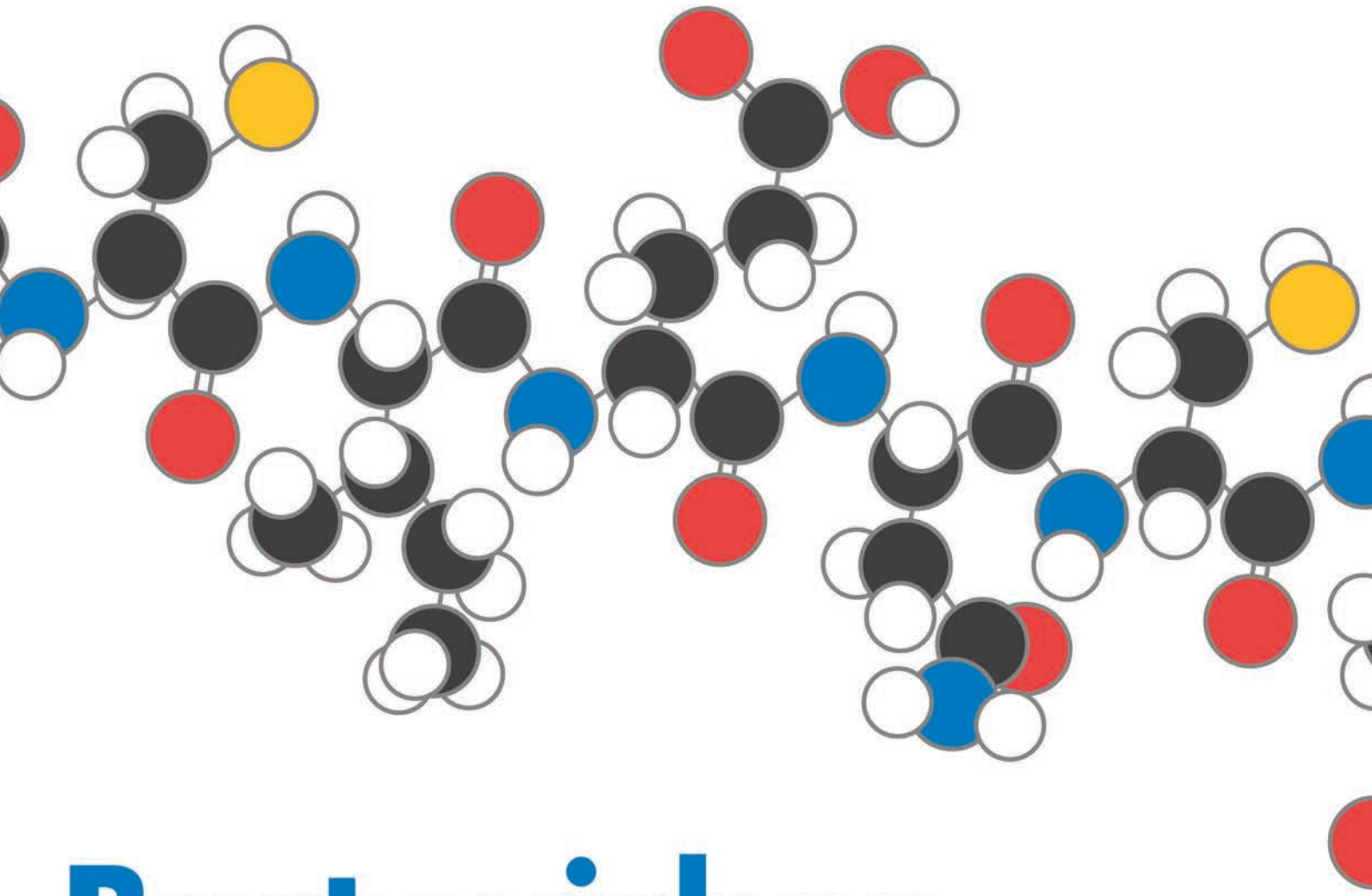
Vol. 18 / No.1 / January 2019

ASBMB TODAY

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

THE WELLNESS ISSUE



Best wishes in 2019!

Together, we'll continue to advocate for science, connect researchers around the world and build a bright future for biochemists and molecular biologists everywhere.

WWW.ASBMB.ORG/RENEW

ASBMB
American Society for Biochemistry and Molecular Biology

CONTENTS

NEWS

2
EDITOR'S NOTE
On being well

3
NEWS FROM THE HILL
In 2019, advocacy will be all down hill

4
MEMBER UPDATE

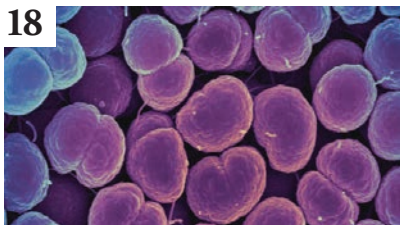
6
RETROSPECTIVE
Thomas A. Steitz (1940 – 2018)

10
A YEAR OF (BIO)CHEMICAL ELEMENTS
For January, it's atomic No. 1

11
NEWS
11 ASBMB members elect six to council and other offices
12 Celebrating Herb Tabor
14 Student Chapter president sees value in campus groups

15
JOURNAL NEWS
15 The discovery of GABA in the brain
17 A molecular dance of phospholipid synthesis
18 Researchers closer to gonorrhea vaccine after exhaustive analysis of proteins
19 A close-up of nascent HDL formation
20 From the journals

18



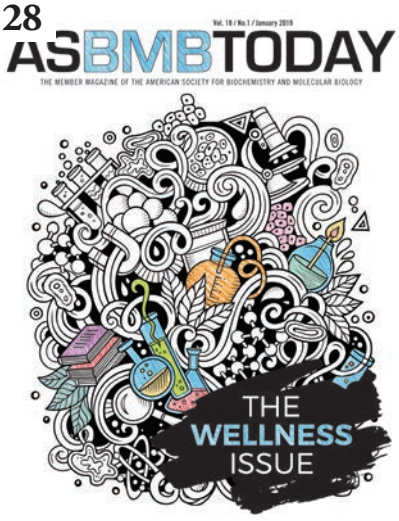
FEATURES

24
HOW TO PATENT AN ANTIBODY
Advice from Charles Craik

28
THE WELLNESS ISSUE
29 Finding the help you need
32 Leadership with a focus on wellness
34 With a little help from my friends
36 Grad students face mental wellness challenges
37 Career wellness: consider your strengths
39 Maternity in grad school — the best and worst of times
41 Holistic mentorship
43 Refreshing my spirit
44 How I learned to stop worrying about grad school and to love climbing rocks
46 For many college students, hunger can 'make it hard to focus in class'
48 Chronic pain after trauma may depend on your stress gene

24

28



PERSPECTIVES

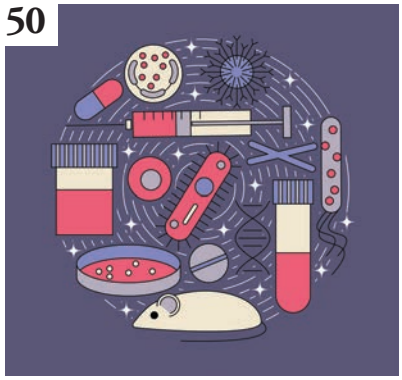
50
ESSAY
Why aren't there quality controls for antibody research?

52
EDUCATION
Catalyst conversation workshop provides tools faculty can use

54
NIGHT SHIFT
Committing for more than one night

55
CARTOON
The 10 commandments of grantsmanship

50



54

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

www.asbmb.org/asbmbtoday
PRINT ISSN 2372-0409

On being well

By Comfort Dorn

Get well soon.

We say that when someone is sick. It's a reflex, like saying "bless you" when you hear a sneeze. It's the sentiment emblazoned on cards, balloons and teddy bears in hospital gift shops.

But wellness is more than the absence of disease. And we know this, right? Even beyond the multi-billion dollar wellness industry with all its potions and pampering, most of us know what it is to feel unwell without being diagnosed as ill.

Yet we're ambivalent about working at wellness — at taking steps to make ourselves (and others) feel our best. That's especially true of people who take their careers very seriously, like (cough) scientists. Who has time for yoga and counseling when you have experiments to monitor, papers to write and breakthrough discoveries to make?

This month, we want to remind you that you can't do any of those things well if you are not well. And beyond that, if you only get one shot at this mortal coil, you might as well feel your best — physically, spiritually and mentally. Maybe you can't cure your own cancer, but for sure you should be able to eke out eight hours of sleep and the occasional moment of serenity.

And because we don't live on private islands, we should look to the wellness of others, whether it's making sure undergrads get enough to eat or helping postdocs recognize their personal strengths.

Wellness is a big-tent topic. In this issue, we offer essays and articles on everything from rock climbing to holistic mentorship. Some, like Paul Craig's account of surviving failure, are deeply personal. Others, like Nathan Vanderford and Teresa Evan's essay on leadership, offer step-by-step guidance and practical tools. And because we are science geeks at heart, we include an article on the genetic cause of pain after trauma.

Have we covered all the bases? Absolutely not. But if you find this issue useful, thought-provoking or even inspiring, let us know. I had such a great time working with all these authors and their wonderful words, I'd be happy to do this again in January 2020.

Be well, and have a very happy new year.

Comfort Dorn (cdorn@asbmb.org) is managing editor of ASBMB Today. Follow her on Twitter @cdorn56.

In 2019, advocacy will be all down hill

By Benjamin Corb

It is the job of the Public Affairs Advisory Committee to advocate for American Society for Biochemistry and Molecular Biology members by communicating your needs to the U.S. Congress, the White House and the federal agencies that support your pursuit of scientific discovery. However, studies show that when individual constituents (that is, voters) talk or write directly to their representatives, those words have greater impact than even the most dedicated advocacy group.

In other words — we need your help.

Your duties as a scientist may limit how much time you have for advocacy. With that in mind, we've designed a three-tiered approach to communicating with government officials, and we're offering a menu of actions to choose from depending on how much time you have.

Here on the East Coast, January brings snow and skiing to mind, so we're using common ski slope terminology to explain how this works.

With tier one or "green circle" (think bunny slope) activities, you can participate in one minute or less. These simple "click here to send a message" tools will direct emails or tweets to your elected representatives. Green circles are the bread and butter of an advocacy campaign. They are an easy way for ASBMB members to get involved. When you do a green circle activity, it helps us contact as many elected officials from across the country as possible and allows you to be an advocate even if you're busy.

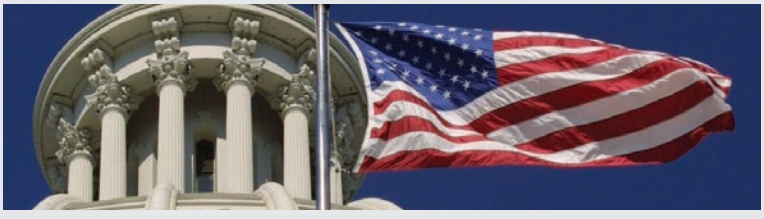
Tier two activities require a little more effort, like "blue square" ski trails. These activities should take you a half-hour or less. A hand-written letter to a member of Congress or a letter to the editor of your local paper are examples of blue square advocacy opportunities. Your added time and attention will help you (and the ASBMB) develop a stronger connection with your elected officials. And the public affairs staff will provide sample text or topics and all the supporting information you need to author a unique piece of writing for a blue square message.

Finally, in tier three "black diamond" activities, passionate ASBMB members can display their expert advocacy abilities. These opportunities take significant effort but have great impact. Organizing a visit to your representative's office or a lab tour for government officials are activities that fall in this category. Not all members have the time or opportunity to organize such events, but if you are willing to take up the challenge, the public affairs office will provide you with support and resources.

The Public Affairs Advisory Committee will run several advocacy campaigns in 2019; they will be posted and updated at www.grassroots.asbmb.org and also include suggested activities at each of the three levels. The first campaign, starting this month, is to educate the freshman class of Congress on the importance of robust federal investments in science. In the spring, we'll highlight what ASBMB members have been doing with increased funding at the National Institutes of Health in recent years. We also plan to talk about immigration and STEM education policies. If you have a topic you think we should address, tell us at publicaffairs@asbmb.org.

We look forward to working with you in 2019.

Benjamin Corb (bcorb@asbmb.org) is director of public affairs at the ASBMB. Follow him on Twitter @bwcorb.



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**.

Member update

By Erik Chaulk

Hanson moves to University of Michigan

Phyllis Hanson was appointed chair of the department of biological chemistry at the University of Michigan Medical School in November.


HANSON

Hanson previously served on the faculty at the Washington University School of Medicine, where she began as assistant professor in 1997 and rose to hold the Gerty T. Cori professorship in the department of cell biology and physiology.

Hanson's research focuses on understanding intracellular membrane organization and trafficking.

In addition to chairing the biological chemistry department, she will hold a joint appointment with the University of Michigan's department of neurology.

Hanson is an associate editor of the Journal of Biological Chemistry.

O'Malley shares Horwitz prize

Bert W. O'Malley is one of three recipients of the 2018 Louisa Gross Horwitz Prize for their work on hormone regulation of distant cells.


O'MALLEY

Presented by Columbia University since 1967, the Horwitz prize honors a scientific investigator or a group of investigators for outstanding basic research in biology or biochemistry.

O'Malley is being honored for demonstrating in the 1960s that steroid hormones modify gene expression, entering the cell and binding to nuclear receptors, which modify gene activity.

He is the T.C. Thompson distinguished leadership professor of molecular and cellular biology and chancellor at Baylor College of Medicine.

The award, which O'Malley shares with Pierre Chambon and Ronald Evans, includes an honorarium and a citation presented at a ceremony in October.

ACS Bader award goes to Broderick

The American Chemical Society has presented the 2019 Alfred Bader Award in Bioinorganic or Bioorganic Chemistry to Joan Broderick.


BRODERICK

Established in 1986, the annual Bader award recognizes outstanding contributions to bioorganic or bioinorganic chemistry research.

Broderick is a professor in the department of chemistry and biochemistry at Montana State University. She is being honored for her research on radical SAM enzymes and biological metal cluster assembly in hydrogenases.

In addition to her research accomplishments, Broderick is highly regarded for her excellence in teaching and mentorship of the students in her laboratory.

She served on the faculties at Amherst College and Michigan State University before moving to Montana State University in 2005.

Gentry receives Landis award

Matthew Gentry is among the first recipients of the Landis Award for Outstanding Mentorship.


GENTRY

Awarded by the National Institute of Neurological Disorders and Stroke, the Landis award will be presented annually to up to five faculty members who have shown outstanding dedication to mentoring students and trainees.

Gentry is a professor in the department of molecular and cellular biochemistry at the University of Kentucky College Of Medicine. He serves as a mentor to students in his lab, where the research focuses on bothglycogen metabolism in humans and starch metabolisms in plants and algae.

Awardees receive $100,000 to support their efforts to develop and mentor students and postdoctoral fellows in their laboratories.

In memoriam: Gordon Shore

Gordon Shore passed away Sept. 7 at the McGill University Health Center Palliative Care Unit. He was 73.


SHORE

Born July 26, 1945, Shore received his Ph.D. from McGill University in 1974 and did postdoctoral work on mitochondria in England with Jamshed Tata.

Shore was a professor emeritus of biochemistry at McGill University, where he taught and did research

ASBMB members elected as 2018 AAAS fellows

The American Association for the Advancement of Science has elected 416 of its members as fellows, in recognition of their extraordinary achievements in advancing science. Of those honored, the 31 listed below are members of the American Society for Biochemistry and Molecular Biology. The fellows will be recognized at the 2019 AAAS annual meeting in February.

Section on biological sciences
Juan D. Alfonzo, The Ohio State University
Paul N. Black, University of Nebraska-Lincoln
Mary Dasso, National Institute for Child Health and Human Development/NIH
Savithramma P. Dinesh–Kumar, University of California, Davis
Joseph Jez, Washington University in St. Louis
Kristen Marie Johansen, Iowa State University
Megerditch (Mike) Kiledjian, Rutgers, The State University of New Jersey
Carla M. Koehler, University of California, Los Angeles
Iris Lindberg, University of Maryland, Baltimore
Hua Lu, Tulane University
Neil Osheroff, Vanderbilt University School of Medicine
Linda Joy Pike, Washington University School of Medicine in St. Louis
Kevin L. Schey, Vanderbilt University
Madeline A. Shea, University of Iowa
Binghui Shen, Beckman Research Institute, City of Hope
Holger Sondermann, Cornell University
Allen Taylor, Tufts University
Stephen Halley White, University of California, Irvine
Dong-Er Zhang, University of California, San Diego

Section on chemistry
Wonhwa Cho, University of Illinois at Chicago
Neil K. Garg, University of California, Los Angeles
Carlito B. Lebrilla, University of California, Davis
Glenn D. Prestwich, University of Utah, College of Pharmacy

Section on medical sciences
Eric R. Fearon, University of Michigan
Isaac Ness Pessah, University of California, Davis
Lawrence I. Rothblum, University of Oklahoma Health Sciences Center
Liangyou Rui, University of Michigan
L. David Sibley, Washington University School of Medicine in St. Louis
Gary Arthur Silverman, Washington University School of Medicine in St. Louis

Section on neuroscience
Jonathan Brewer Cohen, Harvard Medical School

Section on pharmaceutical sciences
John L. Nitiss, University of Illinois at Chicago

on cancer. His research focused on the regulation of oncogene-induced apoptosis.

He was also co-founder and chief scientific officer of Gemin X Biotechnologies, which develops small-molecule cancer therapeutics based on the regulation of apoptosis.

He is survived by his wife, Alexandra, and his children, Bobby, Michael, Dominique and Dylan.

Read a remembrance of Gordon Shore by his friends and colleagues John Bergeron and Richard Rachubinski at asbmb.org/asbmbtoday.

In memoriam: Lowell E. Hokin

Biochemist Lowell Edward Hokin passed away in September. He was 93.

Hokin was born in Peoria, Illinois, in 1924. He began his education at the University of Chicago before enlisting in the U.S. Navy V-12 program to study medicine at Dartmouth University.


HOKIN

He earned an M.D. at the University Of Louisville School of Medicine and completed a residency at Michael Reese Hospital in Chicago. Hokin then did doctoral research in biochemistry in England under Sir Hans Krebs.

Hokin joined the faculty at the University of Wisconsin in 1957. He held several positions before being named chairman of the medical school's department of pharmacology, a position he held from 1970 to his retirement in 1993.

An accomplished researcher, Hokin is known for his discovery, along with his first wife Mabel Hokin, of the phosphoinositide signaling system. He also discovered the fundamental biochemical features of sodium-potassium ATPase.

He is survived by his wife, Vivian, three children and three grandchildren.


Erik Chaulk (echaulk@asbmb.org) is a peer-review coordinator and digital publications web specialist at the ASBMB.

Thomas A. Steitz (1940–2018)

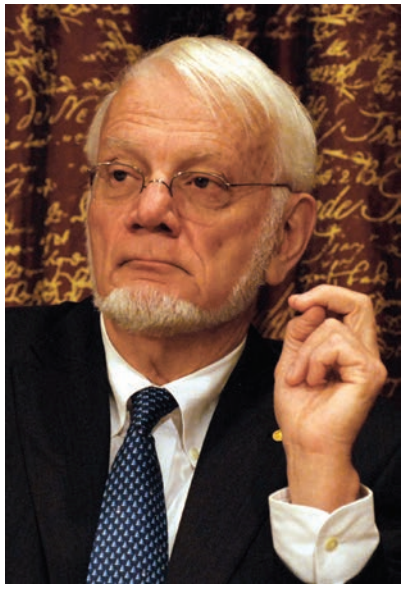
By Martin Schmeing

Thomas Arthur Steitz was a remarkable person, scientist and mentor. He was a Sterling professor of molecular biophysics and biochemistry at Yale University, a Howard Hughes Medical Institute investigator, a Nobel laureate and a giant in the field of structural biology. His death on Oct. 9 left a void in the scientific community and for those who knew him as well as a legacy of fundamental discoveries.

Tom was born Aug. 23, 1940, in Milwaukee, Wisconsin. His childhood in a family of five siblings was filled with classic Americana — tennis and skating and summers spent picking vegetables on his grandfather's farm. In high school, Tom became a skilled saxophonist, developing his lifelong love for music. He also excelled academically, initially spurred on by his younger brother's higher grades.

Tom earned a scholarship to Lawrence College, where he majored in chemistry and credited the humanities courses for maturing his world view. Robert Rosenberg, a mentor at Lawrence, inspired him to pursue a career in science. As a rising senior, Tom attended a conference at the Massachusetts Institute of Technology held by the American Biophysical Society to promote graduate study in biophysics; impressive talks by Alex Rich and Paul Doty had the desired effect. Tom enrolled at Harvard for graduate studies in biophysics in 1962.

Tom intended to study nucleic acids at Harvard until he was wowed by lectures given by Max Perutz, who was visiting from England. Max showed 3D slides of the structure of myoglobin, the first atomic resolution protein crystal structure, an achievement that had won Max a Nobel Prize in 1962. To Tom, seeing was believing: Visualizing a macromolecule was clearly the way to understand its function. This was echoed throughout Tom's career as generations of graduate students at Yale were asked, "Why don't you just crystallize it?"



PROLINESERVER/WIKIMEDIA COMMONS

Tom Steitz at the Nobel Prize press conference at the Royal Swedish Academy of Sciences in 2009.

Upon learning that Bill Lipscomb (Nobel laureate for chemistry, 1976) was using crystallography to study proteins, Tom joined his group at Harvard. Working with five postdocs, and most closely with Martha Ludwig, Tom calculated progressively higher electron density maps of bovine carboxypeptidase A, culminating in a 2.0 Å structure of the protein.

At Harvard, Tom met Joan Argetsinger, a fellow Midwesterner and a graduate student in Jim Watson's lab. Tom and Joan married in 1966, and from then on they were the power couple of molecular biology. Their careers were independent, and they published together only rarely, but it is hard to imagine a more balanced, honored and impactful couple in modern science.

Tom joined David Blow's lab at the Laboratory of Molecular Biology in Cambridge, England, as a postdoctoral fellow and worked with then-graduate student Richard Henderson (Nobel laureate for chemistry, 2017) on solving structures of chymotrypsin bound to its substrates. These studies led to a mechanistic understanding of the serine protease family and of its substrate recognition. Tom often said the years in Cambridge were his most scientifically fulfilling, and they shaped his view of the optimal scientific environment. He recalled stimulating discourse, always about science, with whichever world-leading scientist (perhaps Fred Sanger, Francis Crick or Sidney Brenner — Nobel laureates all) was sitting next to him in the canteen for lunch. It was a stress-free and wonderful time, he said, with no worries, just exciting science. Asked later about the pressure to produce results to secure a faculty position, Tom replied, "Ah, yes, well. I did have a faculty position waiting for me at Berkeley."

As it turns out, he was only at Berkeley for two months. Starting as an assistant professor in 1970, Tom asked the department chair to consider interviewing Joan for a faculty position, as she had also done successful postdoc research in Cambridge. The chair told him promptly that females were best suited to be research assistants and that no female

COURTESY OF MARTIN SCHMEING

Tom Steitz poses with his ribosome trainees in Stockholm after winning the 2009 Nobel Prize in chemistry. Pictured, from left, Poul Nissen, Tom Steitz, Martin Schmeing, Jeff Hansen and Nenad Ban.

scientist would be considered for a faculty position. (This seems shocking now, when Berkeley is thought of as liberal, but Tom said back then, in general, the students were liberal and the faculty members were conservative, which helped explain why it was a frequent site of protests.) Tom and Joan both received offers at Yale, so they left California for New Haven.

At Yale, Tom started working on the structure of hexokinase, the first enzyme in the glycolysis pathway, a subject recommended to him by Brian Hartley at Cambridge. Hexokinase structures with and without substrates were Tom's first big success as an independent researcher. This work with his postdoc Robert Fletterick visualized Dan Koshland's induced fit model, according to which binding of the cognate substrate to an enzyme caused a conformational change to enable activity. These hexokinase crystals were notoriously robust. In later years, if a trainee was short on crystals for soaking experiments, Tom would recall that when more hexokinase crystals were required, they would simply saw them in half and, "Voila! Twice the crystals."

Tom had been recruited to Yale by pioneering structural biologist Fred Richards. At about the same time, Don Engelman and Peter Moore were hired, and together with Hal Wyckoff, they formed what became the Yale Center for Structural Biology. By the mid-1990s, this group included Jennifer Doudna, Paul Sigler and Axel Brünger. This concentration of leading structural biologists made for an exciting and dynamic environment that powered each group's research.

After hexokinase, Tom embarked on a broad research scheme that defined the rest of his career: studies of Crick's central dogma of molecular biology. Starting in the late 1970s, Tom and his lab made seminal discoveries that provided fundamental understanding about every part of the central dogma (see box: The discoveries).

Most famously, in a collaboration with Yale colleague Peter Moore spearheaded by postdocs Nenad Ban and Poul Nissen, Tom determined the first structures of the large ribosomal subunit. The ribosome structures provided insight into how proteins are made and showed the ribosome to be a ribozyme, making the logical link between the primordial "RNA world" and the modern world dominated by protein enzymes. He also solved structures (with the author) representing each chemical step of the ribosome linking amino acids together, and (with Jeff Hansen) of the ribosome bound by clinically important antibiotics. For this ribosome work, he

The discoveries

These seminal discoveries made in Tom Steitz's lab provided fundamental understanding of every part of Francis Crick's central dogma of molecular biology.

DNA to DNA

- The first structure of a DNA-binding protein (the catabolite gene activator protein), solved first in the absence and then later in the presence of DNA
- The first structure of a DNA polymerase and structures of many DNA polymerases at mechanistically important states, which together allowed the proposal of the two-metal ion mechanism for phosphoryl transfer reaction, with universal implications for polymerases and ribozymes
- Structures of the homologous recombination enzyme RecA
- Structures of the site-specific recombinase gamma delta resolvase

DNA to (and from) RNA

- A comprehensive series of structures of the RNA polymerase from phage T7, visualizing initiation, elongation and termination of transcription
- The first structure of HIV reverse transcriptase, the key polymerase in the AIDS-causing virus, in complex with a non-nucleotide inhibitor, revealing its mechanism of inhibition

RNA to protein

- The first structure of a tRNA synthetase bound to tRNA, explaining the tRNA recognition that is important for ligating the right amino acid on the right tRNA, and other tRNA synthetase structures illuminating an important proofreading mechanism
- Structures of enzymes required to add the last three nucleotides in a nontemplated fashion onto some tRNAs so they can be used in protein synthesis
- Pioneering ribosome structural biology, including the first structure of the large ribosomal subunit, and co-complexes of the ribosome with substrates, antibiotics and translation factors

Remembrances

These are excerpts from remembrances written by scientists who worked with Tom Steitz. Read the complete texts at asbmb.org/asbmbtoday.

The group that Tom established was like a family; we spent so much time together immersed in the science, learning from each other and helping each other grow under the watchful gaze of our fearless leader. We will never forget the phrase, "just because it's more interesting doesn't mean it's more difficult."

— Andrea Berman and Satwik Kamtekar

Tom would come down to C10 (a room in the basement of Kline Tower at Yale) almost every afternoon and half-teasingly ask whether you had solved your structure yet. For lunch, everyone would decamp to the cafeteria on top of Kline, often to discuss what was going on in science at Yale and elsewhere. It was during one of those lunchtime conversations that I first heard Tom and Peter (Moore) discuss how to approach solving the structure of the ribosome.

— Lorena Beese

I was first exposed to Tom Steitz's enthusiasm for structural biology when I visited Yale as a prospective graduate student in 1986, and he showed us the very first structure of a DNA polymerase. Many aspects of his mentorship still serve me well today: He taught crystallography in a mathematically rigorous but intuitively logical way, he always kept the biological "big picture" in mind, he taught us how make clear figures, and he never treated female trainees differently than male ones.

— Phoebe A. Rice

One time, someone wanted an inside scoop on a yet-to-be published structure and asked Tom what the bending angle of a bound DNA was. Tom hesitated for a hundredth of a second and said, "Larger than 0 and less than 90 degrees." That person wrote a review predicting a 45-degree bending angle. The actual bend is 60 degrees. We all had a good laugh.

— Wei Yang

I remember when we named the RNA motif where exposed adenosines pack into the minor groove of another RNA helix. I presented a range of suggestions for names; he was not very impressed with any of them but then was delighted with one of his own: A minor. Music-based puns ensued.

— Poul Nissen

COURTESY OF MARTIN SCHMEING

Tom Steitz and his family in Stockholm for Nobel week in early December 2009. Pictured from left, daughter-in-law Katherine, son Jon, wife Joan and Tom.

shared the Nobel Prize in 2009 with Venki Ramakrishnan and Ada Yonath.

Tom trained generations of outstanding students at Yale. He had a reputation for bluntness but was a supportive mentor. He effectively conveyed his excitement for important fundamental science and knowledge for the sake of knowledge. Continuing the advocacy that inspired him to leave Berkeley, he believed that talent and drive, not gender, should be determinants of success and embodied this with egalitarian mentoring. He fostered a rigorous attitude to performing science where the most direct route to a clear answer was prized, a virtue visible in many of his lab alumni.

All his trainees fondly recall go-to Tomisms such as "if it doesn't crystallize, add another component to the complex," "always set up crystal trays before you go on vacation so experiments are still happening while you are skiing" and "if your crystallization drop doesn't have precipitate in it, you haven't done the experiment."

Complementing his no-nonsense attitude to science, Tom had an earnest sense of humor, full of dad jokes and puns, often made with a pause and a telling smile. The antibiotics that blocked peptide movement through the ribosomal tunnel caused "molecular constipation." The so-called "thumb" domain in polymerases structures that resemble a right hand had to be coloured green in reference to gardening. In his Nobel autobiography, he referred to a spanking as an application of the "board of education" to his "seat of knowledge." And he would start serious advice in the style of Yogi Berra, "The hardest thing to predict is the future …"

Outside the lab, Tom loved skiing, which led to the annual Steitz-Engelman lab ski trip; the annual "Riboski" trip with RNA-loving colleagues including Tom Cech, Jim Dahlberg, John Abelson and Olke Uhlenbeck; and trips with his son, Jon. Tom was a loving and proud father to Jon, who was born in 1980. Tom and Joan hosted memorable lab picnics and Halloween parties, sometimes serving bottles from Tom's prized wine collection. He was a keen gardener, at times battling the local Stony Creek rabbits and deer. He also enjoyed hiking in the mountains and sailing among the Thimble Islands.

Tom was at his home overlooking these Thimble Islands when he died from pancreatic cancer. He will be dearly missed.

Some information for this article was sourced from the Thomas A. Steitz Biographical Essay, nobelprize.org.

Martin Schmeing (martin.schmeing@mcgill.ca) is an associate professor of biochemistry and Canada research chair at McGill University.

For January, it's atomic No. 1

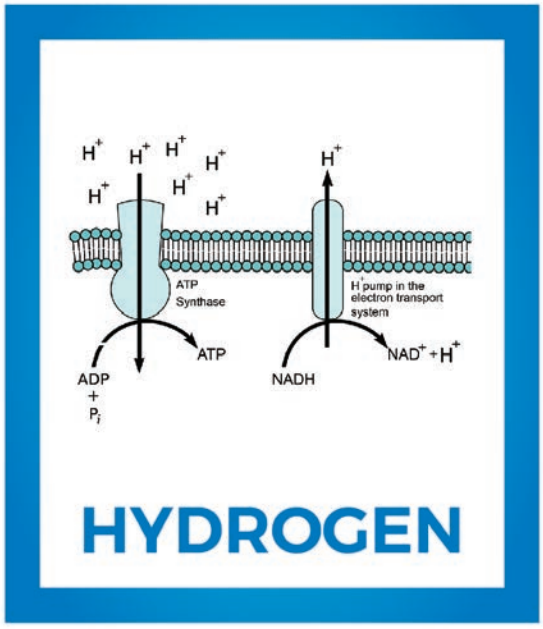
By Quira Zeidan

Following a proposal initiated by the International Union of Pure and Applied Chemistry and other global scientific organizations, the United Nations has declared 2019 the International Year of the Periodic Table of Chemical Elements, or IYPT2019.

The designation commemorates the 150th anniversary of the first publication of Russian chemist Dmitri Mendeleev's periodic table in 1869. Mendeleev's table was not the first attempt to arrange the just over 60 chemical elements known at the time, but it was the first version to predict the existence of unidentified elements based on the periodicity of the elements' physical and chemical properties in relation to their atomic mass.

Today's periodic table contains at least 118 confirmed elements; of these, only about 30 are essential to living organisms. Bulk elements such as hydrogen, carbon, nitrogen and oxygen are abundant structural components of cells and tissues, whereas trace elements (iron, zinc, copper and magnesium, for example) occur in minute amounts as enzyme cofactors and stabilizing centers for protein complexes.

To celebrate IYPT2019, we are launching a yearlong series that features at least one monthly element with an important role in the molecular life sciences.



WIKIPEDIA

High-energy electrons (from the oxidation of food, for example) passed along the electron-transport chain release energy that is used to pump H^+ across the membrane. The resulting electrochemical proton gradient serves as an energy store used to drive adenosine triphosphate synthesis by the adenosine triphosphate synthase.

Hydrogen

For January, we selected the first element of the periodic table, hydrogen, whose atomic number 1 indicates the presence of a single proton in its nucleus. Hydrogen can occur as a single atom designated as H, as diatomic gas, or H_2, in molecules such as water or natural organic compounds (such as carbohydrates, lipids and amino acids) or as negative or positive ions — H^- or H^+, respectively — in ionic compounds.

Living organisms use hydrogen in oxidation-reduction, or redox, reactions and electrochemical gradients to derive energy for growth and work. Microbes can uptake H_2 from the environment and use it as a source of electrons in redox interconversions catalyzed by enzymes called hydrogenases. The transfer of electrons between H_2 and acceptor molecules generates H^+, and it's accompanied by substantial energy changes that can be used for cellular metabolism such as synthesis of molecules, cell movement and solute transport.

Cells also use H^+ to generate energy from the breakdown of foods such as sugars, fats and amino acids in a process called cellular respiration. In a cascade of metabolic reactions, nutrients like glucose are oxidized and split into smaller molecules, yielding reduced nicotinamide adenine dinucleotide, or NADH, and reduced flavin adenine dinucleotide, or $FADH_2$, as biochemical intermediates.

Under aerobic conditions, a series of proteins that comprise the electron transport chain transfer electrons from NADH and $FADH_2$ to cellular oxygen while pumping H^+ across a membrane. This process generates a strong H^+ electrochemical gradient with enough force to drive the activity of the adenosine triphosphate synthase, resulting in biochemical energy production as the gradient dissipates.

The potential energy in H^+ gradients can be used to generate heat for thermogenesis in the brown fat tissue of hibernating mammals, to power flagellar motors in bacteria, to transport nutrients into cells or to generate low pH inside vacuoles. These examples highlight the ubiquitous role of a single element — hydrogen — in essential-for-life biochemical reactions across multiple kingdoms.

Quira Zeidan (qzeidan@asbmb) is the American Society for Biochemistry and Molecular Biology's education and public outreach coordinator. Follow her on Twitter @quirazeidan.

ASBMB members elect six to council and other offices

By Comfort Dorn

Members of the American Society for Biochemistry and Molecular Biology have elected some new and some familiar faces to leadership positions in the society.

Three new members of the ASBMB Council were elected to three-year terms; they will serve from 2019 to 2022.


LAMB

Audrey Lamb is a professor in the department of molecular biosciences, University of Kansas. She studies structural and functional analysis of enzymes associated with iron uptake and the goal of her lab is to understand the structure-function relationships that drive the biosynthesis of siderophores, compounds linked to virulence and pathogenesis in a variety of deadly bacteria.


NTAMBI

James Ntambi is a professor of biochemistry and Steenbock professor of nutritional sciences at the University of Wisconsin–Madison. His research interest lies in the genetic regulation of metabolism in health and disease. He researches, adipocyte biology, differentiation, hormonal and dietary regulation of gene expression. In recent years, he has used a multidisciplinary approach to unravel the physiological role of the stearoyl-CoA desaturase genes in lipid and carbohydrate metabolism of obesity, diabetes and fatty liver disease. He won the 2013 ASBMB Award for Exemplary Contributions to Education.


TEN HAGEN

Kelly Ten Hagen is a senior investigator and section chief in the National Institute of Dental and Craniofacial Research at the National Institutes of Health. Her lab studies the biochemistry and biological roles of the enzyme family responsible for the initiation of a conserved protein modification (mucin-type O-linked glycosylation) to better understand how aberrations in glycosylation may contribute to disease susceptibility and progression. She is a member of the ASBMB Meetings committee.

Other offices


CONAWAY

Treasurer-elect **Joan Conaway** is an investigator and holds the Helen Nelson distinguished chair at the Stowers Institute for Medical Research. She studies the mechanisms of gene transcription and her work helped define mechanisms that regulate initiation and elongation of mRNA transcripts by the enzyme RNA polymerase II. She has previously served on the ASBMB Council and the finance and meetings committees.


ORTH

Kim Orth was elected to the Nominating Committee. She is the Caruth scholar in biomedical research and holds the Forsythe chair in biomedical science at the University of Texas Southwestern Medical Center. Orth works to elucidate the activity of bacterial virulence factors on the molecular level, providing insights into how bacteria cause disease and how eukaryotic host cells signal in response to infection. She serves on the ASBMB Awards Committee and won the 2018 ASBMB-Merck Award.


RADISKY

Evette Radisky was elected to the Publications Committee. She is a professor of cancer biology at the Mayo Clinic. Her long-term research focus is on the molecular recognition between proteases and protein protease inhibitors, and her research interests include many aspects of cancer biology, including the role of proteases in tumor progression and metastasis. She previously served on the ASBMB Meetings Committee.

Comfort Dorn (cdorn@asbmb.org) is managing editor of ASBMB Today. Follow her on Twitter @cdorn56.

Celebrating Herb Tabor

Longtime Journal of Biological Chemistry editor Herbert Tabor turned 100 on Nov. 28. As part of the journal's celebration in Tabor's honor, friends and colleagues shared their best wishes and appreciation for him on the journal website. Below are some of the snapshots they contributed to the virtual scrapbook. See more at jbc.org.

Big cake on the big day

American Society for Biochemistry and Molecular Biology Executive Director Barbara Gordon and Senior Director for Publications Nancy Rodnan paid Herb Tabor a visit at his home on the National Institutes of Health campus in Bethesda, Maryland on Nov. 28. The cake they brought with them was tastefully decorated; it was also tasty, according to ASBMB staffers who sampled the leftovers.

THE COUNTY COUNCIL OF
montgomery county
maryland

Proclamation

WHEREAS, Herbert Tabor was a senior investigator at the National Institutes of Health (NIH) and a resident of Montgomery County for more than 70 years and will be honored by the American Society for Biochemistry and Molecular Biology and the bioscience community on his 100th birthday on November 28, and

WHEREAS, after earning his bachelor's and medical degrees at Harvard, Dr. Tabor interned at Yale-New Haven Hospital, where he participated in the first major clinical trial of penicillin in the U.S. in 1941 and then served as the sole medical officer on the USS Duane during World War II; and

WHEREAS, assigned to the NIH in 1943 by the U.S. Public Health Service, Dr. Tabor went on to study polyamines with his scientific and life partner, Celia White Tabor, for more than five decades, during which time the couple raised their four children on the Bethesda campus, while also mentoring the many young researchers who trained in and visited their lab; and

WHEREAS, as chief editor of the Journal of Biological Chemistry for more than 40 years, Dr. Tabor was both a pillar and pioneer in the bioscience community — firm in his fidelity to scientific integrity and prescient in leading the journal to become the first of its kind to go online, which changed the course of scientific publishing.

NOW, THEREFORE BE IT RESOLVED that the County Council of Montgomery County, Maryland, hereby recognizes the achievements and contributions of

DR. HERBERT TABOR

AND, BE IT FURTHER RESOLVED, that the County Council hereby proclaims November 28, 2018 as Dr. Herbert Tabor Day in Montgomery County.

Presented on this 26th day of November in the year 2018.

Hans Riemer
Council President

Officially 'Herb Tabor Day'

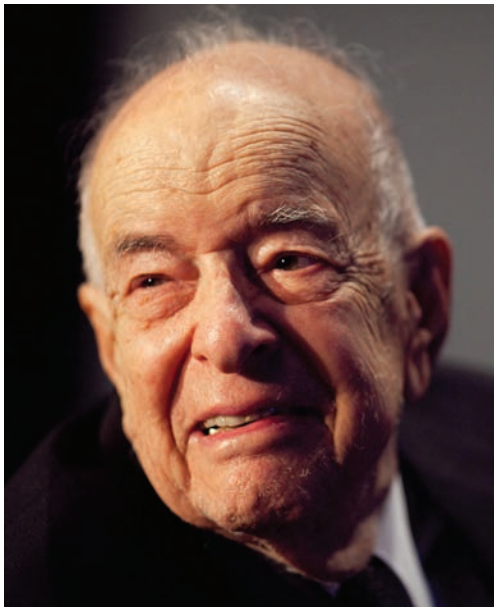
The Montgomery County (Md.) Council recognized Herb Tabor's contributions to science, the scientific community and the world by designating Nov. 28 Herb Tabor Day in an official proclamation (above). The state of Maryland, meanwhile, provided a governor's citation to honor Tabor. Download them both at jbc.org.

'You tutored me on how to be an outstanding journal editor'

Three ASBMB journal editors — Ralph Bradshaw (Molecular & Cellular Proteomics), Herb Tabor (JBC) and Edward Dennis (Journal of Lipid Research) — celebrate Tabor's 40 years of JBC service on April 26, 2010. The snapshot was shared by Dennis, who said, in part, that Tabor tutored him "on how to be an outstanding journal editor." Read Dennis' full submission and Bradshaw's at jbc.org.

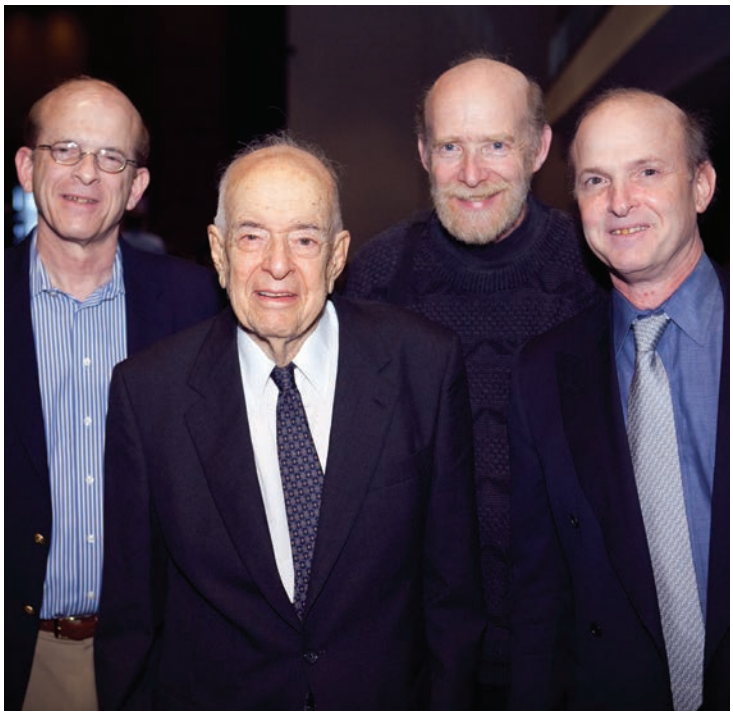
Grand opening

Anthony Pegg, Laurence Marton, Shin-ichi Hayashi and Herb and Celia Tabor prepare for a sake barrel opening ceremony at the 1996 Tokyo International Symposium on Polyamines in Shonan Village Center. The picture was taken "just before the big splash," according to Olle Heby of Umeå University and Lo Persson of Lund University, who submitted it. Heby and Persson wrote: "Dear Herb, Many congratulations on your 100th birthday! Thank you for your great contributions to the polyamine field!"



'What a wonderful human being you are'

Norma Allewell wrote of Tabor, in part: "Because of JBC's stellar reputation and the role that you have had in building it, I was in awe of you for many years. It was only when I had the opportunity to interact with you regularly as an associate editor, that I came to understand what a wonderful human being you are and how much your personal integrity, wisdom and warmth have contributed to JBC's success." Read more at jbc.org.



They've got his genes

Herb Tabor's children, all of whom were raised on the National Institutes of Health campus, where the family lived, joined the JBC associate editors in toasting Tabor's service to the journal in 2011. Here are Tabor and his sons, from left, Ed, Richard and Stan.

Here for the polyamines

From left: Jim Coward, Peter McCann, Herb Tabor, Celia Tabor, Erkii Holta, Tony Pegg, and an unidentified scientist from Finland. This photo was taken by K.-Y. Chen at the Phoenix Temple, Nara, Japan on July 19, 1986, after the International Symposium on Polyamines in the Life Sciences held at Lake Yamanaka, Japan, from July 14 to 18, 1986. Photo courtesy of James K. Coward.

Student Chapter president sees value in campus groups

By Elizabeth Stivison

When Victoria Mak joined the American Society for Biochemistry and Molecular Biology Student Chapter during her freshman year at St. Louis University, the group had been active for a few years but was small, unchartered by the university and limited to the medical campus.

Thanks to the work of Mak and others, the chapter now has more than 50 members and a presence on the main campus. The group is chartered by SLU and hosts numerous speakers, workshops, and outreach and social events.

Mak is now a senior, and she doesn't like to sit around. She's involved with multiple honor societies and student groups at SLU, and she studies ballet. As she looks back over her undergraduate career, one of the things she's most proud of is her role in the thriving ASBMB Student Chapter.

As a freshman, Mak was drawn to the chapter because of its basic science focus and the friendliness and approachability of its members, she said. She wanted to get the chapter chartered because she could see the value ASBMB provided.

"I thought we offered more to the students than we could really show," she said. If the chapter was chartered, "so many more students would be interested; if we were chartered, then we could reach (them)."

So Mak, a few other motivated students and the group's faculty advisor, Dr. Uthayashanker Ezekiel, began the process. They started by demonstrating that the ASBMB chapter was unique, had members and really offered something. More than a year and several committee votes later, they were fully chartered and had the resources of SLU behind them. Such groups on campus are important, Mak said, because they "allow the attendees to bring out the best in themselves."

COURTESY OF VICTORIA MAK

Victoria Mak, president of the ASBMB Student Chapter at St. Louis University, says balancing academics and extracurricular activities has enriched her college experience.

The SLU ASBMB chapter hosts an annual Day in the Clinical Laboratory when local high school students visit to learn and perform lab techniques to complete a case study. SLU students and faculty volunteers run the free event, Mak said, and the high schoolers also can get advice from Doisy College of Health Sciences faculty on college applications and other learning opportunities for area students interested in scientific careers.

Mak is an investigative and medical sciences major, which she hopes will prepare her well for medical school. She loves the problem solving and troubleshooting required in research and gets satisfaction from figuring out why a protocol didn't work as expected.

Outside of biology, Mak loves languages and the way they allow her to interact more deeply with people she meets when traveling. At home in Hawaii she speaks English and Cantonese. In school she has become fluent in French, Mandarin and Japanese as well. She co-founded a Hawaii student club at SLU.

These days, you'll likely find Mak on the move somewhere on campus — dancing, pipetting, organizing an event for ASBMB members, starting a new group to fill a need on campus or maybe even studying for her classes.

The best part of college so far for Mak?

"Being able to balance academics and extracurriculars," she said. "I love using them interchangeably to make my experience richer."

Elizabeth Stivison (elizabeth.stivison@gmail.com) is a Ph.D. student at Columbia University studying mechanisms of DNA repair.

The discovery of GABA in the brain

By Martin J. Spiering

Some scientific discoveries land with a boom only to fizzle out and become a small blip — but there are times when this order is reversed. Such was the case with the discovery of gamma-aminobutyric acid, or GABA, in the brain.

In a study published in 1950 in the **Journal of Biological Chemistry** preceded by a brief conference report, Eugene Roberts and Sam Frankel not only identified GABA as a major amine in the brain but also reported that it is produced and preferentially accumulates in that organ.

The initial response to the discovery was rather muted. In the five years following Roberts and Frankel's report, which was accompanied by two other articles on GABA in the brain in the same JBC issue, according to PubMed only four additional studies of GABA in the brain were published.

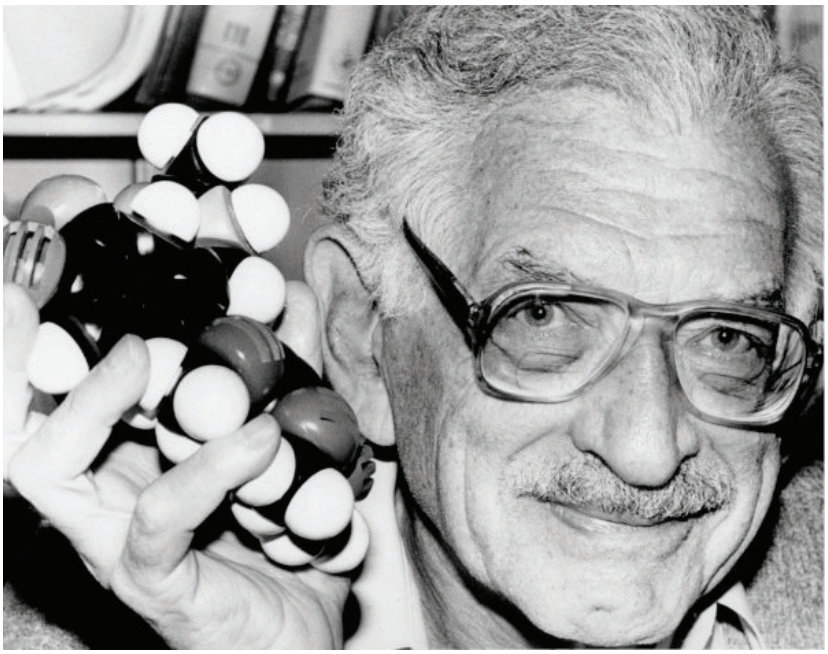
Whether the research community was stunned into silence or this lackluster reaction simply reflected a lack of methods to quickly test GABA's function is difficult to tell as we approach the 70-year mark of this finding. But we do know that at first no one seemed to have an inkling what GABA might be doing in the brain.

GABA's activity in the brain was clarified in 1957 when researchers in Canada reported that an unknown compound having inhibitory activity on crayfish neurons was, in fact, GABA.

Baruch Kanner of Hebrew University Hadassah Medical School in Israel is a member of the JBC editorial board who studies GABA transporters.

"The GABA receptors mostly have an inhibitory input," Kanner said, "and they are the major inhibitory receptors in the brain."

It is now clear that Roberts and Frankel's discovery marked a major milestone in the quest to unravel how neurotransmitters control brain activity.



SCHOLARPEDIA

Eugene Roberts first reported in 1950 that GABA is a major amino compound in the brain.

Roberts' research career and the story of GABA in many ways exemplify how discoveries and careers can be molded from humble and obscure beginnings.

Roberts' personal history as a first-generation immigrant mirrors that of legions of researchers working in the United States. Born Evgeny Rabinowitch in 1920 in southern Russia, Roberts arrived in the U.S. in 1922, settling with his parents in Detroit. Awarded a scholarship from Wayne State University when he was only 16, Roberts graduated magna cum laude with a bachelor's degree in chemistry in 1940. He went on to study biochemistry, earning a master's in 1941 and a Ph.D. in 1943 from the University of Michigan in Ann Arbor.

After a short stint as an assistant head of the Manhattan Project's inhalation section at the University of Rochester in New York, where he worked on the toxicology of uranium dusts, Roberts moved to Washington University in St. Louis in 1946. There, he became interested in amino acids in the brain, studying them in normal and neoplastic brain tissues.

This was at a time when "metabolomics" and "proteomics" would have been considered bizarre, futuristic terms, when even mass spectrometry and other tools now considered standard in analytical chemistry were far off on the horizon or too laborious and time-intensive for the task at hand. Instead, Roberts used paper chromatography and ninhydrin, a chemical dye that reacts with and stains primary amines, to isolate and identify free amino acids in mouse brain extracts.

As he meticulously analyzed these extracts, Roberts came across a ninhydrin-reactive compound whose migration on paper chromatograms

did not match any known amine-containing compounds. What's more, this mysterious amino acid–like metabolite apparently accumulated at much higher levels in the brain than in other tissues. Acid treatments of brain tissues didn't increase these levels, suggesting that this amine exclusively occurs in the free form in the brain. Luckily, it was a lone wanderer, migrating far enough from other ninhydrin-staining compounds that Roberts and Frankel were able to extract it from strips cut from the chromatograms.

The researchers ran the strip-extracted compound along with carefully prepared reference standards in different solvent systems. A technique called the isotope derivative method developed by a colleague at Washington University, Sidney Udenfriend, helped them to home in on the unknown amine. Through this multipronged approach, Roberts and Frankel concluded that the brain-associated amine was GABA. Taking it a step further, using radioactive labeling of potential GABA precursors, the research duo demonstrated that brain tissues can convert another common cerebral amino acid, glutamic acid, to GABA.

The 1957 finding revealing that GABA inhibits the firing of action potentials in neurons presented another novelty. Other amine-containing neurotransmitters whose activities were known at the time, such as norepinephrine and acetylcholine, are activating (excitatory) ones.

The amino acid glycine also can inhibit brain neurotransmission, but Kanner pointed out, "GABA is clearly the most abundant one."

Accordingly, researchers are interested in targeting the GABA system to manage epilepsy, which arises from over-excitation of the brain's neurons. An initially promising avenue has been to prevent or slow reuptake of GABA once it is released into synapses by targeting its transporter, a strategy that has been successful for several brain neurotransmitters to manage other disorders.

"By inhibiting the GABA transporter, GABA is staying around (at the synapse) for a longer time," Kanner said. "Then you get more inhibition, and that could be potentially an anti-epileptic drug because the inhibitory input becomes bigger."

However, although they show promise, compounds that prevent GABA reuptake or stimulate its receptor have not yet made it beyond clinical trials, probably because of side effects, Kanner said.

These snags notwithstanding, GABA's discovery has spurred many research activities; as of this writing, a search of PubMed for "gamma-aminobutyric acid" and "brain" returns about 30,000 papers on the topic.

These efforts include those of Kanner, who is studying the mechanism by which the GABA transporter operates. Kanner said he recalls meeting Roberts some 40 years ago and talking with him about his own research plans and findings on GABA.

"I think it must have been quite gratifying for him to see how (important) this molecule that he discovered in the brain is and how all the aspects of its action are being investigated," Kanner said. "I think it's wonderful that his central contribution will be remembered."

Roberts died in 2016; he would have turned 100 in 2020.

This article originally appeared in the Journal of Biological Chemistry as a JBC Classic. It has been edited for ASBMB Today. Read more JBC Classics at jbc.org.

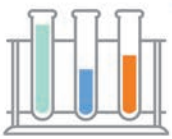
Martin J. Spiering (mspiering@asbmb.org) is the technical editor at the Journal of Biological Chemistry. Follow him on Twitter @Spieringmj.

Upcoming ASBMB events and deadlines

JAN
22: ASBMB–DEUEL Conference on Lipids abstract deadline and registration closes
30: Annual meeting late-breaking abstract and early registration deadline
31: Honor Society nominations due

FEB
4: Communications Winter Course begins
16: Annual meeting outstanding Student Chapters award deadline

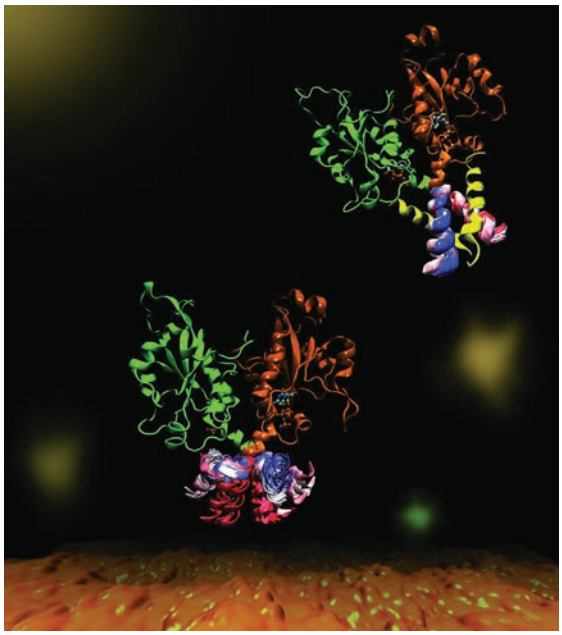
MARCH
5–8: ASBMB–Deuel Conference on Lipids



A molecular dance of phospholipid synthesis

By Sasha Mushegian

The most abundant molecule in cell membranes is the lipid phosphatidylcholine, or PC, commonly known as lecithin; accordingly, the enzymes responsible for synthesizing it are essential. Research published in the **Journal of Biological Chemistry** used computer simulations to gain insights into how one of these enzymes activates and shuts off PC production. The results could help researchers understand why small changes in this enzyme can lead to conditions like blindness and dwarfism.



MOHSEN RAMEZANPOUR AND JAEYONG LEE

CCT is a key enzyme that maintains a balanced composition of cell membrane phospholipids. This image highlights the dynamics of a portion of the enzyme CCT that is essential for regulation of its functions.

Rosemary Cornell, a professor of molecular biology and biochemistry at Simon Fraser University in Canada, studies the enzyme CTP:phosphocholine cytidylyltransferase, or CCT. CCT sets the rate of PC production in cells by binding to cell membranes with low PC content. When bound to membranes, the CCT enzyme changes shape in a way that allows it to carry out the key rate-limiting step in PC synthesis. When the amount of PC making up the membrane increases, the CCT falls off the membrane, and PC production ceases.

"The membrane is this big macromolecular array with lots of different molecules in it," Cornell said. "How does this enzyme recognize that 'Oh, I should slow down because the PC content of the membrane is getting too high?'"

Cornell and her project team — a collaboration with Peter Tieleman and graduate student Mohsen Ramezanpour at the University of Calgary and Jaeyong Lee and Svetla Taneva, research associates at SFU — thought the answer must have to do with the enzyme's dynamic changes in shape when it binds to a membrane. But these changes are difficult to capture with traditional structural biology methods such as X-ray crystallography, which take a static snapshot of molecules. Instead, the team used computational simulations of molecular dynamics, which use information about the forces between every individual atom in a molecule to calculate the trajectories of the enzyme's moving parts.

"What it looks like (when you visualize the output) is your big molecule dancing in front of your eyes," Cornell said. "We set up the molecular dynamics simulation not once, not twice, but 40 different (times). It took months and months just to do the computational parts and even more months trying to analyze the data afterward. We actually spent a lot of time once we got the data just looking on the screen at these dancing molecules."

The simulated dance of the CCT molecule showed that when the M-domain, the section of the enzyme that typically binds to the membrane, detaches from a membrane, it snags the active site of the enzyme, preventing it from carrying out its reaction. When the snagging segment was removed from the simulation, the team saw a dramatic bending motion in the docking site for the snagging element and speculated that this bending would create a better enzyme active site for catalyzing the reaction when attached to a membrane. They confirmed these mechanisms with biochemical laboratory experiments.

Previous genetic studies had shown that mutations in the gene encoding CCT are responsible for rare conditions like spondylometaphyseal dysplasia with cone-rod dystrophy, which causes severe impairments in bone growth and vision, but it was not known how these changes in the enzyme could lead to such dramatic consequences. Cornell hopes that understanding how the enzyme works could help researchers find the causes of these conditions.

"If you have just one small change in CCT, then how is that going to make this whole process of synthesizing PC defective?" she asked. "That's what we're studying right now."

DOI: 10.1074/jbc.RA118.002053

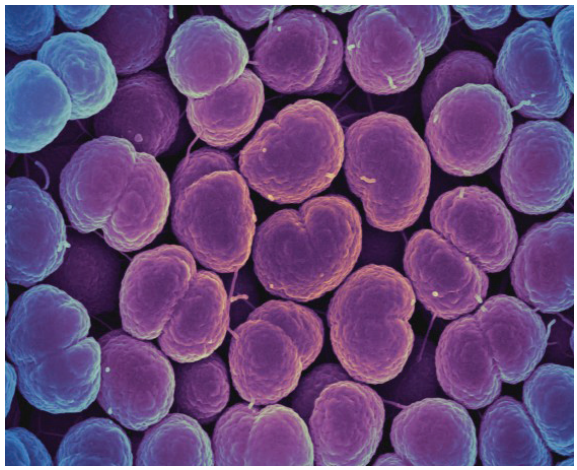
Sasha Mushegian (amushegian@gmail.com) is a postdoctoral fellow at Georgetown University. Follow her on Twitter @sash_mu.

Researchers closer to gonorrhea vaccine after exhaustive analysis of proteins

By Steven Lundeberg

In a study of drug-resistant gonorrhea strains historic in its scope, researchers at Oregon State University have pushed closer to a vaccine for gonorrhea and toward understanding why the bacteria that cause the disease are so good at fending off antimicrobial drugs.

The findings, published in the journal **Molecular & Cellular Proteomics**, are especially important since the microbe Neisseria gonorrhoeae is considered a "superbug" because of its resistance to all classes of antibiotics available for treating infections.



NIAID

Neisseria gonorrhoeae, the bacterium that causes gonorrhea, is shown here in a scanning electron micrograph.

Gonorrhea, a sexually transmitted disease that results in 78 million new cases worldwide each year, is highly damaging if untreated or improperly treated. It can lead to endometritis, pelvic inflammatory disease, ectopic pregnancy, epididymitis and infertility.

Babies born to infected mothers are at increased risk of blindness. Up to 50 percent of infected women don't show any symptoms, but those asymptomatic cases still can lead to severe consequences for the patient's reproductive health, miscarriage or premature delivery.

Aleksandra Sikora, a researcher with the OSU College of Pharmacy and Oregon Health and Science University's Vaccine and Gene Therapy Institute, helped lead an international collaboration that performed proteomic profiling on 15 gonococcal strains.

Among the isolates in the study were the reference strains maintained by the World Health Organization that show all known profiles of gonococcal antimicrobial resistance.

For each strain, researchers divided the proteins into those found on the cell envelope and those in the cytoplasm. More than 1,600 proteins — 904 from the cell envelopes and 723 from the cytoplasm — were found to be common among all 15 strains, and from those, nine new potential vaccine candidates were identified.

A vaccine works by introducing an "invader" protein known as an antigen that triggers the body's immune system and subsequently helps it quickly recognize and attack the organism that produced the antigen.

Researchers also found six new proteins that were expressed distinctively in all of the strains, suggesting they're markers for or play roles in drug resistance and thus might be effective targets for new antimicrobials.

In addition, scientists looked at the connection between bacterial phenotype — the microbes' observable characteristics and behavior — and the resistance signatures that studying the proteins revealed; they found seven matching phenotype clusters between already-known signatures and the ones uncovered by proteomic analysis.

Together, the findings represent a key step toward new weapons in the fight against a relentless and ever-evolving pathogen.

"We created a reference proteomics databank for researchers looking at gonococcal vaccines and also antimicrobial resistance," said Sikora, co-corresponding author on the study. "This was the first such large-scale proteomic survey to identify new vaccine candidates and potential resistance signatures. It's very exciting."

The findings add new momentum to a vaccine quest that also received a boost in summer 2017, when a study in New Zealand showed that patients receiving the outer membrane vesicle meningococcal B vaccine to prevent Neisseria meningitis were 30 percent less likely to contract gonorrhea than those who didn't get the vaccine.

"All previous vaccine trials had failed," Sikora said.

Gonorrhea and meningococcal meningitis have different means of transmission, and they cause different problems in the body, but their source pathogens are close genetic relatives.

DOI:10.1074/mcp.RA118.001125

This article is republished from the EurekAlert website (eurekalert.org).

Steven Lundeberg (steve.lundeberg@oregonstate.edu) is a news writer at Oregon State University.

A close-up of nascent HDL formation

By Laurel Oldach

Oil and water don't mix. But our aqueous blood is full of hydrophobic lipids — including cholesterol. To travel via the bloodstream, those lipids must hitch a ride on an amphipathic carrier. In a paper in the **Journal of Lipid Research**, scientists at Boston University report an advance in our mechanistic understanding of how one such carrier forms.

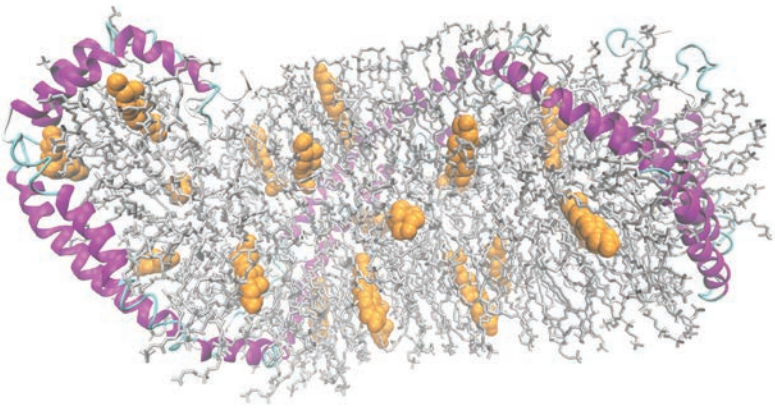
"Lipoproteins are like boats that deliver and remove cargoes of fatty substances to and from our cells," said David Atkinson, chair of the physiology and biophysics department at Boston University School of Medicine and senior author on the JLR paper.

The subset of those "boats" that carry cholesterol and other lipids to the liver from other parts of the body are called high-density lipoproteins, or HDL, aka "good cholesterol." HDL can remove cholesterol from distal cells — such as macrophages in the walls of arteries, where cholesterol accumulation can lead to heart attacks — and deliver it to liver cells, a process known as reverse cholesterol transport. The liver disposes of excess cholesterol by converting it into bile acids secreted into the small intestine.

According to Atkinson, a biophysicist, most of what is known about HDL formation comes from experiments that take a cell biological tack. In such studies, he said, "You can see (HDL formation) happening, and you can quantitate what happens, but you don't understand the driving interactions that cause it to happen."

HDL is built on a scaffold protein, apolipoprotein A-I. This apoA-I is thought to collect cholesterol and phospholipids from the cell membrane. Atkinson's team wanted to better understand that process.

ApoA-I depends on a lipid transporter protein, ABCA1, that pumps cholesterol from the inner to the outer leaflet of the cell membrane. Because the cholesterol that ABCA1 transfers usually ends up bound to apoA-I, some researchers suspected a physical interaction between apoA-I and ABCA1. Others argued that cholesterol and phospholipids could diffuse passively and bind to apoA-I.



WU ET AL/JBC 2009

A model of a high-density lipoprotein particle shows apolipoprotein A-I in pink, phospholipids in gray and cholesterol in yellow.

"Even if you demonstrate that apoA-I binds to the cell surface, you don't actually know that it's bound to ABCA1. It's just bound to the cell surface," Atkinson said. So he asked his team to see if they could "demonstrate that interaction actually happening in the isolated components."

The team, led by graduate student Minjing Liu and supported by Xiaohu Mei and Haya Herscovitz, used isolated apoA-I and ABCA1 to test for a physical interaction. They were able to show immunoprecipitation of apoA-I with purified ABCA1.

The lab earlier had designed a mutant apoA-I with a little extra wiggle in an already flexible hinge region. For this study, they used the mutant to show that higher flexibility increased apoA-I lipidation, or the formation of nascent HDL. The team has not yet tested whether the extra-flexible mutant binds to ABCA1 better or whether binding of either form of apoA-I activates ABCA1.

But about one thing Atkinson is certain: "It's the apoA-I/ABCA1 interaction which then enables the nascent HDL particle formation to happen as the membrane components are being transported out by ABCA1."

Increasing reverse cholesterol transport may be a way to reduce atherosclerosis and heart disease. Atkinson is optimistic about the promise of understanding the physiological processes better.

"Translational research might be in vogue," he said, "but remember that if you don't do foundational basic discovery research, you will not have anything to translate."

DOI: 10.1194/jlr.M084376

Laurel Oldach (loldach@asbmb.org) is a science communicator for the Journal of Lipid Research and Molecular & Cellular Proteomics and a staff writer for ASBMB Today. Follow her on Twitter at @LaurelOld.

From the journals

By Nathalie Gerassimov, Dawn Hayward & Sasha Mushegian

We offer a selection of recent papers on a variety of topics from the **Journal of Biological Chemistry**, the **Journal of Lipid Research**, and **Molecular & Cellular Proteomics**.

Fresh CRISPR-Cas delivery

The bacterial CRISPR-Cas9 system can be used to edit genes with single-nucleotide precision, but current methods of delivering the system remain inefficient in real-world therapeutic settings. Currently, most methods deliver nucleic acids encoding Cas9, which subsequently are translated in the cell. Delivering already synthesized Cas9 protein and guide RNA into cells would be a more direct approach. Yuefei Shen and colleagues at University of Massachusetts Medical School developed CRISPR delivery particles built on amphipathic peptides to do just that. As proof of concept in the **Journal of Biological Chemistry**, they used these particles to edit a gene in fat cells to convert white adipocytes into energy-burning brown adipocytes.
DOI: 10.1074/jbc.RA118.004554

Polyunsaturated fatty acids in dividing T cells

As cells grow and prepare for cell division, they also synthesize the lipid components of the cell membrane, some of which do double duty as signaling molecules. However, mammals cannot synthesize from scratch all the fatty acids they need, such as most polyunsaturated fatty acids, or PUFAs. The initial building block for omega-3 and omega-6 PUFA is an 18-carbon fatty acid with two or three double bonds derived from the diet.

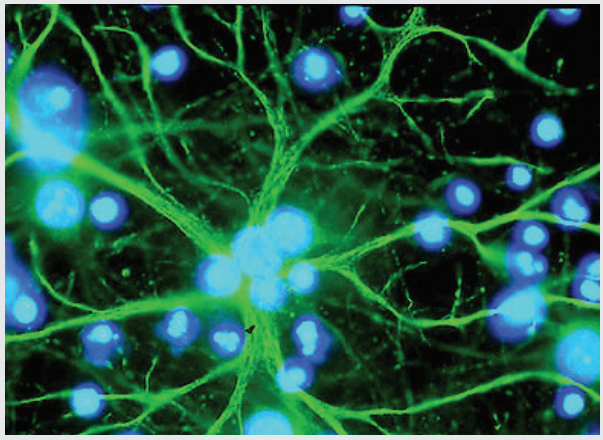
Linking diabetes to cognitive decline

Chronic diabetes has a well-known yet little understood effect called cognitive decline. In fact, patients with diabetes are more likely to develop cognitive disorders such as dementia than those without. To determine the link between the two, Liangcai Zhao and colleagues at Wenzhou Medical University performed a metabolomics study on the brains of diabetic rats. This work was published in **Molecular & Cellular Proteomics**.

First, the researchers treated rats with the drug streptozotocin, which selectively attacks pancreatic beta cells, causing hyperglycemia and other symptoms associated with diabetes. After observing the cognitive decline in these rats using behavioral tests and brain scans, they looked at which metabolites changed with diabetes, specifically in the hippocampus. Lactate, a metabolite in the glycolysis pathway, was higher in the diabetic rats' brains than control animals, especially when the disease became chronic.

While glycolysis generates some energy, cells usually move to the next step, the tricarboxylic acid cycle, to make even more energy. In chronic diabetic rats' brains, however, cells use glycolysis for energy exclusively, and the enzyme used to make lactate had higher activity in these animals.

Not all of this lactate was utilized, however. Lactate transporter levels decreased during the chronic stage such that excess lactate accumulated between astrocytes, a type of brain cell with a range of important roles. The excess dysregulated a specific signaling pathway involved in the transcription of genes in learning and memory, thus providing a link between diabetes and cognitive decline. To alleviate lactate's hold on cognitive decline, researchers blocked its production with an inhibitor. Diabetic rats showed improvement on behavioral tests, which indicated better memory, and brain scans showed less atrophy than previously observed.



WIKIMEDIA

Astrocytes in the brain can accumulate the metabolite lactate between cells during chronic diabetes in rats, contributing to cognitive decline.

The authors suggest that blocking the production of lactate in diabetic patients may be a way to limit cognitive decline.
DOI: 10.1074/mcp.RA118.000690

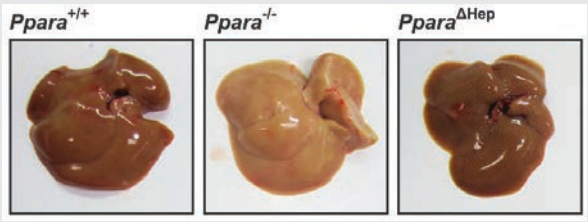
— Dawn Hayward

Protecting the liver — a full-body job

To survive fasting, humans and other mammals can shift their metabolism from reliance on glucose and fat derived from food to reliance on fat stores. Peroxisome proliferator-activated receptor alpha, or PPARA, is a major regulator of lipid homeostasis and is critical for surviving fasting and starvation. PPARA, a transcription factor found in the liver and some other tissues, upregulates genes that contribute to the catabolism of free fatty acids, or FFAs.

In a paper published in the **Journal of Lipid Research**, Frank Gonzalez and his team at the National Cancer Institute together with collaborators in China demonstrated that PPARA in tissues outside the liver can protect a liver that lacks PPARA during fasting. The investigators compared the liver phenotype of normal mice and mice lacking PPARA either in the entire body or only in the liver after one day of fasting.

Food deprivation is associated with elevated fat-derived FFAs circulating in the blood, which are taken up by the liver. In normal mice, these FFAs are broken down to generate energy and are used in gluconeogenesis. Mice completely lacking PPARA still can uptake FFAs into the liver but cannot catabolize them, leading to an abnormal lipid accumulation in the liver called hepatosteatosis. In mice lacking PPARA in only the liver, the researchers found that this phenotype was dramatically redced. PPARA activity from outside the liver boosted fatty acid oxidation and lipase activity, reduced the systemic lipid load and reduced lipid accumulation in the liver.



BROCKER ET AL./JLR

Mice lacking PPARA in the entire body develop abnormal lipid accumulation in the liver during fasting, pictured in the center, which makes the liver appear paler than a normal liver, at left. When PPAR is missing only in the liver, at right, this phenotype is ameliorated.

PPARA function is decreased in several diseases affecting the liver such as nonalcoholic fatty liver disease and hepatitis C. This research suggests that PPARA from outside the liver could compensate for low hepatic PPARA, which may help develop novel approaches to treat these diseases.

DOI: 10.1194/jlr.M088419

— Nathalie Gerassimov

Once in cells, enzymes elongate and desaturate these 18-carbon PUFAs to generate even longer and more unsaturated PUFAs. While several enzymes have been shown to catalyze these reactions, which of them play a significant role in proliferating cells is unknown. In a paper published in the **Journal of Lipid Research**, Marc Surette and colleagues at the universities of Mancton and Quebec, Canada, characterized the PUFA profiles and the responsible enzymes in resting and proliferating primary human T cells and in the Jurkat cell line. The investigators found that both primary and cultured cells had a greater capacity to incorporate, elongate and desaturate exogenous PUFA when proliferating. Furthermore, they identified ELOVL5 as the key elongase in this process. Future studies will show whether changes in PUFA profiles are necessary for successful cell division and how PUFA misregulation contributes to diseases with proliferation defects, such as cancers.

DOI: 10.1194/jlr.M090050

The call is coming from outside the house

During nutrient shortages, cells' nutrient sensors can trigger autophagy to recycle cellular components. This process is dysregulated in cancer and metabolic diseases. Maria Gubbiotti and colleagues at Thomas Jefferson University showed that an important nutrient sensor is located outside the cell, in the extracellular matrix. The extracellular proteoglycan decorin was required to induce autophagy in cardiomyocytes in fasting mice. This study, published in the **Journal of Biological Chemistry**, hints that the extracellular matrix doesn't just hold cells in place but plays an active role in cellular metabolism.

DOI: 10.1074/jbc.RA118.004563

A new way to quantify your favorite protein

Tracking where a protein is inside a cell and exactly how much there is isn't trivial. Scientists use mass spectrometry, antibodies, tags and other means to find and follow their favorite protein, but these methods cannot be used for real-time intracellular imaging. Chromobodies (nanobodies with a fluorescent tag) can be injected into cells and bind endogenous proteins. Bettina-Maria Keller and colleagues at the University of Tuebingen in Germany optimized a chromobody to improve its sensitivity in tracking endogenous proteins. The

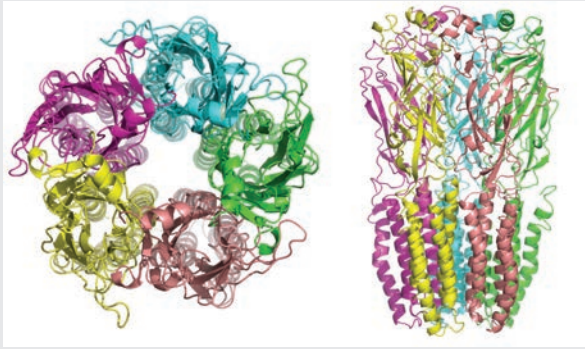
Why a pain drug failed in humans

Everyone knows that humans aren't rats, but in the context of preclinical laboratory studies, we've got to do our best with what we've got. Many drugs show promise during rodent trials and subsequently fail in humans. To make such studies more efficient, it's important to understand how humans differ from model species at the molecular sites that potential drugs target.

Neuropathic pain is caused by the nervous system misfiring rather than by stimulation of typical pain receptors. Potential drug targets for neuropathic pain are the nicotinic acetylcholine receptors, or nAChRs, in the dorsal root ganglia. However, the sensitivity of receptors such as nAChRs differs in rodents and humans. In a recent example, a conotoxin peptide — a venom produced by carnivorous marine snails — alleviated neuropathic pain in mice but not in people.

In a study published in the **Journal of Biological Chemistry**, Arik J. Hone and colleagues at the University of Utah investigated the molecular basis of this difference in effectiveness between conotoxin inhibition of human and rat nAChRs. They found that, on the whole, the pocket on the receptor that binds ligands like conotoxins looked very similar in the two species.

But three amino acids were different, and one of these differences was critical: The substituted amino acid slightly changed the orientation of the conotoxin as it attempted to bind the human receptor, resulting in reduced potency. Changing the same amino acid in the rat receptor did not affect its potency, suggesting that differences elsewhere in the receptor also affected how the receptor and ligand interacted.



WIKIPEDIA

The five subunits of nicotinic receptors are arranged symmetrically around a central pore, and each subunit comprises four transmembrane domains with both the N- and C-terminus located extracellularly.

Understanding the molecular details of species-specific drug targets may help researchers to better predict which pharmacological findings will be translatable from animal models to humans.

DOI: 10.1074/jbc.RA118.005649

— Sasha Mushegian

work, published in **Molecular & Cellular Proteomics**, introduces these destabilized chromobodies. To make the chromobody sensitive to time-dependent changes in concentration, researchers altered its N-terminal sequence so it was degraded immediately by the cell if it did not specifically bind its antigen. After pathway induction or drug treatment, the amount of chromobody, and therefore fluorescence, tracked the increases and decreases in protein concentration in real time. This new and improved chromobody now can be used instead of traditional methods to track a scientist's favorite protein sensitively.

DOI: 10.1074/mcp.TIR118.000914

A new heme catabolite

Hydrogen sulfide is a gaseous signaling molecule important for many biological processes. Toshitaka Matsui and colleagues at Tohoku University report a new reaction pathway in which hydrogen sulfide induces heme oxygenase to produce new isomers of sulfur-containing biliverdin, or SBV, and describe the mechanism of the formation of these catabolites. Biliverdins, the bile pigments responsible for the greenish color of bruises, increasingly are recognized as antioxidants. The new SBV-producing pathway was less dependent on oxygen concentration than canonical heme oxygenase activation, leading the authors to speculate that it allows mammalian cells to degrade heme and produce antioxidants under hypoxic conditions. The study was published in the **Journal of Biological Chemistry**.

DOI: 10.1074/jbc.RA118.004641

Cholesterol-lowering drug target discovered

About a quarter of deaths in the United States are caused by heart disease, according to the Centers for Disease Control and Prevention. Hypercholesterolemia, or high cholesterol, is a major risk factor for cardiovascular disease. However, cholesterol, a component of lipid bylayers, is essential for life. Mammals can either synthesize cholesterol or absorb it from food using the intestinal transmembrane protein Niemann–Pick C1-like 1, or NPC1L1. This transporter resides in lipid rafts, which are membrane microdomains used for cell–cell interaction and cell signaling that are enriched in cholesterol as well as gangliosides — a group of galactose-containing glycolipids. In a paper in

the **Journal of Lipid Research**, Jinichi Inokuchi from Tohoku University in Japan and colleagues show that NPC1L1-dependent intestinal cholesterol uptake requires the ganglioside GM3 and the enzyme that synthesizes it, GM3S. Cholesterol uptake is decreased in GM3S-deficient cells, and GM3S-deficient mice fed a high-cholesterol diet show a lower susceptibility to hypercholesterolemia. This research proposes a new viable target for cholesterol reducing therapies.
DOI: 10.1194/jlr.M089201

Crystals, cataracts and hot potatoes

Highly stable crystallin proteins in the lens of the human eye are never replaced over a lifetime. With age, though, they accumulate oxidation-induced disulfide bonds, which can lead to formation of protein aggregates and cataract disease. Eugene Serebryany and colleagues at Harvard University examined disulfide bond formation in mixtures of wild-type and cataract-associated human γD-crystallin. They identify a "redox hot potato competition" wherein the disulfide bonds are exchanged dynamically between molecules and can be trapped in aggregation-prone intermediates. This study, published in the **Journal of Biological Chemistry**, thus reveals a new enzyme function for crystallins and provides potential insights into the evolution of exceptionally long-lived proteins.
DOI: 10.1074/jbc.RA118.004551

Decorating bacterial walls

The teichoic acids in the cell walls of Gram-positive bacteria are modified frequently, altering bacterial growth, aggregation and resistance to antibiotics. Understanding how these modifications are introduced is therefore important for combating these bacteria, but the pathways are difficult to characterize. In the **Journal of Biological Chemistry**, B. McKay Wood and colleagues at Harvard Medical School write that they developed a suite of assays, including a partially reconstituted model system, to examine steps in the teichoic acid D-alanylation pathway. They found that a previously uncharacterized membrane protein in the pathway attaches alanine onto lipotechoic acid, defining one new step and setting the stage for further investigations.
DOI: 10.1074/jbc.RA118.004561

Negative effects of controlled malaria in pregnancy

Malaria during pregnancy can result in detrimental fetal effects, such as low birth weight. After parasite infection, the mother's immune response restricts parasitic growth to the placenta, but chemokines and other immune cells can infiltrate and prevent nutrient flow to the fetus. Clearance by drug treatment, while helpful, does not reverse all fetal effects. Rebeca Kawahara and colleagues at the University of Sao Paulo in Brazil did a proteomics study on placental tissues from uninfected and previously infected mothers and used a mouse model to look at cellular changes in controlled placental malaria. This work was published in **Molecular & Cellular Proteomics**. Using mass spectrometry and statistical analysis, they identified proteins with altered expression levels, their associated cellular processes and post-translational modifications indicative of changes in regulation. Mapping the resultant networks revealed that in the placenta of the previously infected mothers, processes such as apoptosis, cell signaling and oxidative stress were dysregulated, an observation also seen in the mouse model. This means that, although the infection was cleared, placental cells could face cell death, alteration of intracellular pathways and increasing cellular stress. The authors say that these pathways, though harmful to the placenta and fetus, could be used as markers in the clinic, making it easier to detect the effects of malaria in pregnancy.
DOI: 10.1074/mcp.RA118.000907

Regulation by membrane curvature

Some proteins can be found in both the plasma membrane and the endoplasmic reticulum membrane. One example is diacylglycerol kinase epsilon, or DGK-epsilon, which carries out important functions in the phosphatidylinositol cycle. José Carlos Bozelli and colleagues at McMaster University investigated whether DGK-epsilon activity is affected by the properties of the membranes in which they can be embedded. They found that, when embedded in a locally flat membrane, the kinase had low activity and broad acyl chain specificity; curved membranes, in contrast, improved activity and specificity by allosterically regulating DGK-epsilon activity. Thus, membrane shape, in addition to lipid composition, may be an important regulator of lipid signaling. The study was published in the **Journal of Biological Chemistry**.
DOI: 10.1074/jbc.RA118.005293


Nathalie Gerassimov (nathalie.gerassimov@gmail.com) is a Ph.D. student at the Johns Hopkins University School of Medicine.


Dawn Hayward (dhaywar5@jhmi.edu) is a graduate student at the Johns Hopkins University School of Medicine.


Sasha Mushegian (amushegian@gmail.com) is a postdoctoral fellow at Georgetown University. Follow her on Twitter @sash_mu.

How to patent an antibody

Advice from Charles Craik

By Laurel Oldach

Charles Craik knows a lot about patenting research findings.

The University of California, San Francisco, professor of pharmaceutical chemistry and protease expert is named as an inventor on 16 patents with six under review, most recently a series of antibodies targeting the urokinase-type plasminogen activator receptor pathway to both image and treat aggressive and recurring cancers. He also has taught in a course involving intellectual property at UCSF for several years. Craik sat down with ASBMB Today writer Laurel Oldach to talk about Amgen Inc. v. Sanofi et al., a lawsuit over antibody patents that has generated a lot of buzz in biotechnology. Their conversation has been edited for length and clarity.

Do you think a lot about patents and patenting?

I definitely think about it a lot. I'm an academic professor, so that's my job 100 percent of the time. But in my spare time, I have started companies, and I've learned certain things in the lab that have been very practical. I'm still learning. Perhaps more than an average person, I think about the practical applications of my work.

As an assistant professor, I helped validate HIV protease as a therapeutic target in 1990. I don't have the patent on HIV protease — we got the crystal structure, and we made it available — but I did work with companies so they could develop compounds that could target the enzyme and provide the basis for making a pharmaceutical.

I definitely believe that it's good to patent things, because in my opinion, if pharmaceutical companies are going to invest their money in developing a drug, they need to have it protected so they can try to recoup some of those costs.

I don't think everything should be patented, and I don't spend all my time just thinking about patents, but when there is something that can be a practical invention, I enjoy going through the process of figuring out how to get it protected so someone can make money off it and the cycle can continue for the development of future drugs.

And I've been told multiple times by companies, big and small, "If you don't get a patent, Charly, we will not be able to work with you."

Of all of the monoclonal antibodies patented last year, about a quarter came out of academic research institutions. A large subset of those worked with a commercial co-applicant. How does that process work?

It's very hard to make one generalization about the whole process. But imagine yourself running a lab. You're in a university; you're making discoveries. You're pushing the edge of the field, really trying to do something completely novel that no one's ever thought of or done before. That's what drives us.

If you come across something that could be of practical interest, one of

CINDY CHEW/UCSF

Charly Craik, pictured here in his office at the University of California, San Francisco, says he enjoys figuring out how to protect an invention "so someone can make money off it and the cycle can continue."

the first things you usually do is file a disclosure. A disclosure means going to your university and saying, "I think I have something that's of value here." You write down the information associated with why you think it's valuable, what the concept is, when the experiments occurred that reduced it to practice — that really showed that it happened. That's filing a disclosure. It doesn't cost anything, just filling out a form. But it puts it on record at the university.

The university evaluates whether it's worth filing a patent. Now, it costs money to file a patent. Depending on the lawyer, it can be very inexpensive and not very good, or it can cost between $10,000 and $15,000. Let's say it's roughly that amount of money. If every university filed on every idea, they'd break the bank really fast. So there's an evaluation process.

As a professor, particularly in a university that doesn't have a company behind it, these filings can really drain the bank. The hope is there will be some big winners and there'll be a jackpot, and that supports the whole thing. But it can be pretty risky.

So the cost is for a lawyer to make the patent watertight?

That's a way to put it. But it is a judgment call — no one knows exactly how to write a patent. In the Sanofi-Amgen case, there were highly qualified lawyers. In one case, you could say that he or she failed. On the other hand, the patent was upheld. So it's divining tea leaves in some cases.

When a lawyer talks to you, they're charging by the hour; if they write stuff up, they charge you for that. I've got ways of keeping those costs down: I write a lot of the stuff myself, and they turn it into legalese; that saves a huge amount of time. If I'm about to publish something, a lot of it is already written.

The university has to decide whether they're going to pay those costs. Sometimes they say, "Well, we don't think this is of interest; can you do some more work?" or they go out and market it, speaking in very vague terms. They can say, "We have a potential cure for cancer," and they haven't told anything. Or they say, "We've targeted this particular pathway, and we've found this particular enzyme," and that's still not giving a

1. A binding agent that specifically binds urokinase-type plasminogen activator receptor (uPAR) wherein said agent competes with an integrin for binding to uPAR.

2. The binding agent of claim **1**, wherein said integrin is a β1 integrin.

3. The binding agent of claim **2**, wherein said integrin is α5β1 or α3β1 integrin.

4. The binding agent of claim **1**, wherein said agent competes for binding to uPAR with an antibody from clone 3C6.

5. The binding agent of claim **1**, wherein said agent comprises:

a) a V_HCDR1 comprising an amino acid sequence of a 3C6 V_HCDR1 as set forth in FIG. **1**;

b) a V_HCDR2 comprising an amino acid sequence of a 3C6 V_HCDR2 as set forth in FIG. **1**; and

c) a V_HCDR3 comprising an amino acid sequence of a 3C6 V_HCDR3 as set forth in FIG. **1**.

CHARLES CRAIK

The first five claims from a patent Craik and two colleagues filed in 2010 describe their invention of antibodies that bind to urokinase-type plasminogen activator receptor, blocking its interaction with integrins. This application listed 39 claims in total.

whole lot away.

Companies will sometimes reach out to the university and say, "Oh, we're interested in this area; we'll sign a confidentiality disclosure agreement." And now the researcher is allowed to go and talk to that company.

Sometimes a company is just gathering information. They have no intention of ever licensing your patent. As you get into this, you can smell that pretty quickly. If they're genuinely interested, they might say, 'OK, we'll co-develop this with you." If it was all done at the university, they say, "We'll license it." There are lots of ways. But that disclosure is the beginning.

Do you wish someone had told you about the patent process when you were starting out?

I was fortunate enough to have exactly that. When I was an assistant professor, when we had HIV protease, a lawyer worked with us. He and I got along really well, and he taught me a lot off the clock about how to write a good patent. He took the time to teach me 30 years of his life in a few weekends.

That was extremely valuable. So I started a course at UCSF to introduce students to the process of intellectual property and how to develop their ideas beyond publishing important papers. If they want to start a company, what are the fundamental points about the whole process? I bring in experts to teach that sort of thing.

If you've ever seen a patent, it can be 15 pages. It can be 60 pages. It's an intimidating document. The language is somewhere between Shakespeare and science, and it's just not easy reading.

Not to say that all that prose isn't important, but to keep things simple, go straight to the claims. They are the essence of the patent. And the claims are also prioritized. The No. 1 claim is the most important thing to read. If you're writing a patent, make sure that first claim is really substantive. Everything flows from there.

It's like trying to write a research paper. I teach my students to focus on the data. Just tell me what the story is on the data, and then the paper is going to come. It's the same on a patent. Get your claims.

You've applied for a lot of patents, and a good number have been awarded or licensed out and are in commercial development.

What's the ratio of hits to misses?

That's hard to generalize. Sometimes I think if I were better, they'd all be licensed out. That's always the thought that haunts you as a scientist: "God, I wish I were better at this."

I think I've gotten better as time goes on. At the very beginning, HIV protease was a pretty big hit. But like I said, we initially published that freely. We did file for some inhibitors, but it's the job of pharmaceutical companies to make drugs. So once they had the target, it was a free-for-all; they were off and running. My lab

was academic; we had a few chemists making some molecules compared to 350 chemists at Merck. And Merck developed some good inhibitors.

So back to your question; maybe 10 percent of the things we file disclosures on actually make it into a patent that's then awarded, that then is licensed out.

And then is perhaps considered for development?

Yes. And it's sometimes said that a patent is only as good as its ability to be defended.

Some patents never are contested. A lot of money can be made from them, and they run out before there's a problem. But usually, if a patent is effective, valid, licensed and valuable, when it starts making money it's going to be tested.

That's exactly what happened in Amgen v. Sanofi. Statins were going off patent, and so this whole market was wide open for something new. This PCSK9 antibody potentially could keep your cholesterol levels below what a statin could, particularly for people who aren't responsive to statins, and this was a pretty cool thing. There was a big race, and a lot of money was involved that drove some exciting new science.

What do you think about the appeals court's decision in the Amgen v. Sanofi case — that knowing about a newly characterized antigen is not enough to give an inventor a patent on a whole class of antibodies that bind to it?

I have to choose my words on this one.

I find it very disappointing that this is the direction patents are going with antibodies, because it's slicing the salami so thin that you can't get a meal off of it. So that's a disappointment.

In the law, it always comes down to a particular unique situation. But you still want the broad claims.

For example, I tried in the 1990s to get a patent for an antibody inhibiting any protease. No one had done it, no one had filed; there were no examples where an antibody could trap a protease in its active state versus an inactive state. It was a big idea, right? The examiner came back and said, "No. Too broad." And in the end they gave me any antibody that would inhibit this particular protease. That was a disappointment.

But now, reading this Amgen v. Sanofi case, I wouldn't even get that. They would only give me that particular antibody inhibiting that particular protease, just like PCSK9. That's all you're getting: just one particular antibody. So if someone gets another antibody with a different sequence, it's not protected.

The pendulum swings, and in my opinion it's getting too specific. To have any value to a patent, so that someone would go through the whole process, it should cover more space.

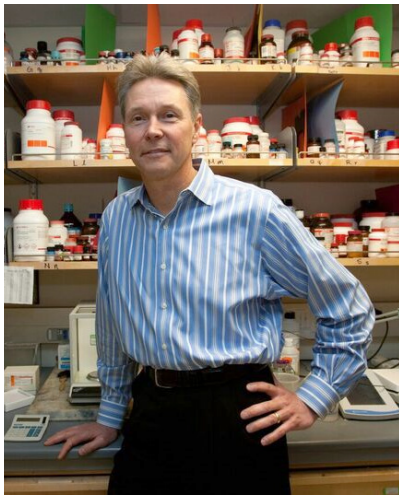
You sound pessimistic.

I don't think this is the end of getting good patents in the antibody space. There's still a lot of meat on those bones.

There are so many opportunities in the antibody space right now; immunotherapy has taken over, but you can do other things with antibodies. They can translate into the clinic as diagnostics, as imaging agents, as therapeutics at the margins of tumor environment, and the list goes on and on and on.

I can't say Amgen v. Sanofi is just a speed bump, but the road isn't completely washed out. We just have to figure out how to navigate around it.

Laurel Oldach (loldach@asbmb.org) is a science communicator for the Journal of Lipid Research and Molecular & Cellular Proteomics and a staff writer for ASBMB Today. Follow her on Twitter at @LaurelOld.



CINDY CHEW/ UCSF

Charly Craik, pictured here in his lab at University of California, San Francisco, worked early in his career with an attorney who taught him how to write a good patent. "He took the time to teach me 30 years of his life in a few weekends," Craik said.

More on antibodies

When ASBMB Today science writer Laurel Oldach interviewed Charly Craik for her December feature, "The antibody patent question," their conversation about patenting one's academic discoveries went beyond the scope of that article, so we decided to offer this extended version of his comments. And if you haven't yet read enough about antibodies, check out Daniel Bojar's essay, "Why aren't there quality controls for antibody research?" on page 50 of this issue.

THE WELLNESS ISSUE

To start the new year right, we offer here a collection of articles, essays and tips on taking care of yourself and others. And to start the collection off right, we offer you this page to color. Studies have shown that coloring can reduce anxiety and stress while improving mood and enhancing mindfulness. So get out your crayons and improve your wellness. You're welcome.

Finding the help you need

By Paul A. Craig

Failure. None of us want to encounter it or admit it has happened, but it's a part of the career of every successful scientist. This article is written specifically for students who hope to embark on that career, to help you deal with and overcome failure wherever you are on your path.

COURTESY OF PAUL CRAIG

In a photo from the early 1980s, Paul Craig, second from left, is shown with his research adviser, Eugene E. Dekker, left, and Prasanta Datta, Harry Winter and Thomas Riggs at the University of Michigan.

My story

When I was an undergraduate student, I experienced the faculty as people who challenged me but in a supportive way. They expected everyone to succeed and graduate. My teachers encouraged me, and I received lots of positive feedback.

Graduate school was different.

I was the first person in my family to pursue a graduate degree. I was so naive that I appeared for my grad school interview in a suit — I thought that was how it was done. I had a strong undergraduate record, so I had been a big fish in a small pond. When I arrived at graduate school, I found that I was an average student, and it seemed to me that others in my class had arrived with much better preparation.

The pressure of grad school was new to me and not comfortable at all. Up to that point, going to school was all about getting good grades. Now I had started on a path for which the roadmap was unclear. (This is one reason I am such a strong supporter of undergraduate research — I want my students to learn early in their careers how to respond when the answer to a question is not known.)

The faculty members were all good people, but they were driven by the need for success and productivity in terms of papers, grants and reputation. I sensed the pressure they felt to publish and win grants. I soon realized that I was part of a larger system that was expected to be successful. I saw that a significant number of students did not complete their degrees.

I went home for Christmas break after my first semester uncertain whether I would return. It had been a difficult term — for the first time, I did not have any family nearby, so I was quite lonely.

I did return, and I remember one event from the following summer very well. My aunt and uncle visited Michigan in August, and they invited me to go with them to Greenfield Village and the Henry Ford Museum in Dearborn. It had been a tough summer — research was new to me, and I was making very little progress. When I went to meet them, I wasn't sure if I would laugh or burst into tears. We ended up having a wonderful time.

I struggled a bit with classes in my second year but was able to pass my qualifying exams to become a Ph.D. candidate the following June. That was when the real struggles began.

I had picked up a project that involved characterizing an enzyme that a previous graduate student from my lab had purified. The procedure was clearly written out, and the prior student had repeated the purification successfully a number of times. It should have worked on the first try if I followed the directions properly, but it didn't. It also didn't work on multiple attempts over the next twelve months, and I grew despondent. My advisor was on sabbatical. I kept sending him reports about my failures, and he wrote back long letters that were encouraging but also questioned my motivation. I still have those letters, but I have been unable to read them again.

I needed help to deal with the

Five things you need

I'd like to share a few things I've learned about surviving and thriving.

1. ***Have a sense of personal well-being and fulfillment.*** This is discussed at length in Great Jobs, Great Lives, a study by Purdue University and Gallup. This survey of 30,000 college graduates measured the impact of different factors on preparing undergraduates to become fully engaged in their careers. They identified five elements of well-being (quoted here) and found a direct correlation between engagement at work and the number of elements found to be present in the life of the graduates, according to the Gallup-Healthways Well-Being Index.
   - ***Purpose well-being:*** Liking what you do each day and being motivated to achieve your goals
   - ***Social well-being:*** Having strong and supportive relationships and love in your life
   - ***Financial well-being:*** Effectively managing your economic life to reduce stress and increase security
   - ***Community well-being:*** The sense of engagement you have with the areas where you live, liking where you live, and feeling safe and having pride in your community
   - ***Physical well-being:*** Having good health and enough energy to get things done on a daily basis

   While not foolproof, asking ourselves whether these elements are present in our lives provides a good test to assess where we stand each day.
2. ***Get honest with someone***, particularly your advisor. Over time, I found that the more honest I was with my advisor, the better things went for me. If things were not working, I needed to assess the failure, try some solutions and present my findings without excuse or justification. We could then look together at the cold, hard facts and decide the best next steps.
3. ***Find a support group and stick with it.*** My support group was my faith community, but there are many other choices. One of my friends in graduate school practiced aikido, which for him combined physical and spiritual well-being. Unfortunately, some of us find ourselves drawn to the dangerous excesses of addiction. The January 2017 issue of ASBMB Today contains a wonderful essay about ongoing recovery from addiction titled "A Journey to Sobriety" by Dr. 24hours. If you are drawn to abuse alcohol or other substances or find yourself involved in compulsive gambling or sexual behavior, you may be able to seek help from a 12-step group, such as Alcoholics Anonymous.
4. ***Stay connected to your family.*** My move to graduate school left me isolated from family. I finally became desperate enough to look up some more-distant relatives. Eventually, I met a second cousin, and we became fast friends. His farm became a weekend retreat for me while I was finishing my Ph.D. and completing my postdoc.
5. ***Be open to real connections from unexpected sources.*** During my last year of graduate school, I was asked to host a biochemistry graduate student from North Carolina who was visiting a Christian fellowship that I had joined. Bob Bateman and I quickly became fast friends, and he has stood beside me in many challenging and joyful situations. I remember calling him when I was awaiting my tenure decision. He urged me to stop talking so fast. Then he pointed out that I would have my family and friends no matter how that decision turned out. We have shared many wonderful moments together with our families over the last 34 years. I continue to be grateful for his friendship, advocacy and advice, even though I never expected to meet him.

emotional impact of failure.

Fortunately, I was not isolated. As a practicing Christian, I looked for fellowship with other believers. That summer I was living in a training/discipleship house with about 30 young men led by a few older men. Perhaps it was the testosterone in the air, but every night as we ate supper together, people talked about their personal and professional successes. I was heartbroken because I had none to share. I remember the night when one of the house leaders asked me why I was so quiet at suppertime. I told him it was because I had no successes to report. He challenged me to share my failures and to ask the others for help and prayer. So I did the next night. My friends surrounded me, encouraged me and promised to continue praying for me.

Things did not change immediately, but I lost my hopeless feeling and started looking for solutions. I found a recently published paper that pointed me in a new direction for purifying the enzyme. It took about two months of methodical effort to work out a new purification scheme and another two months to convince my professor that this was the right thing to do.

From that point, it took another two-and-half years to complete my graduate work, but that was more about learning persistence than fear of failure.

What I've learned

Each of us has unique experiences in our careers. In my story, I emphasize the role of my faith because it was central to my experience. I hope that aspect of my story doesn't lead you to dismiss the discouragement, loneliness and challenges I faced for the first time when I entered graduate school. I believe these are common experiences for people in all walks of life and certainly for those pursuing scientific careers. I also experienced encouragement, voices of wisdom and love.

In graduate school, you will be surrounded by lots of talented people: established investigators who have been publishing and overseeing funded research for decades; the new stars — assistant professors who just completed postdocs with famous scientists and are on a path to greatness; talented postdocs; and more senior grad students. They all know more than you do, and many of them have what you want — a life as a scientist, including the pursuit of knowledge in a stable career that, perhaps, one day will include recognition at the local or even national level. You will start out with other new and talented students who share your dreams. To reach those dreams, you need to work hard. You will encounter frequent challenges, and sometimes they will be more than challenges. I hope my story will encourage you to find the help you need as you pursue those dreams.

COURTESY OF PAUL CRAIG

Paul Craig, right, is pictured with Eugene E. Dekker, his research adviser at the University of Michigan, in the early 1980s.

As you engage in a scientific career, your life will be filled with ups and downs. In academia, papers are accepted or rejected. For most of us, grants are rejected more often than they are funded. We face anxiety as we seek tenure (in academia) and promotion (everywhere).

Our lives have great potential for joy, but here I am focused on the challenges the scientific life brings. Failure is part of our lives. We must learn how to cope so that it is only a temporary state.

If you enjoyed reading this article, please feel free to reach out to Paul at paul.craig@rit.edu.

Paul A. Craig (paul.craig@rit.edu) is a professor of biochemistry and head of the School of Chemistry and Materials Science at the Rochester Institute of Technology. He won the 2018 ASBMB Award for Exemplary Contributions to Education.

Pulse points: Out of the dark

From their labs to their personal lives, scientists now are addressing wellness and working to raise awareness about mental health issues. Throughout this issue of ASBMB Today, you will find short summaries of work in this area, including a study on how sleep deprivation can lead to loneliness, an initiative to improve heart health and research on worms under extreme stress. Check out our website (asbmb.org/asbmbtoday) for links to more information.

Susanna Harris is a graduate student studying microbiology at the University of North Carolina School of Medicine. Last summer, she gave a talk for The Monti, a series of live shows in which guests share personal stories. In her talk, she shared her experience with depression after failing an exam in graduate school and how she came through the other side of what she described as "months of crushing darkness." Watch her talk: vimeo.com/286214085. Follow her on Twitter at @susannalharris.

Leadership with a focus on wellness

By Teresa M. Evans & Nathan L. Vanderford

"Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less."

— Marie Curie

Leaders often portray themselves as confident and fearless, but as leaders we are often the opposite. Confused leaders, misunderstood leaders, overwhelmed leaders and sometimes even scared leaders is more like it.

Whether as a graduate student mentoring an undergrad in the lab, a faculty member overseeing a research team or a department chair leading a group of faculty, we all question our leadership ability and are unsure of ourselves at times. Therefore, we need to reflect on our own leadership styles to better understand the critical role they play in our health and well-being as well as the health and well-being of those we lead.

As scientists, we often are influenced first by the leadership styles we see in graduate school. We see how our laboratory advisor reacts to successes and failures in research, and we begin to adapt to these reactions. Over time, we become conditioned to react one way when our advisor congratulates us on successfully completing our qualifying exam and another when this same advisor scolds us about a failed or incorrectly controlled experiment.

As leaders in the sciences, we have plenty of room to improve how we lead; in particular, scientific leaders should work to put more focus on ensuring that wellness is considered as a key variable in the success of their trainees. We suggest that scientists take advantage of what is known about leadership both from the academic sector and the business world and work to be transformational leaders.

Transformational leadership

Transformational leaders are dedicated to incorporating the ideas and taking into account the needs of all members of their organization, working to build a team that can achieve its goals efficiently and effectively.

We all know that being a good leader is not about wearing a tie, having a title or giving instructions. A leader should embrace transformational leadership, support the needs of the team and incorporate new ideas to ensure the team's needs are being met.

Transformational leaders work to reduce fear in their teams through increasing understanding. As we know from the fundamentals of neuroscience, experiencing fear hinders our ability to think critically and make rational choices. To ensure that the team can function at its fullest potential, we must determine our team members' needs. For example, as a mentor in the lab, we should determine a new student's knowledge level before assigning tasks. This often requires asking more than yes-or-no questions.

Q1: Have you used a pipette before?

A1: Yes.

Q2: Can you tell me about your experiences doing so?

If, in the scenario above, the mentor stopped with the "yes" response, they might assign a task beyond the scope of the student's ability rather than listening to the student and understanding their needs and concerns. The answer to the second question is very telling.

A2: I have used a pipette in my introduction to biology course, but my professor said that I needed more practice.

This answer shows a clear need for additional training to ensure that the student is confident and capable. As leaders, we need to make sure to set our teams up for success; sometimes that means taking a step backward to ensure that everyone is trained and prepared.

Emotional intelligence

Another way to ensure that we are working to understand the needs of our team members is to engage our own emotional intelligence. This EI is essential for managing our own emotions and for ensuring that we are aware of the emotions within our team.

The EI of their leaders is what motivates 87 percent of millennials to help their employers succeed, according to a 2017 survey by the Lenovo Institute. EI is defined in three ways:

1. Notice, label and define what YOU are feeling.

2. Notice, label and define what OTHERS are feeling.

3. Use this information to GUIDE your thinking and behavior.

Mastery of EI will help us understand not only our own emotions but also the emotions of our teams so that

we can respond effectively. We all have known leaders with varying degrees of EI and can reflect on how that made us feel. To promote the well-being of a team, leaders should work to understand the impact that actions and words have on them as well as how to communicate effectively about emotions.

The ABC model

To understand the impact of our actions on our own emotions and those of others, we can use the ABC model. This model is designed to help us understand the interactions among thoughts, emotions and behaviors.

Think about the last time you did not handle your emotions well. Now go through the steps below. You should have a new way of looking at the initial event that allows you, in the future, to react in a more emotionally intelligent way.

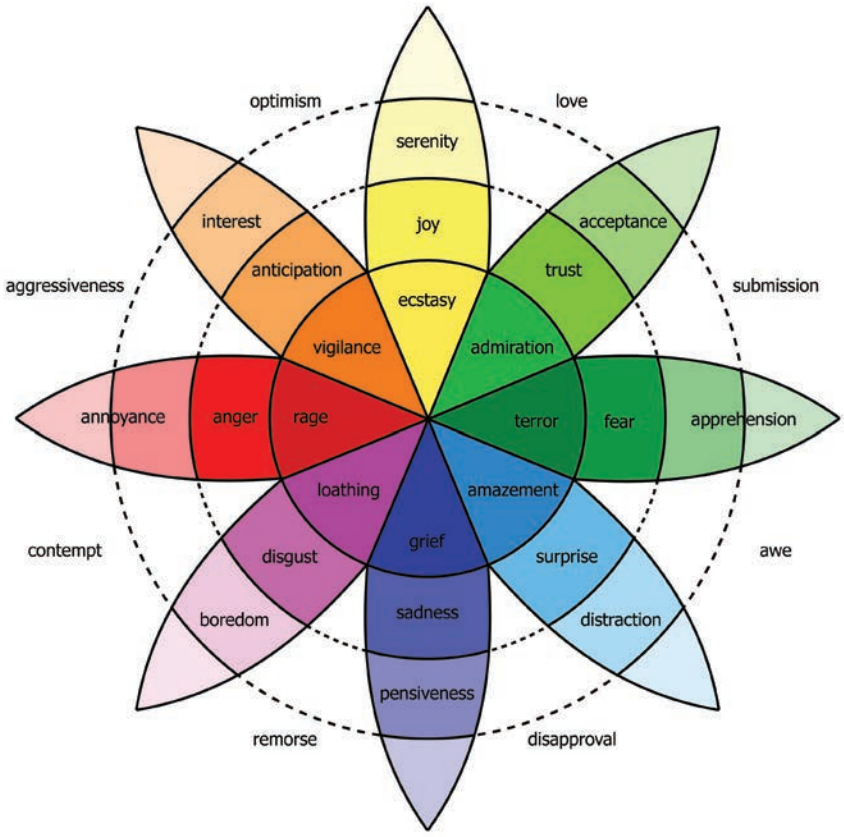
A: Activating event — Something happens to you or within the environment around you. Example: "Someone turned off my experiment while I was away."

B: Beliefs — You have a belief or interpretation regarding the activating event. Example: "They are trying to ruin my results."

C: Consequences — Your belief has consequences that include feelings and behaviors. Example: "I believe they are out to get me."

D: Disputations of beliefs — Challenge your beliefs to create new consequences. Example: "Maybe they just made a mistake."

E: Effective new beliefs — Adoption and implementation of new adaptive beliefs. Example: "I will turn it back on and assume the best until I have a definite reason to believe otherwise. I will talk to them and ask that they be more cautious next time."



This colorful wheel, designed in 1980 by Robert Plutchik, a psychologist, identifies eight basic emotions and their combinations.

By regularly using the ABC model, we can train our behaviors and work to align better with those of a transformational leader. The ABC model is also a great tool for discussing tough situations and reactions with a team to ensure that we are building strong communication.

Wheel of emotions

A leader needs a robust and nuanced emotional vocabulary to communicate effectively and to promote open communication of emotions by team members.

Plutchik's wheel of emotions identifies eight basic emotions and combinations of those basic emotions within a colored wheel. This can help promote the effective and clear communication of emotions, which is called emotional literacy.

When leading a team that struggles with emotional literacy, consider using this wheel to guide the conversation and ensure accurate perception of each person's emotions. For example, a leader might perceive that a team member is showing rage after being asked why they were late for a meeting, but in reality that team member is simply annoyed by the traffic that made them late.

Be a role model

A leader should be a role model in their organization, laboratory or department. A good leader should, therefore, be aware of the need for wellness in the organization and work to embrace wellness programs that

CONTINUED ON PAGE 35

With a little help from my friends

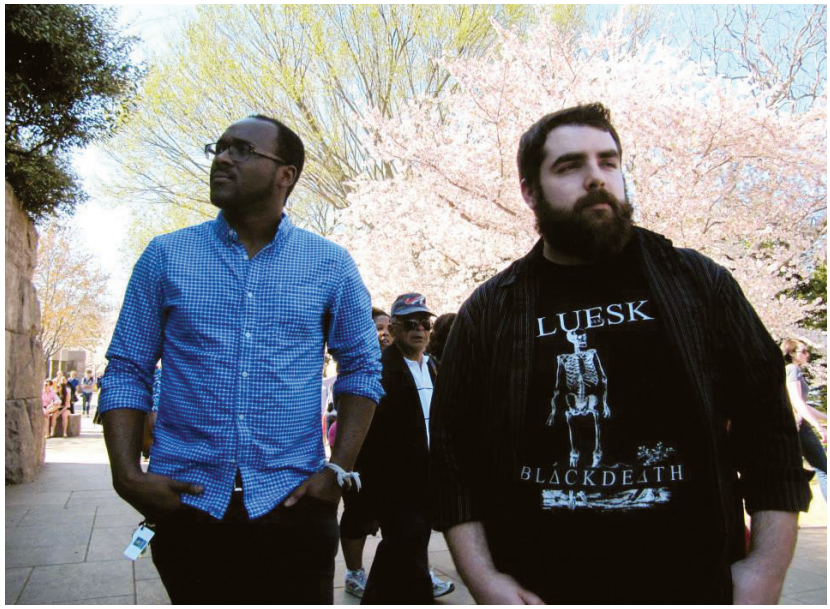
By Mark Zbinden

"He is going to be so upset."

That was my first thought when the head nurse in the emergency psychiatric ward told me they needed to notify my emergency contact of my situation. "He" wasn't my PI. Nor was he my father or any other blood relative.

He was my friend.

It was my fourth year of graduate school, and things were not going well. My project refused to cooperate, my relationship with my PI was strained, and I simply couldn't handle it. I had made an appointment to speak with a therapist, and within half an hour of our meeting, she was escorting me to the hospital across the street. I was terrified. But as traumatic as the whole ordeal seemed, I was most concerned how my best friend, now an objectively successful postdoc at MIT, would react to the news.



RISA BURR

Mark Zbinden, right, and Jarrett, the friend who helped Zbinden after his hospitalization, at the Cherry Blossom Festival in Washington, D.C., in 2014.

A recent report in the journal Nature Biotechnology shows that my story is not uncommon among my peers. Around 40 percent of students surveyed reported experiencing depression, and a similar number reported anxiety. The study also suggests that these experiences are correlated with students having negative feelings about relationships with their mentors.

Graduate students also experience an inordinate amount of stress. I know plenty of students who report working 50-plus hours in a week, and many take on additional debt to make ends meet when their stipends fall short. Often, they've entered their program right after college, and this is their first full-time job experience. On top of that, they likely have moved to an unfamiliar place, crippling whatever local support system they had before starting the pursuit of their advanced degree. More is expected of them than ever before, and they try to meet those expectations with as small a support structure as they've ever had.

So what can graduate students do to overcome this common and untenable situation? In addition to others detailed in this issue of ASBMB Today, I'd like to put forth a resource that rarely is talked about in any depth: friendship.

When I was released from the hospital the next morning, I was greeted by some very concerned text messages from my friend. After I told him I was home, he dropped his lab work and came to meet me at my apartment. I was waiting outside on the stoop, and he sat down next to me. What followed was a long silence, which I broke:

"Thanks, man."

After his laughter subsided, he responded, "No problem."

We talked for a long time, and after a while, it dawned on me just how much I appreciated this person. He, along with the rest of the friends I made in graduate school, meant more to me than I knew — until that very moment.

Throughout the next few weeks, I made it a point to talk to each one, telling them what I was going through and that I appreciated them. I was dumbfounded by their responses: offers of support and love, without fail or hesitation. My story

wound up having a happy ending, and I've compiled some advice here on friendship so that yours can too.

Advice

Before I continue, I'd like to plead with anyone who is having thoughts of self-harm to talk to someone about it immediately. There are people who want to help and care about you. Which brings me to my first bullet point:

• **Psychiatrists, therapists and mental health counselors can help you.** And a psychiatrist can work with you to treat any neurochemical imbalances you may have. If you have an opportunity to see a professional, and you think you need to, I urge you to take advantage of it.

• **We're all in this together.** Your classmates and older graduate students have some understanding, at least, of what you are feeling. Although it can be anxiety-inducing to introduce yourself to someone new, remember: they're in the same position you are.

• **Don't be afraid to tell your friends how you feel.** The strongest foundation of any relationship is honesty, and friendships are no different. When things are going well, tell them. And when things aren't great? Tell them. Your friends care about you, and they'll help you if they can.

• **It's a two-way street.** Your friends will need you as you will need them; be sure to listen to and care for them, if doing so doesn't overly tax you. It's always OK to say no if you're uncomfortable, but reciprocal effort in any relationship is critical.

• **Friendship doesn't have to mean hanging out.** Time and money are short in graduate school, but luckily, friendship doesn't require either of those things. Coffee breaks taken together and exchanged text messages are great ways to catch up and remind yourself that you are not alone in this. That said …

• **Make special plans together.** Planning and taking vacations together cuts down on costs and promotes a healthy work-life balance, and it is a more concrete commitment to time away from the lab than "I'll try not to go to the lab this weekend." Additionally, spending time with people you care about will reinforce the bonds between you, and all involved will be better for it.

No one is an island, and no one can do this alone. Make friends, care for them and build on each other's strengths. Lean on them and offer your hand when they need it.

Even though graduate school threatened to capsize me, my friends were my bulwark.

And they still are.

Mark Zbinden (mark.a.zbinden@gmail.com) is a scientific project coordinator at a small biotech company in Boston. Follow him on Twitter @_PhDnD.

CONTINUED FROM PAGE 33

promote the well-being of the team. As leaders, we should educate ourselves and our team members about EI and emotional literacy.

We can cultivate EI in our teams by encouraging emotional responsibility through promoting team service projects. A leader who wishes to promote EI also should aim to create an honest work environment where transparency is held in the highest regard. Most importantly, we must lead by example and develop our personal EI as leaders.

Conclusion

As scientists, we focus on collecting data, publications and grants, hoping that one day we will accumulate enough to be rewarded in our work lives, and only then will we allow ourselves to start enjoying life. With this mindset, we can find ourselves dedicating most of our time to work and neglecting our wellness.

As researchers, we spend most of our time in the laboratory or our offices, so it is imperative that faculty, academic leaders and mentors embrace the importance of wellness both in themselves and in their team members. We must model positive EI and wellness for those we lead to promote a culture that embraces leading through wellness.

Teresa M. Evans (evanstm@uthscsa.edu) is an assistant professor in the department of pharmacology at the University of Texas Health Science Center at San Antonio.

Nathan L. Vanderford (nathan.vanderford@uky.edu) is an assistant professor in the department of toxicology and cancer biology at the University of Kentucky.

Pulse points: Stressed worms

Researchers funded by the National Institutes of Health investigated the impact that environmental stress can have on the nervous systems of roundworms called Caenorhabditis elegans. A news release from the NIH explained that when C. elegans are exposed to a stressor, such as starvation, they stop developing temporarily and then continue growing after the stressful situation has passed. Researchers studying worms before and after a period of stress concluded that stress rewired the worms' nervous systems.

GRAD STUDENTS FACE MENTAL WELLNESS CHALLENGES

Recent studies have drawn attention to the mental health challenges of graduate students. Hironao Okahana wrote about it in an April article on the Council of Graduate Schools website. Okohana, the CGS associate vice president for research and policy analysis, noted that Ph.D. students face many more mental health challenges than the general population. Read the article at cgsnet.org.

39%

OF GRADUATE STUDENTS FELL INTO MODERATE TO SEVERE DEPRESSION

A 2018 study in Nature Biotechnology reports that 39 percent of participants, mostly doctoral candidates, had moderate to severe depression, as compared with the 20 percent of American adults who experience mental illness in any given year. (Among this study's authors are Nathan Vanderford and Teresa Evans, who write about leadership on page 32 in this issue.)

HALF

OF PH.D. STUDENTS HAVE EXPERIENCED PSYCHOLOGICAL DISTRESS

The problem is not new. Studies in the Journal of Nervous and Mental Disease (2013) and the Journal of College Student Development (2006) reported that half of all Ph.D. students have experienced psychological distress and one-third are at risk of a common psychiatric disorder.

63%

OF GRADUATE DEANS AGREED STUDENTS STRUGGLE MORE THAN 5 YEARS AGO

Graduate deans are mindful of the mental health challenges faced by master's and doctoral students, Okahana writes. In the 2018 CGS Pressing Issues Survey, 63 percent of these deans agreed or strongly agreed that current grad students struggle to maintain mental wellness more than grad students did five years ago.

> "Notably, nearly half of responding graduate deans indicated that their institutions are doing a poor or very poor job of informing and training graduate faculty members, faculty advisers, PIs, and dissertation/thesis chairs."
>
> — Hironao Okahana

Career wellness: consider your strengths

By Natalie Lundsteen

Dhruba Deb began his postdoctoral training at the University of Texas Southwestern Medical Center with mixed feelings. He was confident in his scientific training and knowledge, and he felt prepared to begin work on a project developing novel lung cancer therapeutic strategies. He knew he could succeed at the bench, but he was wary of taking on senior lab leadership responsibilities in this new phase of life. He came from a large city in India but found the culture of Dallas a challenge, and he knew that postdoctoral research is often solitary and sometimes isolating.

From the start, Deb became involved in postdoctoral leadership activities, which presented him with opportunities for self-assessment, finding camaraderie and feeling like part of a team. Increasing his knowledge of his own talents, skills and values had a profound impact on his personal development and well-being. He learned about successful teams and how to thrive in them, seeing that everyone contributes something to group work settings.

"Till this moment of my life, everything was about me," he said. "My studies, my grades, my papers, my grants. For the first time, I realized now the priority is shifting. It is about the paper of the graduate student training with me, the poster of the summer student I taught, the collaborative multi-PI grant that I'm writing with four other postdocs. Suddenly, it is not about just me anymore. It is more about how others around me perform, and their states of mind and wellness as well."

Starting his postdoc, Deb immediately picked up on a crucial aspect of workplace wellness and happiness — self-awareness makes you a stronger individual contributor and a better team member.

Why strengths matter

I advise biomedical science trainees on career development, and I've found that a process of self-reflection can move a trainee forward if he or she feels stuck in any way, whether it's setbacks at the bench, indecision about next career steps or a general lack of confidence.

Postdocs and graduate students are probably familiar with individual development plans; trainees create these personal road maps as a tool to strategize their professional choices and skills development, which can help determine career preferences and values. But so much of a scientist's training is about learning new things. While building skills and identifying areas for improvement, scientists often don't consider consciously those aspects of self where they are naturally accomplished. They rarely work to identify strengths.

One of my favorite resources for personal/professional development is specifically focused on strengths — the CliftonStrengths Assessment (formerly known as the StrengthsFinder), created by the Gallup consulting company. I first took this assessment about 15 years ago when I was a university consultant and the dean wanted to see how I would fit in with the rest of our working group. I learned that my love of building relationships and helping other people directly correlates to a few of my top strengths, including communication, positivity and "WOO" (winning others over). I like motivating people and helping them see possibilities, so I'm happy that I get to use my natural strengths in my job every day. It makes my work seem less like work.

I've seen CliftonStrengths make a difference for many grad students and postdocs who are finding their way as

scientists, learning about professional options and making choices about what to do after their scientific training. But CliftonStrengths is not about choosing a particular career path. Instead, the tool helps you see aspects of yourself that can help you make better career decisions and choices about activities and settings where you can thrive, including working in teams or groups.

Gallup has found that people who spend more of their day using their strengths are less likely to be stressed, worried and sad — and I agree. It makes sense to choose, if possible, a career path where you will be naturally adept. You spend most of your waking hours at work; how you make a living and the people with whom you work certainly affect your quality of life. Career setbacks, career activities and even thinking about career choices cause stress and anxiety, especially for scientists in training or professional transition.

I like the CliftonStrengths assessment because it gives immediately useful results that can have a positive impact on someone who feels stuck in a work or personal situation or who is uncertain about making choices. Being reminded of the things you are naturally good at is a powerful confidence boost, and I think everyone makes better choices when minimizing stress and tension. (Do you see my positivity at work?)

To give some examples of identifying what strengths you naturally might possess, consider these questions: Have you been told that you are a great listener? Do you have a knack for sizing up people or seeing the big picture? Are you great at finding patterns and analyzing data? Those are strengths. If you find a career where you regularly can use your strengths, you will probably enjoy your work almost every day, and knowing your strengths is also powerful in day-to-day interactions and situations with family and friends.

CliftonStrengths results outline your natural talents and how they influence the way you live. The online assessment takes about 20-30 minutes to complete and asks you to make choices between pairs of words in order to produce a Signature Themes Report of your top five talents and how to maximize them. There are a total of 34 strengths organized into four domains (executing, influencing, relationship-building and strategic thinking). The odds of two people having the same top five strengths in the same order is one in 33 million, so your results are truly personalized and individual.

Cost to identify your top five talents is $20. It's definitely worth the price, in my opinion, but since it is a popular tool in higher education settings, you should be able to take CliftonStrengths through a workshop or course at your institution. You do not need a coach or counselor to review CliftonStrengths results, which is one of the great things about it, but I've found that it helps my trainees to debrief and discuss their strengths in groups or one-on-one. I also recommend that non-native English speakers take the version in their first language, if possible; CliftonStrengths is available in more than 25 languages.

Team-building with strengths

Once you know your own strengths, it's also useful to know the strengths and talents of others in your immediate circle. Most activities, whether in your personal or professional life, involve interacting with others, so knowing more about what motivates or discourages others in your team, lab or organization can result in better harmony and a smoother path toward accomplishing goals.

Laura Banaszynski, assistant professor of obstetrics and gynecology in the Green Center for Reproductive Biology Sciences at the University of Texas Southwestern Medical Center, incorporated understanding of strengths when planning a recent program retreat. Faculty, staff, postdocs and students all took the CliftonStrengths assessment before the off-campus event and then used their personal results during retreat activities to spark conversations about lab and team dynamics, getting the most from collaborative activities and interactions, and developing understanding of individual work styles.

Having the common language of the CliftonStrengths assessment "was a positive, morale-building way to strengthen our academic community," Banaszynski said. "Everyone felt good about it. It helped our group be more personal and to understand each other while also having fun."

Postdoc Dhru Deb was happy to discover not only his top five strengths but also those of his colleagues, he said. "This training gave me confidence to talk about my own strengths in job interviews, and also made me aware of a 'magic list' of talents for the people who I can collaborate with to execute tasks requiring certain skills that I lack."

Resources

You can find the StrengthsFinder at gallupstrengthscenter.com. Pair it with other resources:

- the MyIDP tool at sciencecareers.org
- the occupational path exploration tools at biocareers.org and versatilephd.com

Often, taking even a small step in learning about yourself and your options can put you in a better frame of mind to get past feeling stuck and start thinking about your future.

Natalie Lundsteen (natalie.lundsteen@utsouthwestern.edu) is assistant dean for career and professional development in the Graduate School of Biomedical Sciences and assistant professor of psychiatry at the University of Texas Southwestern Medical Center.

Maternity in grad school — the best and worst of times

By Nathalie Gerassimov

The doctor placed my tiny, naked daughter on my chest. It was Jan. 15, 2018, and I was in the sixth year of my Ph.D. graduate studies. The timing was perfect. At the same time, there is never a perfect time to have a baby.

I agonized and analyzed the timing of my potential pregnancy for years, hoping my family planning would not interfere with my career. Turning 30 pushed this issue to the forefront, especially since I'd just married the wonderful man I'd been dating for many years. A female PI said once that having a baby while you are writing your thesis works well, so that was my goal.

Like most Ph.D. journeys, mine was a series of ups and downs. Just as I started to gain confidence as a scientist, my graduate lab decided to move to a different state, and I knew I wouldn't go with them. Luckily, my graduate advisor arranged for me to continue my project with her but to do my work in a new lab. This arrangement was supposed to last for one year, and I decided to postpone starting a family. When the arrangement was extended for another year, I decided it was time to get pregnant.

To be completely honest, I had reason to believe that I might have difficulty conceiving. If I waited until I was 35 to start trying and then had fertility problems, I would be furious with myself for not starting sooner.

I was pregnant three months later.

§

The first month, when I still didn't know I was pregnant, I was incredibly tired and emotional. The science was not going as I'd hoped; I felt sorry for myself. I was relieved to learn I was pregnant. Now I understood why I'd been having such a hard time.

COURTESY OF NATHALIE GERASSIMOV

Nathalie Gerassimov and her daughter, age one month, who was born while Nathalie was working on her Ph.D.

Determined not to be the emotional pregnant woman in the lab, I focused on controlling my thoughts, and through that I was able to hold my feelings in check. Previous dabbling in yoga and meditation helped. I'm an anxious person, excellent at worrying about what could happen. After more than a decade of self-created emotional pain, I finally learned how to breathe: inhale into left nostril, exhale from right nostril, inhale into right nostril, exhale from left nostril … Miraculously, breath control calmed me in less than two minutes.

In the second trimester, I was full of energy, and I channeled all of it toward my research (I had arranged all things pertinent to baby — such as registry — during my first trimester). Being pregnant put a tangible clock on my time in grad school, and I became better at prioritizing.

Sleeping became a challenge as my belly got bigger. I credit my sanity to the Snoogle — a large C-shaped

pillow that supported my entire body. However, no pillow could help with the urgent need to empty my bladder at least once a night.

During my third trimester, I became a master time planner. I was diagnosed with gestational diabetes, and my life circled around management of the disease. I had to inject insulin three times a day and measure my blood sugar four times a day. My meals were calculated precisely, and I had to walk 30 minutes after each meal to help regulate my blood sugar. At that point, I was doing a lot of imaging, and I walked miles in the hall outside the microscope room while the images were being acquired. I also had lengthy appointments twice a week during which I could see my baby hiccup in my belly.

Sleeping got even more challenging. Instead of having to pee once or twice per night, I was usually up four times. This is clearly nature's joke on women; getting out of bed with a large belly is ridiculously hard.

Despite all that, I was better at balancing life and work. I constantly reminded myself what really mattered: Yes, I needed to do due diligence in my research, but these nine months would affect my baby's whole life. So when I could, I worked hard for long hours, which was 80 percent of the time. And when I couldn't, I went home and cuddled with my husband.

My water broke to announce my baby girl's arrival. What followed was hands down the most terrifying and painful experience of my life. As they say, it's called labor for a reason. I'd tried to prepare myself with more frequent meditation and yoga practice, but in the end I opted for the pain meds — which only worked on one side of my body.

Countless times I had imagined the moment I would meet her, gazing at my baby through a rosy mist of love. Instead, all I cared about was stopping the pain.

§

Someone said once that unconditional love comes from selfless actions repeated over and over again. I had a chance to test that hypothesis during the eight weeks allocated by the Johns Hopkins University School of Medicine's new extended maternal leave policy.

The first two weeks, I slept on average two hours a day and functioned whenever my baby needed me, despite being sick, hurt and tired beyond imagining. Every day, I was reduced to tears of exhaustion. I kept reminding myself that nothing is as intense or painful as giving birth. My meditation and yoga practice did help me through this period. It was also crucial to talk to people I trusted about my fears and anxieties — like my need to check every 30 minutes that my baby was breathing. The first month was incredibly hard, but my heart melted in those moments when she slept peacefully in my arms.

When it came time for me to return to grad school, my daughter was sleeping though most nights. My mother was able to come and stay with us for six months, and my husband was fully involved in our baby's care. All I have accomplished rests on their support of my goals and the sacrifices they made for me.

I had four months to finish my experiments, write my thesis and figure out what to do next. I had to work like crazy. With my mom watching my baby, I felt less guilty about being gone for long hours. I'd heard that mothers always feel guilty. I worked at focusing on what I was doing when I was doing it and reminding myself that I was only human, with limited time and energy. I also felt less guilty because I was able to breast feed my baby (I am grateful for the breast pump and maternity room at my school). I abandoned my yoga and meditation practice at this point (due to what I called mother interference syndrome — both from being a mother and having my mother there), but Mom and I went to the gym several times a week, which helped me sleep and regulate my stress.

I managed to finish my graduate work and secure two internships to help me figure out what I want to do professionally. I am now an intern in the biotech industry, and I love it.

My mom had to leave, but we found a wonderful nonprofit child-care center that awes me with its quality of care, even though it costs my entire graduate stipend (my husband pays the rest of our living expenses). I still work long hours and use breast-feeding and my supportive husband to feel less guilty about being gone so much. My daughter just got her first tooth and cries "Mama" when she is hungry or upset. Most nights she sleeps well, and so do we.

Maternity transformed me; I am stronger, more determined and less afraid. I am also consumed by the desire to make this world — the world that my daughter will be living in — better in whatever way I can.

Nathalie Gerassimov (Nathalie.gerassimov@gmail.com) is a Ph.D. student at the Johns Hopkins University School of Medicine.

Pulse points: Shunned and sleepless

Researchers at the University of California, Berkeley, demonstrated that sleep-deprived people not only feel lonelier, but also alienate others. Matthew Walker told Berkeley News: "The less sleep you get, the less you want to socially interact. In turn, other people perceive you as more socially repulsive, further increasing the grave social-isolation impact of sleep loss." The team used brain imaging, simulations and other tools to measure the social implications of poor sleep. Visit asbmb.org/asbmbtoday to learn more and see the simulations.

Holistic mentorship

Tips for supporting graduate students and postdoctoral fellows

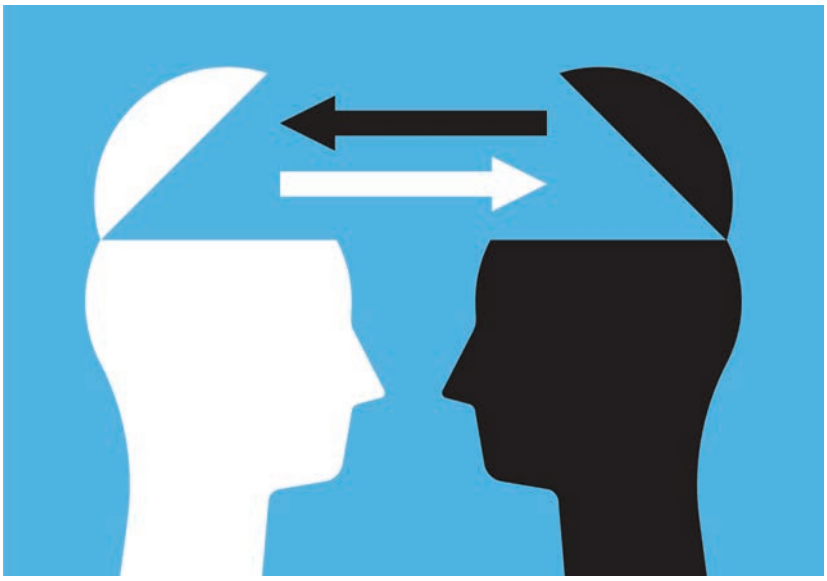
By Kelly Edwards, Ziyan Bai & Bill Mahoney

Holistic: relating to or concerned with wholes or with complete systems rather than with the analysis of, treatment of, or dissection into parts
— Merriam–Webster Unabridged Dictionary

Graduate students in the sciences work to understand or create something novel and present these findings to the larger community, with the goal of moving on to an independent career solving bigger and more complex problems. Postdoctoral fellows feel added pressure to own a piece of the work and to be seen as the creator and keeper of this knowledge as they explore careers inside and outside of academia.

- The pressures experienced by graduate students and postdocs are often overwhelming:
- Will there be enough funding?
- Will my experiments work?
- Will anyone be interested in my findings?
- Will someone beat me to them?
- Do I have what it takes to be successful?

As faculty members working to support graduate students and postdocs in an uncertain and high-stakes environment, we have developed a set of approaches that serve us and other mentors in the academic community. We advocate for building a mentoring team; a single primary research advisor has difficulty meeting all the needs and interests of a trainee. A team can provide support on all sides, and feeling supported goes a long way to enhancing a trainee's productivity, resilience and overall satisfaction.



Graduate students and postdocs are more than their work in the lab. They have complex lives. They may be responsible for a family or be living far from their family (or both). Personal commitments beyond current research projects may provide the fuel and fire for their further training; perhaps they bear the expectations, or assumptions, of others. They have financial stresses and feel self-doubt about how they choose to invest in their future.

Here are some suggestions for mentors to holistically support the development and success of graduate students and postdocs.

Ask open-ended questions

Instead of assuming we know what's going on with a mentee, we should be curious. We can be surprised to learn what's happening in their lives and with their thinking. Before we start lecturing or offering advice, if we show genuine interest and listen, we can better align guidance with where the mentee actually is. For example, either before or after a research-focused conversation, ask how the grad student is feeling about the work and check in about other things (interests and stressors) going on in their lives.

Set clear expectations

Many students enter graduate school or a postdoctoral fellowship knowing little about the unique milestones of academic progress — qualifying exams, masters' theses, finding a primary faculty advisor or developing a line of independent research. Demystifying these steps can be helpful, especially for students who may be the first in their families to earn a college degree or international students who have experienced a different educational system.

Create connections

We sometimes assume that students just will figure out how to seek the things they need or are interested in. We who have worked in university settings for decades can forget easily that these things are not all obvious. Isolation — from peers or faculty — can be a risk, particularly for students who see asking for help as a weakness or who believe it is not safe to be vulnerable. It's helpful to schedule regular advising meetings as a routine check-in. This setting can help normalize feedback so it becomes routine to talk about what's going well so trainees can build confidence in their strengths. Regular feedback also creates a safe opportunity for trainees to learn what they might do differently to do better in the future.

Create a culture of belonging

We have heard from some students that others make them feel that they were admitted to graduate school only because of diversity priorities. They experience micro- or macroaggressions from classmates, faculty or staff — hurtful comments that question whether someone who is not from the dominant culture can really fit in. What can we as mentors do to highlight the unique contributions every person brings to a program or training environment? We need to stress that diversity in backgrounds and training is best for advancing any field. The unique gifts and experiences of each team member should be celebrated. Invite trainees to attend departmental, professional or community meetings that are important to the work — this helps expand the circle of belonging within the professional community.

Show that being vulnerable is OK

As mentors, we need to talk about our own support structures and self-care practices. The more honest we are, the more students can trust us with their concerns and needs. Failure is part of our academic lives — we all have missteps, and we need to recharge and refuel. Demonstrating how we seek support can be our best gift to a trainee (and by practicing self-care, we can offer our best selves as mentors without burning out). We suggest sharing a true story from when you were a graduate student or postdoc about having a paper rejected by a journal or being questioned about research methodology at a national conference; talk about your feelings and how you reached out for help. Explain how you were able to draw upon these experiences the next time you hit a tough patch.

Stay focused on the why

Tapping into a trainee's passion and purpose — the why of why they are in graduate school or pursuing a postdoctoral fellowship — is key to helping them sustain energy and commitment for the long haul. Here too, we can get curious, ask questions and then, as allies, remind them of their passion and purpose when the going gets tough.

Help broaden their networks: None of us knows everything about all potential employment sectors. We need to connect our mentees to people within our own networks or those of our colleagues and friends if their interests align. When we share our network, our trainees can build more relationships as collaborators, mentees, friends or future colleagues.

If we are lucky, each of us is both mentor and mentee throughout our career. Mentorship, peer connections and access to support, whether for academic skills or emotional health, can help our mentees shift from surviving to thriving.

Kelly Edwards (edwards@uw.edu) is the associate dean for student and postdoctoral affairs at the University of Washington graduate school and a professor of bioethics in the UW School of Medicine. She has focused her research and leadership on how educational environments shape people both personally and professionally.

Ziyan Bai (baiziyan@uw.edu) is a doctoral candidate in the University of Washington College of Education and graduate staff assistant in the office of postdoctoral affairs. She is interested in graduate education policy, practice and the financing of higher education.

Bill Mahoney (wmahoney@uw.edu) is co-director of the University of Washington Office of Postdoctoral Affairs and is an associate professor in pathology at the UW School of Medicine. He has a longstanding interest in STEM professional development, focusing on graduate students, postdoctoral fellows and junior faculty.

Pulse points: Feel like a fraud?

Julia Omotade, Jamie King and Richard A. Kahn wrote in this magazine in February 2017 that the term "imposter syndrome" is used "to describe the chronic and potentially lifelong feelings of inadequacy and self-doubt that affect performance and professional outcomes." Have you experienced these feelings in your educational or professional career? If so, you're not alone and there are ways to overcome them. Elizabeth Cox answers the question "What is imposter syndrome and how can you combat it?" in a TED-Ed animation.

Refreshing my spirit

By Edward Eisenstein

Silence.

You may be skimming this issue of ASBMB Today rather quickly before turning back to the rapid pace of your everyday life. As we become absorbed by today's increasing demands of science and teaching, with information bombarding us through every medium, it is a wonder that we find any time to pause and reflect on our mental, physical or spiritual well-being.

ED EISENSTEIN

Ed Eisenstein attends meeting at the meetinghouse at Sandy Spring, Maryland, where Quakers have gathered since 1770. Initially, a log house was used for worship; this current brick structure was built in 1817.

Although many of us enjoy and even thrive on the excitingly rapid pace of science and discovery, teaching and counseling, and contributing to our local and global communities, how do we restore ourselves and reconnect with our values in order to persevere when life events are overwhelming?

There is now greater appreciation for the importance of wellness in our lives, and accordingly, many avenues are available to us for physical rejuvenation. But how does one revive the spirit? For me, I restore and nourish my spirit at a meeting among Friends.

So, what do I do at a Quaker meeting?

My Quaker meeting is held in silence. Deep silence. Before I arrive at the meetinghouse, I don't review a to-do list, read the newspaper, look at my smartphone, scroll through email or even listen to the radio. Instead, I try to clear my mind and avoid anything that might distract me from experiencing meeting for worship.

Once I arrive, I sit on a simple bench in an old, unadorned building. Our meetinghouse was built in 1817 — though Quakers have gathered on the site since 1753 — and it hasn't changed much since then. The hand-hewn pews face one another with no altar or pulpit but simply an open space in the center of the room.

Although there aren't many distractions, it isn't always easy to center myself — for life reasons or because of the sounds of traffic or someone coughing. But being in a sacred place with so much history helps me become still.

Then there is the silence

When I am able to settle myself fully, first my body and then my mind, I am able to open myself to silent prayer. I begin by meditating on the gratitude I feel for all the joy in my life, for my family and community, for the ability to discern my direction so that, as a way opens in my search for truth, I can meet the challenges ahead of me more readily. I ask for faith, forgiveness, equality and peace. And I do this silently.

The silence is important. Not simply for reflection but so I can listen, carefully, to the "still, small voice" that Quakers believe dwells in everyone's heart. The silence enables me to be more receptive to revelation

CONTINUED ON PAGE 45

How I learned to stop worrying about grad school* and to love climbing rocks

*at least for a little while

By Richard Sima

Every Tuesday, I find myself sweating and holding onto a wall for dear life.

I recently started bouldering, which is rock climbing without the rope or associated safety gear. As the name implies, the sport historically involved climbers attempting to conquer boulders outdoors. Nowadays, there is an indoor option with human-designed walls, artificial lights and padded floors.

My previous forays into building an exercise regime inevitably petered out. The touted benefits of an aerobic workout did little to outweigh the pain and boredom of running; though my mood was heightened in the hours and days after a good run, the anticipated wheezing, groaning and misery meant I never looked forward to lacing up my running shoes. In the face of this dread, I stopped putting on my running shoes at all.

Climbing was different from the start. I have to be mentally present every time I'm on the rock wall because inattention has immediate consequences. Not checking the placement of my feet before shifting my entire body weight will lead to a fall. Not judging clearly the distances between two handholds will lead to a fall. Becoming distracted by thoughts about experiments and analyses waiting back at the lab also will lead to a fall. In this way, climbing has a meditative quality. The danger I feel hanging even a few feet off the ground is enough to focus my attention on the task at hand as opposed to the myriad ideas, internal monologues and latent

HANNAH AHN

Richard Sima nearly slips off a rock wall at an EarthTreks gym in Baltimore but manages to catch himself.

anxieties I would otherwise occupy myself with.

The climbing routes are distinguished from one another by color, each assigned a difficulty and quirkily named — "Long Way Home," "Time for Coffee," "You Have Feet." The beginner routes include many platforms, called holds, that are large or have hand-conforming edges, making them easy to grab or stand on. Five months in, I'm climbing at a V3 level, which is solidly intermediate. The routes I now climb feature smaller holds, tougher transitions and increased soreness post-climb.

Each step up the wall is gratifying, mentally and physically. Bouldering forces me to move and sense my body in ways I've never done before. My fingers and hands are more sensitive to the weight and pressure I put on them, even as the skin on my palms becomes increasingly calloused with use. I've learned to move my feet and legs with greater precision and to trust the weight I can put on even just the toe of my shoe as I reach for a higher hold. Feeling the pull of gravity is thrilling as I let go with one hand and rebalance myself. When I'm clinging to a wall some ten feet off the ground, my lab experiments are far from my mind.

For me, climbing is a way of getting over the fear of failure through what amounts to exposure therapy in a low-risk setting; by being repeatedly exposed to something that provokes anxiety in a low-stakes environment, I can habituate myself to that stress of failure. Research shows this to be a benefit of hobbies outside the lab. Bouldering gives me a chance to fail often and publicly. If you aren't failing at climbing, then you aren't trying to push yourself to improve.

This is something I've had to get used to. It's easy to feel self-conscious approaching a new problem or climbing route, getting my hands on the starting holds and then immediately realizing I have no idea what to do next. I contort my body in various angles and directions, trying to find purchase on the next step, which initially seemed so easy and obvious. No doubt I look very silly.

I notice, however, that climbers with years of experience go through this same awkward dance on difficult problems that are new to them. There's nothing wrong or embarrassing about it. They also have to drop down as their strength gives way or they lose their balance. Even the seasoned veterans fall. The key is to then brush oneself off, take a deep breath and try again. Each attempt decreases my anxiety and makes the eventual success that much sweeter.

The climbing gym I frequent is well-suited for those keeping typical graduate student hours: it opens early and closes at 11 p.m. Unlike tennis, my previous sport of choice, bouldering does not require a partner, so there is no need to wrangle conflicting schedules or deal with dropped plans due to an experiment that took longer than expected.

Climbing is a social activity, however, and the community has been very open and welcoming. We all learn from watching one another, and we sometimes share pointers on different approaches to a route we're struggling with. As a neophyte, I find it inspiring to see children a fifth my age and a third my height scramble up routes I have not yet dared to attempt. I see how far I have to go in improving my physical strength and skill. But I also see how far I've come, and I take pride in what I have learned thus far.

I'm not sure where I'll be when I (fingers crossed) finish my thesis later this year. But I know many more routes will be left to climb, and I'll take each of them one step at a time.

Richard Sima (rsima1@jhu.edu) is a Ph.D. candidate in the neuroscience department at the Johns Hopkins University School of Medicine. Follow him on Twitter @richardsima.

CONTINUED FROM PAGE 43

and to connect with the others who are worshipping at the meeting.

Often, in deeply gathered meetings, nothing breaks the silence. But sometimes a Friend will receive a message that requires vocal ministry and will feel that it must be shared with those present. Do I ever receive a message? Certainly. But sometimes I think it is meant only for me, and sometimes I think it isn't ready to share with the meeting. When I am led by spirit so strongly that I must share with the meeting, I recall, as a good rule of thumb, a quote attributed to Albert Einstein: "I like to keep things as simple as possible. But not any simpler."

The meeting is over when one member, appointed as clerk, stands and shakes the hand of another. We then gather in friendship, sharing updates in our lives and hearts, and talk to newcomers who doubtless have questions about the hour that just passed. We connect with one another, our spiritual community, strengthened by the mystical bonds we have nurtured, and prepare to face the world and let our lives speak.

Edward Eisenstein (eisenstein@umd.edu) is an investigator at the Institute of Bioscience and Biotechnology Research and a faculty member of the Fischell Department of Bioengineering at the University of Maryland. He is a member of Sandy Spring Monthly Meeting of the Religious Society of Friends.

For many college students, hunger can 'make it hard to focus in class'

By Michelle Andrews
Kaiser Health News

As students return to campus this winter, many will hunger for more than knowledge. Up to half of college students report that they were either not getting enough to eat or were worried about it, according to published studies.

"Food insecurity," as it's called, is most prevalent at community colleges, but it's common at public and private four-year schools as well. Student activists and advocates in the education community have drawn attention to the problem in recent years, and the food pantries that have sprung up at hundreds of schools are perhaps the most visible sign.

Some schools are also using the Swipe Out Hunger program, which allows students to donate their unused meal plan vouchers, or swipes, to other students to use at campus dining halls or food pantries.

Those "free dining passes have given me chances to eat when I thought I wouldn't be able to," one student wrote to the program. "I used to go hungry and that would make it hard to focus in class or study. [The passes] really helped my studying and may have helped me get my GPA up."

Pantries and food passes are good band-aids, but more systemwide solutions are needed, advocates say.

"If I'm sending my kid to college, I want more than a food pantry," said Sara Goldrick-Rab, professor of higher education policy and sociology at Temple University in Philadelphia, who founded the Hope Center for College, Community and Justice. "I want to know that they're addressing high food prices on campus and taking steps to ensure no student goes hungry."

Part of the disconnect may stem from a misperception about what today's students are really like, said Katharine Broton, an assistant professor in educational policy and leadership studies at the University of Iowa who has published research on food and housing insecurity in colleges. Many of them don't fit the profile of a "typical" student who attends a four-year institution full time and doesn't have a job, Broton said. Rather, about 40 percent of students today are working in addition to going to school, and nearly 1 in 4 are parents.

The juggling act can be hard to maintain. "Most of the students, we find, are working and receiving financial aid, but still struggling with food insecurity," Broton said.

Adding to the stress is the fact that while tuition and fees continue to rise, financial aid hasn't kept pace. In the 2017-18 school year, after accounting for grant aid and tax benefits, full-time students at two-year colleges had to cover $8,070 in room and board on average, while those at four-year public institutions faced an average $14,940 in room, board, tuition and fees.

Anti-hunger advocates credit students with both sounding the alarm about hunger on campus and in some cases offering ingenious solutions.

Rachel Sumekh, who founded the Swipe Out Hunger program with friends at UCLA several years ago, said they wanted to do something useful with the unused credits from

the meal plans that they were required to buy. The program now counts 48 schools as participants, and Sumekh said in the past year they've seen a "dramatic" increase in the number of colleges that are reaching out to them about getting involved.

The University of California, Berkeley, is part of Swipes, as the program is known. It's one element in a multipronged effort that targets students who may need extra support to meet their basic housing, food and other needs, said Ruben Canedo, a university employee who chairs the campus's basic needs committee. (He also co-chairs a similar committee for all 10 UC campuses.)

According to a survey of Berkeley students, 38 percent of undergraduates and 23 percent of graduate students deal with food insecurity at some point during the academic year, Canedo said. The school targets particular types of students, including those who are first-generation college-goers, parents, low-income or LGBT.

Canedo said a key focus last fall was to enroll eligible students in CalFresh, the California version of the federal Supplemental Nutrition Assistance Program(SNAP), formerly known as food stamps.

Under federal rules, students generally must work at least 20 hours a week to qualify for SNAP, something many cannot manage. But states have flexibility to designate what counts as employment and training programs, said Elizabeth Lower-Basch, director of income and work supports at CLASP, an anti-poverty advocacy organization. In California, for example, students who participate in certain educational programs at school are eligible for CalFresh.

"That's our first line of defense," Canedo said. "Students are being awarded about $192 per month."

For students who don't qualify for CalFresh, the school sponsors a parallel food assistance program that also provides benefits.

There's a food pantry that offers regular cooking demonstrations. But what Canedo said he's particularly proud of is a 15-week nutritional science course that students can take that teaches them about healthy eating, prepping food, budgeting and grocery shopping, among other things. Some of those skills can help students learn to manage their money and food to get them through their time at school without running short.

This article was originally published on Kaiser Health News, a nonprofit news service covering health issues. It is an editorially independent program of the Kaiser Family Foundation, which is not affiliated with Kaiser Permanente.

KHN
KAISER HEALTH NEWS

Michelle Andrews (andrews.khn@gmail.com) is a writer for Kaiser Health News. Follow her on Twitter @mandrews110.

Pulse points: Healthy hearts

Researchers at the Centers for Disease Control and Prevention and Agency for Healthcare Research and Quality project that there will be about 16.3 million cardiovascular events and upwards of $173.7 billion in hospitalization costs between 2017 and 2021 if interventions in clinical settings and communities are not implemented. For those reasons and others, the CDC and Centers for Medicare & Medicaid Services launded the Million Hearts initiative. The initiative brings together state and federal agencies and private-sector partners to prevent 1 million cardiovascular events by 2022.

Chronic pain after trauma may depend on your stress gene

By Sarah Linnstaedt

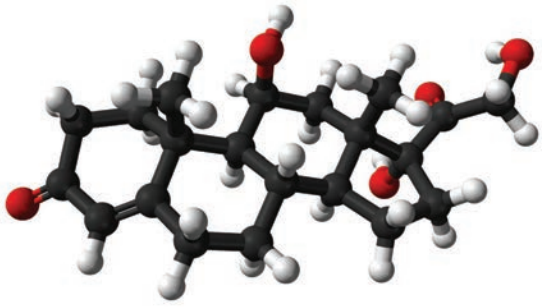
Almost every person in the world will experience at least one traumatic event, such as a car crash, an assault, war combat or a natural disaster, during their lifetime. Many will endure more than one.

Most people recover from a traumatic incident, but a substantial percentage develop chronic problems, including post-traumatic stress symptoms, depression and chronic pain.

Chronic pain? Isn't pain caused by nerve injury? Not always. Chronic pain can develop and is quite common after trauma exposure. This might seem surprising given the fact that many traumas involve little or no tissue damage.

I am a geneticist and molecular biologist studying predictors and mediators of chronic pain and other chronic neuropsychiatric conditions that develop after a traumatic experience. I am particularly interested in understanding the biological reasons why some individuals are more vulnerable to chronic pain than others.

Based on previous findings from our research group and others, my colleagues and I hypothesized that individual genetic variation affects who develops pain and who recovers after trauma exposure. To test this hypothesis, our group at the Institute for Trauma Recovery, led by Samuel McLean, enrolled individuals in a study of European-Americans and African-Americans who had been involved in a traumatic motor vehicle collision. We collected blood samples from more than 1,500 such individuals and assessed their DNA and their pain levels six weeks after the car crash.



PUBLIC DOMAIN

This ball-and-stick model represents a molecule of cortisol, known as the "stress hormone." Cortisol and adrenaline have been shown to sensitize peripheral nerves directly, which enables cortisol to signal pain in the absence of nerve injury.

Trauma, then pain

Before I go into details about this study, let's brainstorm how chronic pain might develop after trauma. If we know how pain develops, we can find treatments to prevent its onset. And by preventing the onset of chronic pain, we eliminate the need to use addictive and potentially deadly opioids.

Exposure to traumatic events causes our stress system to activate. This stress system sends signals between the hypothalamus in the brain, the pituitary gland and the adrenal gland, ultimately resulting in the release of cortisol, commonly known as the "stress hormone."

Cortisol is a critical link between trauma and chronic pain. This is because cortisol and another stress hormone called adrenaline have been shown to sensitize peripheral nerves directly, which enables cortisol to signal pain in the absence of nerve injury. For this reason, it is vital for our bodies to regulate cortisol levels carefully and to resolve the stress response quickly and effectively.

Regulating the stress hormone

Our bodies have natural regulators of blood cortisol levels. Typically, a protein called the glucocorticoid receptor, or GR, binds to cortisol that is released after stress exposure and causes cells to alter activities of the immune system and brain. But another protein called FKBP5 also can manipulate cortisol levels by binding GR and preventing it from binding cortisol.

If FKBP5 levels are high, that sequesters the GR and prevents the GR from binding and lowering blood cortisol levels. Consequently, levels of cortisol in the blood can rise and potentially cause harm by binding nerve endings and causing pain. Previous studies have shown that a person's genes can influence relative levels of these proteins.

Based on this knowledge, our group hypothesized that the ability of FKBP5 to regulate cortisol and potentially affect pain levels might originate in our DNA. We tested this hypothesis using data from our more than 1,500 car crash survivors.

Importantly, these individuals experienced trauma but did not have bone fractures or tissue injury.

We chose motor vehicle collision as our trauma exposure because it is common and highly traumatic, and we can capture data in the immediate aftermath of the traumatic incident. Physicians in emergency departments across the country helped us enroll individuals and collect blood from them so that we could measure DNA, RNA, microRNA and hormone levels. This was important because for this study we wanted to understand how all of these types of molecules are related and how their composition can vary from one individual to the next.

Our pain and our genes

Our group discovered that which genetic variant of the FKBP5 gene a person carries is predictive of how much post-traumatic chronic pain that individual will experience following motor vehicle collision.

Our study of car crash survivors showed that rare variants TG and GG in the stress response gene FKBP5 increase vulnerability to developing chronic pain.

Both African-American and European-American individuals carrying at least one copy of the less common variants FKBP5-TG or FKBP5-GG experienced more pain than the individuals carrying only the more common FKBP5-TT variant. (We all have two copies of every chromosome, so we can carry two different versions or variants of the same gene.)

We then wanted to know how these variations affect the stress response and subsequent chronic pain.

We knew that individuals with the less common variants FKBP5-TG or FKBP5-GG are more likely to experience pain after trauma exposure. We predicted that in these individuals, FKBP5 regulation of cortisol would be abnormal. We measured cortisol in these individuals and found that their cortisol levels were higher with respect to FKBP5 levels than the cortisol levels of individuals carrying the FKBP5-TT variant, who have less pain.

The common TT gene variant causes less cortisol to build up in the blood and less pain. The rare TG and GG variants cause cortisol levels to surge, and this can trigger chronic pain.

The effect on microRNA binding

We wanted to find the molecular mechanism through which this genetic variant alters FKBP5 and related cortisol levels. Our first clue was that the gene variant we were studying is located in the 3'untranslated region, or UTR, of the FKBP5 messenger RNA. The 3'UTR contains many regulatory elements that control the amount of protein produced from a gene. One such type of regulatory element is a microRNA binding site.

microRNAs bind to mRNA, usually in the 3'UTR region, and silence the bound genetic message. Humans have more than 2,000 different microRNAs, which bind to mRNA through specific base pairing. Our group and others have shown that microRNAs such as miR-320a and miR-15 can bind FKBP5. Therefore, we examined the genetic sequence surrounding the FKBP5 gene variant we had shown to be associated with post-traumatic chronic pain and found a predicted miR-320a site just over 100 nucleotides upstream of the variant.

With more than 100 nucleotides separating the genetic variant and the potential miR-320a binding site, it was clear that the genetic variant did not influence microRNA binding directly in the same way seen in a previous study. However, in collaboration with Alain Laederach's group at the University of North Carolina at Chapel Hill, we determined that the genetic variant influenced the ability of the FKBP5 RNA to fold into a secondary structure.

The exact folding of the RNA secondary structure differed depending on whether the FKBP5 gene contained the TT variant or the TG/GG variant. Using RNA structural modeling called SHAPE, we showed that the RNA structure varied significantly in the region of the miR-320a binding site, such that miR-320a could bind in the presence of the protective variant but could not bind efficiently in the presence of the risk variant.

Therefore, in people with the TG or GG genetic variants, the variant causes the FKBP5 RNA to fold into a secondary structure that inhibits miR-320a silencing of FKBP5. This disinhibition leads to increased FKBP5 levels and increased post-traumatic chronic pain.

Overall, this recent discovery by our group suggests a way that humans can develop chronic pain following trauma exposure without experiencing tissue injury. It also highlights a gene involved in the development of post-traumatic chronic pain that could be a promising new target for drug therapies. And it proposes a mechanism through which this gene is regulated naturally.

This last point can help us in our quest to discover specific types of therapeutics, because, for instance, if we didn't want to try to target FKBP5 directly, we could mimic the action of this naturally occurring regulatory mechanism. Our work suggests that with such a potential therapeutic, we could preferentially treat individuals with the DNA variant that causes more pain.

A version of this article was published in The Conversation website under a Creative Commons license. Read the original article at theconversation.com.

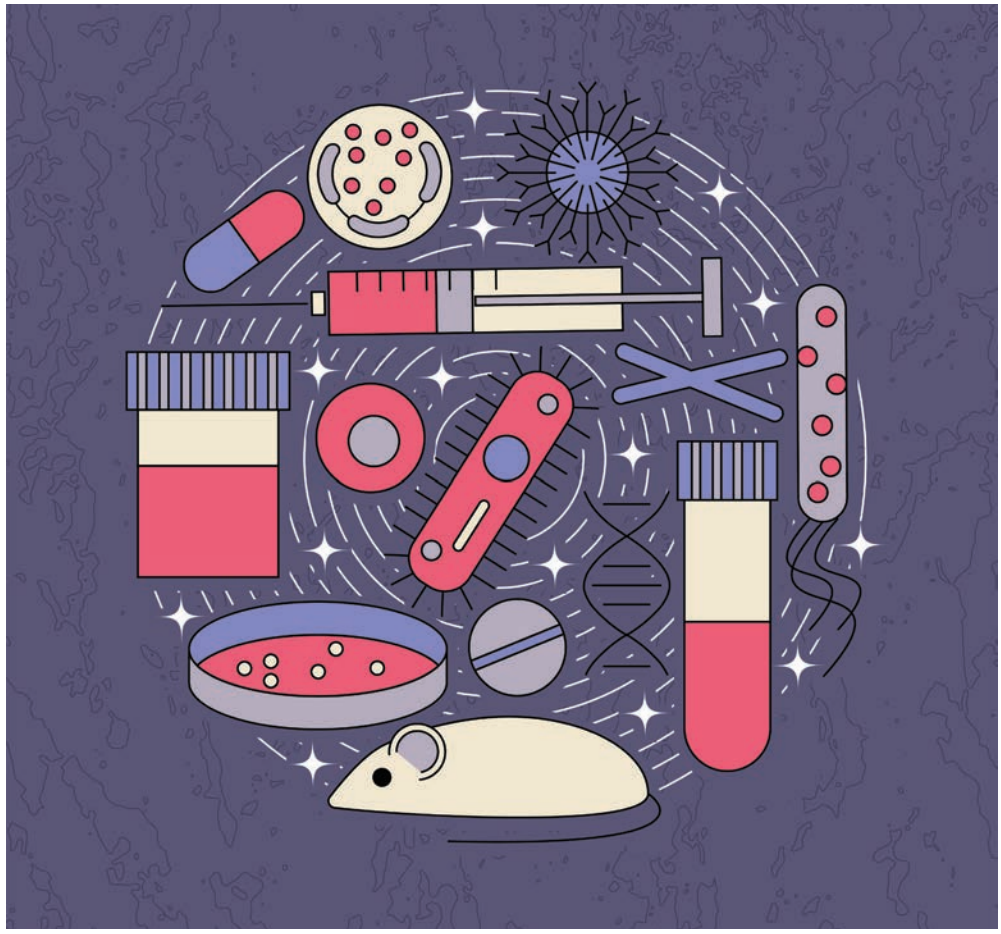
THE CONVERSATION

Sarah Linnstaedt (Sarah_Linnstaedt@med.unc.edu) is an assistant professor of anesthesiology at the University of North Carolina at Chapel Hill.

Why aren't there quality controls for antibody research?

One of science's most helpful tools gives an alarming number of false results

By Daniel Bojar



Many people know antibodies as our bodies' safeguard against infections. They keep us healthy by recognizing surface features on bacteria or viruses and alerting the immune system: attack! But they also play a crucial role in life science research. Their ability to recognize exactly one protein makes them ideal precision tools for detection, quantification and, in some cases, even treatments.

Of course, that's only true if the antibodies do what they're supposed to. Bad biological substances such as poor-quality antibodies are major drivers of scientific studies that can't be reproduced.

Reproducibility is one of the gold standards of sound science — to be considered trustworthy, a lab's results have to be repeatable by others. But around 36 percent of all research that has been flagged as irreproducible is caused by bad biological substances, making up a good third of the staggering $28 billion wasted every year due to irreproducible preclinical research.

The quality of everyday research substances — an issue that seems fundamentally mundane — impedes the progress of medicine and costs every one of us dearly, financially as well as personally. Currently, there are no official standards for the quality of commercially available antibodies or evaluations by third-party institutions before commercial availability. As these unreliable preclinical studies, partly caused by poor-quality antibodies, distort entire scientific fields and endanger the lives of citizens relying on future health care, distributors of commercial antibodies have to take action by imposing stricter quality

A good third of the staggering $28 billion wasted each year on irreproducible preclinical research is caused by bad biological substances.

standards.

Two studies that comprehensively investigated the quality of commonly used antibodies tell a disconcerting story. In the first, published in 2010 in the journal Nature Structural & Molecular Biology by the group of Jason D. Lieb located at the University of North Carolina at Chapel Hill, all 246 of the commonly used antibodies in the field of DNA-binding protein modifications were tested. Of these, 25 percent bound multiple targets instead of the one that they were supposed to do. Four antibodies were perfectly specific — to the wrong protein. In the second study, published in 2008 in Molecular & Cellular Proteomics by the laboratory of Mathias Uhlén at the Royal Institute of Technology in Stockholm, Sweden, researchers tested the quality of around 6,000 of the most commonly used commercial antibodies. The results were dismal; less than half of the antibodies were sufficiently specific for their supposed target protein.

Eleftherios Diamandis, a cancer researcher at the Mount Sinai Hospital in Toronto, Canada, is one researcher who fell prey to this widespread issue. He just wanted to contribute to the fight against pancreatic cancer. As in practically every type of cancer, early detection is key, as it can increase the five-year survival rate from 5 percent up to 20 percent. What better way to detect cancer early than by a biomarker, a molecule whose presence in unusual amounts indicates cancer, measurable by a quick blood test? He and his collaborators found a promising protein from the pancreas, CUB and zona pellucida-like domains protein 1, or CUZD1, which seemed to reliably indicate the presence of pancreatic cancer.

To determine elevated levels of CUZD1, they used a commercial testing kit, an enzyme-linked immunosorbent assay, or ELISA. Briefly put, in an ELISA, an antibody specific for the target protein, such as CUZD1, binds to the target protein, and then a second antibody (specific for the first antibody) coupled to an enzyme is added. The amount of enzyme then is measured by, say, a color change induced by an enzymatic reaction. From this the initial amount of CUZD1 can be inferred. Commercial availability from a major distributor of laboratory substances typically indicates standardization and reliability, which is why it usually is preferred to a self-made solution.

But something was rotten in the state of biomarker detection. When Diamandis and his team investigated whether their ELISA truly recognized their protein of interest (something most researchers would never attempt to do with a purportedly reliable commercial product), they found the horrible truth: Their expensive product did not detect CUZD1 at all. Instead, it measured the cancer protein CA125.

No wonder it presented a good biomarker for cancer — it literally was cancer. A poor-quality antibody in the commercial ELISA kit cost the Diamandis lab around $500,000 and many months of hard work. And worst of all, only a hair's breadth away: If they hadn't questioned their results, an obvious next step would have been a clinical trial to test whether early detection with this novel biomarker led to a better patient outcome. People could have died from the error, as the detection of cancer wouldn't have happened at an early stage but at a later stage when the cancer protein CA125 was present.

Tackling an abstract problem such as the reproducibility of preclinical research is notoriously hard, as actionable procedures are not immediately obvious. One approach is to apply practical solutions to the much more tangible root causes of this problem. Poor-quality antibodies are one of these root causes. So what can we do about it?

Every link in the chain of the great human endeavor of research has to play its part to achieve improvement. Manufacturers of antibodies need to implement more stringent quality standards, testing their antibodies with multiple methods. These quality standards ideally should be set by an independent organization (at least partly consisting of scientists) that would certify the antibodies prior to their usage. Funding organizations should demand this antibody quality standard prior to the start of a project, and editors as well as reviewers of scientific journals should demand them after the end of a project.

We should demand an improvement in the groundwork for clinical trials, starting with mandatory quality controls of commercial antibodies. We all entrust our lives and health to these quality standards.

This essay was originally published in August on Massive Science (massivesci.com).

Daniel Bojar (daniel.bojar@bsse.ethz.ch) is a doctoral student in the department of biosystems science and engineering at ETH Zurich. Follow him on Twitter @daniel_bojar.

Catalyst conversation workshop provides tools faculty can use

By Ann Aguanno

I never liked workshops.

Starting in graduate school and continuing through my postdoc and early faculty positions, I attended workshops on lab techniques, mentoring undergraduates and teaching strategies. The goal was often unclear or not aligned with the workshop's title, the participants were unengaged, the activities lacked guidance and direction and, in the end, I took very little home with me.

This began to change when I joined the American Society for Biochemistry and Molecular Biology and got involved in a series of workshops organized by the Educational and Professional Development Committee and held over a five-year period that focused on concept-driven teaching strategies in biochemistry and molecular biology. As a participant and eventually a host and organizer, I finally saw what a workshop could be — an engaged group of faculty from diverse institutions working together to improve student learning in the molecular life sciences.

When those workshops concluded a few years back, the steering committee of the ASBMB Student Chapters, of

Feedback

Participants in the March workshop were asked to describe something they learned and, if they were presenters, something they hoped others learned from their presentations.

I learned some important strategies for improving student learning, such as how to strategically use pre-lecture or pre-lab quizzes, as well as using augmented reality as another way to study protein structure. We also discussed how to work on math skills in our classes and how to encourage crossover between biology and chemistry topics to enhance learning.

I hope that the workshop participants came away from my presentation with some new ideas about how to present the links between DNA and protein structure, as well as the impact of mutation on protein structure and human disease. I presented some possible lab exercises that could be used as a substitute for "wet lab" exercises.

—Tricia Melloy, Fairleigh Dickinson University

I learned that ideas and reflections take on more pixels and color when they are shared with others. It helped me to explain more fully my thoughts and ideas when I shared with colleagues.

My presentation was on a pre- and post-test on threshold concepts in biochemistry, and I have students with varying chemical backgrounds in my class. I hope people saw that student learning is not just about how many previous classes a student has taken but how deeply they learned about these abstract topics.

—Kelly Keenan, Stockton University

Scientific literacy is an important and integrated part of critical thinking skills, including interpretation and representation of scientific data; problem solving using quantitative skills; evaluation of scientific information and sources; recognition of evidence to support hypothesis; understanding of research design; and making justifications, predictions and conclusions based on quantitative data.

—Yufeng Wei, Seton Hall University

I enjoyed hearing about the innovative practices other faculty were using in their classrooms. Since lots of us are finding similar challenges as we try to employ active learning practices, it is good to have a chance to hear about some works in progress to get suggestions and share ideas.

I have been developing a course-based undergraduate research, or CURE, project for a nonmajor's lab and talked about some aspects of this that have been rewarding and some that have been challenging. I hope that for other faculty who are developing or plan to develop CUREs, it gave them ideas for things to try and things to avoid, and also the willingness to try a good idea that will engage students even if there are some kinks still to work out.

—Amy Springer, University of Massachusetts Amherst

which I was member, recognized that faculty still looked to the society for a collaborative experience where best teaching practices could be explored. The steering committee decided to offer a new series of education workshops that would build on the model and success of those organized by the EPD Committee.

In March, we hosted the first in this new series of faculty development workshops called Catalyst Conversations for Undergraduate Educators. Hosted by Montclair State University in New Jersey and funded by the ASBMB, the event included a dozen chalkboard talks, each focusing on a class activity or pedagogy approach, followed by general discussion.

Pam Mertz of St. Mary's College of Maryland, Celeste Peterson of Suffolk University, Quinn Vega of Montclair State University and I organized the workshop. Both ASBMB members and nonmembers were invited, with a maximum of 25 participants to ensure ease of collaboration and networking.

Participating faculty, mainly from East Coast colleges and universities, explored the use of the primary literature in the classroom, innovative approaches to lab activities, strategies for teaching core concepts and the use of computational and bioinformatics sources as teaching tools. With handouts to help synthesize each presentation — including the activity's objective, implementation, assessments and potential challenges — each participant walked out of the workshop with tools in hand.

Ann Aguanno (aaguanno@mmm.edu) is a professor of biology, chair of the department of natural sciences and a recruiter at Marymount Manhattan College.

More conversations

The ASBMB and La Sierra University will host a Catalyst Conversations for Undergraduate Educators on Feb. 24 in the Troesh Conference Center on the La Sierra campus in Riverside, California.

Educators will exchange ideas about teaching practices in biochemistry and molecular biology and navigating the research landscape in the undergraduate environment.

The session themes are as follows:

- **Research at a PUI: Challenges, opportunities and funding**, led by Jessica Bell, University of San Diego
- **BMB for a new generation**: Concepts and assessment, led by Marvin Payne, La Sierra University
- **Developing NSF funding for your undergraduate research**, a working lunch and discussion led by Christopher Meyer, California State University, Fresno
- **CURE: Theory and implementation**, presented by Ellis Bell and Joseph Provost, both from the University of San Diego

Participants will also have an opportunity to give short chalk talks, share instructional materials, and discuss implementing new ideas into their own teaching and research.

To register or submit an abstract for a chalk talk (you do not need to submit an abstract to participate), go to asbmb.org/catalystconversion.

The ASBMB and the University of Wisconsin–La Crosse will host a Catalyst Conversation for Undergraduate Educators within the North Central Region on March 16 at the Myrick Park Center in La Crosse, Wisconsin.

The session themes are as follows:

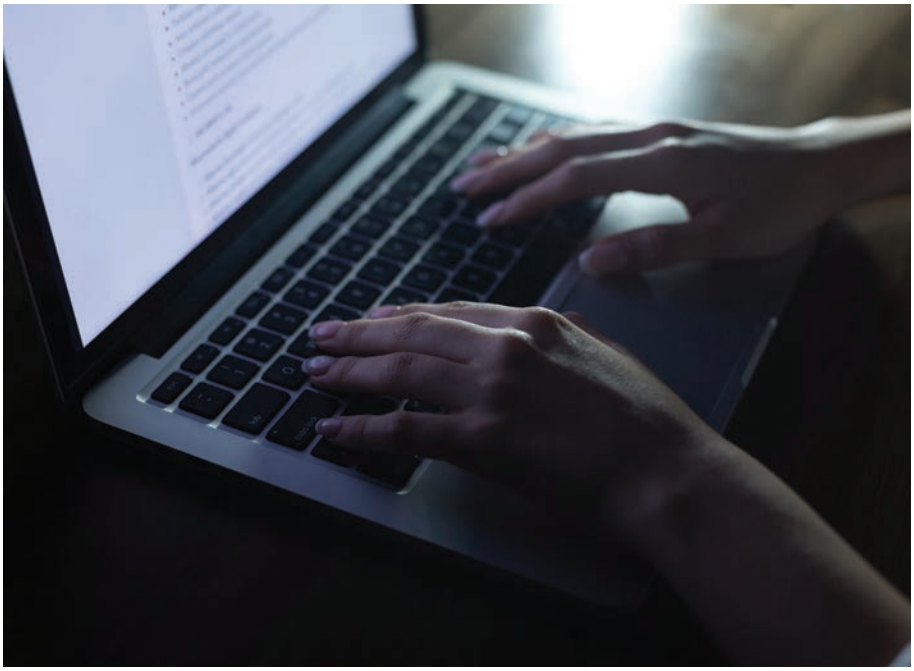
- **Best practices in science lab building design**, led by Todd Weaver and John May
- **Career planning for the molecular life science major**, led by Basudeb Bhattacharyya
- **Strategies to develop an inclusive undergraduate research lab**, led by Daniel Grilley and Kelly Gorres
- **Applying to graduate school for the molecular life science major**, led by Basudeb Bhattacharyya and Todd Weaver

The final session will give faculty at primarily undergraduate institutions an opportunity to share teaching materials and discuss best practices in biochemistry and molecular biology education.

Both workshops are free and include a continental breakfast and catered lunch. Email questions to Stephanie Paxson at spaxson@asbmb.org.

Committing for more than one night

By Adriana Bankston



I often have many things on my mind — and I usually do my best work — at odd late-night hours. Snuggled on the couch with familiar music or a movie in the background, I can focus on detailed tasks and big questions.

Work defines me, brings me joy, fulfills me and is often my refuge from the rest of the world. So it's no surprise that when I found work that I enjoyed and could pursue freely, I jumped on it.

I was volunteering at the Future of Research, a nonprofit, on a project researching postdoc salaries, which grew into an interest in studying the postdoc position as a whole. I happily could pursue this topic no matter the time of day (or night). I frequently found myself reading, just for fun, National Academies' reports on postdocs and other publications on the state of the research enterprise.

Realizing that this was more than a fleeting interest, I decided to ask our executive director, Gary McDowell, if I could contribute to a book chapter he was writing on postdoc reforms. When I asked him on a Friday afternoon, he replied, "I don't want to commit you."

We would need to work intensely on the chapter to submit it before the deadline. Gary is a nice person and likely already felt bad that I was working as a volunteer — somewhat ironic, since we were advocating for better postdoc pay.

But I could see the potential for this book chapter to increase transparency around the postdoc position. So, instead of having the intended effect, Gary's statement made me realize how committed I was already becoming to postdoc advocacy. I didn't care what time it was; I just knew I had to work on this book chapter. If someone like me, who had been through postdoc training, didn't advocate for postdocs, who would do it?

I remember sitting the following Thursday night at the desk in my office, covered by a blanket as I often am when writing. It was probably raining. I was tired; it had been a long day, and I could barely keep my eyes open at times. I drank lots of coffee.

We used the postdoc salary work as a case study, and as I wrote about it, I realized how much this work meant to me. I remember thinking how valuable volunteer work can be. I felt validated; the book chapter symbolized the larger potential to create change by volunteering, by just showing up and committing to a cause.

The more I wrote, the more fun it became. I never felt any writer's block, and I just continued writing without realizing what time it was. I enjoyed the tremendous teamwork and commitment we both had to this crazy deadline.

We divided up the work pretty

much 50-50, and while Gary would say I had the harder task (a detailed section about our data), I watched in amazement as he framed the beginning of the chapter in a larger context and detailed recommendations from several National Academies' reports. And there was something symbolic about two former postdocs writing this chapter late at night on why postdocs should be treated better.

While writing, I was relaxed; I knew that I had found what I was looking for, and I was soaking it in. At the same time, I felt random bursts of excitement because I couldn't believe I'd been given the opportunity to work on this topic.

I realized how well we worked together. We were collaborating on a pretty significant write-up in addition to a previous publication. Gary was very good with the vision and the big picture, while I filled in the details and pointed out holes in the argument. It was a pretty good combination of talents, and it was fun.

As I felt myself almost falling asleep, I wondered how Gary just couldn't and wouldn't stop this advocacy work, no matter what time of night. That motivated me to keep going, and I kept writing. I gained new appreciation for the work's importance as well as for Gary's ability to inspire enthusiasm. His dedication was contagious; I couldn't stop working on it either. At that moment, it was clear that I had developed a passion for this topic.

At around 3 a.m. on Friday, we were still going, and neither of us planned to sleep until it was done. I quickly wrote a conclusion. To date, it's still one of the best things I've ever written, because by then I could see both the broad vision of the chapter and the details, and I knew exactly what I wanted people to take away from it. I was surprised that Gary trusted me to write this section and made only a few small edits. I remember thinking what a great privilege it was to work with someone who gave me intellectual freedom and trusted my judgement.

We proofread the entire document and made more edits. At about 4:30 a.m., Gary told me he was going to take care of the references and I should go to sleep. I said, "No, I will not sleep until this is done."

We finished about 5 a.m., and Gary submitted the chapter.

I went to bed utterly exhausted but elated. This night elicited a lot of emotions. I felt appreciated and valued for the work and realized that I had to be more involved with Future of Research, because it had become a large part of who I was as a person.

So in a sense, I committed for more than one night. I committed to something life-changing in terms of discovering my professional direction. That late night working on the chapter solidified my passion for postdoc advocacy, and I was satisfied to have completed something so large.

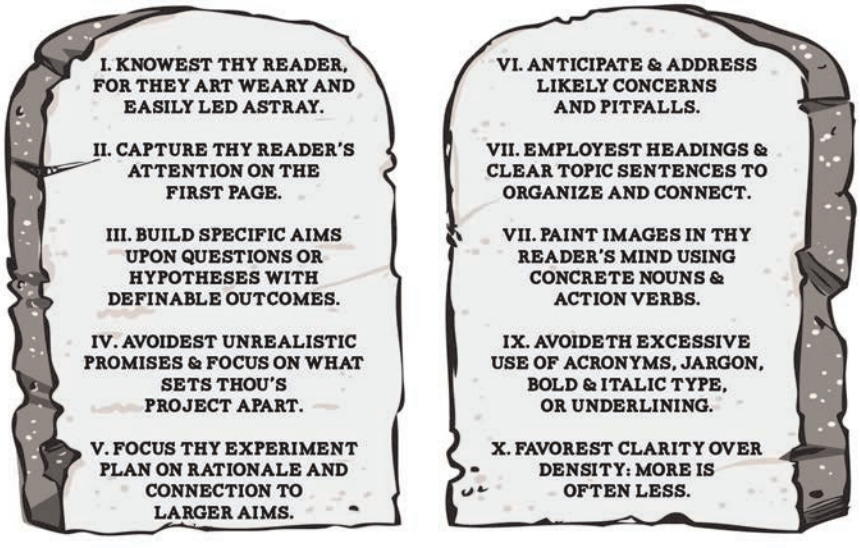
I wondered later whether it's unusual to be so engrossed in work. Why did writing a book chapter until 5 a.m. seem normal and make me so happy? When I knew I'd found my passion and was working toward a larger goal, that kept me motivated, even when I could barely stay awake.

And after you've had a night like that, you commit for more than one night.

Adriana Bankston (abankston81@gmail.com) is a former bench scientist with a passion for improving training and policies for junior scientists. She is a policy activist with the Future of Research.

The 10 commandments of grantsmanship

Peter Kennelly, a professor of biochemistry at Virginia Tech, recently gave a seminar on grantsmanship. He put together his top-10 takeaways in a biblical format. Aspiring grant writers might want to cut this out and post it prominently.



CALL FOR SUBMISSIONS

ASBMB Today is launching two essay series in 2019:

What I wish people understood about _____

Is there an aspect of your life, personal or professional, that others just don't get? Fill in the blank in this sentence, and then set the record straight.

Night shift

Life does not end when the sun goes down, and our experiences are often heightened at night. Tell us a story about what you do while others sleep.

For information, email asbmbtoday@asbmb.org or go to asbmb.org/asbmbtoday and click SUBMIT.

ASBMBTODAY

CLASSIFIEDS

Whitworth University:
Visiting Assistant Professor of Biology (Molecular)

WHITWORTH UNIVERSITY

The Biology Department at Whitworth University invites applicants who are passionate about teaching molecular and developmental biology to a diverse group of undergraduate biologists. The successful candidate will have the opportunity to teach upper division molecular genetics, developmental biology, or cellular biology, with the potential of also teaching introductory cell biology and/or biochemistry, as well as one or more courses in a specialized area of their expertise. Although the specifics can vary, a typical teaching load includes two lecture courses with labs per semester and one course during the January term. We seek scholars who enjoy collaborating with undergraduate students and who seek the challenge of inspiring students to reach their full potential. We also seek candidates that value evolutionary theory as foundational to an education in biology. We are particularly interested in individuals who have experience and/or demonstrated passion for working with and mentoring students from underrepresented backgrounds.

asbmb.org/careers/jobs/78589

Rutgers University-Camden:
Assistant Teaching Professor

RUTGERS

The Department of Chemistry at Rutgers University, Camden campus seeks applications for a full-time, 10-month non-tenure track (NTT) Assistant Professor appointment in Chemistry with an emphasis on teaching and coordinating courses in General, Organic and Biological Chemistry for both chemistry and non-chemistry majors enrolled in the Nursing, Health Sciences, Biology, or Forensic Sciences Programs. This is a 2-year appointment with possibility of renewal. The teaching load is 4 courses per semester, with possible course releases allowing time for administrative duties.
Qualified applicants should upload a cover letter, CV, a 1-2 page statement of teaching philosophy and a sample syllabus at https://jobs.rutgers.edu by Feb 28, 2019 for consideration.

asbmb.org/careers/jobs/78659

Arizona State University:
Associate Director and Professor in the School of Mathematical and Natural Sciences

ASU Arizona State University

The School of Mathematical and Natural Sciences (SMNS) in the New College of Interdisciplinary Arts & Sciences at Arizona State University (ASU) invites applications for a full-time, benefits-eligible, Associate or Full Professor with an administrative assignment as Associate Director to the school. The successful applicant will be expected to work with the Director to provide administrative vision, leadership, and management for the School; to foster and contribute to the School's interdisciplinary teaching and research missions; to encourage and support undergraduate research in the School and develop innovative ways to engage a broad demographic of students in faculty research; to develop new programs and initiatives both with the community and in the School; to grow the student body and help develop innovative methods for student teaching, learning, and retention; to coordinate efforts to acquire research funding that draws upon the diverse capabilities of SMNS faculty; and to engage in research and teaching that complement and strengthen current offerings and emphases in SMNS.

asbmb.org/careers/jobs/78666

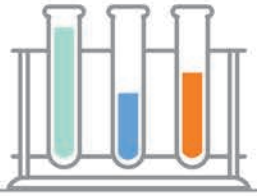
University of CA, Davis, Dept. of Biochemistry and Molecular Medicine:
Postdoctoral researcher position in Medicinal Chemistry and/or Chemical Biology

UCDAVIS UNIVERSITY OF CALIFORNIA

A postdoctoral researcher position is available immediately in the collaborative Cancer Nanotechnology & Drug Development Program between the Department of Biochemistry and Molecular Medicine and NCI-designated Comprehensive Cancer Center at the University of California, Davis. The position offers competitive salary and benefits. The successful candidates will have the opportunities to work with world renowned experts in cancer biology, PK/PD, pharmacology, cancer nanotechnology, immunology and molecular imaging to rapidly translate innovations from bench to bedside. The program is funded by multiple NIH grants and the wet lab setup is appropriate for the synthesis and characterization of new drugs and novel nanomaterials, drug development/screening, molecular biology and cell biology, multiple types of animal experiments, PK/PD and immunology. Multiple types of NMR, HPLC, MS, LC-MS, optical imaging, MRI, SPECT, micro-PET & PET/MRI, metabolomics, genomics and proteomics instruments are available.

asbmb.org/careers/jobs/78753

To see a full list of jobs, please visit **asbmb.org/careers**.



Interested in posting a job in ASBMB Today and on our online job board?
Visit **asbmb.org/advertise** to learn more.

ASBMB

EB ORLANDO

EXPOSURE EMERGES BEYOND

When you present your research at the ASBMB annual meeting at EB 2019, you receive deserved recognition and critical feedback that will help you advance your work. Submit your abstract to be considered for inclusion in this year's poster presentations.

All who attend will have a chance to discuss their work with influencers in their area of specialty, connect with peers in the life sciences community and gain inspiration to take back to the lab.
Sign up by the early registration deadline to save 30 percent.

KEY DEADLINES:
Jan. 30: Late-breaking abstract | Feb. 5 Early registration

Visit ASBMB.org/meeting2019 to view abstract topics and register.

ASBMB '19
ANNUAL MEETING
ORLANDO | APRIL 6-9

Held in conjunction with Experimental Biology