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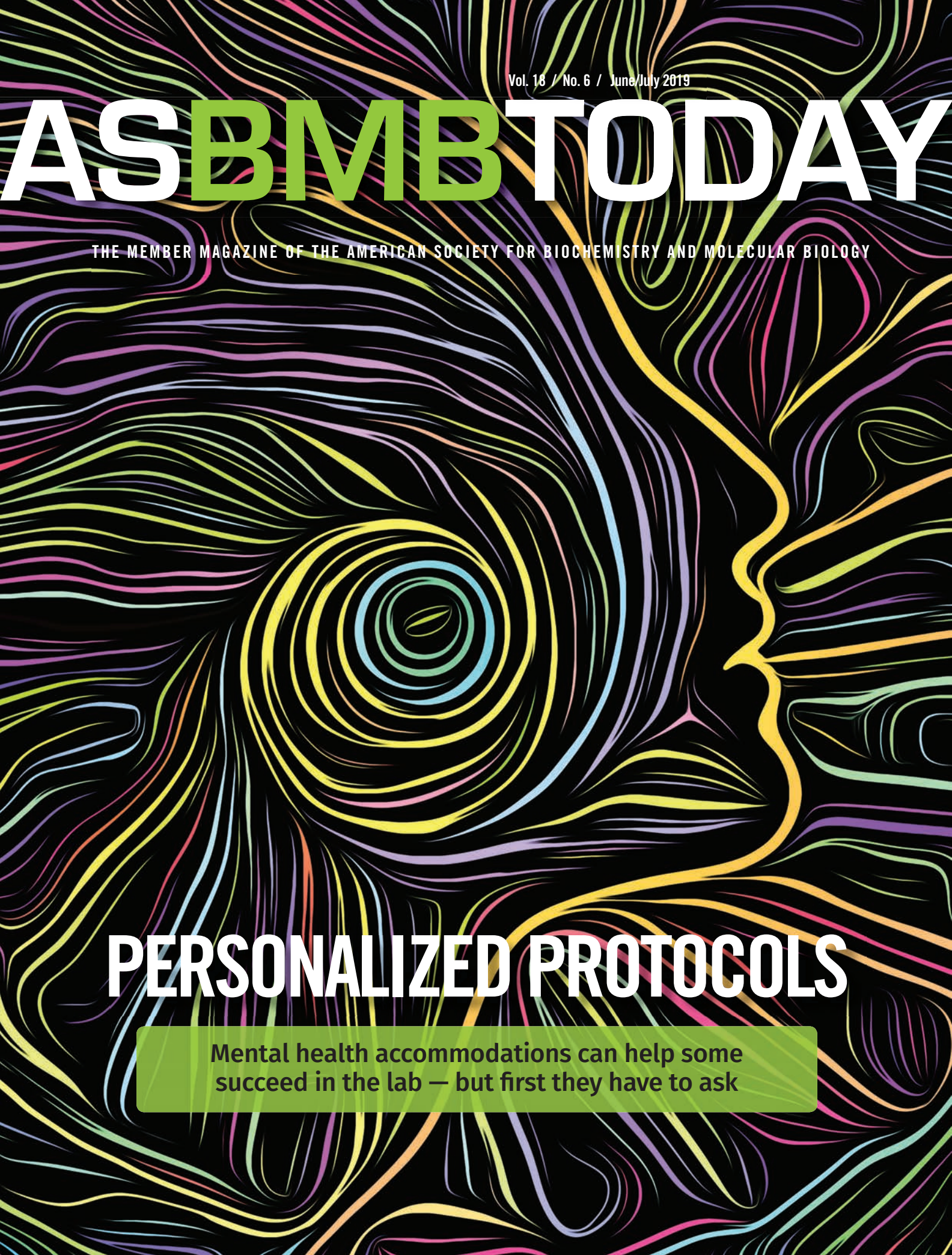
ASBMB TODAY

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



PERSONALIZED PROTOCOLS

Mental health accommodations can help some succeed in the lab — but first they have to ask

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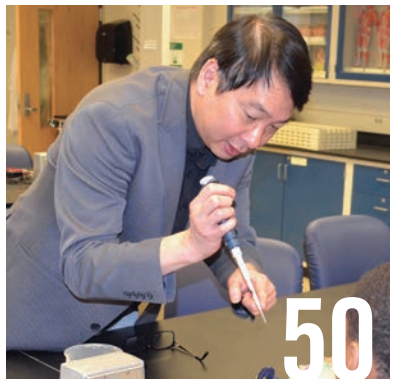

ASBMBTODAY

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

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Magazine life

By Comfort Dorn

After more than two years of procrastinating, I got a library card last month, and one of the first books I checked out was Ruth Reichl's "Save Me the Plums." In case that name doesn't ring a bell, Reichl has been the food editor at the LA Times, restaurant critic for The New York Times and editor of Gourmet magazine. Quite the dream career for anyone who likes food.

Reichl also has written several autobiographical bestsellers, and this latest is about her stint at Gourmet. Because I too am a magazine editor (admittedly on a vastly different scale), I take a particular interest in her detailed descriptions of the job, complete with quirky coworkers and mystifying jargon. Coincidentally, years ago, I edited a short-lived magazine that died because we didn't sell enough ads — so I feel a sad bond reading about Gourmet's demise in 2009.

For most of its 69 years, Gourmet was a specialized publication, what some would call a niche product, tightly focused on recipes and restaurants (with a smattering of travel). My grandmother sent me a gift subscription for a decade or so, pre-Reichl, and I loved that escapist quality. It was stodgy but soothing.

Under Reichl's leadership, Gourmet came out of its luxe-life bubble, running articles about the horrors of fish farms or how the food industry tried to sabotage a scientist who linked trans fats to cancer. There were still recipes with caviar, but there were also sloppy joes. The reality of food, in all its complexity, turned out to be much more interesting than the airbrushed fantasy.

And (to bring this back home), I think that's where magazines belong. Perched between the first-draft-of-history breathlessness of newspapers and the weightiness of books, a good magazine can use its theme (food, fashion, woodworking, biochemistry) as a prism for viewing the complexities of the world that theme inhabits.

So as much as I love running stories about amazing science, I have a special fondness for stories about issues: sexual harassment, faculty diversity — or John Arnst's article on page 26 about accommodations for scientists with mental illness. Both kinds of stories really need to run in tandem. If we don't make sure that students and early-career researchers have what they need to succeed — be it time off for therapy appointments, noise-canceling headphones or a dog to raise oxytocin levels — we will never see their potentially amazing science.

And, cheesy as it sounds, the more we understand the challenges in our world, the better our chance of making it better.

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

Advocating for more than money

By Benjamin Corb

When I write about the actions of Congress, I often focus on appropriations and funding. And rightly so. As glucose fuels the mitochondria in a cell, Congress' support for federal science-funding agencies fuels the engine that powers American leadership in research and innovation. So it's no surprise that the 12 appropriations bills our legislators wrangle each year get the lion's share of my ink.

But Congress can walk and chew gum at the same time. Hundreds of bills are introduced every year in both the House and the Senate, and only a small fraction of those have a direct effect on funding the agencies we care about. In fact, people I talk to are often surprised when I tell them we spend at least half our time on Capitol Hill talking about things other than money for science.

Right now, the American Society for Biochemistry and Molecular Biology public affairs team is tracking more than 100 pieces of legislation; these focus on topics such as sexual harassment in science; rules and regulations that dictate how federal advisory committees (and review panels) operate; and a package of bills to improve science, technology, engineering and mathematics programs in higher education. You may be familiar with that last bit from our spring advocacy campaign.

Many bills are introduced but don't become law. In the 115th Congress (January 2017 through January 2019), some 13,000 pieces of legislation were introduced, and only 3% (443) were enacted. The failure rate for legislation is high, but we learn a lot even from bills that never come to a vote.

Introduced legislation helps us identify which members of Congress truly support the American scientific enterprise. By tracking who introduces what pieces of legislation, we know where to focus our resources and build relationships. If a member of Congress introduces a bill to support STEM scholarship programs, for example, we know we can go to that member when we want to discuss policies that will support the next generation of scientists.

This year — for the first time — our advocacy efforts have moved beyond Washington, D.C., to state capitals. Studies show that state legislatures are more effective at passing legislation than Congress, with some data suggesting states are six times more successful at enacting laws than the federal government.

Like scientific research, advocacy is a long game. We need persistence and patience if we're going to see future successes. And like working at the bench, our efforts include a lot of trial and error.

With that in mind, the ASBMB public affairs team recently worked with J.P. Sredzinski, a Republican who represents the communities of Monroe and Sandy Hook in the Connecticut House of Representatives and a friend of mine, to draft legislation supporting a state program to retain minority STEM students in public colleges and universities. We researched the issue, helped draft the bill's language and testified before a joint committee on higher education in Hartford, Conn. The legislation received bipartisan support and was passed out of committee before it stalled due to the estimated cost of implementation.

We will review and modify the bill and then work with Sredzinski to reintroduce it in the next legislative session. While our proposal stalled (like 97% of bills in Congress), we built new partnerships that will serve us well in the future.

Like scientific research, advocacy is a long game. We need persistence and patience if we're going to see future successes. And like working at the bench, our efforts include a lot of trial and error.

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

Member update

By Erik Chaulk

Ravid named Mass. academy president


Ravid

Boston University professor **Katya Ravid** has been named a fellow and president of the Massachusetts Academy of Sciences.

The nonprofit academy seeks to promote scientific literacy and awareness and provides a platform for research networking across the commonwealth of Massachusetts.

Ravid is a professor of medicine and biochemistry at the Boston University School of Medicine, a professor of biology and health sciences at Boston University and a Fulbright research scholar.

Her research explores platelet production and function as well as the roles of purine receptors in platelet and vascular biology in health and pathology.

Ravid founded the Evans Center for Interdisciplinary Biomedical Research and is founding director of the Boston University interdisciplinary biomedical research office.

She began her three-year term as president of the academy in 2018.

Gierasch wins Merrifield Award


Gierasch

Lila Gierasch, editor-in-chief of the Journal of Biological Chemistry, has received the 2019 Merrifield Award from the American Peptide Society.

Named in honor of Nobel laureate R. Bruce Merrifield and his wife, Libby, the award recognizes outstanding lifetime achievement in peptide science.

Gierasch is a distinguished professor of chemistry and biochemistry and molecular biology at the University of Massachusetts Amherst. Her research focuses on protein folding, structure and function, with an emphasis on how proteins fold in vivo. The American Chemical Society previously recognized Geirasch for her contributions to peptide science with the Ralph F. Hirschmann Award. She received the 2014 Mildred Cohn Award in Biological Chemistry from the ASBMB.

Gierasch received the Merrifield Award and gave a lecture at the 26th American Peptide Symposium in June; the award includes a $25,000 honorarium.

Strahl, Dohlman honored as mentors


Strahl


Dohlman

Brian Strahl and **Henrik Dohlman** were among 10 faculty members at the University of North Carolina at Chapel Hill to receive Excellence in Basic Science Mentoring Awards earlier this year.

Established by the university's office of graduate education, the awards recognize outstanding faculty members affiliated with the biological and biomedical sciences program who demonstrate excellence in mentoring graduate students.

Strahl is a professor and vice chair of the department of biochemistry and biophysics and an Oliver Smithies investigator. His research focuses on histone proteins.

Strahl also serves as faculty director of UNC's high-throughput peptide synthesis and array facility.

Dohlman is the Sanford Steelman distinguished professor and chair of the department of pharmacology. His research is centered on G proteins and G–protein–coupled receptors. Dohlman is an associate editor for the Journal of Biological Chemistry.

The two were recognized at a ceremony in January.

LaRiviere named associate dean


LaRiviere

Washington and Lee University associate professor of chemistry and biochemistry **Fred LaRiviere** was appointed associate dean of the college in February.

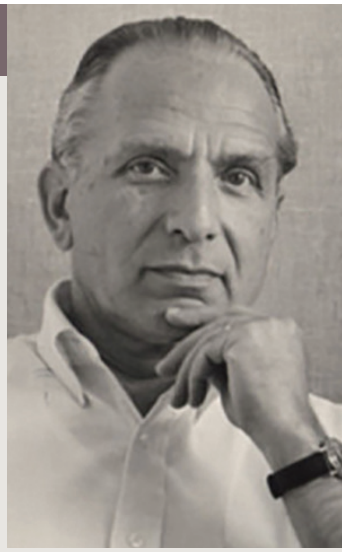
In this new role, LaRiviere focuses on academic performance and support as well as improving faculty development programs and strategic priorities.

LaRiviere joined the faculty at Washington and Lee in 2006 after holding postdoctoral research and teaching positions at Brandeis University and Colby College.

His research explores RNA biochemistry, focusing on understanding the fundamental aspects of ribosome metabolism in eukaryotes.

He has supervised more than 35 student–researchers during his tenure at Washington and Lee and has received numerous grants and fellowships for his research.

In memoriam: Jerard Hurwitz



American biochemist Jerard Hurwitz died in January at the age of 90.

Highly regarded for his work on the biosynthesis of DNA and RNA, Hurwitz was one of the discoverers of RNA polymerase, an enzyme that transcribes DNA into messenger RNA. His work on RNA polymerase led to a general understanding of how the genome is replicated in dividing cells and paved the way for future breakthroughs in genetic engineering.

After receiving his Ph.D. in biochemistry from Case Western Reserve University, Hurwitz joined the microbiology department at Washington University in St. Louis in 1956. There he began his work on RNA polymerase.

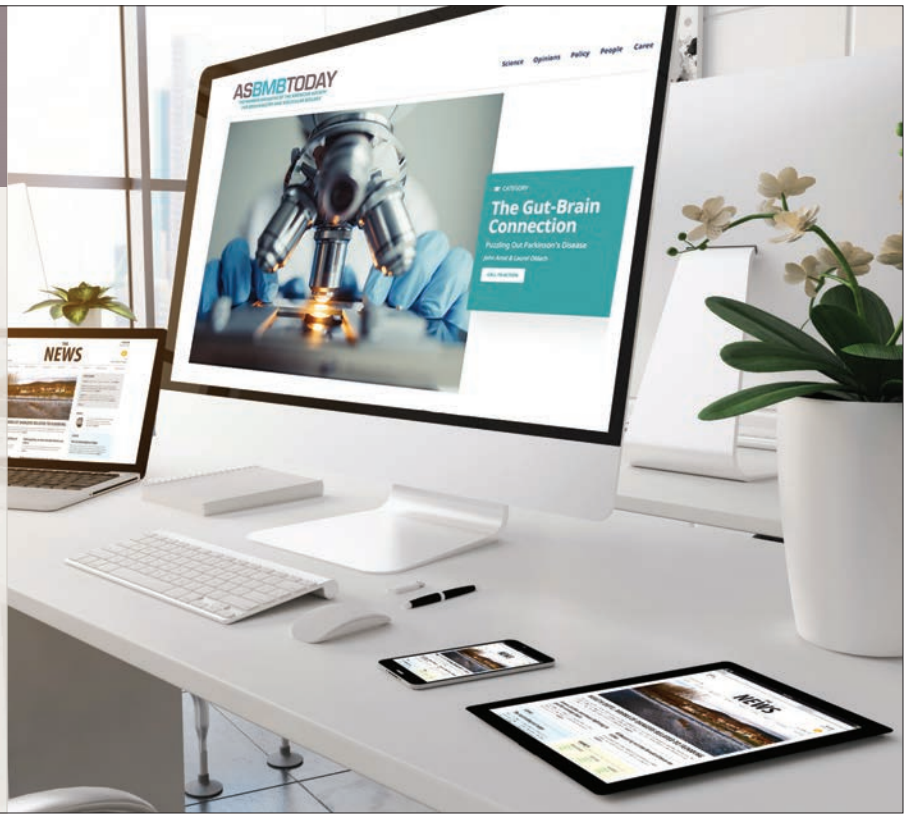
Hurwitz joined the faculty at New York University in 1958 as a professor of microbiology. In 1965, he moved to the Albert Einstein College of Medicine, where he was a professor and chair of the department of developmental biology and cancer.

In 1984, Hurwitz joined the Memorial Sloan Kettering Cancer Center as chair of the molecular biology program. He served as MSK's vice chair from 1991 to 2003.

Hurwitz was elected to the National Academy of Sciences in 1974 and received numerous awards for his research throughout his career, including the Eli Lilly Award in Biochemistry in 1962 and a Guggenheim Fellowship in 1968.

SEND US YOUR NEWS

Have you recently been promoted or honored? Do you have good news to share with your fellow ASBMB members? Email it to us at asbmbtoday@asbmb.org — and don't forget to include a photo!



James Bangs

Isabelle Coppens

John Gerlt

Ekaterina Heldwein

Robert Kranz

Sue Lin-Chao

Dominique Missiakas

Charles Rock

Eight members named microbiology fellows

Eight members of the American Society for Biochemistry and Molecular Biology are among the 109 newly elected fellows of the American Academy of Microbiology.

An honorific leadership group within the American Society for Microbiology, the academy elects new fellows every year on the basis of scientific achievement in the field of microbiology.

The newly elected fellows join more than 2,400 scientists who have demonstrated scientific excellence, originality and leadership in microbiology research, teaching, public health, industry and government service. Congratulations to the following ASBMB members.

- James Bangs, University at Buffalo
- Isabelle Coppens, Johns Hopkins Bloomberg School of Public Health
- John Gerlt, University of Illinois at Urbana–Champaign
- Ekaterina (Katya) Heldwein, Tufts University School of Medicine
- Robert Kranz, Washington University in St. Louis
- Sue Lin-Chao, Institute of Molecular Biology, Academia Sinica
- Dominique Missiakas, University of Chicago
- Charles Rock, St. Jude Children's Research Hospital

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

Fatih Abasiyanik, University of Chicago

Aitor Aguirre, Michigan State University

Saadman Ahmad, California State University, Northridge

Alby Alex, St. Bonaventure University

Anne Alexander, Milwaukee School of Engineering

Ohoud AlMalki, Georgetown University

Nasser Alotaiq, University of Glasgow

Justus Alvarez, Stephen F. Austin State University

Trisha Anand, University of Texas at Austin

Leonard Anderson, Morehouse School of Medicine

Polina Anipchenko, Saint-Petersburg State Academy of Veterinary Medicine

Giulia Antoniali, University of Udine

Ludmilla Aristilde, Cornell University

Pablo Artigas, Texas Tech University Health Sciences Center

Rahul Awasthi, Spartan Health Sciences University

Joshua Baker, Nashville State Community College

Gertrude Bassey, Bon Secours Mercy Health

Robert Bauer, Columbia University

Ariel Bazzini, Stowers Institute for Medical Research

Nirajan Bhattarai, Idaho State University

Amanda Biederman, Ohio University

Anja Bielinsky, University of Minnesota

Caymee Bigham, University of Texas at Austin

Jaylin Billie, University of Central Florida

Darlene Blount, City of Hope National Medical Center

Milena Bone, Rensselaer Polytechnic Institute

Matt Borglin, California Polytechnic State University at San Luis Obispo

Sreyashree Bose, Texas A&M University

Francesco Botre, Sapienza University of Rome

Sergei Boudko, Vanderbilt University Medical Center

Maria Boza, University of Central Florida

Aaron Bradford, Regis College

Deanna Broadwater, Michigan State University

Ol'ha Brovarets, Institute of Molecular Biology and Genetics of the National Academy of Sciences of Ukraine

Kelsey Bruce, Linfield College

Violeta Burns, West Virginia University

Kyle Cavagnini, Johns Hopkins School of Medicine

Madison Champine, Winona State University

Courtney Chandler, University of Maryland, Baltimore

Karthick Chennakesavan, Temple University

Emily Cianflone, Winona State University

Joanne Clement, University of Florida

Junru Cui, Johns Hopkins School of Medicine

Ngozi Dagbaue, Spartan Health Sciences University

Neil Daily, InvivoSciences Inc.

Haider Dar, University of Pittsburgh

Brandon D'Arcy, University of South Alabama

Srinivasan Dasarathy, Cleveland Clinic

Saptashwa Datta, Sri Ramaswamy Memorial Institute of Science and Technology

Michelle Davis, Plymouth State University

Samuel DeCero, Medical College of Wisconsin

Victoria Deery, University of Massachusetts Boston

James Del Signore, Florida Institute of Technology

Mark Vincent dela Cerna, University of Louisville

Robert Devor, Oklahoma State University

Jenelle DeVry, Xavier University of Louisiana

Salonika Dikshit, Spartan Health Sciences University

H. Diessel Duan, University of Kentucky

Maria-Berenice Duran, Keiser University

Jean Elick, University of Saint Francis

Hannah Erskine, University of New Hampshire

Saja Fakhraldeen, Kuwait Institute for Scientific Research

Brooke Farrugia, University of Melbourne

Bruna Ferreira, University of Tampa

Jennifer Fishovitz, Saint Mary's College

Bethann Flint, West Virginia University

Sona Fokum, University of Illinois at Chicago

Lacy Fowler, Hillsborough Community College

Kasey Freshwater, West Virginia University

Melody Fulton, University of Georgia

Vrushali Furia, Spartan Health Sciences University

Sachika Gandhi, Spartan Health Sciences University

Jian Gao, Second Affiliated Hospital of Dalian Medical University

Ravisha Gautam, Spartan Health Sciences University

Fabio Gomez Cano, Michigan State University

Richardria Goodson, Huntingdon University

Samer Gozem, Georgia State University

Nicholas Graves, University High School

Ying Gu, Pennsylvania State University

Ritik Gupta, Spartan Health Sciences University

Eric Gurzell, Western Illinois University

Caio Ricardo Gutierrez Silva, University of North Carolina at Greensboro

Emery Haley, Van Andel Institute Graduate School

Seth Hall, Ohio Northern University

Mallory Handlin, unaffiliated

Jorg Hanrieder, University of Gothenburg

Nancy Hart, Peace Health St. Joseph Hospital

Andrew Hines, Huntingdon College

William Hines, University of New Mexico School of Medicine

Katie Hollis, Van Andel Institute

Peter Huang, Van Andel Institute

Tyler Hurd, Merrimack College

Abhay I, Spartan Health Sciences University

Surtaj Iram, South Dakota State University

Rabia Islam, Deakin University

Jane Jackman, Ohio State University

Divya Jain, Spartan Health Sciences University

Guochun Jiang, University of North Carolina at Chapel Hill

Benjamin Johnson, Van Andel Institute

Tierra Johnson, University of Maryland, Baltimore School of Medicine

Heather Junqueira, BioScentK9

Hala Kaaki, University of South Florida

Malika Kadirova, University of Utah

Sahithi Kaligota, Spartan Health Sciences University

Rishabh Kandwal, Spartan Health Sciences University

Rezaul Karim, University of South Florida

Richard Kennedy, Lord Fairfax Community College

Katelyn Kerod, Montclair State University

Jessica Kissinger, University of Georgia

Christopher LaRock, Emory University

Johan Larsbrink, Chalmers University of Technology

Thu Le, Pacific Lutheran University

Konstantinos Lekkos, University of Aberdeen

Andreia Leopoldino, University of São Paulo

Guanyu Liao, University of Wisconsin–Madison

Yang-Tsung Lin, Michigan State University–U.S. Department of Energy Plant Research Laboratory

Sara Lindén, University of Gothenburg

Amelia Linnemann, Indiana University

Michael Lisanti, University of Salford

Pengda Liu, University of North Carolina at Chapel Hill

Amber Lobb, Winona State University

Benjamin Loef, University of Wisconsin–Stevens Point

Lucia Lopes, University of São Paulo

Arimar Lopez, University of Central Florida

Tamara Maes, Oryzon Genomics S.A.

Sahil Mahajan, Washington University in Saint Louis

Misa Mai, Clark University

Andrew Maliszewski, Georgia Gwinnett College

Dana Malo, University of Illinois at Chicago

Rosann Marattil, University of Illinois at Chicago

Seth Margolis, Johns Hopkins University School of Medicine

Lenore Martin, University of Rhode Island

Sara Martire, University of Texas Southwestern

Michael Marvin, Rockhurst University

James McCarthey, Vanderbilt University Medical Center

Caitlin McDermott, University of Florida

Lauren Grace McGee, Huntingdon College

Antonio Mele, University of Central Florida

Richard Melvin, University of Minnesota School of Medicine

Jagadeeshaprasad Mashanipalya Guddadarangaiah, Penn State College of Medicine

Marissa Mielke, College of St. Scholastica

Mary Miller, Rhodes College

Eric Morrow, Brown University

Rima Mouawad, Michigan State University

Disha Mukadam, Spartan Health Sciences University

Pratik Mulay, Spartan Health Sciences University

Goutham Narla, University of Michigan

Premkumar Natraj, Jeju National University

Madeline Niblock, Michigan State University

Cole Niebuhr, Global Science Directive

Nicki Nouri, University of Illinois at Chicago

Sara Nowinski, University of Utah School of Medicine

Udochukwu Obodo, City of Hope National Medical Center

Mijung Oh, Samsung Medical Center

Lindsey Ohmstede, Stephen F. Austin State University

Samuel Okpechi, Louisiana State University Health Sciences Center, New Orleans

Marcos Oliveira, São Paulo State University

Laura Ott, University of Maryland, Baltimore County

Vijayakanth Pagadala, Glycan Therapeutics

Kinjal Pancholi, Spartan Health Sciences University

Cinta Papke, University of South Alabama

Sui Par, Georgia Institute of Technology

Dhruv R Patel, Spartan Health Sciences University

Shubham Patel, Spartan Health Sciences University

Pruthvik Patel, Spartan Health Sciences University

Nisha Pawar, University of Maryland Baltimore

Sandhya Payankaulam, Michigan State University

Stephanie Phillips, El Paso Community College

Michael Piacentino, California Institute of Technology

John Pietrzyk, Biolog Inc.

Adrian Pintado, University of Malaga

Kirill Plemyashov, Saint-Petersburg State Academy of Veterinary Medicine

Briana Plourde, Waubonsee Community College

N**atalia Podlutskaya,** University of Alaska Fairbanks

Danielle Porier, Virginia Polytechnic Institute and State University

Jaideep Prasad, Michigan State University

Lynne Prost, University of Wisconsin–Madison

Jonai Pujol–Giménez, University of Bern

Yanrong Qian, Ohio University

Li Qiang, Columbia University

Weihua Qiu, Virginia Commonwealth University

Ayesha Qureshi, Spartan Health Sciences University

Muzammil Qureshi, Spartan Health Sciences University

Charles Radloff, U.S. government

Md Rahman, Qatar University

Ana-Maria Raicu, Michigan State University

Sudhanshu Raikwar, University of Missouri and Harry S. Truman Memorial Veteran's Hospital

Matthew Rardin, Amgen

Mortezaali Razzaghi, University of Iowa

Aviv Regev, Broad Institute of the Massachusetts Institute of Technology and Harvard

Hongxia Ren, Indiana University School of Medicine

Joshua Renfroe, Lectenz Bio

Christian Reynolds, Wayne State University School of Medicine

Shiva Rijal, Touro College

Jonathan Roberson, University of Central Florida

C**arol Robinson,** University of Oxford

Shavon Rochester, Delaware State University

Angela Rogers, Arizona State University

Norbert Rolland, Centre national de la recherche scientifique

Rosalind Rosemond, Wellstar Health System

Jeffrey Sagan, University of California, Davis

Jascinta Santavanond, La Trobe Institute for Molecular Science

Matthew Saunders, Lectenz Bio

Macleod Sawyer, DNX Research Foundation

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Rameen Shah, New Jersey City University

Simi Sharma, University of Illinois at Chicago

Ben Shurina, Miami University

Amy Silva, University of Wisconsin–Stevens Point

Manvendra Singh, Duke–National University of Singapore Medical School

Olivia Sirpilla, Walsh University

Courtney Smith, Brigham Young University

Scott Soleimanpour, University of Michigan

Shanel Sosa, Wesleyan University

Wei Sun, Chinese Academy of Medical Sciences

Mohammed Houssaini Tahri Squalli, Worcester State University

Avrohom Teitelbaum, Touro College

Danelda Theron, St. Bonaventure University

Christopher Tinkey, Georgia Gwinnett College

Sankalp Tripathi, Spartan Health Sciences University

Michael Trites, University of Alberta

Sarah Tulin, Canisius College

Ayushi Umrigar, Spartan Health Sciences University

Audrey Uridil, Iowa State University

Jazmin Urrutia, University of Texas at Austin

Rachana Vaidya, University of Massachusetts Dartmouth

Dylan Valencia, University of California, Los Angeles

Ana Vergara, Washington State University

Katherine Vest, University of Cincinnati College of Medicine

Alexandra Votintseva, Saint-Petersburg State Academy of Veterinary Medicine

Yung-Chun Wang, University of Georgia

Zhiyi Wei, Southern University of Science and Technology

Abby Wicks, Wayne State University

Torsten Wittmann, University of California, San Francisco

Wei Xia, Sun Yat–sen University

Jianfeng Xu, Arkansas State University

Tulsi Yadav, Spartan Health Sciences University

Jinyi Yang, Massachusetts Institute of Technology

Alan Yocca, Michigan State University

Tai-Soon Yong, Yonsei University College of Medicine

Sara Young–Baird, National Institutes of Health

Xianghui Yu, Jilin University

Lisa Yun, Michigan State University

Ningning Zhao, University of Arizona

Bin Zhao, Stanford University

Chenghao Zhu, University of California, Davis

Tongtong Zhu, Icahn School of Medicine at Mount Sinai

Christina Zito, University of New Haven

Mark Zweigart, University of North Carolina

2019 honor society inductees

ASBMB

ASBMB Student Chapter regional directors Erin Sayer of the University of Nebraska–Lincoln (*left*) and Debra Martin of Saint Mary's University of Minnesota (*right*) flank new Chi Omega Lambda members at the ASBMB annual meeting in Orlando. The pictured students are (*from left)* Erin Bertone, Rebekah Dalton, Mary Doan, Jeffrey Gabell, Clark Hamor, Enessa Kalontar, Jovan Mirkovic, Sarah Neshat, Mallory Soska and Giang Vo.

The American Society for Biochemistry and Molecular Biology Honor Society (Chi Omega Lambda) recognizes exceptional undergraduate juniors and seniors pursuing degrees in the molecular life sciences at colleges or universities with ASBMB Student Chapters. Students are recognized for their scholarly achievement, research accomplishments and outreach activities. An induction ceremony was held in April at the ASBMB annual meeting in Orlando.

Erin Bertone, University of Nebraska–Lincoln
Caleb Carr, University of Massachusetts Amherst
Brett Daiger, Hendrix College
Rebekah Dalton, Otterbein University
Mary Doan, Drexel University
Julia Furnari, Marymount Manhattan College
Jeffrey Gabell, University of Nebraska–Lincoln
Colton Hageman, University of Nebraska–Lincoln
Clark Hamor, University of St. Thomas
Drew Harrahill, University of Nebraska–Lincoln
Spencer Jones, University of Nebraska–Lincoln
Enessa Kalontar, St. John's University
Nicholas Kite, University of Nebraska–Lincoln
Benjamin Laliberte, University of Massachusetts Amherst
Jamie Loughlin, Stockton University
Sean MacBride, University of Nebraska–Lincoln
Edelina Marzouk, Wesleyan University
Kelly McAleer, The College of New Jersey
Jovan Mirkovic, St. John's University
Mackenzie Mitchell, Wesleyan University
Kevin Mora, Manhattan Marymount College
Karen Nga Tana, Goucher College
Meghan O'Neil, Rochester Institute of Technology
Sarah Neshat, Northeastern University
Rebecca Prest, Missouri Western
Ashlyn Rairdin, University of Nebraska–Lincoln
Mike Slaza, Stockton University
Madison Smith, Purdue University
Mallory Soska, Otterbein University
Brandon Tran, Manhattan Marymount College
Caitlyn Turner, Trinity College
Giang Vo, St. John's University
Quin Waterbury, Purdue University

Biochem, with a side of advocacy

By Elizabeth Stivison

Kelly McAleer, a rising senior at the College of New Jersey, has turned her longstanding passion for science and science advocacy into action. Last fall, she founded an American Society for Biochemistry and Molecular Biology Student Chapter at TCNJ that supports both current and potential students as well as research in general.

In the summer of 2018, McAleer participated in the first session of the ASBMB's Advocacy Training Program. Two months into the training, she realized that an ASBMB chapter at TCNJ could provide opportunities and resources for students to take action on political issues that affect research. In addition, she thought a chapter would fill a specific niche at TCNJ, since the college has biology and chemistry departments but no distinct biochemistry department. So, without missing a beat, McAleer organized a meeting in October to gauge interest, and the chapter was officially founded in December with McAleer as president.

McAleer launched the chapter with an eye to both advocacy and community outreach. "I think if we don't advocate for science, there will be no science," she said. "We need our government and our representatives to realize the importance of federal funding for science."

To this end, the new ASBMB chapter held a Government 101 information session where students learned the basics of how government works, from how budgets are made to how a bill becomes a law.

COURTESY OF KELLY McALEER

Kelly McAleer founded the ASBMB Student Chapter at the College of New Jersey with an eye to both advocacy and community outreach.

"If people want to advocate at the federal level, they need to understand those bare basics," McAleer said.

Chapter members also hosted a Donuts and Policy event where they talked about the current Congress. They have been brainstorming a trip to Washington, D.C., for a day on Capitol Hill (modeled on the ASBMB's annual Hill Day) when the students would speak directly with their representatives about government support of science.

On the community outreach side of things, many chapter members volunteer at a nearby high school, acting as tutors and mentors in science classes. McAleer knows how important mentors and teachers can be to future scientists who otherwise wouldn't know a science career is possible. She describes having no connection to any scientists when she was growing up, no family or friends who were scientists.

"My first real exposure to science came from the classroom," she said. "I had a lot of really great teachers, and in high school I began to become serious about pursuing an education in science."

All this planning, coordinating and organizing, in addition to her studies and playing violin in the college orchestra, doesn't seem to tire McAleer out in the least. She finds it energizing to lead others and see her vision become a reality. Her time in college and her work with the ASBMB have expanded her idea of what is possible in her life, she said, and she has become interested in a wider range of biomedical careers. Becoming a physican–scientist, for example, is intriguing her now.

"It's always been medicine," she said of her goals. "It still is — but it's not just that now."

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

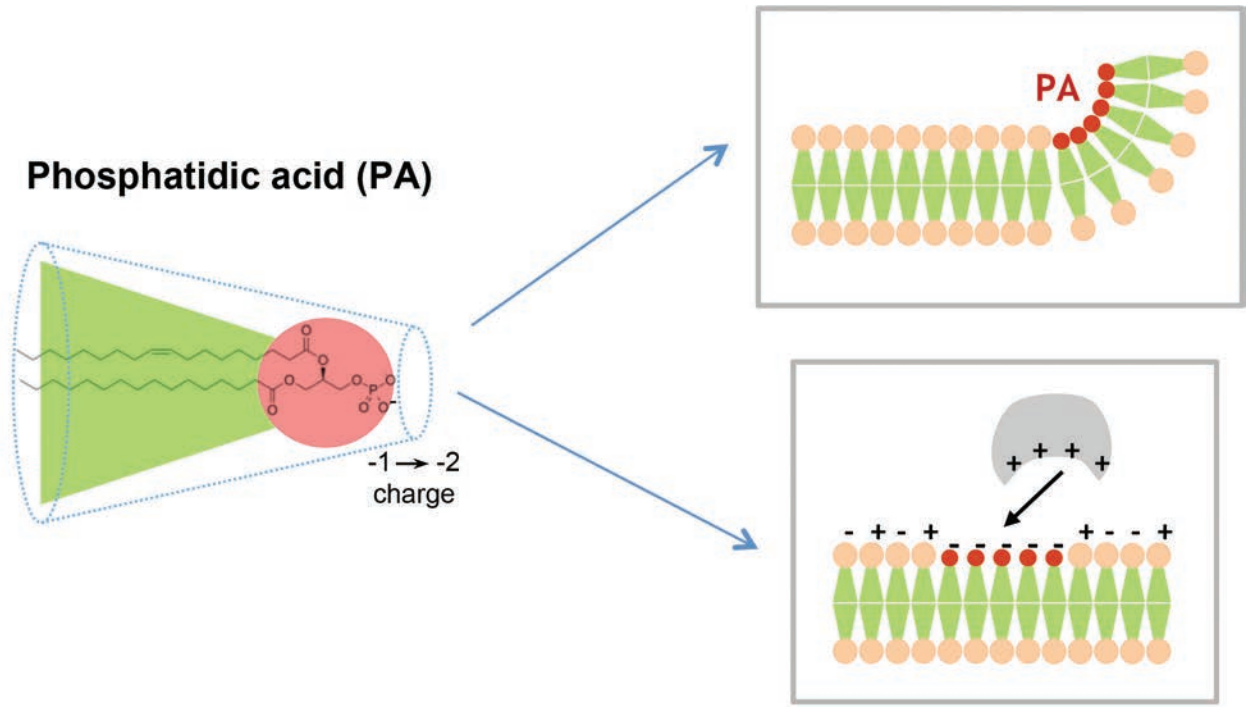
An ever-growing role for a tiny lipid

By Nicolas Vitale

Critical signaling functions have been attributed to phosphatidic acid, or PA, the smallest building block in phospholipid biosynthesis. With a small head group and a net negative charge ranging from -1 to -2 depending on pH, PA can modulate local membrane geometry and recruit a large set of specific proteins to confined membrane subdomains; a recent review by Emeline Tanguy and colleagues summarizes both of these essential actions for PA's signaling function. PA is versatile and challenging because it can be produced and metabolized by a large set of enzymes.

Although PA is present at low levels in most cell types, it appears to be critical for neuronal and glial cell function. Several neurological diseases maybe attributed, at least in part, to altered PA synthesis and/or catabolism. For example, Ricardos Tabet and colleagues proposed in 2016 that an alteration of the PA/diacylglycerol balance could be a main cause of fragile X syndrome, a genetic cause of intellectual disability. They showed that diacylglycerol kinase-kappa, or DGK-kappa, mRNA was the main target of fragile X mental retardation protein and that reduced DGK-kappa expression impaired PA synthesis in neurons from mice bred not to express FMR1, a protein that male fragile X patients lack. Silencing DGK-kappa in pyramidal neurons from the CA1 region of the hippocampus largely reproduced fragile X symptoms. This PA/DAG imbalance is thus likely to affect DAG and PA downstream signaling required for both maturation of dendritic spines and establishment of correct synaptic plasticity.

Maria Zeniou–Meyer and colleagues in 2008 proposed that the loss of expression of the kinase RSK2, which leads to Coffin–Lowry syndrome (a rare syndromic form



NICOLAS VITALE

Phosphatidic acid is defined by its shape and charge. This conical lipid generates negative membrane curvature and is negatively charged, thereby recruiting positively charged proteins.

of mental retardation), reduced PA synthesis and distorted neurosecretion. Increased PA synthesis has been reported in gliobastoma, the most frequent and aggressive brain cancer. A link between brain PA levels and Alzheimer's disease also is starting to emerge, but the exact effects of PA imbalance in neurodegeneration and cognitive deficits has not been identified. Finally, reduced PA synthesis may contribute to fetal alcohol spectrum disorders, as ethanol leads to phospholipase D-mediated phosphatidylethanol production at the expense of PA.

Many cellular pleiotropic functions of PA rely on its ability to regulate actin cytoskeleton dynamics and to modulate membrane-involved functions. The former occurs mainly through PA's ability to modulate the activity of small GTPases, including Rho and Arf members. The latter probably results both from the original cone shape structure of PA favoring negative membrane curvature and from PA's net negative charge allowing local recruitment of specific proteins. One remaining challenge is to define precisely sites of PA synthesis within the brain and at the subcellular level in neurons. Recent improvements in lipidomics allow for sensitive quantification of dozens of PA species made with different fatty acids. According to a study by Nawal Kassas and colleagues, the development of novel genetically encoded PA sensors also will be crucial in localizing and potentially quantifying changes in PA and perhaps different PA species.

Despite PA's low abundance, its relative simplicity, and the complexity of its metabolic and signaling pathways, improved understanding of its multiple functions in brain development and function is now within reach.

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Outfitting T cell receptors for special combat

By Jonathan Griffin

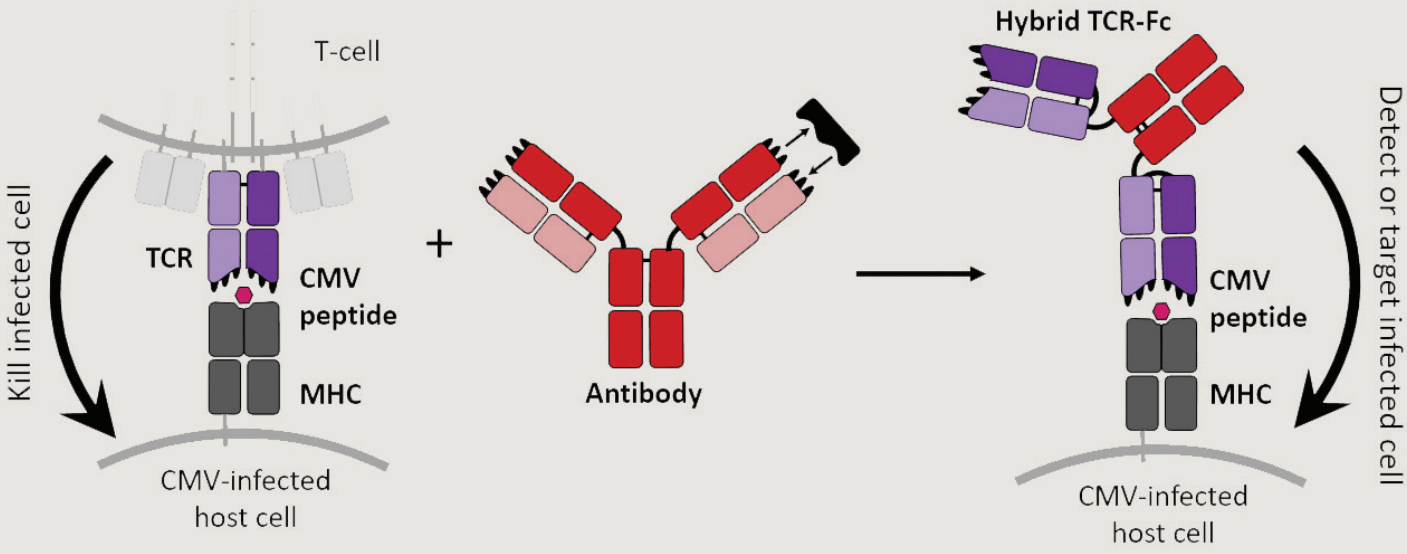
Researchers have engineered antibodylike T cell receptors that stick to cells infected with cytomegalovirus, or CMV, which can be deadly for patients with weakened immune systems. These receptors potentially could be used to monitor or destroy the virus and might also be able to target brain tumors.

CMV causes lifelong infection in more than half of all adults by age 40, but the virus lies dormant in most. T cells normally circulate through the body and use their membrane-bound T cell receptors, or TCRs, to detect disease-associated proteins hiding inside infected cells. TCRs then can instruct T cells to destroy the infection. For immunocompromised patients, however, this defense mechanism is diminished, leaving them vulnerable to the virus.

Researchers have used T cells to treat disease before, but engineering and transplanting whole T cells is costly and invasive. In a study published in the **Journal of Biological Chemistry**, a team of researchers took an alternative approach, producing CMV-detecting TCRs that float freely in the body and bind tightly to their diseased targets.

"Right now, we've got a molecule that looks like an antibody but it binds to a (CMV-associated) peptide that would normally be recognized by a TCR," said Jennifer Maynard, a professor of chemical engineering at the University of Texas at Austin and senior author of the study. "Antibodies cannot normally access these molecules, so that's a big deal."

Researchers frequently use bacterial or yeast cells as miniature biomolecule factories, but their nonmammalian molecular machinery often introduces defects in human TCRs, Maynard said. To provide a more suitable environment, the authors used hamster ovary cells to produce the receptors.



JENNIFER MAYNARD, ELLEN WAGNER/UNIVERSITY OF TEXAS

This new hybrid protein combines the cell targeting properties of a TCR with the tight binding and free-floating nature of an antibody to create a new molecule able to tag CMV-infected cells specifically.

> **Our protein could be used to specifically target glioblastoma cells, and it would provide a very unique marker.**
>
> —Jennifer Maynard

TCRs naturally bond loosely with their targets, but the authors wanted theirs to bind and not let go. To strengthen these connections, the authors randomly mutated the DNA of the TCR component that detects the CMV peptide. They inserted many versions of the mutated DNA into the hamster cells, which then manufactured about a million types of TCR, Maynard said.

The researchers measured bonding strength by exposing those myriad TCR variations to the CMV peptide.

"We found one that was our favorite," Maynard said. "We improved the binding affinity 50-fold."

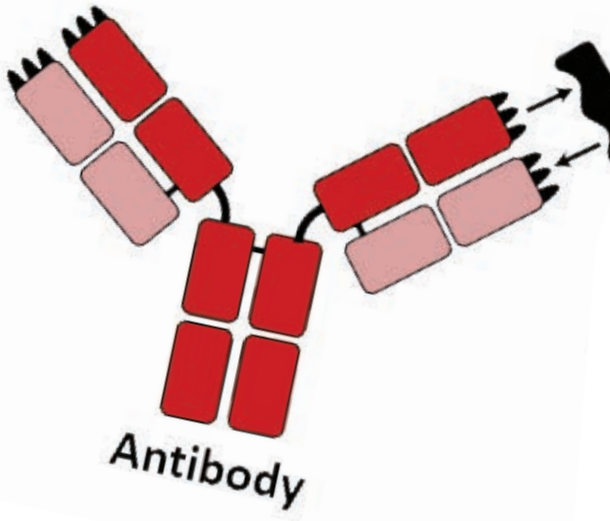
To liberate the TCRs from the T cell membrane, the researchers further edited the DNA so the TCRs would attach to the protein stem of Y-shaped antibodies. And to help these proteins hold their shape, they added a bond inside the TCR and prevented sugars from attaching.

These new TCRs could track disease progression in patients or evaluate new vaccines. They also might restore immune response in patients by instructing their cells to attack CMV infections, Maynard said.

This new molecule could be effective in treating glioblastoma as well. Although these brain tumors do not produce many distinct markers, they do suppress the immune system, which in CMV-infected patients can bring the virus back to life in tumors, Maynard said.

"Our protein could be used to specifically target glioblastoma cells, and it would provide a very unique marker," Maynard said. "We would use this to monitor or kill some of those tumor cells."

DOI: 10.1074/jbc.RA118.007187



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How do protein tangles get so long?

By Laurel Oldach

Long before Alzheimer's disease patients notice any symptoms, neurofibrillary tangles composed of tau protein filaments begin to form in their brain cells. How toxic these aggregates are and how well they spread depend on their size — that is, the number of tau monomers they contain. However, scientists studying tangle formation have not been able to explain why different sizes of tau aggregates appear in disease.

But now researchers have discovered that instead of adding just one protein at a time, fibrils of various lengths can join end-to-end to create one larger filament. The finding, published in the **Journal of Biological Chemistry**, helps explain how fibrils can grow to hundreds of nanometers. It also could help researchers understand mechanisms of an emerging group of drug candidates designed to inhibit tau aggregation.

A common simple model of tau aggregation and fibril formation includes two steps. First, two tau proteins bind slowly; additional tau molecules latch on quickly.

Carol Huseby, then a graduate student in Jeff Kuret's lab at the Ohio State University, worked with Ralf Bundschuh to expand this mathematical model to include other known ways that tau fibrils behave. Scientists have observed, for example, that sometimes one fibril fragments into two. Or a new fibril can nucleate in the middle of an existing fibril.

The simple model predicted many short fibrils. But Huseby knew that, under a microscope, aggregated tau appears as a smaller number of long fibrils. That discrepancy suggested that something was happening in the real world that hadn't been accounted for in the model. They hypothesized that short fibrils could attach end-to-end to get longer.

To test the hypothesis, Huseby labeled tau proteins with three fluorescent colors and allowed them to aggregate in separate test tubes. Then she mixed the different colored fibrils in a fourth test tube.

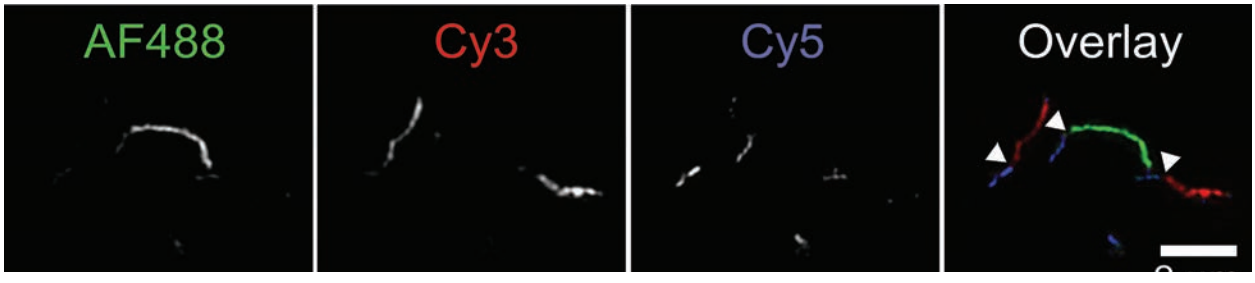
Images taken with a super-resolution fluorescence microscope showed long fibrils with short sections of each color, indicating that fibrils from the original test tubes had joined ends to form longer fibrils. Control experiments established that this can't be explained by labeled molecules' preference for like labels.

After Huseby incorporated this new mechanism into the model, it produced a better description of what purified tau proteins were doing as they formed aggregates. This study is the first to show that the fibrils can elongate by more than a single tau protein at a time.

Alzheimer's disease researchers still are trying to discern whether tau fibrils are a cause or simply an effect of the disease. Transmission of fibrils from one cell to another may contribute to the spread of disease in the brain. A very long fibril, according to Kuret, is unlikely to spread in this way. "But once it's broken up into little pieces, those can diffuse," he said, "facilitating their movement from cell to cell."

This study used just one type of tau. Six isoforms are known, and phosphorylation and other changes increase the protein's complexity. The researchers plan to incorporate these variables in future work and to use the model to understand how tau inhibitors change the protein aggregates' behavior.

DOI: 10.1074/jbc.RA118.006943



CAROL HUSEBY/OHIO STATE UNIVERSITY

Tau proteins labeled with three fluorescent dyes were allowed to aggregate in separate test tubes, shown in the three images at left. The different colored fibrils were mixed in a fourth test tube, at right, resulting in long fibrils with short sections of each color.

Cascading errors

How can a mutation in one lipid-turnover pathway cause problems in others?

By Laurel Oldach

Lysosomal storage disorders are genetic diseases. When any one of a number of enzymes in the lysosome loses its function, the molecule it breaks down accumulates, slowly building to levels that are toxic to cells. An article in the **Journal of Lipid Research** gives a clue as to why complex lipids known as gangliosides accumulate even in lysosomal storage disorders that don't affect ganglioside metabolism directly. The work was led by Konrad Sandhoff, who discovered a lysosomal storage disorder (since named after him) in 1968.

The ganglioside GM2 is found mostly in the outer plasma membranes of cells in the nervous system. In Sandhoff disease, which is caused by mutation of the enzyme that cleaves the complex sugar in GM2's head group, GM2 quickly accumulates in patients' neuronal lysosomes. This accumulation can be neurologically debilitating and is often fatal.

After undergoing endocytosis as part of normal membrane turnover, GM2 becomes part of the surface of a vesicle in the lysosome (see figure). The enzyme that breaks down GM2, which resides in the lysosomal lumen, depends on binding between GM2 and an accessory protein called GM2AP to find and break down its substrate. Until now, researchers didn't know whether GM2AP recruits the enzyme to the vesicle surface or delivers the lipid to the enzyme in solution.

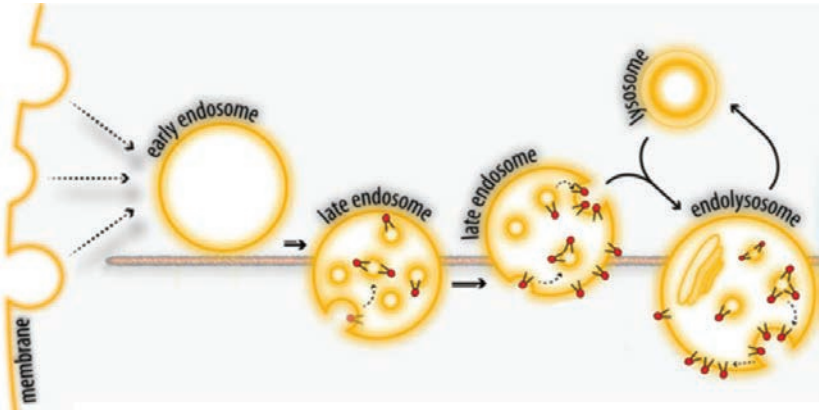
Using surface plasmon resonance, scientists in Sandhoff's lab led by postdoctoral fellow Susi Anheuser showed that GM2AP extracts gangliosides from the membrane of intraluminal vesicles. They also showed that GM2AP activity depends on the lipid makeup of those vesicles. If the vesicle has a negative surface charge, as is typical in healthy cells, GM2AP can extract gangliosides and ferry them to the relevant enzyme. If the quantity of neutral or positively charged lipids increases, the researchers observed, then that extraction is less effective, and ganglioside breakdown slows.

"GM2 degradation activity is regulated by molecules in the microenvironment of the reaction," Sandhoff explained. "If the lipids are changed, you change everything."

In addition to building up in some disorders as the main storage product, gangliosides can accumulate in disorders that primarily affect other lipids, such as cholesterol or mucopolysaccharides. Before now, scientists couldn't explain why that secondary buildup occurred. This paper suggests that raising the concentration of these other lipids in the lysosomal vesicle disrupts ganglioside degradation by affecting the interaction between GM2AP and the vesicle surface.

Richard Proia was not involved with this JLR paper, but he studies sphingolipids at the National Institutes of Health. "Normally, simple-mindedly, you think of each enzyme carrying out a single reaction and working by itself," he said, adding that this work complicates that view. "If one lipid is stored, and that has a negative effect on some other pathway, then the other pathways are now going to store lipids. That explains a phenomenon that's been known for a long time."

DOI: 10.1194/jlr.M092551



ADAPTED FROM PRIBASNIG ET AL./JBC 2015

After endocytosis, membrane-spanning proteins or lipids that become part of an endosomal vesicle can face into the lumen of the late endosome and the lysosome. This makes parts of the molecule that were once on the cell surface accessible to enzymes in the lysosome.

Study shows long-term effects of weight loss on the proteome

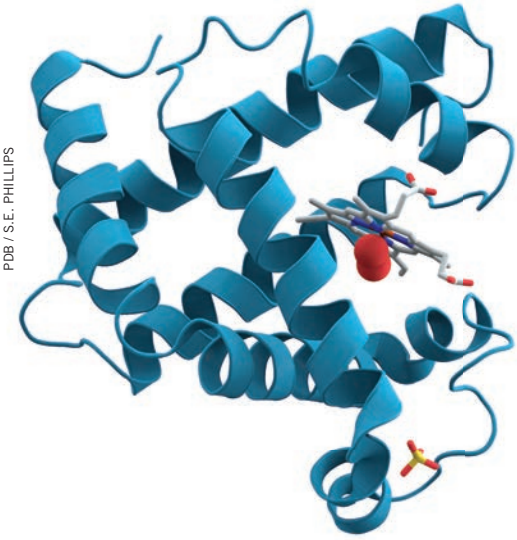
By Laurel Oldach

As hard as weight loss is, long-term maintenance can be even more of a challenge. But research published in the journal **Molecular & Cellular Proteomics** indicates that the hard work of maintaining weight loss can pay previously unknown health dividends.

Using plasma samples from a study that followed people as they lost weight and worked to keep it off, researchers at a Swiss proteomics company called Biognosys, in collaboration with a team at Nestlé, studied how weight loss affected participants' blood proteome. They observed that while chronic inflammation subsides immediately after weight loss, it takes some time for added beneficial effects to kick in.

The diet, obesity and genetics study, or DiOGenes for short, was designed to test the benefit of various diets in maintaining weight loss. Among the 550 participants who lost 8 percent or more of their starting weight and stayed in the study for another six months, researchers reported in 2010, those who followed a high-protein, low-glycemic-index diet were most successful at keeping it off.

More recently, researchers at Biognosys led by Lukas Reiter used a streamlined proteomics approach to analyze patient plasma samples from the start of the study, the end of its eight-week weight-loss phase, and six and 12 months into the maintenance phase. Consistent with other weight-loss studies, the team saw a dramatic, lasting drop in inflammatory signaling linked to atherosclerosis and an increase in lipid metabolism soon after weight loss.



PDB / S.E. PHILLIPS

Proteomics researchers found that many plasma proteins, such as myoglobin, shown at left, increase in nonenzymatic glycation after patients lose weight. It takes six months to a year of sustained weight loss for glycation to drop below baseline levels.

Because of the depth of their proteome coverage, the Biognosys researchers could add a look at protein glycation. Nonenzymatic glycation occurs when high concentrations of sugar react with proteins in the plasma. Many of the glycated proteins that changed significantly during weight loss, including albumin, myoglobin and some apolipoproteins, were unexpectedly more abundant after the study's initial weight-loss phase. It took more than six months on the weight-maintenance diet for those glycated proteins to drop back below their baseline levels. Because glycated proteins can activate the immune system, the researchers wrote, the effect of longer-term weight loss is positive.

In future studies, the researchers who own the data hope to move from looking at the whole cohort's proteome to correlating each study participant's outcomes with the composition of that individual's proteome at baseline in search of biomarkers that could help predict how future dieters will fare. Meanwhile, the Biognosys team wants to use its analytic abilities to power high-throughput proteomics for clinical trials.

DOI: 10.1074/mcp.RA118.001288

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From the journals

By Courtney Chandler, Isha Dey & Jonathan Griffin

Olive proteins and Parkinson's disease

Aggregates of alpha synuclein, or alpha SN, are primary components of Lewy bodies, which are linked to the degeneration of dopaminergic neurons in Parkinson's disease. In the search for therapeutic molecules, researchers have found that phenolic compounds from olive fruit protect against neurodegeneration and exhibit antioxidant properties. Hossein Mohammad–Beigi and an international team screened extracts from 15 olive varieties and found that Koroneiki olives had the most potent effects on alpha SN aggregation. The authors fractionated the extract and identified three compounds that drove alpha SN monomers to form oligomer chains with reduced toxicity. The study was published in the **Journal of Biological Chemistry.**
DOI: 10.1074/jbc.RA118.005723

Tregs help fight fatty liver disease

Consumed by people around the world, alcohol is a leading cause of illness and mortality. The liver is the organ primarily responsible for alcohol metabolism and can be damaged by excessive or prolonged consumption. This progressive damage leads to alcohol-induced liver disease, or ALD, which presents as a spectrum of symptoms and severities. Fatty livers are the earliest and most common pathology. Recent studies suggest that fat accumulation makes the liver more vulnerable to inflammation, which is further exacerbated when immune cells called T regulatory cells, or Tregs, are deficient.

A recent paper published in the **Journal of Lipid Research** gives insight into the role Tregs play in ALD. Qin Ning and colleagues from Huazhong University of Science and Technology in China used mice to model alcohol-induced fat accumulation in the liver. They found that diseased mice had depleted Tregs as well as aberrant macrophage activation and cytokine production. Treg transfer to the diseased mice relieved inflammation and lipid metabolic disorder and inhibited macrophage activation and cytokine production. They also found that the effects of Tregs are dependent partially on the cytokine IL-10. Their data show a novel role for Tregs in ALD and highlight a potential therapeutic target.
DOI: 10.1194/jlr.M083568

Counting proteins of a single cell

Computer simulations can help scientists understand complex cell signaling pathways, but, to ensure model accuracy, researchers need parameters determined by experiments with live cells. Akira Komatsubra and colleagues in Japan have established a way to measure protein concentration and dissociation constants at the single-cell level. By attaching EGFP and HaloTag genes to the ends of MAPK1 and RSK2 genes, respectively, the authors enabled fluorescence imaging of proteins encoded by the two modified genes and calculated their concentrations and dissociation constants. The study, published in the **Journal of Biological Chemistry**, demonstrates an approach to quantifying parameters that could improve the performance of simulation models.
DOI: 10.1074/jbc.RA119.007685

Rethinking a vaccine for malaria

Caused by parasites belonging to the Plasmodium family, malaria is transmitted to humans by female Anopheles mosquitoes. This life-threatening disease is prevalent in developing countries, and the only approved vaccine is largely ineffective, so much recent research has been directed toward developing more potent protection against the parasite. Studies have shown that some attenuated parasite proteins can protect humans, but researchers have been unable to find malaria proteins that confer this protection.

Using malaria parasite–infected mice as models, a study by Anthony Siau and colleagues at Nangyang Technological University and Singapore Immunology Network employed immunomic and proteomic techniques to identify a repertoire of parasite proteins associated with protection against Plasmodium yoelii, the parasite used in labs to infect mice. Using such criteria as reproducibility and immunoreactivity, the authors categorized these proteins based on how likely they were to protect against blood-stage malarial infection — the stage when the parasites divide in red blood cells and that is responsible for all clinical malaria symptoms. Their findings were published in the journal **Molecular &**

Viral cue sharpens arthritis drug's aim

Tumor necrosis factor, or TNF, protein coordinates inflammatory responses after binding to immune cells, but defects can occur in regulatory pathways that lead to overproduction of the protein, causing chronic inflammation and autoimmune disorders. The drug etanercept, marketed as Enbrel, a soluble form of a TNF receptor, has been approved to treat autoimmune disorders such as rheumatoid arthritis. However, it also blocks essential molecules, including lymphotoxin alpha, or LT alpha, thus increasing a patient's vulnerability to infections, lymphoma and heart failure.

In a study published in the **Journal of Biological Chemistry**, Sergio Pontejo and colleagues at the Autonomous University of Madrid introduced a component of a poxvirus into etanercept, producing a variant with less than one-sixtieth of the original LT alpha-blocking activity and a mostly retained ability to inhibit TNF proteins.

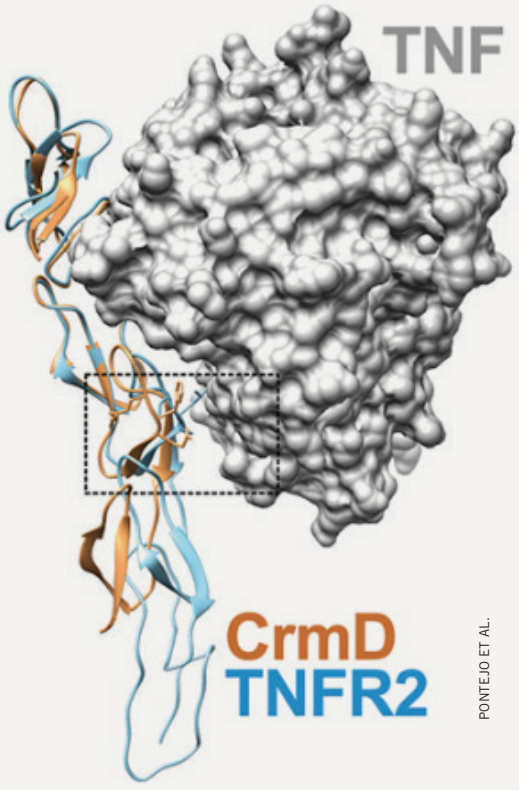
To evade host immune responses, poxviruses deploy proteins called viral TNF decoy receptors that inhibit native TNF molecules. One of these decoy receptors, CrmD, which is produced by the mousepox-causing ectromelia virus, neutralizes both TNF and LT alpha proteins in mice but does not interfere with LT alpha in humans. The authors of the study sought to understand CrmD's unique binding ability at a molecular level.

By analyzing how several mutations in CrmD's binding region affected its binding to TNF and LT alpha, the researchers zeroed in on a motif of three amino acids that prevents the protein from inhibiting human LT alpha. They then mutated etanercept to include this motif and found that the mutation reduced LT alpha-blocking activity more than sixtyfold while weakening TNF inhibition threefold.

This safer form of etanercept might replace the traditional form of the TNF inhibitor in clinical use.

DOI: 10.1074/jbc.RA118.005828

—Jonathan Griffin



PONTEJO ET AL.

Overlaid crystallographic structures of CrmD in yellow and etanercept in blue bound to TNF. The dashed box surrounds the region of the CrmD that is key to preventing inhibition of lymphotoxin alpha.

Cellular Proteomics. When extended to Plasmodium species affecting humans, this extensive data set could be used to help validate and characterize new vaccine formulations for better prevention of malaria.

DOI:10.1074/mcp.RA118.000997

Staph bacteria's copper resistance

Many hospital surfaces are copper because the metal has antimicrobial properties that can block the spread of disease, but some strains of Staphylococcus aureus have evolved mechanisms to resist copper's effect. Zuelay Rosario–Cruz of Rutgers University and a team of researchers identified two genes, copB and copL, that enable S. aureus' copper resistance. Genetic evidence suggested that the CopB protein plays a role in copper export, while nuclear magnetic resonance identified CopL from Bacillus subtilis, a close relative of S. aureus, as a membrane-bound lipoprotein that could bind extracellular copper. These findings, published in the **Journal of Biological Chemistry,** suggest mechanisms by which S. aureus thwarts copper and could aid in the development of methods to better limit infections.

DOI: 10.1074/jbc.RA118.004723

Reversing mutant accumulation in cancer

The transcription factor p53 functions as a tumor suppressor; in more than half of cancer patients, this protein is mutated and accumulates inside cells. Luciana Rangel and colleagues at the Federal University of Rio de Janeiro report that the small molecule PRIMA-1, which can return mutated p53 to a natural shape, also reverses accumulation of the protein. Their study, published in the **Journal of Biological Chemistry**, showed that exposing cancer cells to PRIMA-1 reduced aggregates of p53, initiated programed cell death and inhibited the ability of mutant p53 to trigger aggregation of native p53. The authors suggest these results point toward p53 as a valid drug target.
DOI: 10.1074/jbc.RA118.004671

Digging into the phagosomal proteome

In the process of phagocytosis, immune cells eat up foreign pathogens. The primary phagocytes in the human immune system are dendritic cells, or DCs, which break down pathogens in dynamic compartments called phagosomes and present the resulting antigen to T cells to start an immunogenic response. A phagosome changes its protein composition during its development and in response to various stimuli, but that phagosomal proteome is poorly understood.

In a collaborative study published in **Molecular & Cellular Proteomics**, Eik Hoffmann and an international team investigated changes in the phagosomal proteome in DCs derived from resting bone marrow versus those stimulated for immune response by lipopolysaccharide, or LPS. Using label-free mass spectrometric analysis, the authors found that upon LPS stimulation, these phagosomes recruit fewer proteins that help them mature and more proteins that help them present the antigen to T cells, thus changing their proteome. The study also identified other proteins previously not known to participate in phagosome function. This preliminary finding paves the way for better understanding of the phagosomal proteome and its dependence on external stimuli.
DOI:10.1074/mcp.RA119.001316

Isotope labeling may affect kinetic studies

Kinetic reactions and metabolic pathways can be studied using isotopically labeled substrates. Reactants are labeled by replacing specific atoms with their isotopes and can thus be tracked through time. Serine palmitoyltransferase, or SPT, is the first enzyme in sphingolipid biosynthesis and often is investigated using isotopically labeled L-serine.

In a recent study in the **Journal of Lipid Research**, Dominic Campopiano of the University of Edinburgh and an international team used SPT from humans and the bacteria Sphingomonas paucimobilis to investigate the effect isotope labels may have on catalysis. SPT is conserved among all organisms capable of producing sphingolipids, yet the eukaryotic isoform is membrane-bound whereas the bacterial isoform is soluble and found in the cytoplasm. Campopiano and colleagues monitored SPT-catalyzed reactions using a series of L-serine substrates that differed in the position of an isotopic label. While the human and bacterial forms of SPT showed similar kinetics in many cases, one substrate revealed a kinetic isotope effect in the bacterial SPT that was absent in the human form. This suggests subtle catalytic differences between cytoplasmic and membrane-bound forms of SPT and that the position of isotope labeling should be considered carefully during kinetic experiments.
DOI: 10.1194/jlr.M089367

Molecular bridges help patch up DNA

Double-strand breaks, or DSBs, in DNA can be lethal to cells, but mechanisms have evolved to correct errors in the genetic code. The protein Ctp1 is key to the initiation of DSB repair, but exactly how it interacts with DNA was until recently unknown. To find out, Sara Andres and colleagues from the National Institute of Environmental Health Sciences and the University of North Carolina performed atomic force microscopy imaging of Ctp1-DNA complexes. The authors write in the **Journal of Biological Chemistry** that they observed polymerized Ctp1 tetramers on dsDNA, forming bridges between strands; when Ctp1 was mutated, cells were sensitized to DNA damage. These images provide valuable mechanistic insights for studying disease-causing DSB repair defects.
DOI: 10.1074/jbc.RA118.006759

Protons and calcium ions shall not pass

Channelrhodopsins, or ChRs, are light-activated ion channels used in neuroscience to induce activity in neurons. But activating ChRs also can allow passage of protons and calcium ions, which may trigger undesirable responses such as glial acidification or intracellular calcium release. To avoid these effects, Yong Ku Cho and colleagues

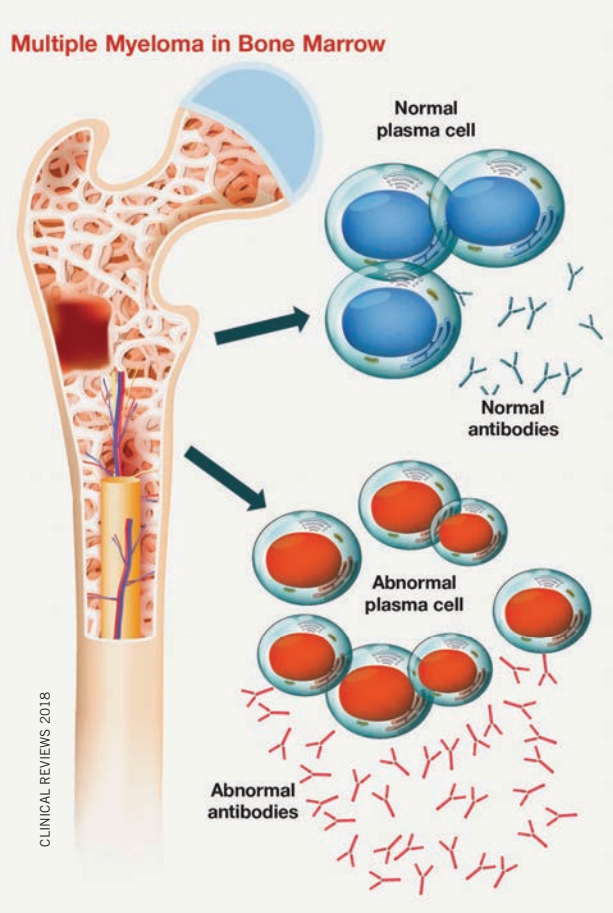
Tackling an incurable blood cancer

Multiple myeloma, or MM, is a cancer of the plasma cell, a white blood cell responsible for making antibodies, in bone marrow. It is the second most common blood cancer in the U.S. after non-Hodgkin's lymphoma. MM starts out as a benign condition called monoclonal gammopathy of undetermined significance, or MGUS, and then becomes malignant via an intermediate stage known as smoldering multiple myeloma, or SMM. The lifetime risk of getting MM in the U.S. is less than 1%. The disease's progression is poorly understood and it has no cure, so recent research has sought to understand the microenvironment that contributes to the pathophysiology of MM.

A feature of cancer progression is induction of tumor hypoxia as a result of reduced oxygen and nutrient delivery to the tumor cells. MM cells can adapt to hypoxia, which contributes to disease progression. To understand this process better, Astrid Slany and colleagues in Austria and Germany profiled the proteome of primary human MM cells in response to hypoxia induced as the cancer progresses. They analyzed plasma cells from bone marrow of patients with MGUS, SMM and MM and looked for proteins expressed in myeloma cells that aided in their survival, proliferation, and mechanisms to evade apoptosis and immune response. In comparison to nondiseased plasma cells, myeloma cells showed significant changes in the expression of proteins that regulate metabolic processes leading to cell proliferation under hypoxic stress. Also, pro-apoptotic proteins were downregulated, while proteins involved in escaping cell death and immune response were upregulated in hypoxia-stressed MM cells. Their findings were published in the journal **Molecular & Cellular Proteomics**.

These results indicate that myeloma cells' adaptation to hypoxia plays a key role in disease progression. Unique proteins in advanced-stage myeloma cells could serve as novel targets for development of improved anti-myeloma treatment strategies.
DOI:10.1074/mcp.RA119.001390

—Isha Dey



This cartoon shows plasma cells in bone marrow with and without multiple myeloma. Researchers are studying this incurable cancer's adaptation to lack of oxygen.

at the Massachusetts Institute of Technology engineered ChRs that permit the passage of only certain ions. By generating and screening hundreds of ChR2 mutants, they found a combination of mutations that produced a ChR variant with tenfold reductions in calcium and proton flux. Their methods offer a means to customize ChRs and could reveal new principles of optogenetic protein engineering. The study was published in the **Journal of Biological Chemistry.**
DOI: 10.1074/jbc.RA118.006996

Lipid signaling may help prevent atherosclerosis

Atherosclerosis is caused by the buildup of fatty plaque deposits in the arteries and can lead to heart attack and stroke. Lysophosphatidic acid, or LPA, is a lipid that functions in signaling in vascular smooth muscle and endothelial cells. While LPA has been shown to be increased in atherosclerotic lesions in mice, the specific roles of LPA and LPA receptors in blood and vascular disease remain an active area of research.

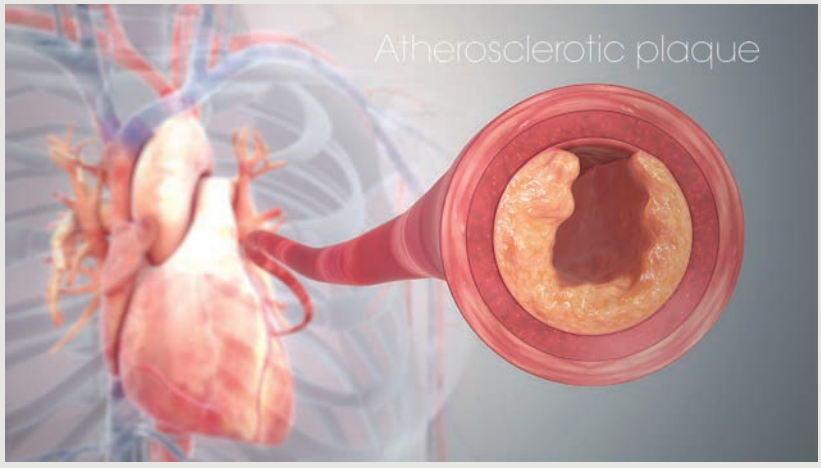
In a recent study published in the **Journal of Lipid Research**, Susan Smyth of the University of Kentucky and colleagues investigated the role of a specific LPA receptor called LPAR4 in the development of atherosclerosis in mice. They found that while cholesterol levels and lipoprotein distribution were similar in wild-type and Lpar4-knockout atherosclerotic mice, the knockout mice had overall less atherosclerosis and the atherosclerotic lesions that were present were smaller in size.

Previous studies have shown that LPA can promote inflammatory responses, including the switch between M1-type macrophages that are associated with inflammation and M2-type macrophages that are associated with tissue repair and healing. When Smyth and colleagues used LPA to stimulate macrophages isolated from wild-type and Lpar4-knockout mice, they found that macrophages from the knockout mice upregulated a marker associated with M2-type activation. They also detected higher levels of markers indicative of M2-type macrophages in the aortic and coronary arteries from the knockout mice compared to the wild-type mice.

These results suggest that LPAR4 may be involved in recruiting specific immune cell subsets or regulating the phenotypic switch of macrophages from M1- to M2-type, which in turn may promote resolution of plaque inflammation. Furthermore, their research supports the idea that therapeutic development to target LPA pathways may provide an anti-inflammatory approach to prevent some of the complications associated with atherosclerotic disease.
DOI: 10.1194/jlr.M091066

—Courtney Chandler

MANU5/WIKIMEDIA COMMONS



Fatty plaque buildup in the heart's artery causes atherosclerosis, reducing its surface area and hence its oxygen-carrying capacity.

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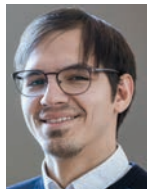


For June and July, it's atomic Nos. 6 and 7

By Quira Zeidan

This series of articles on chemical elements important for life marks the International Year of the Periodic Table in 2019. To date, we have introduced hydrogen, iron, sodium, potassium, chlorine, copper, calcium and phosphorus. This month, we continue the series with carbon and nitrogen.

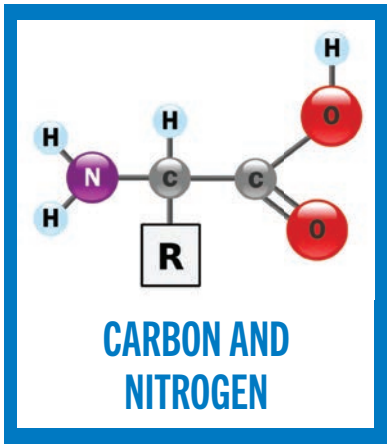
Carbon, with symbol C and atomic No. 6, and nitrogen, with symbol N and atomic No. 7, are reactive nonmetals that generally share electrons with other atoms by forming several covalent bonds. A carbon atom has four electrons and four vacancies in its outermost shell and can combine with other atoms via four covalent bonds. Nitrogen has five valence electrons in its outermost orbitals, three of which are high-energy unpaired electrons that each can form a covalent bond. Nitrogen typically connects with other atoms through these bonds.

Carbon is the fourth most abundant element in the observable universe and the 15th most common in the Earth's crust. Carbon is produced in the core of stars when two helium nuclei collide to form highly unstable beryllium, which fuses with another helium particle to produce a stable carbon nucleus. When massive stars explode as supernovae, carbon disperses into space. It accumulates in the Earth's atmosphere where it combines with oxygen as carbon dioxide, or CO_2. Carbon is dissolved in all of Earth's water bodies and is a common constituent of large carbonate rocks — such as limestone and marble — and coal.

Nitrogen is produced in supermassive stars when carbon reacts with hydrogen to produce nitrogen, oxygen and helium in a cycle that generates light and heat. Nitrogen is the seventh most abundant element in the Milky Way and the solar system, and it represents about 78% of the Earth's atmosphere in the form of dinitrogen gas, or N_2. Nitrogen makes up about 0.002% of the Earth's crust, where it is trapped from the atmosphere during mineral formation, and it dissolves in the oceans via precipitation or sediment runoff.

Both carbon and nitrogen are exchanged continuously in the environment. In the carbon cycle, atmospheric carbon dioxide is converted to organic carbon via photosynthesis. Organisms cycle carbon back into the atmosphere or soil by respiration, excretion and decomposition. In addition, carbon trapped in fossil fuel reservoirs during older geological events is released continuously into the environment by erosion, volcanic emission and human activity, contributing to the present cycle.

Unlike carbon, atmospheric nitrogen cannot be used directly by plants. Instead, nitrogen gas is combined with oxygen or hydrogen by soil bacteria and converted into nitrates and ammonia, respectively. Plants — and subsequently animals — use fixed nitrogen to build biological molecules such as proteins and nucleic acids. Organic nitrogen is returned to the soil by excretion and decomposition and cycled back into ammonia by bacteria and fungi.



General structure of an amino acid (with the exception of proline). The alpha carbon in the center is bonded to four groups: an amino group (NH_2), a carboxyl group (COOH), a hydrogen atom (H) and a variable side chain (R group). The R group determines the overall structure, size, electric charge and polarity of the amino acid (in glycine, R is another hydrogen atom).

The chemistry of life is organized around carbon. Carbon atoms can react with each other to form very stable carbon–carbon bonds. Multiple carbon atoms linked together can exist as linear chains, branched trees and cyclic rings. These structures, called carbon skeletons or backbones, combine with various chemical groups to make the biomolecules and organic compounds found in living cells.

In addition to carbon–carbon interactions, carbon forms single bonds with hydrogen atoms and both single and double bonds with oxygen and nitrogen. Carbon skeletons bonded

Carbon and nitrogen occur in all known life. Together with hydrogen and oxygen, they form stable compounds … where the four elements combined make up between 96% and 99% of any living organism's mass.

only to hydrogen are called hydrocarbons, and they include the tails of fatty acids, methane and methyl groups. Other biomolecules contain carbon atoms bonded to oxygen in several chemical arrangements, including hydroxyl groups in alcohols such as glycerol, carbonyl groups in aldehydes and ketones represented in monosaccharides, and carboxyl groups in carboxylic acids like in amino acids.

Nitrogen combines with carbon, forming ring configurations such as purines and pyrimidines that constitute nucleic acids. Biomolecules that contain carbon and nitrogen also include amines and amides. Amines contain the amino group R-NH_2, which ionizes to R-NH_{3+} in aqueous solutions due to its reaction with an H^+ from water. Amines occur in amino acids and some neurotransmitters. Amides are formed by the combination of an acid and an amine, such as during formation of peptide bonds that join amino acids in proteins. Enzymatic deamination of the amino acid arginine produces nitric oxide gas that readily diffuses across cellular membranes, acting as a signaling molecule. In animals, nitric oxide regulates smooth muscle contraction and activates macrophages and neutrophils to kill microorganisms.

Carbon and nitrogen occur in all known life. Together with hydrogen and oxygen, they form stable compounds commonly found in biological molecules, where the four elements combined make up between 96% and 99% of any living organism's mass.

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Upcoming ASBMB events and deadlines

JULY

UV Safety Month
- Mass Spectrometry in the Health and Life Sciences abstract deadline (July 7)
- ASBMB–BSC Symposium on the Interplay Between Epigenetic Regulation and Genome Integrity early registration deadline (July 20)
- Emerging Roles in Nucleolus oral abstract deadline (July 25)
- Serine Proteases in Pericellular Proteolysis and Signaling oral abstract and early registration deadline (July 26)
- Transforming Education in the Molecular Life Sciences (July 25–28)

AUGUST
- Mass Spectrometry in the Health and Life Sciences registration deadline (Aug. 1)
- Emerging Roles in Nucleolus early registration deadline (Aug. 2)
- **Fungal Disease Awareness Week begins Aug. 13**
- Serine Proteases in Pericellular Proteolysis and Signaling poster and registration deadline (Aug. 15)
- Mass Spectrometry in the Health and Life Sciences (Aug. 18–22)
- ASBMB–BSC Symposium on the Interplay Between Epigenetic Regulation and Genome Integrity abstract deadline (Aug. 30)
- Emerging Roles in Nucleolus poster abstract deadline (Aug. 30)

SEPTEMBER

Pain Awareness Month
- Communication Course applications open (Sept. 3)
- Emerging Roles in Nucleolus registration deadline (Sept. 10)
- Peer review week (Sept. 10–15)
- Serine Proteases in Pericellular Proteolysis and Signaling (Sept. 12–15)
- Postdoc appreciation week (Sept. 16–20)

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PERSONALIZED PROTOCOLS

Mental health accommodations can help some succeed in the lab — but first they have to ask

By John Arnst

Sitting at her desk in the National Institutes of Health's Theoretical Molecular Biophysics Section, Robyn Stix sometimes reaches down to pet Agnes, her white-gold Labrador retriever. The petting releases oxytocin that helps Stix, a postbaccalaureate fellow, cope with her chronic anxiety.

When Shauna Otto, a Ph.D. candidate at Oregon State University, is working through a bipolar episode and finds herself unable to reach out to others in her lab, her contact at the university's Disability Access Services acts as a buffer, relaying messages between Otto and her primary investigator until she's well enough to re-enter the lab.

Both Agnes' presence and Otto's mediator are considered reasonable accommodations under Title I of the Americans with Disabilities Act; they allow individuals with disabilities to do their work to the same extent as people without disabilities. Rather than specifying which medical conditions constitute disability, the ADA considers a person to have a disability if they have a mental or physical impairment that substantially limits one or more major life activities.

The protections of the ADA and the right to request and receive accommodations extend to students at the primary, secondary and postsecondary levels for a gamut of visible and unseen disabilities, which includes the mental illnesses that a number of recent studies have found graduate students are more likely to have than the general population.

While accommodations can be clear-cut in an undergraduate setting — additional time for tests, an assignee to help with taking notes or even a student helper to lend an additional set of hands in a chemistry laboratory — the informal nature of research laboratories may leave graduate students and postdoctoral fellows feeling uneasy about disclosing their conditions to their PIs and requesting the accommodations they need.

While anecdotes suggesting a mental health crisis among graduate students had been circulating for years, a number of recent papers helped bring greater attention to the scale of the problem.

A paper in the journal Psychology Research and Behavior Management in March found that 23.7% of a surveyed 325 doctoral students at China Medical University in Shenyang exhibited signs of depression, and 20% exhibited signs of anxiety. In a paper published in November 2018, researchers at Harvard University found that graduate students in economics programs experienced moderate or severe symptoms of depression and anxiety at rates more than three times greater than the general population.

Both of those papers came in the wake of a paper published in March 2018 in Nature Biotechnology, wherein 41% of a surveyed 2,279 graduate students were found to have moderate to severe anxiety, and

around 39% of the students were found to have moderate to severe depression. The authors, Teresa Evans and Nathan Vanderford, pointed out those rates are much higher than those in the general population, as reported in other research studies and by various health organizations. Their results prompted an unprecedented flurry of news coverage and concern among the higher education community.

"There's a lot of evidence showing this paper has been received by the community in a positive light and that it has catalyzed an ongoing discussion," said Evans, an assistant professor at the University of Texas Health Science Center at San Antonio.

Over the past year, Evans and Vanderford have spoken at universities across the United States about the results of their survey and the actions that PIs, students, faculty and administrative leaders can take to address the issue. They often are invited by trainees who want to see increased support for mental wellness.

One of the most prominent voices — or rather, faces — of the conversation about mental health among graduate students has emerged on social media. Susanna Harris, a graduate microbiology student, started an Instagram account called The PhDepression.

Since the first post — in which Harris discussed her own experience with depression and anxiety as a graduate student at the University of North Carolina at Chapel Hill — more than 100 early-career scientists with mental illnesses including PTSD, postpartum depression, bipolar disorder and borderline personality disorder have shared their stories. The PhDepression, now a social media limited liability company, also has accounts on Facebook and Twitter as well as a blog for longer stories.

"What's striking to me is the similarity of stories," Harris said.

Teresa Evans of the University of Texas Health Science Center at San Antonio and Nathan Vanderford of the University of Kentucky, published a study in the journal Nature Biotechnology last year about mental health among graduate students. The results, Evans said, have "catalyzed an ongoing discussion" about what can be done to improve graduate students' well-being.

Susanna Harris and her team share photos across The PhDepression's social media accounts that are a conscious contrast to the stock photos often used to typify depression, such as those that ran with coverage of Evans and Vanderford's Nature Biotechnology paper. "It all was accompanied by a photo of a woman crying in a window," Harris said, "and that was really the impetus to start PhDepression on Instagram — to put that smiling face that everyone sees in academia and include a story that is often not told."

"The general tone is 'I had a history of a little bit of imbalance, I knew that something was a little off in college, then I got to grad school and it was just this pressure cooker that precipitated all of these issues. Instead of having the resources and support that I did in undergrad, where I had an outside mentor or a counseling group or an RA or a roommate, I don't have that and I don't have the financial resources to feel comfortable getting them.'"

Reasonable accommodations

At the University of California San Diego, Joanna Boval and her staff handle accommodations requests for undergraduates and graduate students, some of whom are navigating the onset of mental illness.

"I think that if they are experiencing these things for the first time, it's very isolating and scary," said Boval, the director of the Office for Students with Disabilities at UCSD.

Under Section 504 of the Rehabilitation Act of 1973, which bans discrimination against individuals with disabilities in any program or activity receiving federal funds, public schools at all levels are required to make a reasonable effort to accommodate students in these activities. For Boval, accommodations are a matter of equity.

"We talk about leveling the playing field, right?" Boval said. "So, a reasonable accommodation usually differs from person to person, depending upon the impact of the disability and also the particular environment in which they are working or learning or doing a task."

At a postsecondary institution such as UCSD, a request for a reasonable accommodation is processed by the university's Office for Students with Disabilities, or OSD. This can be initiated by a student or by a referral from the university's counseling and psychological services or student health services.

After a student has provided medical documentation of a functional limitation, they meet with a disability specialist from the OSD to review their planned coursework and discuss potential accommodations. Boval and her staff work with about 500 students each quarter, more than half of whom receive accommodations for psychological disabilities.

From elementary through high school, a student's parents and their interactions with teachers usually drive the accommodations process. Modifications such as waiving course requirements might be made to curriculum in a K-12 setting but are not an option at a university.

Adult options

"The responsibility is on the student to self-identify (and) to ask for what it is he or she feels they need in this particular environment," Boval said. "It can be challenging if students don't really understand what their disability is or how it really impacts them."

If a professor or PI resists making an accommodation for a student, Boval may have to resort to asking other faculty members for support.

"If I have difficulty getting through to a tenured faculty person about a situation accommodation … I will call a member of my faculty advisory committee and I'll say, 'Hey, look, here's the situation. This is what we need to have happened. Can you talk to your colleague?'" she

said. "More often than not, when the first faculty has heard from who they consider their peer, they are more likely, even if they do it reluctantly, to acquiesce."

If those methods fail, students can seek recourse through the Office for the Prevention of Harassment and Discrimination and, externally, the Office for Civil Rights, the U.S. Department of Education or private legal means.

In professional settings, if an employer refuses to provide a reasonable accommodation to an employee with a disability, the primary avenue of recourse is the Equal Employment Opportunity Commission, the federal agency responsible for enforcement of the ADA.

According to Linda Carter Batiste, the principal consultant and legislative specialist at the Job Accommodation Network, employers are responsible for accommodating an employee's needs up until making an accommodation would be considered "undue hardship."

Undue hardship is "a very, very broad term that encompasses a lot of things," Carter said. "There are some specific things that employers don't have to consider doing, and that's things like creating new jobs, removing essential functions, providing personal need items like medications, things like that."

The Job Accommodation Network, which provides free guidance on workplace accommodations and disability employment issues, suggests a number of potential accommodations for people with depression, including alternative lighting, flexible scheduling, noise-canceling headsets and removing nonessential tasks.

"Sometimes, they'll ask to have marginal functions removed," said Melanie Whetzel, the lead consultant on JAN's cognitive/neurological team. "Maybe some little tasks that they do that could be given to someone else, and then they would have more time to spend on the essential functions."

If an employee and employer are unable to work out a reasonable accommodation, or an employee is denied an accommodation, the employee can file a complaint. The outcome depends on a number of factors, Carter said. These can include whether there was a valid reason for the request, whether the employer determined that the employee didn't need an accommodation, whether the employer made a good faith effort and whether there were any accommodation options or any that would not create an undue hardship.

"In general, it's important that an employer make and document that it made a good faith effort to try to accommodate," Carter said. "If, ultimately, the employer determines that it cannot make an accommodation, the documentation of effort can be critical if the employee files a complaint.

"Also, it can be helpful to communicate with an employee about why an accommodation is being denied. Sometimes, if the employee understands why, the employee might not be as likely to file a complaint."

Canines and convalescence

At the NIH, where Robyn Stix simulates the molecular dynamics of membrane proteins, Agnes often can be found sleeping under the desk. "She's a lazy dog," Stix said. "I think my lab mates would like it if she were a little more exploratory."

When Stix was an undergraduate at Skidmore College, she was diagnosed within one year with both Crohn's disease and anxiety. In addition to the oxytocin released by close contact, which helps alleviate anxiety, Agnes also assists Stix with the painful gut flare-ups caused by Crohn's, through deep pressure therapy.

While Agnes' presence beside Stix is considered a reasonable accommodation, she may have been

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Robyn Stix, a postbaccalaureate fellow at the National Institutes of Health campus in Bethesda, Maryland, goes everywhere with a small pouch of treats and plastic bags for her service dog, Agnes, whose red vest bears the words "Not all disabilities are visible." Stix has anxiety and Crohn's disease.

Shauna Otto didn't know accommodations were available to her when her she was grappling with a mood disorder as an undergraduate. She was well into her graduate studies at Oregon State University when an on-campus psychiatrist referred her to the office for students with disabilities. There, she was assigned a counselor who helps her stay in touch with her lab when she suffers a debilitating episode.

considered undue hardship in a lab where a dog might cause stress in lab animals. When Stix interviewed with her PI, José Faraldo-Gómez, she was forthright in requesting Agnes be allowed with her in the lab.

"I like to be upfront, because I want to be sure it's a good environment. If someone's going to be different because I have a service dog, I don't want to end up in a lab like that," Stix said. By her account, Faraldo-Gómez was happy to oblige. "When I visited, Jose made sure to ask where we would fit best in the room."

When a mental health issue prevents someone from physically being able to get into a lab space, the best option may be to give that person time and space to work through their depressive or anxiety episodes.

"I would say, with individuals who have a chronic mental health challenge or who have a chronic health issue, one of the reasonable accommodations may be something like occasional absences, because the disability is so impactful that they physically can't get into the space," said UCSD's Boval.

When Shauna Otto was in the depths of a depressive episode last winter, a psychiatrist on campus at Oregon State referred her to the university's disability access services at the Office of the Dean of Student Life. There, she and a staff member were able to work out the details of a reasonable accommodation in which the counselor would act as a communications buffer when Otto found herself unable to reach out to the members of her lab.

Otto, who first began experiencing bipolar disorder near the end of her time as an undergraduate, said she didn't know accommodations were an option during the years she fought against her anxiety and depression.

"We ended up deciding that she would just be my contact and liaison," Otto said. "Sort of a safe third party who would be able to keep in contact with me while I'm working through my stuff or bouncing back from an episode. She would email my PI and anybody else in the department that needed to get ahold of me and sort of be a Shauna concierge."

Now nearing what will likely be the final year of her Ph.D. program, Otto said she feels optimistic about her ability to manage the depression-compounding anxiety that left her temporarily homeless near the end of her senior year of college and with mixed success during a postbaccalaureate program.

"I feel a lot better, even just reporting issues immediately to my adviser," Otto said. "Just having that crutch, having a safe person to help me manage communication."

'More than a pair of hands'

Akshat Sharma was diagnosed with major depressive disorder in 2012. His depressive episodes and medication seemed a thing of the past when he left his graduate school support network at the University of Wisconsin-Madison for a postdoctoral fellowship at the University of Texas Health San Antonio last year.

In Madison, Sharma had been a part of the local theater community. In San Antonio, he was daunted by the musical-heavy theater scene, which he saw as difficult to break into. He didn't know anyone outside his lab and felt alienated by his new

neighborhood. Two men he'd known and admired back in the Midwest died by suicide in quick succession.

In the San Antonio lab, Sharma was tasked with wrapping up a departing postdoctoral fellow's project, which involved dissecting 20 mice in a day and processing four tissues from each for flow analysis.

"That was his jam," Sharma said. "It was not mine. My idea of a big day in lab was when I would bleed five people and work with their samples. So this was all really new and terrifying."

All these factors contributed to a depressive episode that came to a head after a large experiment failed. Although his mistakes were only a small factor, Sharma took the whole of the blame on himself, he said, which pushed his depression and suicidal ideation beyond any past point.

"It's like the depressive and the suicidal ideation are two guys on Tinder who swiped right on each other but have yet to make a date," Sharma said. "But this was the one time that I think was terrifying because it was the one time that I was very seriously planning on — on doing it."

When Sharma's PI realized the gravity of the situation, she contacted Sharma's doctoral adviser at UW-Madison, who reached out to Sharma.

Soon afterward, Sharma began working with a psychiatry resident at the medical school. After an adjustment period, he resumed taking medication for his depression.

Once the worst of Sharma's depression had passed and he wanted to get back to work, his PI removed him from larger projects to ease him back into a routine, which he initially misinterpreted as being shut out due to incompetence.

"I think she just felt like I needed a break, but the state of mind that I was in I was like 'My god, they're shutting me out of experiments, because I'm incompetent.'"

When Sharma talked to his PI, he said, she told him she was trying to help him by reducing his stress — though experts might contend that an unrequested accommodation is not the most advisable course. When he told her he was embarrassed that she had to deal with his problem, he said, she responded by asking if he'd be embarrassed if he broke his leg and couldn't work.

"(That) crystallized a lot of things for me," Sharma said. "It showed that she saw me as more than a pair of hands; she was willing to be accommodating to make sure that the environment in lab was one where I could grow and feel comfortable."

The lab as family unit

While Otto, Stix and Sharma found themselves with supportive PIs, not all early-career scientists are as fortunate. While hard statistics on graduate students' relationships with their advisors are difficult to come by, accounts of the toxic relationships between students and their primary investigators or advisers abound on Twitter and various corners of the web.

"I think one of the biggest struggles for Ph.D. students is the lab environment," said Paige Bentley, the director of counseling and wellness services at Wake Forest University. "It's a small environment and it has characteristics of a family unit, so all of the dynamics that would come up

Paige Bentley, director of counseling and wellness services at Wake Forest University, thinks many Ph.D. students struggle in the lab environment. "All of the dynamics that would come up in a family show up in a lab as well," she said.

Peter J. Kennelly, a professor at Virginia Polytechnic Institute and State University, saying having a structured accommodations process and sticking to it "saves the student from having to repeatedly negotiate with instructors and relieves the instructor of trying to act as an amateur psychologist."

Each fall, the graduate school at the University of Georgia offers a brown-bag workshop on mental health for faculty members and students. "It is our most highly attended offering of the entire year — every single year," said Suzanne Barbour, the dean.

in a family show up in a lab as well."

For Beth Haas, an assistant professor of chemistry at Misericordia University, a history of dealing with mental illness has helped inform interactions with students who might be struggling themselves.

"I learned in graduate school that this terrible monster feeling I had that would grip me from time to time had a name, and that name was Anxiety, and that Anxiety at times led to depression," said Haas.

During graduate school, Haas said, she had a supportive adviser who both affirmed Haas' decision to seek counseling and asked what else she could do to help Haas.

"I'm kind of also passing that along, you know, paying it forward by telling my students, "It's OK to not feel OK sometimes, and you're not alone in that,'" Haas said.

At Misericordia University, a liberal arts college in Dallas, Pennsylvania, small class sizes give Haas the ability to get to know her students better than when she was a visiting professor at Michigan State University, she said.

"Because there are a few of them, and I get to know them so personally, I noticed things that I couldn't notice in a room of 125 (students)," she said. "So I'm noticing individual distress. And I'm also able to talk to that person because they know me and I know them."

By opening up to her students about her own history, Haas has been able to offer them a safe space to share their anxieties and illnesses.

"(A student) told me in my office hours one day that she had appreciated that I had told the class that I am a shy person and can be very anxious about meeting new people," Haas said. "That doesn't mean you have to tell everybody on the street, 'Hey, hi, I have anxiety! Nice to meet you!' But having that sense that if you had a physical health issue, people would be understanding and supportive and sympathetic and all of that. Mental health doesn't have to be different. Right?"

Extra instruction

At Virginia Polytechnic Institute and State University, Peter J. Kennelly, a professor of biochemistry, approves accommodations for some of his students almost every semester.

"In general, interacting with students through this structured process has gone smoothly. The students seem comfortable approaching instructors to discuss their need for accommodations," Kennelly said.

Most of the accommodations he sees as a lecturer fall under the umbrella of expanded test-taking options.

"In recent years, faculty at my university have been informed that we are to refer students to the counseling office rather than attempting to assist students with emotional and other issues," Kennelly said. "My own sense is that placing the decision — as to whether or not a student has a legitimate need for an accommodation — in the hands of a professionals with whom students can interact privately works well. It saves the student from having to repeatedly negotiate with instructors and relieves the instructor of trying to act as an amateur psychologist."

According to Nathan Vanderford, an assistant professor in the department of toxicology and cancer biology at the University of Kentucky and author on the 2018

Nature Biotechnology study, even if PIs have a successful history of mentoring, they sometimes feel ill-equipped to handle many sensitive topics, including the mental health struggles of their trainees.

"There's a great need for more faculty training in broad areas of mentorship to include mental health and well-being issues, because most faculty currently receive no training on how to be an effective mentor, much less on how to deal with important health and wellness issues," Vanderford said. "When Teresa and I speak about our graduate student mental health work, we make it clear that we're not healthcare professionals in this area. PIs or mentors shouldn't feel like they need to be healthcare professionals in this area either, but we all need to be equipped with the basic information on how to connect trainees and colleagues with helpful resources."

According to Suzanne Barbour, a professor and the dean of the graduate school at the University of Georgia, faculty members at UGA are encouraged to direct students who may be in a crisis to the university's Student Care and Outreach Center.

"They are kind of the nexus to direct students to services that can help them get out of crisis, whether it's an academic crisis, a financial crisis, a mental health crisis, a behavioral crisis," Barbour said. "It's a unit to which faculty can refer their students when a faculty member may say, 'Well, I just don't know how to help.'"

Additionally, the graduate school at UGA starts every academic year with a "lunch and learn" for faculty and students focused on mental health.

"It is our most highly attended offering of the entire year — every single year. We get some people who come back every year, but there are always new faces," Barbour said. "We give them a sense of what mental health resources we have on campus for students … but a lot of times, it's just them asking questions, saying, 'This is what's happening with my students. What should I do?'"

At the University of Texas Medical Branch at Galveston, David Niesel and other faculty members work similarly to inform graduate students about the resources available on campus.

"One of the things that we thought would be important was to immunize students very early in their careers," said Niesel, senior vice president and dean of the graduate school of biomedical sciences.

The faculty sought to do this through adding material about survival skills for burnout and depression to a pre-existing longitudinal course about ethics, in addition to providing graduate students in the course with information about the office of counseling and psychological services.

At UCSD, Boval and colleagues work with the Teaching and Learning Commons, a section of the executive vice chancellor's executive branch, to increase institutional awareness of the accommodations process. Last summer, the commons mandated that instructional assistants on campus, who lead small discussion sections of 25 to 30 students for large lecture courses, needed to go through an online training program about disability and accommodations.

"The hope is that as our campus grows, we're going to continue to have more instructional assistants on the front line with the students," Boval said. "We're hoping that by having this mandatory training, we give them tools and skills that they can start using their first quarter in their roles, and that they will start educating, in small ways, the faculty that they report to."

Disclosure

As Stix looks to the future of her scientific career, she's uncertain about how PIs might react to her mental health status. (Author's note: For an additional perspective on this conundrum, see Susanna Harris' essay on page 46, "Mental Illness Should Not Disqualify Me.")

"I don't mind saying that I have anxiety or that I'm on SSRIs (selective serotonin reuptake inhibitors), but I know that some people judge you differently because of that," Stix said.

Stix thinks she might stay in her current lab for graduate school but doesn't know how accepting other PIs might be about having a dog in the lab, even with the mandatory protections of the ADA.

"I don't want to limit where I go," she said. "But I also know that, unfortunately, it's a big risk to go elsewhere, because even with interviewing, I might not know how they'd treat me there, how they'd treat her."

Laurel Oldach contributed to this report.

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The fast-acting drug offers a new way to treat depression and fathom its origins. Recent approval of a nasal spray promises to expand access, but much remains unknown about long-term use and the potential for abuse.

At 32, Raquel Bennett was looking for a reason to live. She'd struggled with severe depression for more than a decade, trying multiple antidepressants and years of talk therapy. The treatment helped, but not enough to make it seem worth living with a debilitating mental illness, she says. "I was desperate."

In 2002, following a friend's suggestion, Bennett received an injection of ketamine, an anesthetic and psychedelic party drug also known as Special K. During her first ketamine trip, Bennett hallucinated that God inserted a giant golden key into her ear, turning on her brain. "It was as if I was living in a dark house and suddenly the lights came on," she says. "Suddenly everything seemed illuminated."

The drug lifted Bennett's depression and dispelled her thoughts of suicide within minutes. The effect lasted for several months, and, she says, the respite saved her life. She was fascinated by the drug's rapid effects and went on to earn a doctoral degree in psychology, writing her dissertation about ketamine. Today, she works at a clinic in Berkeley, California, that specializes in using ketamine to treat depression. "This medicine works differently and better than any other medication I've tried," she says.

Listening to ketamine

By Emily Underwood, Knowable Magazine

When Bennett experimented with ketamine, the notion of using a psychedelic rave drug for depression was still decidedly fringe. Since the first clinical trials in the early 2000s, however, dozens of studies have shown that a low dose of ketamine delivered via IV can relieve the symptoms of depression, including thoughts of suicide, within hours.

Even a low dose can have intense side effects, such as the sensation of being outside one's body, vivid hallucinations, confusion and nausea. The antidepressant effects of ketamine typically don't last more than a week or two. But the drug appears to work where no others have — in the roughly 30 percent of people with major depression who, like Bennett, don't respond to other treatments. It also works fast, a major advantage for suicidal patients who can't wait weeks for traditional antidepressants to kick in.

"When you prescribe Prozac, you have to convince people that it's worth taking a medication for several weeks," says John Krystal, a psychiatrist and neuroscientist at Yale University in New Haven, Connecticut. "With ketamine, patients may feel better that day, or by the next morning."

COURTESY OF RAQUEL BENNETT

Raquel Bennett is a postdoctoral fellow in clinical psychology and founder of KRIYA Institute, which works with patients seeking psychotherapy, medication management and ketamine treatment. She received her first ketamine treatment in 2002.

Depression, fast and slow

In 2001, writer Andrew Solomon published a haunting description of the depression that derailed his early 30s: "If one imagines a soul of iron that weathers with grief and rusts with mild depression, then major depression is the startling collapse of a whole structure," he wrote.

When Solomon first fell ill, in the 1990s, many clinicians and researchers presumed that the pathological brain changes underlying depression were inherently slow to repair. This mind-set was rooted in the modest but controversial success of a class of slow-acting drugs that includes Prozac.

Developed in the 1950s, the drugs were first inspired by the chance observation that a hypertension drug called reserpine — an extract of the plant Rauwolfia serpentina, or devil pepper — made people intensely depressed. After discovering that reserpine depletes monoamine neurotransmitters in the brain, including serotonin and norepinephrine, scientists hypothesized that low neurotransmitter levels causedepression. They went on to develop monoaminergic antidepressants, drugs designed to increase circulating levels of these chemicals in the brain.

Today, monoaminergic antidepressants include selective serotonin reuptake inhibitors (SSRIs) such as Prozac, Lexapro and Zoloft, as well as the older and less commonly prescribed monoamine oxidase inhibitors (MAOIs) and tricyclic and tetracyclic antidepressants. Scientists have long debated whether the drugs work at all, but the most comprehensive study to date — published in The Lancet in 2018 — suggests that they do lower depression symptoms in about 60 percent of depressed people, albeit only modestly more than taking a placebo.

The benefits start to show up only after several weeks of treatment, however, and roughly a third of people with major depression disorder – called treatment-resistant patients — don't respond to at least two types of monoaminergic antidepressant.

By the early 2000s, the monoamine hypothesis had unraveled. This was partly due to the antidepressants' mediocre performance in patients, and partly to experiments which showed that depleting neurotransmitter levels in healthy people does not make people depressed. Scientists now believe that drugs like Prozac do not directly treat depression's root cause. Instead, they think the drugs work via an indirect mechanism to subtly boost the growth of synapses and the birth of new neurons, and that this somehow relieves symptoms.

Solomon's bleak metaphor of corrosion was at least partly grounded in science. Many scientists now agree that depression slowly eats away at the neural pathways underlying our sense of worth and well-being, our desire to go to the movies or get out of bed. But research into ketamine holds out new hope that — unlike rusted iron — the depressed brain can be restored, by repairing and strengthening the neural circuits that regulate mood. *—Emily Underwood*

VINAYARAJ/WIKIMEDIA COMMONS

Slow-acting antidepressant drugs were inspired by the chance observation that a hypertension drug called reserpine — an extract of the plant Rauwolfia serpentina, or devil pepper, pictured here — made people intensely depressed.

The buzz around ketamine can drown out just how little is known about the drug. In the April 2017 JAMA Psychiatry, the American Psychiatric Association published an analysis of the evidence for ketamine treatment noting that there are few published data on the safety of repeated use, although studies of ketamine abusers — who typically use much higher doses — show that the drug can cause memory loss and bladder damage. Most clinical trials of the low dose used for depression have looked at only a single dose, following up on patients for just a week or two, so scientists don't know if it's safe to take the drug repeatedly over long periods. But that's exactly what might be necessary to keep depression at bay.

The analysis also warned about ketamine's well-established potential for abuse. Used recreationally, large doses of the drug are known to be addictive — there's some evidence that ketamine can bind to opioid receptors, raising alarms that even low doses could lead to dependence.

Bennett has now been receiving regular ketamine injections for 17 years, with few negative side effects, she says. She doesn't consider herself addicted to ketamine because she feels no desire to take it between scheduled appointments. But she does feel dependent on the drug, in the same way that a person with high blood pressure takes medication for hypertension, she says.

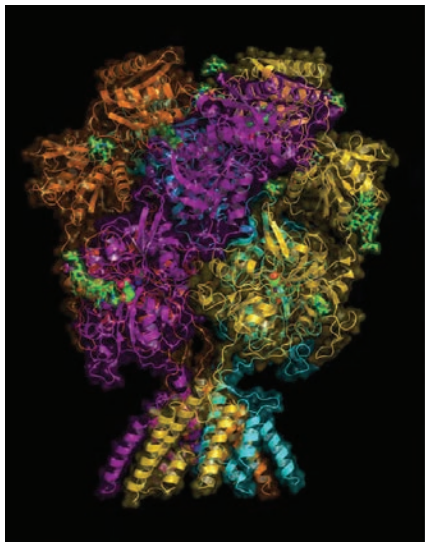
Still, she acknowledges what most clinicians and researchers contend: There simply aren't enough data to know what the optimal dose for depression is, who is most likely to benefit from ketamine treatment and what long-term treatment should look like. "There's a lot that we don't know about how to use this tool," Bennett says. "What's the best dose? What's the best route of administration? How frequently do you give ketamine treatment? What does maintenance look like? Is it OK to use this in an ongoing way?"

Despite the unknowns, pharmaceutical companies have been racing to bring the first ketamine-based antidepressant to market. In March, the US Food and Drug Administration approved a ketamine-derived nasal spray, esketamine, developed by Janssen Pharmaceuticals, a subsidiary of Johnson & Johnson. Only two of Janssen's five phase III trials had shown a benefit greater than taking a placebo. Still, in February an independent panel recommended FDA approval. That makes ketamine the first novel depression drug to hit the market in more than 50 years, notes Carlos Zarate Jr, a psychiatrist who studies mood disorder therapies at the National Institute of Mental Health.

Thousands of people are already flocking to private clinics like Bennett's, which provide intravenous ketamine infusions. Because the drug was approved in the 1970s as an anesthetic, physicians can legally provide the drug as an "off-label" depression treatment. Many ketamine clinics have long waiting lists or are so swamped that they aren't accepting new patients, and Janssen's nasal spray could rapidly expand access to treatment.

But some researchers worry that the nasal spray won't solve many of ketamine's problems and could create new ones. Although

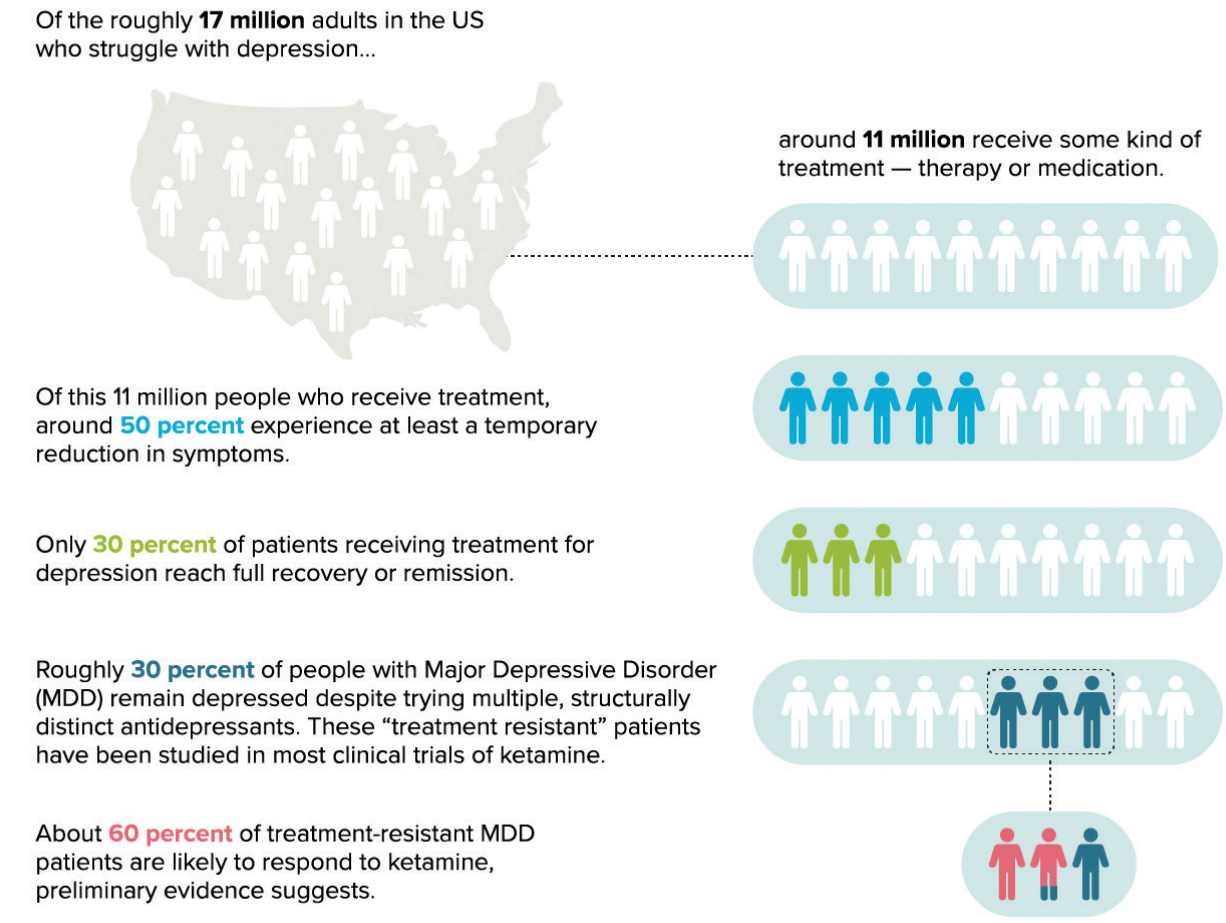
FURUKAWA LAB, CSHL



Central to the controversy over how ketamine works in the brain is the NMDA receptor (illustrated here), which binds to the neurotransmitter glutamate. Some scientists believe ketamine's antidepressant effects hinge on its ability to block NMDA receptors, but others believe the drug works via other mechanisms. Resolving that mystery is key to developing similar drugs with fewer side effects, scientists say.

There simply aren't enough data to know what the optimal dose for depression is, who is most likely to benefit from ketamine treatment and what long-term treatment should look like.

Depression treatment by the numbers



SOURCE: REPORTING BY E. UNDERWOOD

KNOWABLE MAGAZINE

the FDA is requiring that the nasal spray be administered only in a certified doctor's office or clinic, esketamine is "every bit as habit forming as regular ketamine," and will be difficult to keep out of the hands of abusers, says Scott Thompson, a neuroscientist at the University of Maryland and a coauthor with Zarate of a 2019 review on fast-acting antidepressants in the Annual Review of Pharmacology and Toxicology. A nasal spray can't deliver as precise a dose as an IV infusion, Thompson notes. "If someone has got a cold, they're not going to get the same dose."

In Thompson's view, esketamine holds few advantages over generic ketamine, which costs less than a dollar per dose, although the IV infusions in private clinics often cost hundreds of dollars per visit. Janssen has indicated that each esketamine treatment will range from $590 to $885, not including the costs of administration and observation.

Zarate and others are still thrilled to see big pharma investing in ketamine, after decades of stalled efforts to find new psychiatric drugs. "As esketamine hits the market, venture capitalists will come up with better versions and move the field forward," Zarate says. Several drug companies are now testing

other ketamine-like compounds in hopes of developing drugs that have its potent antidepressant potential without its psychedelic and dissociative side effects.

Some researchers are also testing whether ketamine works for conditions beyond depression, such as obsessive-compulsive disorder, as well as in specific subsets of patients, such as severely depressed teenagers. Other scientists are using ketamine to help untangle one of the biggest mysteries in neuroscience: What causes depression? (See Depression treatment by the numbers, page 38.)

Seeking answers in neural wiring

Thirty years ago, the prevailing thought was that low levels of certain brain chemicals, such as serotonin, caused depression. Boosting those could remove symptoms.

"I felt that depression needed months or weeks of treatment — that the plastic changes involved in the healing process would require weeks to reset themselves," says Todd Gould, a neuropharmacologist at the University of Maryland and a coauthor of the recent review paper. But ketamine's speed of action casts doubt on that idea.

Newer evidence suggests that depression is caused by problems in the neural circuits that regulate mood, Gould notes. Much of the evidence for this faulty-wiring hypothesis comes from rodents. Starting in the 1990s, scientists began to discover intriguing abnormalities in the brains of mice and rats that had been exposed to certain stressors, such as bullying by a big, aggressive male.

Stress and trauma are strong predictors of depression in people, but scientists can't ask rats or mice if they are depressed. Instead, they use behavioral tests for classic depression symptoms such as anhedonia, the inability to take joy in pleasurable activities, Thompson says. Depressed animals "give up easily" in experiments that test their willingness to work for rewards like sugar water, or their interest in the intoxicating scent of a potential mate's urine. "They can't be bothered to cross the cage," he says.

Thompson and others have found that there are fewer connections, or synapses, between neurons that communicate reward signals in the brain in depressed animals. Other labs have found shriveled connections in neuronal circuits key to decision-making, attention and memory. Brain imaging studies in people with depression have also revealed abnormal activity in neural circuits that regulate emotion, suggesting that the findings in rodents may also apply to humans.

If faulty neural connections are to blame for depression, the next question is, "How do we get atrophied neural pathways to regrow?" Krystal says.

Circuit training

The answer, many scientists now believe, is the brain's most abundant neurotransmitter, glutamate.

Glutamate is the workhorse of the brain. It relays fleeting thoughts and feelings, and enables the formation of memories by strengthening synaptic connections. Glutamate is the reason you can still ride a bike years after you learned, even if you never practiced.

Not all glutamate activity is good. Too much can cause the equivalent of an electrical storm in the brain — a seizure — and chronically high levels may lead to dementia. Abnormalities in glutamate receptors — specialized proteins on the surface of brain cells where glutamate can dock and bind — are linked to a wide array of psychiatric diseases, including depression and schizophrenia.

To maintain balance, cells called inhibitory interneurons act like brakes, releasing a neurotransmitter called GABA that quiets brain activity. Most mind-altering drugs work by changing the balance between GABA and glutamate — amphetamines and PCP enhance glutamate signaling, for example, while alcohol inhibits glutamate and boosts GABA.

By the 1990s, scientists had discovered that ketamine triggers a gush of glutamate in the brain's prefrontal cortex. This region governs attention and plays an important role in

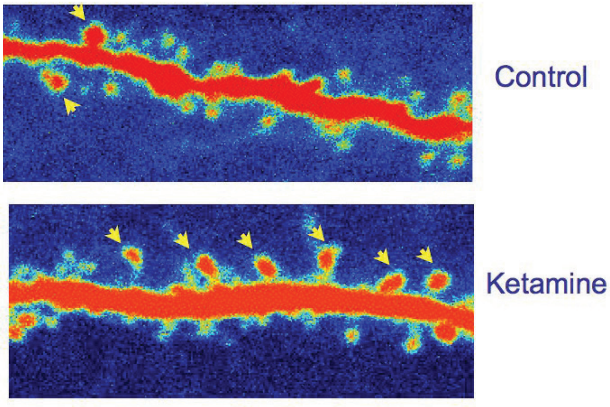
Some researchers are also testing whether ketamine works for conditions beyond depression, such as obsessive-compulsive disorder, as well as in specific subsets of patients, such as severely depressed teenagers.

emotional regulation. The out-of-body sensations that some people experience when they take ketamine may occur because this rapid release of glutamate "excites the heck out of a whole bunch of neurons" in the prefrontal cortex, says Bita Moghaddam, a neuroscientist at Oregon Health & Science University who discovered the drug's glutamate-revving effect on rats while studying schizophrenia.

Scientists aren't sure yet how ketamine forms stronger neural circuits. But the hypothesis goes roughly like this: When ketamine enters the brain, it causes a short-term burst of neuronal activity that triggers a series of biochemical reactions that create stronger, more plentiful synaptic connections between brain cells.

At first, many researchers thought ketamine's antidepressant effects relied on a structure located on the surface of neurons, called the NMDA receptor. Like a key that fits into different locks, ketamine can bind to several types of NMDA receptor, making neurons release the excitatory glutamate neurotransmitter.

This hypothesis suffered a blow, however, when several drugs designed to bind to the NMDA receptor (as ketamine does) failed in clinical trials for depression.



R.J. LIU, G. AGHAJANIAN & R. DUMAN

Ketamine strengthens connections between brain cells. Compared with a control, a rat neuron (red) treated with ketamine has grown more dendritic spines (shown by yellow arrows).

Esketamine also complicates the story. Ketamine is made up of two molecules that form mirror images of each other, R- and S-ketamine. Esketamine is made up of just the S form and binds roughly four times as effectively as R-ketamine to the NMDA receptor. Despite acting much more powerfully on the NMDA receptor, studies in rodents suggest that S-ketamine is a less potent antidepressant than R-ketamine, although it's not yet clear whether or not R-ketamine could work better in humans.

Zarate and others now believe ketamine may work through a different receptor that binds glutamate, called AMPA. By pinpointing which receptor ketamine acts on, researchers hope to develop a similar drug with fewer side effects. One hot lead is a compound called hydroxynorketamine (HNK) — a metabolic byproduct of ketamine that does not affect NMDA receptors but still produces rapid antidepressant effects in rodents. The drug appears to lack ketamine's disorienting side effects, and Zarate and Gould plan to launch the first small clinical trials to establish HNK's safety in humans this year, likely in around 70 people. "I think we have a very good drug candidate," Gould says. (Zarate and Gould, among others, have disclosed that they are listed on patents for HNK, so they stand to share in any future royalties received by their employers.)

Plastic synaptic remodelers

To alter how the brain processes mood, scientists believe ketamine must ultimately change synapses. In experiments in rodents, Ron Duman of Yale University has shown that both ketamine and HNK can harness one of the brain's most important tools for synaptic remodeling: brain-derived neurotrophic factor, or BDNF.

BDNF is a protein intimately involved in shaping synapses during brain development and throughout the lifespan. Healthy brain function depends on having just the right amount of BDNF in the right place at the right time. Many mental illnesses, including

depression, are associated with low or abnormal amounts of the protein. For example, samples of brain tissue from people who have died by suicide often contain abnormally low amounts of BDNF.

Duman and colleagues have found that both ketamine and HNK cause a sharp uptick in the amount of BDNF that is released from neurons. This increase is required for the drugs' antidepressant effects, and for the increase in dendritic spines — the stubby protrusions that form synaptic connections with other neurons. Both ketamine and HNK also seem to reduce inflammation, which has been linked repeatedly to the stress-induced loss of synapses.

Ketamine is not the only compound that can induce rapid synaptic plasticity: Other psychedelics, such as ecstasy (MDMA), acid (LSD), and DMT also trigger similar structural changes in neurons and rapid antidepressant effects in rodents, researchers at the University of California at Davis recently found. The effects don't hinge on getting high, the team reported in March in ACS Chemical Neuroscience. Even very small doses — too low to cause perceptual distortions — can increase synapse density and lift depression.

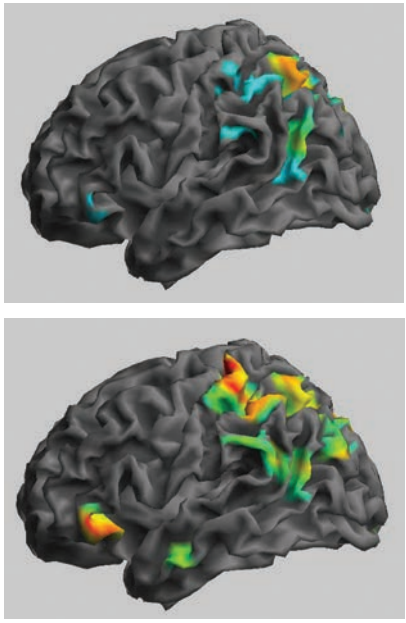
Traditional antidepressants such as Prozac also increase BDNF levels in the brain, but not nearly as fast as ketamine does, Duman says. That is why most antidepressants take so long to remodel synapses and relieve depression symptoms, he says.

Dissecting depression

Beyond promising new treatments, Zarate and other researchers see ketamine as a powerful tool for probing depression's tangled neurobiology. Studies in mice and rats are a good start, but scientists need to study the drug in people to truly understand how ketamine affects the brain. Unlike traditional, slower-acting antidepressants, ketamine lends itself to short-term lab experiments.

Zarate is using neuroimaging tools such as fMRI to study the human brain on ketamine. Past studies have shown that in people with depression, communication among several key brain networks is disrupted. One network, called the default-mode network (DMN), is involved in self-referential thoughts such as ruminating about one's problems or flaws. This network tends to be hyperactive in people with depression, and less connected to more outwardly attuned brain networks such as the salience network, which helps the brain notice and respond to its surroundings.

In one recent study, Zarate and his colleagues found that after receiving an IV dose of ketamine, people with depression had more normal activity in the default mode network, and that it was better connected to the salience network. At least temporarily, the drug seems to help people get unstuck from patterns of brain activity associated with repetitive, negative thoughts. Zarate does caution that the study results need to be replicated.



CARLOS ZARATE, JESSICA GILBERT/ETPP, NIMH

Ketamine appears to strengthen connections between neural networks in people with severe depression. In a study comparing neural activity prior to a ketamine infusion (top) and six to nine hours after an infusion (bottom), a single dose made the brain more responsive to a simple sensory stimulus, the light stroking of a finger.

By pinpointing which receptor ketamine acts on, researchers hope to develop a similar drug with fewer side effects.

Ketamine has been deemed safe to use as an anesthetic in children, but there aren't yet sufficient clinical data to show how low, repeated doses of ketamine used for depression could affect the developing brain.

The team has also used brain imaging to study how ketamine affects suicidal thoughts. About four hours after an infusion of ketamine, a chunk of the prefrontal cortex that is hyperactive in people with depression had calmed down, researchers found, which correlated with people reporting fewer thoughts of suicide.

Ketamine also seems to tune other brain regions that are key to effective treatment. Last year, scientists published a study in mice showing that ketamine quiets abnormal activity in the lateral habenula, a small nodule wedged deep under the cortex. Some researchers have described the lateral habenula as the brain's "disappointment center." The region is responsible for learning from negative experiences, and is hyperactive in people with depression, as if "broadcasting negative feelings and thoughts," Thompson says.

Such studies remain exploratory. As to why ketamine works — and just as important, why its effects are transient — scientists are still speculating. "I think ketamine is resetting neural circuits in a way that improves the symptoms of depression, but the risk factors — whether genetic, environmental or other risk factors — are still present," Gould says. "It seems to help reset things temporarily, but the underlying cause is not necessarily resolved."

Helen Mayberg, a neurologist at Mount Sinai Hospital in New York who specializes in using an experimental procedure called deep brain stimulation to treat depression, suggests that ketamine may be like using a defibrillator on someone experiencing cardiac arrhythmia. "I am not addressing the fact that you have underlying heart disease, but now that your arrhythmia is gone, I can concentrate on other treatments."

It's important to put the potential risks of ketamine into perspective, particularly for people contemplating suicide, researchers emphasize. Most people are willing to tolerate severe side effects for other life-saving treatments, such as cancer drugs, Mayberg points out. "If you can interrupt an extreme suicidal plan and ideation, I'll take that."

Ketamine in teens?

For Krystal, weighing ketamine's still largely uncharted risks and potential rewards ultimately comes down to a deeply personal question: "What would we want for ourselves? For our families? Do we want them to have to go through several failed trials over several months, or even a year, before taking a medication that might make their depression better in 24 hours?"

Some of the hardest decisions are likely to involve children and adolescents. Hospitalization for youth suicide attempts and ideation nearly doubled between 2008 and 2015, leaving many clinicians — and parents — desperate for more effective and rapid treatments. Left untreated, depression is "really bad for the brain" and can cause serious, long-term cognitive and developmental problems when it starts young, Zarate says. "The question is, is that going to be better than the long-term side effects of ketamine?"

Scientists don't yet know. Ketamine has been deemed safe to use as an anesthetic in children, but there aren't yet sufficient clinical data to show how low, repeated doses of ketamine used for depression could affect the developing brain.

On a more fundamental level, scientists don't fully understand the neurobiology of adolescent depression, notes psychiatrist Kathryn Cullen of the University of Minnesota. It may involve abnormalities in brain development, such as the way the prefrontal cortex connects to brain regions that process emotion, but "we don't know if the brain connection abnormalities emerge because of toxic stress induced by depression, or if these abnormalities predispose people to develop depression, or if depression itself reflects abnormal development," Cullen says. "It's critical to figure out how to alleviate the biological changes that are associated with [teen] depression so that the brain can get back on a healthy trajectory."

Two recent clinical trials — one at Yale and another at Minnesota run by Cullen — have found that ketamine can lower symp-

toms in severely depressed teenagers, but neither study was set up to follow the teenagers long-term, says Cullen. Janssen is currently running a trial of its esketamine nasal spray with 145 youths who are suicidal, but the results of that study have not been published yet. Cullen thinks ketamine has potential for use in teens, particularly to avoid suicide, but "there are still a lot of unknowns."

Not just a quick fix

Worldwide, depression afflicts more than 300 million people, making it the leading global cause of disability. When contemplating such overwhelming misery, the vision of a world in which depression can be cured with a single injection or squirt of nasal spray holds obvious appeal.

But — despite the hype — that is not what ketamine offers, Bennett says. Based on her own experience as a patient, and her clinical work, she is troubled by the framing of ketamine as a "rapid" depression treatment if that precludes the slower, more effortful process of psychotherapy. Without psychotherapy, she says, "you're not giving patients any tools to help themselves, just making them dependent on a molecule that has temporary effects. When the effect wears off, they have to go back for more medicine. This is going to be lucrative for the pharmaceutical company but probably not in the patient's best interest."

In Bennett's clinic, ketamine is administered only alongside talk therapy, which she uses to prepare patients before they take ketamine, and afterward to help them process the experience. "I think this is the only ethical way" to administer a drug that can trigger disorienting psychedelic experiences, she says. "This isn't a 'take two and call me in the morning' situation."

There's growing scientific interest in whether ketamine can enhance the effectiveness of therapy by increasing the brain's ability to remodel circuits through experience, Krystal notes. And in 2017 a small Yale study found that providing cognitive behavioral therapy in tandem with ketamine can extend the drug's antidepressant effects.

JANSSEN PHARMACEUTICALS, INC.

Although clinicians are hopeful that Janssen Pharmaceutical's newly approved esketamine nasal spray, Spravato, will expand access to treatment, many also worry about the drug's potential for abuse.

Unlike some researchers and pharmaceutical companies, which consider ketamine's and esketamine's hallucinogenic side effects inherently negative, Bennett thinks that for some people the visions can be positive — particularly in the context of therapy. There's scant scientific evidence to support the idea that such hallucinations are therapeutic, and they can be deeply disturbing for some people. (If people who experience hallucinations do better, it may simply be because they have received a higher dose of ketamine, Krystal points out.)

Still, Bennett thinks researchers and clinicians need to stay open-minded about why ketamine is helping people — and be more attentive to the settings in which ketamine and esketamine are administered. "People consistently report that they experience the presence of God, or their own sacredness," she says. "When someone comes to my office wanting to kill themselves, ready to die — and then they have a transformational moment where they believe their life is sacred — it's indescribable how exciting that is as a clinician."

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FROM ANNUAL REVIEWS

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Understanding the link between metabolism and aging

Princeton postdoc aims to motivate younger scientists

By Courtney Chandler

Growing up in rural Mississippi, Melanie McReynolds used to watch St. Jude Children's Research Hospital infomercials that focused on scientists and their findings; those TV segments sparked her interest in research.

"At a young age, I didn't realize the in-depth scientific process I was learning, but it was so inspirational to hear and see the scientific story unfold and come to life," she said.

"And then in college, I was intrigued by the ability to ask and answer questions of the unknown."

McReynolds followed in her parents' footsteps and attended Alcorn State University in Mississippi for her undergraduate studies. After her sophomore year, she was one of 10 top Alcorn students selected for a research trip to Bangalore, India.

"This was my first experience with biomedical research," she said. "It changed my life and promoted my love for science."

She also participated in the now-defunct Alcorn State/Penn State Bridges to the Doctorate Program, funded by the National Institutes of Health to promote science training for underrepresented minorities. At the program's end, McReynolds had a bachelor's degree from Alcorn and a master's from Penn State, where she did research in Craig Cameron's lab. The Bridges program triggered her interest in diseases related to metabolism and aging.

Now a Howard Hughes Medical Institute Hanna Gray fellow and postdoctoral research assistant at Princeton University, McReynolds studies diseases of aging in Joshua Rabinowitz's lab. She focuses on how the molecule nicotinamide adenine dinucleotide, or NAD+, is produced and used. Because NAD+ can carry electrons between chemical reactions, it is involved in myriad processes within cells.

Previous studies have associated a decline in NAD+ with aging and disease, and McReynolds describes the molecule as a "master regulator" of age-dependent pathology. She investigates NAD+ metabolic flux in young and old mice, using isotope labeling, mass spectrometry and quantitative modeling to understand how the rates of production and consumption of the NAD+ chemical backbone vary between these groups.

"These are fundamental questions the field needs answered," McReynolds said. "Our initial results are exciting and will hopefully be published soon."

This type of metabolic flux analysis isn't new to McReynolds. As a graduate student in Wendy Hanna–Rose's lab at Penn State, she studied NAD+ biosynthesis. She pioneered many mass spectrometric and isotopic labeling techniques to study the physiological roles of NAD+ in the nematode Caenorhabditis elegans.

"I'd never worked with nematodes before, and it was fascinating to integrate genetics, metabolism and biochemistry all together," she said.

She received numerous awards for her work, including the American Society for Biochemistry and Molecular Biology 2016 Best Poster Award in the category metabolism, disease and drug design. She defended her thesis in 2017 and credits Hanna–Rose with molding her as a scientist and teaching her to think outside the box.

"Melanie approached her research with confidence from the start," Hanna–Rose said. "She liked to think creatively about how to approach problems, and it was fun to see her mature in this creativity to start focusing it in productive directions."

Inspired in part by a love of teaching and mentoring, McReynolds decided to stay in academia, leading to her position at Princeton. She also wants to lead by example.

"I want there to be a lot of people of color in tenure positions," she said. "I want to make sure I can be an example for others, or a representation for others, who also want to pursue academic science."

McReynolds has struggled with doubt and adversity. During her second year as a graduate student, she took a four-part candidacy exam that included a paper critique, paper presentation, research proposal and

COURTESY OF MELANIE MCREYNOLDS

In addition to her research, Melanie McReynolds does motivational speaking, sharing her insight with grad students and undergrads.

chalk talk on the proposal.

"I bombed my chalk talk," she said. "I was still getting familiar with the research, was still learning how to approach it, and had to repeat the chalk talk."

McReynolds didn't let this set her back. She learned NAD+ metabolism and biosynthesis in detail, which was important for her current and future research. When the time came for her second chalk talk, her friends showed up with balloons and cheers to show their support. She passed without issue.

"The experience strengthened my foundation," she said. "I could look at it as something devastating, but I look at it as something that strengthened me as a researcher and scientist."

McReynolds also does motivational speaking outside the lab, sharing her insight with graduate students and undergraduates majoring in science, technology, engineering and mathematics at various universities. Her go-to advice is useful for scientists and nonscientists alike:

"Trust the process and trust your science. Stay the course. Trust your ideas and questions, and believe in yourself enough to know you can stand behind what you're producing."

These words keep McReynolds motivated. She likes the ever-changing nature of scientific research and that every day brings new tasks and new questions.

"The big question and the big picture of where this research can go, that's what keeps pushing me," she said. "Plus, the joy of scientific discovery."

Rabinowitz sees McReynolds' positivity in action in his lab. She is a methodical and determined scientist, he said, focused on the greater goal even when challenges arise.

"What truly amazes me is her positive attitude during setbacks. I see that her success on this challenging road reflects a tremendous degree of passion, determination and raw intelligence — plus her fantastic can-do attitude."

Now in her second year of postdoctoral work, McReynolds will continue to analyze NAD+ flux and how it relates to aging and disease. Her HHMI Hana Gray fellowship ensures $1.4 million in funding over eight years. She aims someday to run her own lab focused on metabolism-related diseases of aging and hopes her research will influence drug discovery to combat these diseases.

Courtney Chandler (cochandl@umaryland.edu) is a graduate student at the University of Maryland, Baltimore. Follow her on Twitter @CourtneyEChan.

Mental illness should not disqualify me

By Susanna Harris

Am I emotionally stable? This old question came crawling back when I saw a screenshot of a university recommendation form that asked for an assessment of students' emotional stability.* Nestled between "This applicant shows integrity" and "This applicant is able to give clear, concise oral presentations," the survey offered a multiple-choice response to "This applicant is emotionally stable."

How would I be scored? How would I rate myself, and would that rating matter if they knew my full background?

A memory bubbled up from nearly four years ago. I was preparing my application for the National Science Foundation's Graduate Research Fellowship Program. A professor in my program was assigned to help edit the proposal, and I sat in his office. The scientific research was fine, he said; it was logically sound and relevant to the foundation's goals. The personal statement required major improvements.

"How do you show them you're not just another little white girl?"

I was shocked, but I now appreciate his honesty that my bland story about loving science as a child wouldn't get me very far.

After digging around in my brain, we examined how my love for biology not only started when I was young but also forced me to deal with the crippling social anxiety that had been part of me for just as long. It was a true story of overcoming obstacles through effort, all in the name of science.

The professor told me to make it clear that I was not relying on medication or therapy; otherwise, the application committee might not feel confident in my abilities. Though his words come back to annoy me when I'm introduced as an advocate for mental health, making me feel afraid or ashamed to speak so publicly to my peers, I believe his advice was crucial in winning the fellowship.

My application might have ended up on the desk of a reviewer who understood the value of seeking help and of being wise enough to use it. Such amazing people surround me now. But maybe my story would have been read by one of the many people studies have shown to have subconscious, or even conscious, biases against those of us with mental illness. Maybe it would have been read by someone who, like the professor advising me, couldn't see that a diagnosed and treated mental illness was not a weakness.

In my personal statement, I wrote that I had finished treatment for mental illness. That was true when I submitted the proposal. A year after I was awarded the NSF fellowship, my next mental health crisis occurred.

Would the NSF have funded me if they had known about all of this? I am tenacious, responsible, reliable and intelligent. I love learning and discussing science. I believe academia can be a wonderful place where brilliant minds come together to help each other.

But am I emotionally stable?

When we believe that we have achieved our status by luck or help and that we would be dismissed if our true selves were discovered, that's called imposter syndrome. But what if society at large, knowing our truth, really wouldn't think we belong? If value in academia is based on the ability to think, what happens when a person admits their mind is sometimes broken?

Should we encourage others to be open about mental illness in a space where they might face retribution? It's a valid question when being outed for mental illness really does threaten professional standing and can affect relationships throughout a career.

I am emotionally stable-ish. On medication and with ongoing psychotherapy, I can handle more stress and disturbances than ever before. I became able to do this only by acknowledging that something was wrong in the pipeline of my thoughts and making the terrifying decision to get help. Without a support system of doctors and friends, I operate well below my maximum ability; with care and treatment, I am a successful graduate student, skillful researcher and overall way better human.

Reaching out for support is a

Should we encourage others to be open about mental illness in a space where they might face retribution?

sign of self-awareness and of our strength. Estimates vary, but if a significant minority of graduate students are struggling with symptoms of mental illness, excluding anyone who may be categorized as "emotionally unstable" will debilitate our academic community. Enforcing a system of bias against disclosing mental illness only pushes people to let their illness grow until it overtakes them.

By providing support, we can stabilize almost anything and make it more resilient — including a person. We can change the environment within academia to do just that, and I believe it will make us better as a community. Instead of pressuring our students and professors to hide their mental illnesses or disclose "emotional stability" status, let's create a system that supports them throughout the relatively unstable paths of academia.

**After I asked the university about its recommendation form, the question about emotional stability was removed immediately. It will be a much longer process to remove these same questions from the minds of the application reviewers and the prejudice that comes along with them.*

Susanna Harris (susannalharris@gmail.com) is a Ph.D. candidate in microbiology at the University of North Carolina at Chapel Hill and founder of ThePhDepression, a project to increase visibility of those in academia who struggle with mental health issues. Follow her on Twitter and Instagram @susannalharris.

What I wish people understood about studying science at a small college

By Kerri Beth Slaughter

Sometimes people ask me why I chose to attend a small liberal arts college to pursue a basic science degree. I won't tell you that attending a small school is the best choice for everyone, but it was the right decision for me.

As a kid in public school, I always made good grades, but my teachers thought I was shy. I rarely spoke up to answer questions. I preferred to listen and observe instead of jumping into the discussion. When I began looking at colleges, I was daunted by the idea of attending a large university with freshman classes of 100-plus students.

I eventually interviewed for scholarships at Milligan College, a small Christian school nestled in the Appalachian Mountains of East Tennessee. The campus had fewer students than my high school. During my interview, I met with three professors and the college president. Although I was a little nervous at first, I started to feel at ease as I talked with them about my goals and interests in science. They helped me feel comfortable in my own skin, and I was impressed by how much they enjoyed engaging with students.

A few months later, I sat down at a desk for my first class in the Milligan science building, built in 1972; the funky architecture and funky smells were the first things I noticed. I didn't realize how much I would learn and grow there during my four years in college, not because of the building itself but because of the professors who invested in me.

My professors changed science from words in a textbook to something that I could see, touch and imagine.

Richard Lura taught organic chemistry and biochemistry, two classes that often inspire a love–hate relationship for science students. He never used PowerPoint slides or tried to integrate technology in the classroom. Rather, he transformed a basic science class into an interactive discussion and learning experience.

For the first lecture of each new unit in organic chemistry, instead of plowing through the details of the next chapter, Dr. Lura gave a broad overview of the material. He engaged the class in discussion about where we might find organic compounds in our daily lives or in industry. After studying for the previous unit's exam, this discussion helped me remember the big picture of what I was learning.

Dr. Lura sometimes asked students to act out chemical reactions so we could visualize what happens at the molecular level. These comical demonstrations, such as modeling nucleophilic substitution reactions, helped me develop a deeper understanding of chemistry instead of simply memorizing the material. The class interactions also encouraged camaraderie among the students, and we spent many hours helping each other solve problems to prepare for exams.

My biology professor was Michael Whitney. In one of our cell biology classes, he handed each student a container of Play-Doh, and we spent part of the period molding actin monomers and tubulin dimers to learn about assembly of the cytoskeleton. Beyond being a fun activity for the students, Dr. Whitney's effort to help us become visual learners sparked my fascination with the cytoskeleton, a topic that will be a significant focus of my dissertation research.

At Milligan College, I grew close to the community of science professors and students as we learned together in the lab and classroom. My professors changed science from words in a textbook to something that I could see, touch and imagine. They helped me learn how to ask thoughtful questions about science instead of accepting what I was told as fact.

My professors also taught me how studying science could strengthen my Christian faith, and they provided a safe space to discuss controversial topics. Over time, I found myself speaking up in class more often to answer questions and build on class discussions. I was no longer the shy kid sitting quietly in the corner of the classroom.

Scientists can be born in the absence of state-of-the art research facilities and millions of dollars in funding. Sometimes all you need is a creative professor, an eager student and a bit of Play-Doh.

By senior year, I had decided to pursue a Ph.D. in biomedical science so that I could become a science professor like the ones who influenced me at Milligan College. I am now a doctoral candidate in the biochemistry department at the University of Kentucky, and my small-school background has contributed greatly to my success as a graduate student, scientist and communicator.

I've never been fond of the phrase "coming out of your shell," perhaps because I heard it too often as a kid. However, I wholeheartedly believe that my professors at Milligan College helped draw me out so that I could reach my full potential as a scientist.

Scientists can be born in the absence of state-of-the art research facilities and millions of dollars in funding. Sometimes all you need is a creative professor, an eager student and a bit of Play-Doh.

Kerri Beth Slaughter
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COURTESY OF KERRI BETH SLAUGHTER

Kerri Beth Slaughter, left, and fellow science club members dressed up as elements from the periodic table to hand out candy at Milligan College's Trunk or Treat.

University program aims to serve and inspire future scientists

By Madison Honer & Maura Southwell

When Edwin Li joined the Saint Joseph's University biology department in 2010, he noticed the school's strong culture of community service. As a Jesuit institution, SJU encourages students and faculty members to work for social justice and serve others, a practice described in Latin as "cura personalis," which translates as "care for the entire person."

Li first experienced science outreach at SJU with a molecular biology graduate student, Jessica King, who was a GeoKids fellow. The GeoKids Learning Integrating Nature, Kids and Science, or LINKS, fellowship places graduate and advanced undergraduate fellows into first- through fifth-grade classrooms in Philadelphia. Mentors from the Wagner Free Institute of Science, a museum in the city, work with the SJU fellows who co-teach weekly hands-on lessons in natural science.

"I noticed all of the outreach programs were focused on macro-level biology — teaching elementary students about ecosystems and organisms," Li said.

Li wanted to develop an outreach program based in molecular biology, his area of expertise. He envisioned undergraduate biology majors and high school students learning together and inspiring each other.

In 2013, Li applied for grants from the American Society for Biochemistry and Molecular Biology to fund a partnership between high school teachers and academic researchers. He recruited SJU microbiologist Brian Forster, SJU science outreach coordinator Caitlin Fritz and honors biology teacher Matthew Jurkiewicz from Bishop McDevitt High School in Wyncote, Pennsylvania, to create High School LINKS, modeled on the mentor-based GeoKids program. They developed a curriculum, "Genes, mutations and diseases: Understanding the origins of genetic disorders through experiential learning."

In the program, undergraduate LINKS fellows, mentored by Li and Forster, lead a five-week unit focused on DNA structures and functions, genetic mutation and inheritance, gene expression, and protein structure and functions. The high school students learn techniques such as polymerase chain reaction, electrophoresis, bacterial transformation and enzyme-linked immunosorbent assay. The unit culminates in a field trip to SJU's laboratories, where they analyze the phenotype, chromosomes, proteins and DNA of three samples to determine which patients are diagnosed with sickle cell anemia, Down syndrome and Cri-du-chat syndrome.

Jurkiewicz, an SJU alumnus, now has had LINKS fellows in his classroom for six years. "For many of my students," he said, "the biggest takeaway from the LINKS program is to … see young men and women just a few years older than them with the desire, ability and opportunity to have a career in these fields."

High School LINKS also provides a unique opportunity for the future scientists of SJU. Marly René works as an undergraduate LINKS fellow in Jurkiewicz's honors biology class. "This experience strengthened my presentation and leadership skills," she said. "I also learned to communicate better with students and my peers, which will benefit me in interacting with colleagues, professors and professionals in the future. The students are great and so eager to learn more. It really made me realize how much of an impact outreach has on the community."

High School LINKS expanded in 2017 into Overbrook High School, 10 minutes from SJU's campus. The SJU faculty and undergraduates worked with Overbrook biology teacher Christina Johnson to develop a new curriculum focused on how genetic mutations can lead to biodiversity. During the unit, the Overbrook students visit SJU's biodiversity lab to see fish, reptiles and amphibians up close.

The field trip and the interactions with professors and college students are priceless, Johnson said. "The LINKS program allows our students who would normally not go to a college lab during their high school careers the opportunity to engage and spark an interest. They were able to visualize how genetics can play a major role in the lives of

At right, molecular biologist Edwin Li demonstrates proper micropipetting technique to Bishop McDevitt High School students during their field trip to Saint Joseph's University in March.

Below, an Overbrook High School student completes a scavenger hunt during the field trip to the Saint Joseph's University biodiversity lab in May.

MAURA SOUTHWELL & ASHLEY BLISS

living things such as an albino red ear slider turtle."

On a recent field trip, Overbrook High School students discussed how skin color is determined by genetics. Their observation of the animals' body patterns led them to talk with SJU students and faculty about how genetics influence human skin color. One Overbrook student made the connection that the skin condition vitiligo, where patches of skin lose pigment over time, may be linked to an inheritable genetic mutation.

Li has realized his goal. "The continuation and expansion of High School LINKS has allowed us to capture the interest of a wide range of students," he said. "This is one of the few outreach programs to offer SJU students the opportunity to share their passion for cellular and molecular biology, organismal and evolutionary biology, or both. We have met the diverse interest of our undergraduate students while also fulfilling the educational needs of our high school partners."

LINKS has served hundreds of high school students and has provided more than 20 SJU undergraduates with experience in science outreach and public engagement.

Alison Kloiber graduated from SJU last year and is a High School LINKS alumna. She now works in an internship using the skills she developed in the program. "While three years ago I was clueless about this field," she said, "I am now considering (science outreach) as a potential career path."

Madison Honer (mh641683@sju.edu) recently earned a B.S. in biology from Saint Joseph's University, where she led the High School LINKS program at Overbrook High School. She will pursue graduate work in biology at Saint Joseph's and continue her work in science outreach through the GeoKids LINKS fellowship.

Maura Southwell (msouthwe@sju.edu) is the project coordinator for science outreach at Saint Joseph's University, where she earned a B.S. and an M.S. in biology. Her thesis work focused on the effects of melatonin on adult zebrafish behavior. Follow her on Twitter @SJUscienceout.

LINKS fellow Madison Honer focuses a dissecting scope for Overbrook High School students to see and try to pick a roundworm during their field trip to Saint Joseph's University in May.

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Steven Elledge, *Harvard Medical School*
Matthew Ellis, *Baylor College of Medicine*
Mike MacCoss, *University of Washington*

Marcus Bantscheff, *GlaxoSmithK*

Maria Barna, *Stanford University*

Isabell Bludau, *ETH Zurich*

Chuna Choudhary, *University of Copenhagen*

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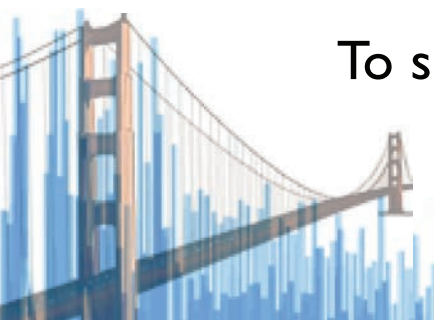

To see full program, register and book housing, visit:

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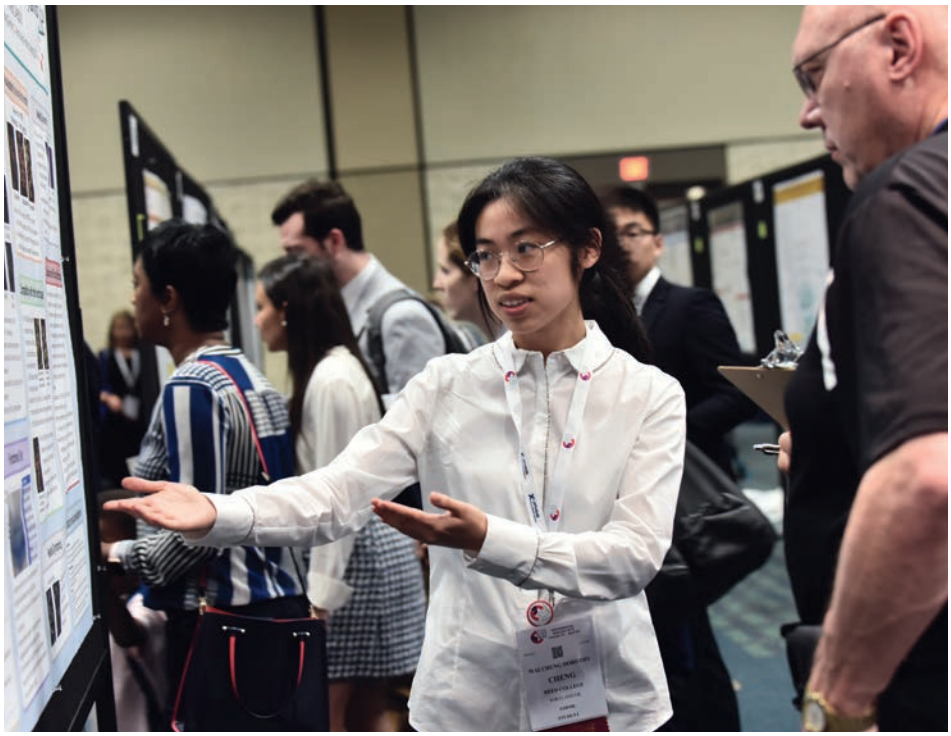
Members of the American Society for Biochemistry and Molecular Biology shared their science, learned from others and made connections at the ASBMB annual meeting held April 6–9 at the Orange County Convention Center in Orlando, Florida. To see more photos, go to asbmb.org/asbmbtoday.



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