a conceptual model for studying all the biological properties (known as the ten hallmarks of cancer) of tumors at the single-cell level. For me, an essential part of this creative idea generation process is the visualization

of such a conceptual model in drawing and painting.

Was it possible that on the other side of the planet someone was thinking just like me? I began to envision a network that would bring together cancer scientist-artists from around the world.

During this time, I also was taking a leadership course aimed at boosting communication skills. As part of my homework, I researched executive editors, founders, directors and CEOs of professional societies, nonprofits and academic journals interested in merging art and science. I made a list of people that I was interested in speaking with about the project and reached out to them.

Cynthia Pannucci, the founder and director of Art & Science Collaborations, or ASCI, in New York City, was the first to reply. She not only encouraged my idea of a cancer, art and science group, which I would go on to name the Cancer ART-SCI Network, but also connected me with Roger Malina, the executive editor of an art and science journal called Leonardo. Malina liked my idea. I published a peer-reviewed article in Leonardo called "Understanding the unpredictability of cancer using chaos theory and modern art techniques." Response was positive, and I proposed an "art and cancer" special section in Leonardo. Malina agreed on the condition that I be the guest editor and form an editorial advisory committee.

"Strange attractor of cancer in its phase space" created by Deb in 2015.

Artworks by the members of the Cancer ART-SCI network in the LuminArté gallery in Dallas, Texas.

The special section aims to document studies where scientific methodologies combined with artistic practices could advance prevention, diagnosis or cure for cancer.

By the time the Leonardo special section was underway, I had made contact with about 10 other scientist-artists who shared my vision. Now that there was a publication willing to cover the intersection of cancer research and art, how could I grow this small network? Was there a way to reach out to cancer scientist-artists worldwide?

Expanding the network

In 2013, I was giving an award lecture about my work on identifying novel therapeutic targets in lung cancer at the Memorial Sloan-Kettering Cancer Center in New York. The talk was on the same day as the Leonardo Art Science Evening Rendezvous seminar, which goes by the acronym LASER, in New York City. I spoke to the organizers of LASER, and they agreed to let me present my cancer-art collaborative work at the seminar.

I literally carried two bags on my shoulder that day — one from the science conference and the other from the art event. The LASER meeting got me a lot of new contacts in New York City. In addition, I was interviewed by the online magazine Sci-Art in America and got featured by ASCI. Soon after, I recorded a podcast on our growing network of cancer researchers and artists at the University of Texas at Dallas and was invited to a meeting arranged by the National Academies on combining art, science, engineering and medicine.

The Cancer ART-SCI Network started getting international attention. Le Scienze in Italy and MedInArt in Greece featured an ongoing visual art project we produced called "Cancer: Finding Beauty in the Beast," on their websites.

I recently curated and participated in a gallery installation to show the works of art created by the members of Cancer ART-SCI Network. It involved paintings, sculptures and photography created by six scientists and artists.

Loving life

Now I am living a life that I love. I am a scientist by day and an artist at night. I would like to stay that way. In the future, if I'm offered the chance to practice both as part of one job, I will take it.

The Cancer ART-SCI Network is a fast-growing community, and it already has members from several countries around the world. At some point, I may create a nonprofit organization to manage its burgeoning activities.

I feel this is just the beginning of a fulfilled life.

Dhruba Deb (dhrubadeb@gmail.com) is a postdoctoral researcher at the University of Texas Southwestern Medical Center, founder of the Cancer ART-SCI Network and guest editor for the "Art and Cancer" section at the journal Leonardo.

Pointers for those curious about careers in industry

By Angela Hopp

This is the first in a series of interviews with Kenneth I. Maynard of Takeda Pharmaceuticals International Inc. about what it takes to launch and propel a career in the pharmaceutical industry. Maynard previously worked for Sanofi, Aventis Pharmaceuticals and Harvard Medical School. He is a member of the National Institutes of Health Common Fund's external scientific panel for the Broadening Experiences in Scientific Training program. This Q&A with ASBMB Today's executive editor, Angela Hopp, has been edited for length, style and clarity.

What tips do you have for students interested in a pharmaceutical industry career?

Network, network, network. You need to learn as much as you can about the pharmaceutical industry and the plethora of available opportunities. Speak with as many people as you can to get to know them and what they do in any pharma company. This helps to understand this vast area.

Know yourself. Knowing what it is that you are passionate about and what role you wish to play in this area is critical. Based on my own experience and on what I know of the pharma industry today, it is best to get trained in academia as long as you possibly can, depending on the amount of responsibility that you want to have in industry. For example, it would be difficult to work your way


Kenneth Maynard

up from a bench scientist to become head of a disease area in a big pharma company. If you wish to be head of a drug discovery unit or head of a therapeutic area, then you're probably better off transitioning from a position as head of a department or chief of a clinical service, because it brings a certain amount of experience and seniority. If you do not wish to be a manager but to remain at the bench doing basic science, research assays, animal models and such, it would be fine to transition out of academia with a master's degree or a newly obtained Ph.D. If you want to be a group leader, I'd say transition after you've achieved a junior faculty instructor or assistant professor position. Think carefully about where to position yourself and when to make that transition.

Which skills, besides scientific ones, are most important for career advancement in industry?

Anyone who has obtained a Ph.D. will have gathered various skills along the way that are important for career advancement in the pharmaceutical industry.

The most obvious of these is written and verbal communication skills. The very best communicators are able to write and speak so effectively that they are able to explain, in a clear and concise manner, concepts and information that are complicated and sometimes not yet codified into law. We can be exceptional communicators if we can provide clarity on topics to people who are outside their field of expertise or who are experts in the field.

Linked to effective communication is leadership skills. John C. Maxwell, the No. 1 global leadership guru of 2016 according to the Global Gurus List of Top 30 Global Leadership Experts, describes leadership as "influence, nothing more, nothing less." Whether we help colleagues develop their own ideas for experiments, lead small lab journal clubs, mediate large group discussions, or facilitate panels at meetings or conferences, we are developing important teaching, mentoring, coaching and leadership skills of influence.

Another skill acquired is that of self and project management, which requires effective work habits and organizational skills. Once we are given carte blanche to pursue a new area of endeavor that has not been studied previously, we soon find that we somehow need to consume a lot of new information, frequently unsupervised, and then identify unanswered questions and prioritize and evaluate them. Once we have decided the questions to which we plan to find answers, we need to set goals and put tasks in place, including learning techniques to help us address the questions. Because this process cannot

continue ad infinitum, we also need to set up timelines in which to accomplish these tasks. We soon learn that whatever time we set aside to perform them is vastly inadequate and probably needs to be doubled, so amid all of this planning we learn to be flexible and use prioritization as a tool to maximize our time spent on performing important and urgent tasks and delegating unimportant and nonurgent tasks. As much as there is a timeline in our academic pursuits, the impact of time in the pharmaceutical industry is even more pronounced, since patients need medicines now. The process from idea to drug continues to increase, so this aspect continues to get worse over time. This skill therefore becomes more and more important in terms of meeting deadlines.

What are the best ways to find jobs in industry for those just coming out of academia?

There is nothing to replace doing the grunt work of seeking opportunities through online searches and reviewing professional journals that typically have jobs advertised. Some professional societies have electronic job boards online, send regular emails listing job opportunities or host job fares at annual conferences, with capacity for speed dating sometimes available.

By far I have found that the best way is through networking with people who work in the pharmaceutical industry. The ideal situation is to have someone bring an opportunity to your attention even before it hits the internet for general consumption. That requires more than just networking but actually developing a relationship with people in the industry who are willing to take the time to make you aware of such opportunities. For that to happen, they will at least need to be convinced that you are a person of value and would be good fit for their company. This is unlikely to occur by simply giving someone your business card.

Pharma companies sometimes approach senior academic investigators with whom they have productive existing relationships. Thus, these key individuals may sometimes know about open positions in companies.

What are some common mistakes people make while interviewing for jobs in industry?

As much as you are being interviewed by the company, they expect that you know who they are, what they do and what drives you to join them. This will not be the case if you are not prepared by knowing the company, such as its key assets, areas in which it works or has products, its culture and what is important to it, and its recent important announcements to the public. These can be found easily on companies' websites or in publicly available annual reports if they are larger companies, but may be more difficult to find if they are small biotech or startup companies.

Once you are fully aware of the company, and even if you were not able to find much on the internet, not asking about or realizing that they may have various positions for which you may be an eligible candidate or not being flexible enough to consider these other opportunities is a potential shortfall. Moreover, asking questions that indicate to the interviewer your insights into the company also may help you gain valuable information that may help you to understand what it is about that position or company that could help you to make your own decision in the event that you get multiple offers from various companies.

Understand that the pharmaceutical industry is one of the most highly regulated industries in the world and employees must live by codes and standards. This impacts the way one's communication and even dress code could negatively inform an interviewer about the candidate's capacity to adapt to the environment. More and more companies and recruitment services are examining not only LinkedIn but also the Facebook pages of potential employees to determine suitability.

What are they looking for? What will they find there?

Although you have submitted your CV or résumé online or to a recruiter, it is possible that some interviewers may not have received it or may not have taken it to the interview because they are running in between meetings, so you need to take extra copies just in case. For this purpose, among others, it is better to have a two- or three-page résumé than a 25-page CV and corresponding length bibliography.

Be prepared to articulate succinctly what unique skills and assets you, the applicant, bring to the position based on your prior position(s) and experience(s). Once you make it past the screening process, many of the candidates look similar on paper. Your unique skills and experiences are what set you apart from the other candidates, and you want to be clear about that and not have them guess at what it might be. This is where that elevator speech will be useful.

Understand at what stage of the application and interviewing process salary and compensation packages may be discussed. This is typically not done at the first telephone interview; however, being ready to have the discussion, just in case, is to be better prepared.

Angela Hopp (ahopp@asbmb.org) is the ASBMB's communications director and ASBMB Today's executive editor. Follow her on Twitter at www.twitter.com/angelahopp.

A mother's letter to biomedical researchers

By E. Gay Grossman

"I need to know if you are on our team," I said into the phone. There was dead silence.

It was 1999. The man on the other end of the line was the first geneticist I had taken our daughter, Lilly, to see. She was 2 years old.

I had gone to see this geneticist because I wanted to have another baby, but I was concerned about Lilly's slow progression. At age two, she wasn't walking. Crawling was difficult, because her arms would suddenly give out beneath her and leave bruises on her banged forehead. But she loved to roll and furniture-walk. Her MRI was normal.

PHOTOS PROVIDED BY GROSSMAN

The Grossmans in 1998.

Lilly's diagnosis was proving to be tricky for medical experts. This particular phone conversation was the first time I felt that we were very much alone in our search for a diagnosis. The feeling kept coming back as we saw more doctors, and I quickly learned that I was the one who had to drive Lilly's case forward. I was told to be patient. I was told not to compare her to other kids. I was reminded that I was a first-time mother. I was asked to bring my husband to appointments. I was told I held her too much. I was told it might just be in my head.

By the time Lilly was two and a half, we'd already taken her to three pediatricians, two neurologists, one endocrinologist and the geneticist I had on the phone. This is the same geneticist who had told me, on the night when we took Lilly to the emergency room because her tremors wouldn't stop, that his wife was angry with him because he was missing a family dinner with his son home from college. I remember wondering if Lilly would make it to college like his son.

Months turned into years. At 8, Lilly couldn't walk and had trouble talking, and her tremors had increased in frequency and strength.

The tremors that started when Lilly was 18 months old were slight but over time developed into out-of-control shaking. It looked like she was having seizures. We had to hold her arms so she didn't scratch her face. She wore socks to bed because her toenails cut her legs and made them bleed. There was a pillow along the wall so she didn't hurt her hands when they flailed against it. All night long, she would be awake, aware and screaming in pain.

We continued to see every doctor anyone suggested. I had random people handing me notes when I was shopping. "Go see this doctor," they'd say. "He might be able to help your daughter." My mantra became, "I will never look back and regret not pursuing something. I will always try everything."

By the time Lilly was in first grade, she had seen more than 35 specialists across the country. By the time she was 8, she'd seen so many that when we'd share her health records, we'd hear, "Every doctor I want to suggest to you, you have already seen."

Being awake all night gives you plenty of time to think. I thought about how difficult it was not to be able to open the windows at night because your child is screaming in pain. I thought about how lucky I was that the social worker came during the day, because if the social worker saw our nights, my child could be taken away from me. Mostly, I thought about how this night was the same as the night before and how the next night would be like tonight. We were alone.

We held down our baby for blood draws, too many to count. We went through the laborious process of collecting urine samples from a baby girl wearing diapers. We heard her cry from spinal taps and cradled her in our arms until the drugs made her

sleepy so they could place her in an MRI machine to look at her brain. We cared for the aftermath of skin, muscle and nerve biopsies. These are things no parent should have to endure. To experience them while having to beg your insurance company to pay for them adds insult to injury.

Then we hit a dead end because we ran out of tests to do. Every test result was normal.

Living this life takes its toll. Both my husband and I suffered from stress-related ailments. A couple of years later, I was diagnosed with stage 2 breast cancer. But for both of us, our ailments and my diagnosis were manageable because they were known and had a plan. We still were searching for Lilly's diagnosis.

When Lilly was 15 years old, whole-genome sequencing was on the horizon. I'd been watching its progress for years. It still wasn't available to the general public, but this didn't stop us from asking about it at every opportunity. I was determined to get Lilly sequenced.

Our first stab at it ended quickly when the study required a sibling to participate. Within six months, another study was available. I reluctantly let the intake nurse know that Lilly didn't have a sibling. But their funding was for a trio — mother, father and affected child.

Lilly Grossman in 2006.

I set about collecting Lilly's information to submit for the study. Her medical records were already on a disc, but I wanted whoever read Lilly's file not to stop thinking about her. I assembled items in a bright pink notebook. I put 8 1/2" x 11" photos on the front and back. The front photo was a perfectly healthy-looking Lilly. The back photo was her confined to a wheelchair. Inside there was the medical disc. There was a letter from Lilly's principal confirming her GPA of 3.5 every semester and a poem Lilly had written expressing her dreams and her frustrations.

The study was to take seven patients. A day after the committee overseeing the study met, I received an email at 10 p.m. that said "You probably know the committee met yesterday, but I wanted to let you know Lilly is patient #1."

There have been only a few moments like this in my life when I couldn't find the words to express the gratitude I felt toward someone for putting Lilly on a to-do list and using grant funding for her.

While we waited for the results from the first study, we agreed to participate in a second study looking at the emotional experience of having our genomes sequenced. I remember Lilly being interviewed. She was asked, "Lilly, what do you fear most while waiting for the results?" She turned her head to me, and a tear dripped down her cheek. I knew her answer: Lilly's greatest fear was that they would find nothing.

A 2015 photo of the Grossman family.

One night, I received an email that said, "They found something. A mutation on the ADCY5 gene, which has treatment options, and the DOCK3 gene, for which very little is known."

We next had a two-hour appointment with Lilly's neurologist, who explained in detail about the genes. There was only one other family with the mutation in the gene for adenylyl cyclase V, or ADCY5. The enzyme is a member of a family of proteins responsible for generating cyclic adenosine monophosphate, better known as cyclic AMP, in cells.

Lilly and I were the only ones known to have a mutation on the DOCK3 gene. We were told Lilly had a normal life expectancy. You don't realize the significance of a shortened life expectancy for your child until it is lifted.

Once we had our mutated genes identified, we realized we were uneducated about the science and had no plan. We dug in and learned the science, went to conferences, networked and scoured the internet. We soon discovered no one else had a plan either.

CONTINUED ON PAGE 58

CONTINUED FROM PAGE 57

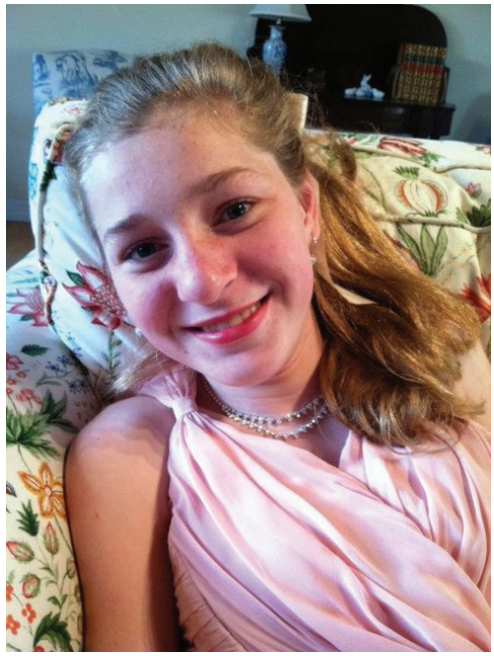
We were the second family to have a child with an ADCY5 mutation; we were the first in the world to have the DOCK3 mutation. Searching for journal articles confirmed no one knew much about either mutation.

Our clinician prescribed Diamox, a carbonic anhydrase inhibitor, which sometimes is used to treat epileptic seizures and has been found to calm tremors. It has brought Lilly great relief, actually eliminating nightly tremors for months at a time. When she began taking it we all slept for a full night for the first time in years. But over time, the drug began affecting her fine motor skills and made typing difficult. Now she stops and restarts it when the side effects cease. Tetrabenizine, which often is prescribed for uncontrollable movement disorders and tics, also has brought relief. We've found that alternating these two medications is the best fix for now.

Having these drugs has been life changing for all of us. Lilly's dorm life would be impossible without them. Traveling and staying overnight in a hotel would not be an option.

These days, we share Lilly's story, sign documents so others can talk about Lilly's case without us being there, and open her records to anyone interested in seeing them. Selfishly, finding families affected by ADCY5 and DOCK3 will bring us the numbers we need so that when someone is ready to study Lilly's mutations, we'll have the necessary critical mass.

Lilly still uses a wheelchair, and she can't walk. Some people have trouble understanding her speech. Lilly has just finished her freshman year in college, living in a dorm with 24/7 care. She pledged a sorority, has had articles printed in the school newspaper and has chosen a major of English with a minor in political science.



Lilly Grossman in 2011.

While Lilly is at school, we are busy creating a foundation called ADCY5.org. In just three years, we have gone from two ADCY5 patients to more than 100 worldwide. The foundation is giving newly diagnosed families a place to land and find support. It's providing a place for researchers to find the papers published on ADCY5. We are seeking help to understand the biology so that we can move toward a definitive treatment. Funded science is the only thing that will get us to our destination.

I hope that someday you'll read my follow-up article about Lilly after a treatment is found. You'll read about her dreams being fulfilled because of science. You'll remember reading this article, and you'll share our relief. Maybe you'll be a part of our journey and find the treatment for the mutations on the ADCY5 and DOCK3 genes.

E. Gay Grossman (gaygrossman@gmail.com) is a founder of ADCY5.org and a patient advocate who speaks widely on living with rare diseases.

The Art of Science Communication

Fall session begins Oct. 3

The Art of Science Communication online course provides participants with fundamental communications training, focusing on how to present science to a nonexpert audience in a formal setting.

Registration deadline: Sept. 19

Take part in the ASBMB class from wherever you are for only **three to four hours** a week.

During the course, you will learn to:

- construct and deliver an effective presentation
- get your message across
- generate interest in your topic
- engage your audience
- effectively use nonverbal communication

The course is **eight weeks** long and **costs $25** for ASBMB members.*

**The cost for non-ASBMB members is $100. Visit www.asbmb.org/join to become a member.*

www.asbmb.org/outreach/training

ASBMB
American Society for Biochemistry and Molecular Biology

Re: Deceased members (June/July 2016)

The list of recent ASBMB member deaths in your June/July issue included Donald Hanahan, a leader in phospholipid biochemistry and founding chair of the department of biochemistry at the University of Arizona College of Medicine. I joined Don in 1967, just weeks before the arrival of the first class of 32 medical students. The college had been planned in the traditional way, with basic science departments quite distinct from pre-existing units on the parent campus. Don was wise enough to see the strength in collaboration, and he oversaw creation of a campus-wide Graduate Committee on Biochemistry. Eventually this became a universitywide department — ironically, some years after Don had left Arizona. But Don's wise influence was felt at Arizona for many years.

Christopher K. Mathews, Oregon State University

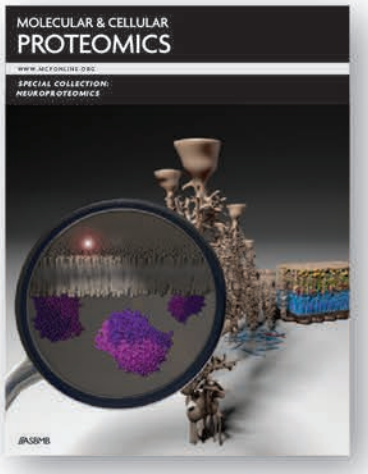
Re: Meet Natalie Ahn, ASBMB's incoming president (June/July 2016)

Having read (Natalie) Ahn's first contribution to ASBMB Today and (Steven) McKnight's last, I was disappointed to find no mention of the educational activities of the ASBMB.

Ellis Bell, University of Richmond

I agree. Considering that Dr. Ahn states that two of her three top priorities are to "recapture the annual meeting's reputation as a must-attend event" and "expand our visibility and membership, especially among young investigators," I believe some mention of the undergraduate poster competition and the many other educational opportunities at the annual meeting would have been appropriate.

Phillip Ortiz, State University of New York



ASBMB JOURNALS

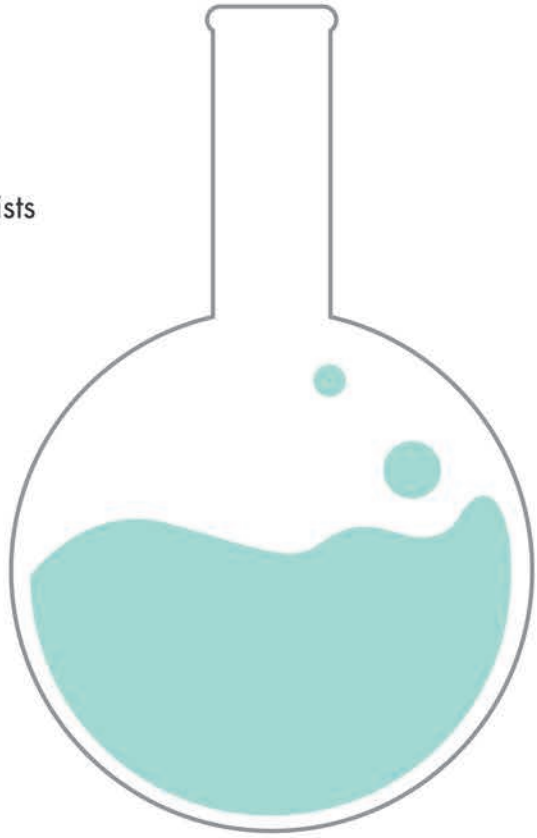
When you submit to an ASBMB journal you can expect:

- No submission fees
- Fair, thorough, constructive peer review by scientists
- Immediate and freely available publication upon acceptance

ASBMB member benefits:

- Discounted page charges and free color figures*
- Complimentary online subscriptions to JBC, JLR and MCP

**ASBMB has eliminated color figure fees for regular members publishing as corresponding authors.*



ASBMB
American Society for Biochemistry and Molecular Biology

www.asbmb.org/publications

2017 ASBMB ANNUAL MEETING

CHICAGO
APRIL 22-26

WWW.ASBMB.ORG/MEETING2017

ASBMB
American Society for Biochemistry and Molecular Biology