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ASBMB TODAY

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

The Wellness Issue





Proteinases and their inhibitors

Feb. 24–26

This meeting covers diverse and vibrant fields of protease research, such as mechanistic studies on proteases in their molecular, cellular and organismic context.

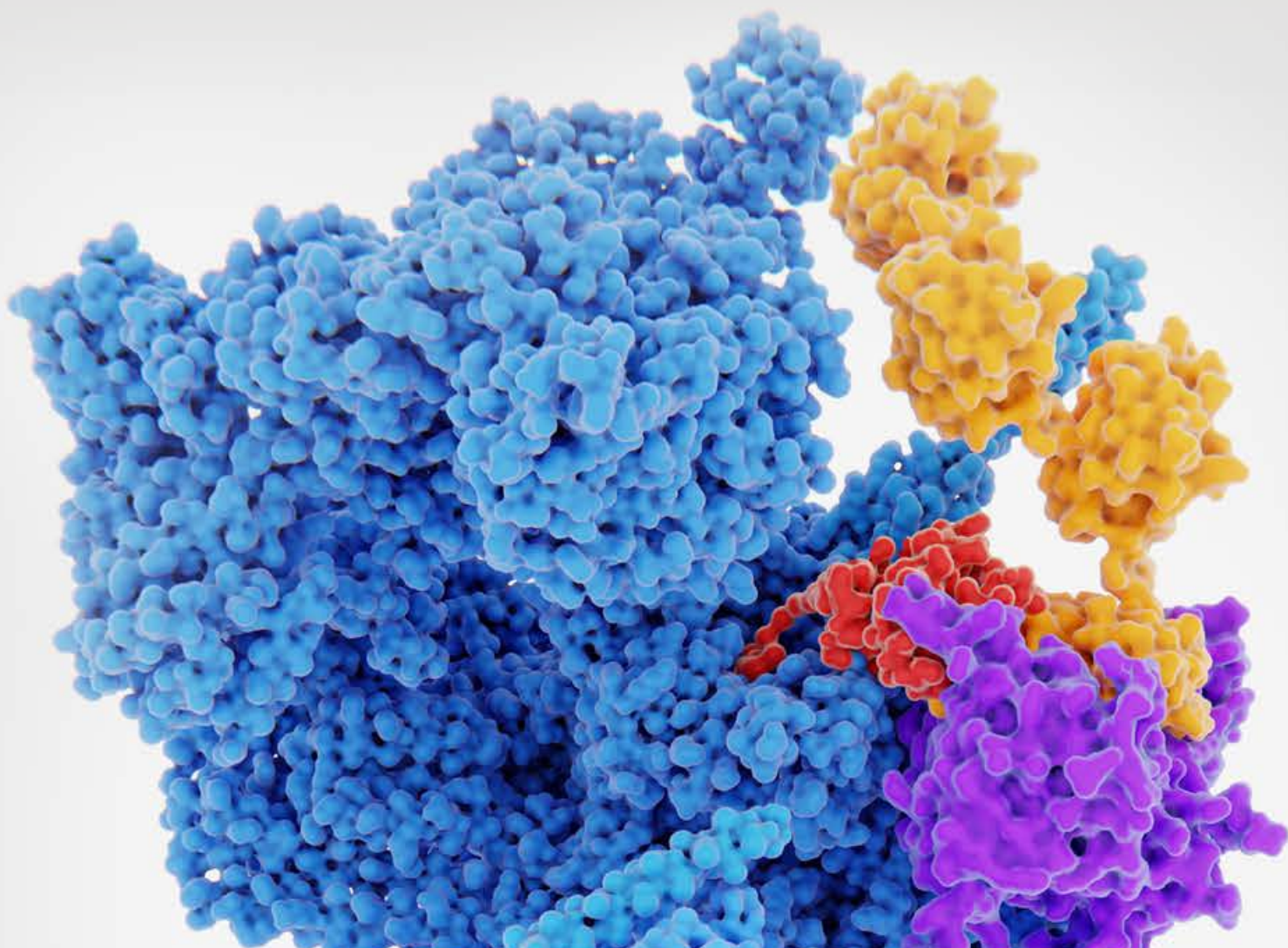
Sessions include:

- proteolysis in cancer
- proteolysis in neurosignaling and neurodegeneration
- proteolysis in blood coagulation
- discovery of protease substrates
- mechanisms and engineering of proteases, ligases, their substrates and inhibitors

Early registration deadline: Feb. 1

Learn more and register at:

asbmb.org/meetings-events/proteinases-and-their-inhibitors



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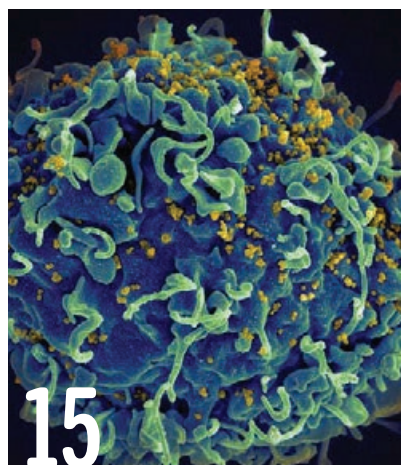
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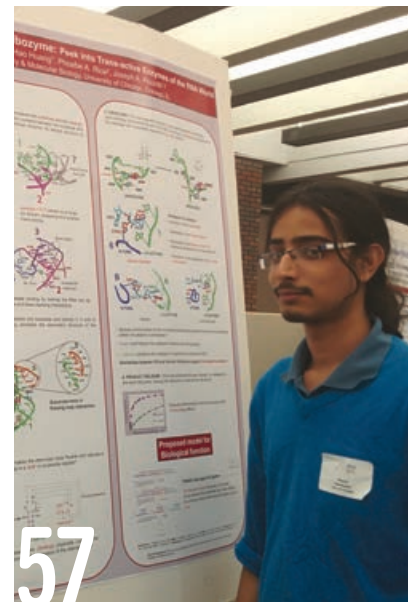
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EDITOR'S NOTE

It's the little things

By Comfort Dorn

Even before we lived under the cloud of a pandemic, I sometimes had trouble sleeping at night. Occasionally, my thoughts would race anxiously about money or my job or my family. The sheets would twist, the pillow was lumpy, and I just could not settle down.

I don't remember when or where, but at some point I read or was told that one way to address this nighttime anxiety and tension was to relax my tongue. It sounds pretty basic, almost silly, but when I unstuck my tongue from the roof of my mouth and settled it so it wasn't touching anything, the rest of me relaxed too. And more often than not, I soon drifted off.

As I read through the essays for this 2021 wellness issue of ASBMB Today, I thought about my tongue.

We asked our contributing writers and our readers to tell us something about how they have been keeping well during this year. In addition to the threat of COVID-19, we've been faced with a wild presidential election (and its aftermath) as well as the biggest racial justice movement the world has seen in more than half a century. Even those people with great self-care habits were thrown for a bit of a loop.

What struck me about the activities described in these wellness essays is how basic they are. Take a walk. Read some books. Eat nourishing food. Reach out to friends and family to create celebrations and share experiences. Ask for help. These are all things that we can and should have been doing all along.

So what is it about a pandemic that brings us back to such fundamentals? First, many of us have had more



unstructured time over the past 10 months. We have not been going to work or school. We have not been traveling or socializing in person. We have been left largely to our own devices — both electronic and mental.

But, more importantly, many of us have realized that we really do need to take care of ourselves. Wellness doesn't just happen. Our collective trauma has given us permission to ask ourselves what we need and then to do whatever it is — to give ourselves the simple care that will keep us going.

As we say goodbye to the excrement fest of 2020, I hope we can hang on to these good, simple habits of wellness. I hope we continue to care for ourselves.

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



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Collins, Kim and Qian receive Pioneer Awards

The National Institutes of Health has announced the 2020 recipients of its Pioneer Awards, a funding opportunity designed “for exceptionally creative scientists pursuing pioneering approaches.” The award, which enables a principal investigator to pursue a new research direction (the application does not require any preliminary data), consists of \$700,000 in direct costs for up to five years. Three of this year’s 10 recipients, Kathleen Collins, Peter Kim and Shu-Bing Qian, are members of the American Society for Biochemistry and Molecular Biology.

Kathleen Collins is head of the University of California, Berkeley’s division of biochemistry, biophysics and structural biology in the molecular and cellular biology department. Collins studies noncoding RNA processing, ribonucleoprotein biogenesis and the biochemistry of polymerases that use an RNA template.

She will use the Pioneer Award funding to support a project titled “Human genetic supplementation without donor DNA or a DNA break,” seeking to overcome challenges that limit the possible usefulness of genetic engineering as a therapy. The research is aimed at developing a method based on retroelements, elements of the human genome that copy themselves into new loci from RNA templates, to introduce new transgenes into nonproliferating cells, such as adult tissue. The lab hopes that this approach will avoid some of the challenges of homologous recombination at double-stranded breaks

(which CRISPR-based genome editing technologies rely on) and of using viral vectors to introduce transgenes.

Peter Kim is a biochemistry professor at Stanford University School of Medicine, a scholar at Stanford ChEM-H and lead investigator in infectious diseases at the Chan Zuckerberg Biohub. Prior to becoming a professor at Stanford, Kim spent 10 years as the president of Merck Research Laboratories. His early research at



KIM

Massachusetts Institute of Technology’s Whitehead Institute focused on the structures of proteins that mediate viral membrane fusion; since returning to academia in 2013, he has studied potential inhibitors of that fusion, focusing on HIV, and on finding ways to target protein surfaces that are difficult to target with traditional small molecules.

Using the Pioneer Award grant, Kim seeks to create “high-resolution, epitope-focused vaccines” that raise immunity against smaller regions on the target protein. In the application, he writes that this eventually could enable vaccine developers to come up with formulations that elicit broadly neutralizing antibodies, which are a tiny portion of the current antibody response to vaccines.



QIAN

Shu-Bing

Qian is a professor of molecular nutrition at Cornell University and a faculty scholar at the Howard Hughes Medical Institute. Qian’s research focuses on translational control in gene expression and

physiological stress conditions as well as the effects of RNA modifications such as adenosine methylation on cellular physiology. His lab also uses ribosome footprinting and related sequencing methods to understand how protein synthesis responds to stress.

The lab recently found that ribosome pausing in response to amino acid starvation can cause transcriptional upregulation of the same genes on which translation had stalled out. The project supported by the Pioneer Grant, “A genetic circuit formed by ribosomes,” will focus on this and other mechanisms by which translation in the cytoplasm can regulate transcription in the nucleus. Qian previously was awarded the New Innovator Award from the NIH, a program similar to the Pioneer Award but for earlier-stage investigators.

McKnight wins Welch award

Steve McKnight, a professor and former chair of the biochemistry department at the University of



MCKNIGHT

Texas Southwestern Medical Center, has received the 2020 Robert Welch Award in Chemistry.

McKnight served as president of the American Society for Biochemistry and Molecular Biology from 2014 to 2016. His career has spanned a number of biochemical research areas; he has researched gene regulation in eukaryotic cells and phase separation in proteins with low-complexity regions.

Based on his gene regulation work, McKnight founded a biotechnology company, Peloton Therapeutics. Last year the pharmaceutical company

MEMBER UPDATE

Merck acquired the company and its library of compounds that inhibit hypoxia-inducible factor 2 alpha, which are being studied as possible cancer therapies.

The award, named for 20th century Texas oil magnate Robert A. Welch, recognizes “basic chemical research that benefits humankind” and consists of \$500,000 along with a gold medallion. In a statement to Chemical & Engineering News, McKnight expressed gratitude to the Welch Foundation for its long-term support of the UTSW biochemistry department.

Three members win Biophysical Society awards

Three members of the American Society for Biochemistry and Molecular Biology — Angela Gronenborn, Carlos Bustamante and Peter H. von Hippel — have won annual awards from the Biophysical Society. They will be fêted at the BPS annual meeting scheduled to be held virtually in February.

Angela Gronenborn, the UPMC



GRONENBORN

Rosalind Franklin chair and distinguished professor of structural biology at the University of Pittsburgh School of Medicine, has won the Biophysical Society’s Founders Award for her

work in nuclear magnetic resonance spectroscopy. Gronenborn, who won the ASBMB’s Mildred Cohn Award in 2019, investigates structure, dynamics and interactions of biological macromolecules.

In a press release, BPS President Catherine A. Royer of the Rensselaer Polytechnic Institute in New York

said, “The Founders Award allows us to call attention to outstanding achievements in biophysics that are now accepted and used by others, whether that acceptance was immediate or over a period of years. Angela was among a few scientists who recognized early on the power of NMR for analysis of biomolecular systems. She played an integral role in transforming NMR into the powerful method that it is today.”

Gronenborn was elected to the National Academy of Sciences in 2007 and the American Academy of Arts and Sciences in 2018.

Carlos Bustamante, the Raymond and Beverly Sackler chair of biophysics at the University of California, Berkeley, won the Biophysical Society’s 2021 Kazuhiko Kinoshita Award in Single-Molecule Biophysics “for his



BUSTAMANTE

pioneering work in measuring and understanding orientations, rotations and dynamics of motor proteins by developing and using single-molecule imaging approaches,” according to a press release.

Bustamante, a Howard Hughes Medical Institute investigator, has been a professor at Berkeley since 1998 and is an honorary professor at the National University of San Marcos in Lima, Peru. The Kinoshita award also recognizes his commitment to outreach and collaboration.

Bustamante was elected to the National Academy of Sciences in 2002 and the American Academy of Arts and Sciences in 2015.

Peter H. von Hippel, an emeritus professor of chemistry and biochemistry and a member of the Institute of Molecular Biology at the University of

Oregon, won the Biophysical Society’s 2021 Ignacio Tinoco Award for his studies of nucleic acids and their interactions. The award, established in 2018, honors the legacy of its namesake, Ignacio “Nacho”



VON HIPPEL

Tinoco Jr., who was a pioneer in RNA folding.

“Peter honors the example set forth by Nacho, and we are pleased to award him for his many years of highly innovative scientific contributions as well as his commitment to fostering inclusive and collaborative research teams,” BPS President Royer stated in a press release.

Von Hippel was elected to the National Academy of Sciences in 1978, to the American Academy of Arts and Sciences in 1979, and to the American Philosophical Society in 2004. He won the ASBMB–Merck Award in 2000 and the BPS Founders Award in 2013.

Wei, DiMaio and Toker receive NCI awards

The National Cancer Institute’s Outstanding Investigator Award supports “accomplished



WEI

leaders in cancer research, who are providing significant contributions toward understanding cancer.” Three ASBMB members — Wenyi Wei, Daniel DiMaio and Alex

Toker — were among this year’s grant recipients.

Wenyi Wei is a professor of

pathology at Beth Israel Deaconess Medical Center and Harvard Medical School. His lab studies cell cycle regulation and ubiquitination pathways in tumor progression, focusing in particular on the Cullin–RING family of ubiquitin E3 ligases. In addition to investigating how these proteins can contribute to tumorigenesis, Wei has also begun to investigate the therapeutic potential of inducing protein degradation with PROTAC technology.

Daniel DiMaio is a professor of genetics, molecular biophysics and biochemistry, and therapeutic radiology at Yale University School of Medicine and a deputy director of the Yale Cancer Center. His lab studies the proteins that facilitate cell entry by cancer-causing papillomaviruses and polyomaviruses. They've also worked on engineering



DiMaio

simple transmembrane proteins that can activate receptors or block viral entry into cells, which may offer therapeutic applications. DiMaio is a fellow of the

American Academy of Microbiology and the American Association for the Advancement of Science.

Alex Toker is a professor of pathology at Harvard Medical School and Beth Israel Deaconess Medical Center. His lab studies the role of phosphoinositide 3-kinase, or PI3K, and AKT signaling in cancer progression. PI3K/AKT, an important growth regulatory pathway, frequently is overactivated in cancer but difficult to control through small-molecule intervention. Toker's

CONTINUED ON PAGE 6

National Academy of Medicine names Finkel, Regev as members

Among this year's 100 inductees to the National Academy of Medicine are two American Society for Biochemistry and Molecular Biology members, Toren Finkel and Aviv Regev.

Toren Finkel is a professor of medicine and director of the Aging Institute at the University of Pittsburgh. He is honored for establishing the field of redox signaling by discovering that reactive oxygen species can work as signaling molecules.



FINKEL

Subsequent research has shown that redox signaling can affect transcription, DNA modification, nutrient sensing and other signal transduction pathways, altering cellular functions including immunity, stem cell renewal and tumorigenesis. Finkel's current work focuses on changes to mitochondrial function and metabolism that accumulate with age, including in autophagy-induced mitochondrial turnover, or mitophagy, as well as mitochondrial calcium control and fatty acid oxidation.

Aviv Regev is the head of Genentech Research and Early Development. Previously, she was a professor at the Massachusetts Institute of Technology, a Howard Hughes Medical Institute investigator and a core member of the Broad Institute. The academy honored her work in single-cell genomics; Regev's lab has developed many experimental and computational methods to advance single-cell RNA sequencing and analysis, such as early approaches to leverage scRNA-seq to study cell types, states, circuits and transitions; scaling up single-cell sequencing for expression profiling of many cells; and using scRNA-seq to study tissue biology in health and disease. The award also recognized Regev's earlier work on groups of genes called modules that are expressed in concert, generating patterns of response that are important for immunity and other cellular pathways.

New NAM members are elected by current members through a process that recognizes individuals who have made major contributions to the advancement of the medical sciences, health care and public health. The newly elected members bring the NAM's total membership to more than 2,200.



REGEV

CONTINUED FROM PAGE 5

lab searches for metabolic vulnerabilities brought about by that excessive PI3K/AKT activation, which may point to more tractable drug targets. Toker is a deputy editor of the *Journal of Biological Chemistry*.



TOKER

Coincidentally, Emily Cohen, now a research scientist at the biotech startup Kronos Bio, was a grad student in DiMaio's lab from 2009 to 2014 and then did a postdoc in Toker's lab from 2015 to June of this year. DiMaio and Toker believe Cohen brought them good luck. For her part, Cohen said both helped her flourish as a scientist: "The NCI award couldn't have gone to two better principal investigators, both for their incredible scientific knowledge, foresight and creativity, and for their work as mentors to their trainees."

Stillman joins Circle Pharma science board

Bruce Stillman, president and chief executive officer of Cold Spring Harbor Laboratory in New York, has been appointed to the scientific advisory board of Circle Pharma, a biotechnology company based in San Francisco.

Stillman, who studies DNA replication in eukaryotes, has worked in yeast and human cells to identify proteins that play important roles at the replication fork and in assembling chromatin. His lab discovered the origin recognition complex, or



STILLMAN

ORC, a protein that binds to replication sites and enables chromosome replication to begin. Subsequent research has illuminated the structure of complexes that ORC forms with helicases before DNA unwinding starts and revealed that ORC stationed at the centrosome

and centromere also is involved in the regulation of chromosome separation. The work has had implications for many diseases, including cancer and rare genetic diseases caused by ORC mutations.

Stillman is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the Australian Academy of Science and a fellow of the American Association for Cancer Research and the Royal Society. He has received many awards including, in 2014, the ASBMB Herbert Tabor Research Award.

Circle Pharma is focused on developing new macrocycles, compounds that contain rings of 12 or more atoms. Well-known macrocycles include the macrolide antibiotics, porphyrin compounds such as heme, and chlorins. Although often bioactive, macrocycles can be complex to synthesize and difficult to deliver into cells. Circle's lead compounds target two cyclins, proteins involved in cell-cycle progression, and the company hopes these will be useful additions to the arsenal of cancer treatments.



Interest groups at the ASBMB annual meeting

The ASBMB encourages its members to hold topic-specific scientific seminars at the 2021 ASBMB Annual Meeting, held in conjunction with Experimental Biology 2021.

The goal is to bring together people with similar scientific interests to facilitate communication and collaboration. During these two- or three-hour events, participants can interact, present, discuss and network within a topic-specific community.

If you are interested in organizing a scientific interest group, please submit your proposal for consideration by the Meetings Committee by Feb. 1.

Donald G. Comb



Donald G. Comb, an environmentalist, biochemist and founder of New England Biolabs Inc., died Oct. 4 at his home in Gloucester, Massachusetts. He was 93.

Born in 1927, he grew up in Detroit, the second of three boys. As a child, he spent his summers in northern Michigan. He loved to fish and became interested in the life cycles of insects. He earned a Ph.D. in biochemistry from the University of Michigan, where he spent time at the university's biological station learning entomology and collecting insects.

Comb took a faculty position in the biochemistry department at Harvard Medical School, where he worked on the function of sugars and small RNAs. In the summers, he collected sea urchins and studied their early development at the Bermuda Biological Station.

After leaving Harvard, he founded New England Biolabs in 1974 as a science cooperative that provided research tools for molecular biologists. NEB was among the first companies to commercialize restriction enzymes, which cleave DNA at specific sequences and are essential tools for recombinant DNA technology. Comb established a research group at NEB to study and find cures for parasitic diseases found in developing countries.

Combs supported environmental education and was an early member of the Sierra Club. He founded a marine sanctuary in the Caribbean, worked on protecting the West Branch of Maine's Penobscot River, and helped establish the Ocean Genome Legacy, a research facility dedicated to preserving the sea's biological diversity. He supported the Union of Concerned Scientists and the Conservation Law Foundation.

A lifelong outdoorsman and fisherman, Comb also loved to sail and enjoyed identifying and collecting mushrooms. In addition to environmental groups, he supported the arts, especially local artists in Massachusetts.

He is survived by his wife, Linda Comb; three children, Michael, Dave (Coleen) and Janis Comb; 12 grandchildren; four great-grandchildren; and his former wife, Marilyn Comb.

Frank C. Greene



AGRICULTURAL RESEARCH/USDA

The American Society for Biochemistry and Molecular Biology learned recently that Frank C. Greene died last year. He was an emeritus member who joined the society in 1988.

Born Sept. 2, 1939, Greene was a plant physiologist at the United States Department of Agriculture's Western Regional Research Center in Albany, California, from the 1960s until his retirement in the early 1990s, by which time he had become the center's lead scientist. He spent most of that time studying protein expression in developing wheat.

While wheat proteins such as gluten sometimes are vilified, they are required for storing energy for the plant zygote. They also are essential for making bread and other baked products, making their expression a matter of commercial interest. Greene studied iron-binding wheat proteins called transferrins early in his career; later, he developed a yeast strain that produced the wheat protein gliadin, a component of gluten, to make biochemical studies of the protein easier.

Greene was a member of the American Society of Plant Physiologists. Colleagues say he was instrumental in the establishment of Grain Genes, an international database for oat, wheat and barley geneticists.

He is survived by his wife, Joyce Sakai, and daughter Beverly Greene. A second daughter, Deborah Greene, died in 2015.

This 1988 photo shows Frank C. Greene checking wheat plants he was using for grain protein studies.

James Siedow (1947–2020)

By Robin A. Smith

James (Jim) Siedow, Duke University's former vice provost for research and a longtime biology professor known for his kindness and quick, Texan wit, died Nov. 15 in Durham after a long battle with Parkinson's disease. He was 73.

DUKE UNIVERSITY



Plant biochemist James Siedow spent 40 years on the faculty at Duke University, 12 of them as vice provost of research. He retired in 2016.

Over the course of his 40-year career at Duke, Siedow made various contributions to our understanding of plant growth. Siedow is the author or coauthor of more than 125 scientific papers on plant respiration, the process by which plants convert the food they make through photosynthesis into the energy they need to grow.

During his tenure as the head of Duke's research enterprise, Duke's research expenditures more than doubled and the university rose in the ranks to become one of the top 10 research institutions in the nation.

One of his major contributions to plant science was working out the details of an alternative form of energy production, known as cyanide-resistant cellular respiration, which was thought to play a role in helping plants survive stress.

"Jim paid a critical role in botany, and later biology, inasmuch as he was often the only professor who could form a bridge over the chasm that separates field studies from molecular studies," said professor and dean emeritus Bill Schlesinger, who rose through the ranks alongside Siedow.

Siedow was born and raised in Houston, Texas. He graduated Phi Beta Kappa from the University of Texas at Austin in 1969 with a bachelor's degree in chemistry and

botany, then went on to earn a Ph.D. in biochemistry at Indiana University in 1972.

There, he met his future wife of 46 years, Mary Dunn Siedow, who was pursuing a Ph.D. in literacy education.

Siedow did postdoctoral research at the University of Michigan and Rice University before joining the Duke faculty in 1976. Here, he taught classes ranging from introductory biology to biophysical plant physiology, receiving the Trinity College Distinguished Teaching Award in 1984.

“He was a remarkable person in so many ways; a world-class scientist, an effective and focused leader and a beloved mentor and teacher,” said professor emeritus Norman Christensen, whose office was adjacent to Siedow’s in the basement of the Biological Sciences building for 15 years. “We were a daily feature in each other’s lives,” Christensen said.

Christensen recalls the years they spent co-teaching an introductory biology course, “referred to by some as the Jim and Norm show.” One time, Siedow “convinced one of our teaching assistants to don a gorilla outfit and jump out of a side closet during one of my lectures,” Christensen said.

“My favorite Jim tale relates to his 40th birthday party for which a group of us had arranged the appearance of a clown, Rainbow the Clown to be exact,” Christensen said. “After making balloon animals and performing similar feats, Rainbow started in on stand-up comedy. Jim was standing next to him and matching him joke for joke. This continued until at some point, Rainbow paused, turned to Jim and said, ‘I work alone!’”

Siedow was promoted to full



At a Journal of Biological Chemistry associate editors dinner in 2013, James Siedow talks with Thomas Vanaman, also a JBC AE and a fellow Duke University professor in the 1970s and '80s, now at the University of Kentucky.

professor in 1987. He became increasingly involved in service to the university and national engagement, shifting his responsibilities from the lab to administration, and later testifying before Congressional committees about university research funding.

From 1988 to 1989 he spent a year in Washington, DC, as program director at the National Science Foundation. He then chaired Duke’s Academic Council from 1994 to 1996, and was the dean of faculty development in Arts and Sciences from 1997 to 1999.

While serving on the Academic Council, he gave Duke’s then-president Nan Keohane a plaque that remained on her desk throughout her presidency. The plaque read: “Have you consulted the faculty?”

Siedow became vice provost for research in 2001, overseeing the Office of Research Support, which provided grant administration for non-medicine faculty, and the Office of Corporate Relations, which seeks research partnerships with industry.

While most of the growth in Duke’s research during Siedow’s tenure was on the medical center side, research expenditures on the campus side grew 73%. By the time Siedow stepped down in 2014, he was managing the annual distribution of more than a billion dollars in research funding.

“I came in at a time when the federal funding spigot looked wide open and ready to run,” Siedow told Duke Today in 2013.

In describing Siedow’s tenure, then Provost Peter Lange said: “The growth in research funding has been superb. Less apparent, but no less noteworthy, has been the growth of multidisciplinary scholarship, the sharply increased numbers of larger multi-investigator grants, and the broadening and deepening of the university’s research portfolio. Jim’s quiet and effective leadership has been crucial to the faculty’s outstanding research and grant efforts.”

Despite having to manage increasingly complex federal regulations

REMEMBRANCES

James Siedow served on the editorial board of the *Journal of Biological Chemistry* from 1998 to 2006 and as an associate editor from 2006 to 2016. On these pages we share some remembrances from his colleagues at JBC and beyond.

I met Jim when I came to Duke for a job interview back in the summer of 1991, right after my wife, Xinnian Dong, got an offer from Jim's department for a faculty position. I remember that Jim went to my seminar, even though the topic of my talk was scientifically far from what he did on the cloning of TGF-beta receptors, and he talked to me briefly after the seminar, telling me that he and his departmental colleagues really wanted both of us to consider Duke for our career development. Through the years, I kept hearing from my wife about how Jim was selflessly helping her with grant submission and manuscript preparations, truly acting as a mentor for her. In addition, I remember that Jim exchanged his lab space, which was bigger, with Xinnian so that she could hire more people with the expanding laboratory, a rare action among faculty who often guard their lab space in any circumstances. Jim's actions as a mentor and colleague were truly exemplary.

I got to know Jim more personally when we both were inducted to become associate editors for JBC in early 2006 and attended AE meetings together in the following years. We also shared one assistant for our editorial duties for the journal, and I learned from my interactions and also sensed from the assistant that Jim was an extremely generous and caring person who would never make others uncomfortable with any demands. During our AE meetings, I also learned from his deep thinking about how to manage the challenges faced by the journal, employing his wisdom accumulated from his years' work in the administration at our university.

I enjoyed very much Jim's humor even when he was presenting serious matters. I fondly recall the last time Xinnian and I had dinner with him about two years ago, when he already had stepped down from his AE position, and the memories that we shared together for all of those wonderful years. Jim will always be with us with such a great memory.

— Xiao-Fan Wang, Duke University

and guidelines for university research, Siedow said he “tried to create an atmosphere of service to the researchers. We've focused on how we can do things, not why we can't do things.”

Siedow was elected a Fellow of the American Association for the Advancement of Science (2002), and a Fellow of the American Society of Plant Biologists (2007), where he also served as president.

Students and colleagues remember the impact he had on their lives.

Plant physiological ecologist Chantal Reid says that when she was a graduate student at Duke in the mid-1980s, Siedow taught a popular graduate-level course where his “view of a plant was a generic stick figure.” Years later she had the opportunity to co-teach with him, and while he had embraced new pedagogical tools, he “still drew on the board his stick figures for a plant.”

Fellow plant molecular biologist Xinnian Dong remembers Siedow for his generous proofreading help, as he often offered a second pair of eyes for her manuscripts and grant proposals.

“I personally consider Jim a born editor,” Dong said. “It was hard at first to figure out his slanted chicken scratch handwritings. But his suggestions always made sense and better than my original writings. I learned so much from Jim through these back-and-forth exchanges.”

Biology professor Tai-ping Sun remembers his mentoring and feedback when she first starting teaching plant physiology as a new assistant professor in the 1990s. “Jim sat in all my lectures,” Sun said.

Norman Christensen, founding dean and professor emeritus at Duke's Nicholas School of the Environment, says it was Siedow's vote of confidence that helped him make the difficult decision to leave the botany department and take the reins of the newly

created Nicholas School, combining forestry, geology and ecology.

“Jim’s encouragement, his assurance that I had the leadership skills and imagination to match the challenge, was very important,” Christensen said.

“Jim was known for his quick wit, colorful turn of phrase, and meticulous attention to whether his books were lined up evenly or all of the clocks in the kitchen read the same,” Schlesinger said.

Friend and colleague David McClay, a biology professor who worked down the hall from Siedow his entire career, recalls, “a discussion with Jim could become quite intense, and often he would stop, pause, and come back with ‘What’s your point?’ So you learned that you couldn’t ramble with Jim.”

Siedow was an avid fan of men’s and women’s basketball at Duke, modern arts and dance, and birdwatching. Before his wife Mary fell ill with cancer, they enjoyed hosting meals around the “big table” in their dining room, inviting friends for slideshows of their many travels, and dancing together at Duke holiday parties.

“Duke underwent so much change during Jim’s 40-year tenure, and he was an important agent for much of that change,” Christensen said.

Siedow will be buried next to his wife Mary in a private ceremony. A memorial service will be planned in the future.

This article was adapted from materials provided by Bill Schlesinger and Lisa Dellwo.

Robin A. Smith (ras10@duke.edu) was a researcher and writing teacher for more than 10 years before joining the news office at Duke University, where she covers the natural sciences across campus.



REMEMBRANCES

Jim’s sense of humor, his kind words, and his willingness to help young scientists are what stand out. I don’t think I’d be a JBC AE if it wasn’t for Jim.

— **Joseph Jez, Washington University in St. Louis**

Jim Siedow’s memorial in Duke Today captures his personality and the impact of his activities as a faculty member and administrator. Jim and I met in graduate school at Indiana University, where Anthony San Pietro was our mentor, and started a friendship that lasted almost 50 years.

Jim recruited me to the JBC editorial board when he was the associate editor for the section on bioenergetics. Working with Jim was a pleasure. The workload was a bit heavy, but there were many interesting manuscripts, and it was a pleasure helping to move these papers along into print.

There were also the manuscripts that wouldn’t go away. Jim’s communications to authors that declined their submissions were diplomatic and very clear as to why such a decision had been made. His comment to me at one point was that I might see a particular manuscript again, but it wouldn’t be as a JBC submission. In spite of his best efforts, however, some authors didn’t give up.

One resubmission was declined again but reappeared within a month. I was assigned the second resubmission for review, and Sandra Finch, Jim’s editorial assistant, passed along a message: “Dr. Siedow says you need to eat more red meat.” The manuscript wasn’t published in JBC. People like Jim Siedow are rare, and we have lost a great deal with his passing.

— **Charles Yocum, University of Michigan**

Jim and I started terms as JBC associate editors the same year, 2006. He was the “plant guy” editor and handled papers in that area of biology, as well as others. I remember the farewell dinner for Jim, which I recall was 2016 —not so long ago. I got (ASBMB Publications Director) Nancy Rodnan to bring in a basketball for a challenge between Jim (Duke) and Linda Spremulli (UNC). He had an unfair height advantage. I enjoyed seeing him at our meetings, and his participation. It’s always sad to see one of your AE siblings go, but it happens. Thanks for the memories, Jim.

— **Fred Guengerich, Vanderbilt University**

Mirror, mirror on the wall, what organs age fastest of them all?

By Nathalie Gerassimov

If you could look into a crystal ball and see your medical future, would you? Michael Snyder argues that you should — and that you actually can.

Snyder and his research team have shown that we each have a unique health baseline and that deviations from this baseline precede symptomatic manifestations of diseases and aging. His lab and several companies he has spun off his research are at the frontier of personalized medicine and clinically relevant molecular mechanisms of aging.

Snyder, the Stanford B. Ascherman professor and chair of genetics and director of genomics and personalized medicine at Stanford University School of Medicine, describes himself as a guinea pig for many of his research ideas. He says he wears at least eight devices designed to measure his personal health baseline continuously (including heart rate, skin temperature, blood glucose and oxygen levels). He loves to tell the story of how he got infected with Lyme disease while helping his brother build fences in rural Massachusetts and detected the infection based on his wearables two weeks later.

A decade ago, Snyder persuaded his then 84-year-old mother to participate in (and be a co-author on) a research study about himself that he published in *Cell*. Around

the same time, he recruited a cohort of over 100 people that his team studied for up to 10 years, which led to the discovery of several cases of early-stage cancers, heart defects and other conditions — so he is also a life saver. Overall, he could be described as a curious visionary, pushing the boundaries of medicine into a new orbit.

In a recent paper published in the journal *Nature Medicine*, Snyder's team describes how the aging process can be detected on a molecular level in individuals over a span of two years. Different people age in different ways, which the researchers refer to as aging types, or ageotypes.

Some ageotypes involve the cardiovascular system, the kidney and liver, and the metabolic and immune systems. Individuals can display one, some or all of the different aging types — Snyder himself is a metabolic, kidney and liver ageotype, and he postulates that there are many more types that his team is not able to detect yet due to insufficient data.

This methodology and conceptual framework can be used to monitor anti-aging strategies on an individual level and potentially intervene. For example, a person with an immune ageotype might eat more garlic or take turmeric as a supplement. It's still in the research stage, but Snyder is working on a commercial test idea.

For Snyder, precision health starts with measuring an individual health baseline. His research and personal experience have shown that a change in heart rate is one of the earliest indicators of many diseases and that a commercial device such as a Fitbit can pick up this deviation from the baseline. This also applies to COVID-19, where he and his team were able to detect an elevation in resting heart rate in 81% of cases a median of four days prior to patients showing symptoms and in some cases as much as 10 days. “Our group has recently developed this into an early alarming system for COVID-19 and other respiratory illnesses,” Snyder said, “and we hope to enroll as many as 10 million participants” in a study of this system.

Snyder is also a big proponent of continuous glucose monitoring. Participants in his longitudinal study were screened for prediabetes and diabetes, and several of them converted from healthy to prediabetic or diabetic during the study. However, the researchers also saw that individuals determined to be healthy by clinical tests such as fasting glucose levels and A1C levels could display large spikes in blood glucose levels after meals, indicating that their bodies repeatedly were unable to deal efficiently with the glucose from the absorbed meals,

STEVE FISCH



Michael Snyder and his team have been able to detect an elevation in resting heart rate in 81% of COVID-19 cases a median of four days prior to the patients showing symptoms, and in some cases as much as 10 days.

Michael Snyder, an associate editor of the journal *Molecular & Cellular Proteomics*, uses more than eight wearable devices to monitor his health baseline continuously. His research has found that deviations from this baseline, such as heart rate changes, precede symptomatic manifestations of disease.

further supporting the idea that existing clinical tests are insufficient to capture disease in its earliest forms. Unfortunately, continuous glucose monitoring is expensive.

Snyder points out that “medical economic modeling supports the idea that in many cases it is cheaper to screen for disease to capture and treat it in its earliest stages,” but he

admits that medical insurance companies have not yet embraced this concept fully.

Nathalie Gerassimov (nathalie.gerassimov@gmail.com) is a postdoctoral researcher at the Carnegie Institution of Washington department of embryology.



How flame retardants could impair neurodevelopment

By Anna Tancredi

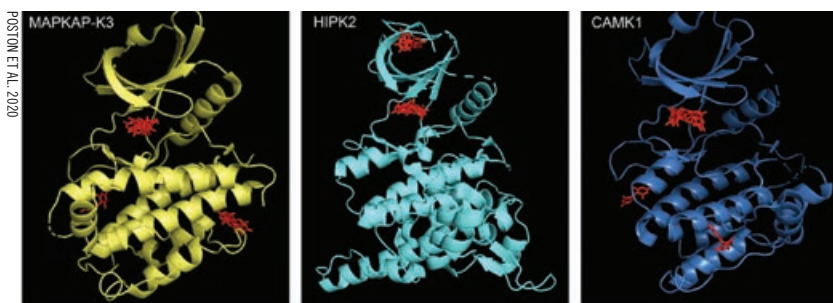
Evidence has been mounting for years that the flame retardants coating our furniture, electronics and construction materials can be harmful to human health. Members of one class of these retardants, polybrominated diphenyl ethers, or PBDEs, have come under increased scrutiny for their potential role in disrupting neurodevelopment, especially in children. Researchers have found that the 209 PBDE subtypes can bioaccumulate in lipid-rich tissues, including in the brain, but the precise mechanism by which these compounds cause harm remains unknown.

Ramendra Saha, an associate professor of cellular and molecular biology at the University of California, Merced, first heard about PBDEs at the National Institute of Environmental Sciences, where he was a postdoctoral fellow. He listened to speaker after speaker describe the potential toxicity of these compounds that seemed to litter every home. As a new father at the time, he wondered how he could keep his son safe.

Armed with a background in neuroplasticity and transcription, Saha delved into the epigenetic effects of PBDEs in neuronal development and function.

Saha's lab found that certain PBDEs can act as promiscuous kinase inhibitors and disrupt a signaling pathway involved in cell growth, division and differentiation known as the mitogen-activated protein kinase/extracellular signal-regulated kinase, or MEK-ERK, pathway.

"We were looking at environmental toxins that have been shown to



Ligand-docking simulation results for the top three hits from the kinase screen. Crystal structures were obtained from the Protein Data Bank, and Autodock-Vina was used to find energetically optimal binding poses for 6-OH (red) with each kinase.

have some correlation with intellectual disability and that act as an inhibitor to signaling cascades that are known to be important to normal neurodevelopment," Saha explained.

A paper in the *Journal of Biological Chemistry* describes how Saha's team proposed a new mechanism by which one particularly toxic PBDE, 6-OH-BDE-47, known as 6-OH, could impair the MEK-ERK signaling pathway. Robert Poston, a Ph.D. student in Saha's lab at the time, noticed that MEK inhibitor PD0325901, or PD, had key chemical structures similar to 6-OH. Using 3D modeling software, the researchers simulated the binding interactions of both 6-OH and PD with MEK1.

The results were encouraging: 6-OH and PD both were calculated to bind in the same allosteric binding site for MEK1. When they tried to demonstrate this binding directly in the lab, however, they were stumped: Increasing amounts of 6-OH added to MEK1 did not lower MEK1 activity.

Teaming up with researchers at the University of Dundee in Scotland, Saha's lab screened 6-OH with 140

kinases that represent most of the human kinome. Simulations of their top hits showed that 6-OH binding was most likely in the well-known ATP-binding pockets of the screened kinases, suggesting this PBDE could be a promiscuous ATP-competitive kinase inhibitor and could explain the complex and diverse effects of PBDE exposure.

Saha's group continues to study how 6-OH exposure can affect mitochondrial function, calcium homeostasis, regulation of synaptic function and other links to the impairment of MEK-ERK signaling.

Has Saha's work in the toxicology field changed his family's behavior? "Absolutely," he said. "We do not buy anything that is labeled 'fire resistant.'"

DOI: 10.1074/jbc.RA119.011138

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How a virus can affect memory: The role of HIV in HAND

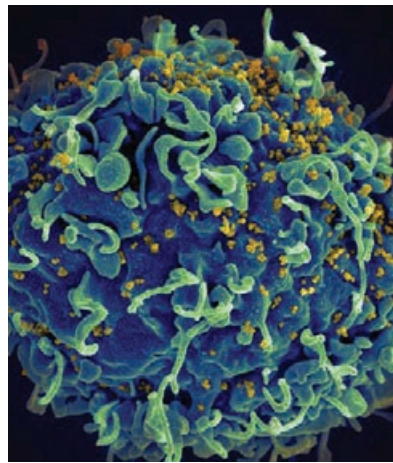
By Nicole Lynn

Human immunodeficiency virus destroys the white blood cells of the immune system, inhibiting the body's ability to fight infection. The stages of HIV range from acute to chronic; left untreated, HIV can progress to AIDS, which can be fatal.

A frequent outcome of HIV infection is HIV-associated neurocognitive disorders, or HAND. These disorders include a spectrum of mental and physical decline that affects behavior, memory and motor functions. While the development of antiretroviral therapy, or ART, has helped reduce the progression and severity of HAND, these disorders persist in 30% to 50% of infected individuals.

The mechanisms by which HIV infection promotes neurodegeneration are largely a mystery. However, ongoing collaborative research bridging the fields of virology and lipid and cell biology have brought researchers one step closer to an answer. In a recent study published in the **Journal of Biological Chemistry**, Dmitri Sviridov of the Baker Heart and Diabetes Institute together with Michael Bukrinsky of George Washington University investigated the relationship between Nef, an accessory protein secreted by cells infected by HIV-1, and the onset of HAND.

Nef is released from cells as cargo within extracellular vesicles; these EVs are lipid bilayer particles unencumbered by the cell membrane. Even with administration of ART, the cells of HIV-infected



Helper T cells are important in directing the immune response against HIV. In this image, a helper T cell (shown in blue) is under attack by HIV (shown in yellow), the virus known to cause AIDS.

individuals continue to secrete EVs containing Nef called ExNef. "A discovery that Nef is secreted in EVs from infected cells even during full suppression of virus production provided an important detail to our concept," Sviridov said.

Research by Sviridov and his colleagues showed that ExNef, which is absorbed rapidly by neural cells in the lab, reduces the abundance of ATP binding cassette transporter A1, or ABCA1, a membrane protein that functions in the homeostasis and transport of cholesterol and lipids.

The researchers found that when ABCA1 is reduced, cellular cholesterol metabolism is disrupted; lipid rafts, or solid regulatory domains in the cell membrane, are modified and increase in abundance.

These changes, a result of the effect of ExNef on ABCA1, promote an accumulation of amyloidogenic proteins. Specifically, the researchers observed an increase in amyloid precursor protein as well as the microtubule-associated protein tau. Both APP and tau play key roles in the pathogenesis of Alzheimer's disease.

The infective mechanism discovered in this study is unique to HIV; however, this research can further our understanding of other illnesses. "In broader terms, this mechanism involving lipid rafts ... may apply to non-infectious neurodegenerative diseases, such as Alzheimer's and other pathogens, including SARS-CoV-2, which causes neurological impairment by an unknown mechanism," Sviridov said.

Sviridov and his collaborators now are investigating therapies aimed at mitigating the effects of ABCA1 downregulation and the subsequent increase in lipid raft modification and abundance as a result of ExNef. They hope therapeutic intervention not only will help mitigate the prevalence of HAND but also may work to treat other metabolic disorders.

DOI: 10.1074/jbc.RA120.014642

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New lipid class may shed light on causes of dental disease

By *Gelareh (Abulwerdi) Vinueza*

M myriad microbial species live in the mouth, and an imbalance in their relative numbers can lead to dental disease. In chronic adult periodontitis, a destructive inflammatory disease, researchers have found *Porphyromonas gingivalis*, of the Bacteroidetes phylum, in increased numbers between the tooth and gum.

Gingivitis precedes development of periodontitis, which occurs when the inflammatory lesion of gingivitis becomes destructive, resulting in bone loss and detachment. Researchers believe virulence factors of *P. gingivalis* contribute to this progression. These factors include lipopolysaccharide that may promote bone resorption, expression of hairlike fimbriae that may help bacteria attach to epithelial cells between tooth and gum, and proteolytic enzymes that may promote tissue degradation. These factors could work together to promote destruction of tissue surrounding a diseased tooth.

Frank Nichols, a professor at the University of Connecticut School of Dental Medicine, described one of the possible mechanisms for delivering bacterial lipids to gingival tissues: “*P. gingivalis* can attach to the epithelium through its cell surface adhesion molecules, including fimbriae on the bacteria’s outer surface, and in so doing, it may deliver its cell wall lipids to epithelial cells through a process of lateral diffusion.”

In a new study in the **Journal of Lipid Research**, Nichols and colleagues describe isolating a new lipid class from lab-grown *P. gingivalis* using high-performance liquid chromatography, or HPLC, and mass



This illustration compares a healthy tooth with one from a patient with periodontitis, a disease caused by the bacterium *Porphyromonas gingivalis*.

spectrometry. “We noticed a small late-emerging lipid peak that eluted well after other lipid classes of *P. gingivalis* total lipids,” Nichols said.

The new lipid peak contained a group of related lipid species, with the most abundant having a negative ion mass-to-charge ratio of 1256; the team had identified a new class of *P. gingivalis* lipid products — Lipid 1256. They later found that this lipid is elevated in diseased tissues and plaque samples from teeth with periodontitis.

The Lipid 1256 class appears to be produced through a lipid synthetic pathway involving addition of amino acid or fatty acid components to the base glycine lipid structure, Lipid 342, with the final step being addition of diacylated phosphoglycerol to the serine dipeptide lipid class Lipid 654.

The researchers found that a neutralizing antibody blocked activation of human embryonic kidney cells transfected with human Toll-like receptor 2, or TLR2, demonstrating that Lipid 1256 engages TLR2. They also found that Lipid 1256 is a strong

ligand for TLR2 when compared to the other serine/glycine lipid classes. Lipid 1256 stimulates release of two cytokines, IL-1 β and TNF- α , from peripheral blood monocytes, both known to increase bone resorptive processes.

“Bacteria of the phylum Bacteroidetes are represented in large numbers in the gastrointestinal tract,” Nichols said, “so we wondered if Lipid 1256 is prevalent in those organisms.” They found that two common GI Bacteroidetes organisms produce Lipid 1256, suggesting that they might affect chronic inflammatory disease of the GI tract by exposing the GI wall to these lipids.

Recovery of Lipid 1256 in the mouth and intestine means that both sources could contribute to diseases such as rheumatoid arthritis or atherosclerosis. Other researchers have found that these diseases may involve engagement of TLR2, which could occur if either the bacterial lipid or the bacteria enters the bloodstream. Future research evaluating the recovery of Lipid 1256 in human tissue samples may implicate lipids of the Bacteroidetes phylum in systemic diseases with a TLR2-dependent chronic inflammatory response.

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A novel technique maps antibodies' epitope specificities

By Laurel Oldach

According to one count, some 5 million commercial antibodies exist, used to target, detect or destroy in contexts from research labs to patients' bodies. Raised in goat, rat, mouse, rabbit, llama and even chicken against fragments of a menagerie of proteomes, these antibodies bind with high affinity to their mostly protein targets.

Determining the portion of a protein surface to which an antibody binds is called epitope mapping. The gold standard approach is to determine the structure of an antibody-target complex. However, structural work can be difficult and may take months per antibody. Researchers also use peptide display technologies, presenting a library of protein fragments on a microarray or the surface of *E. coli* and finding out which ones the antibody binds to through microarray scanning or flow cytometry.

In a recent article in the journal **Molecular & Cellular Proteomics**, researchers in the labs of Xiaodong Zhao, Hua Li and Sheng-ce Tao at Shanghai Jiao Tong University introduced a new, faster method for epitope mapping. Using the new technique, they write, "One technician is able to map the linear epitopes of more than 200 antibodies in one month at an affordable cost."

The approach starts with a random phage display library, a collection of 109 peptides with random sequences, each 12 amino acids in length, expressed on the surfaces of phages. (Although other researchers



previously have used phage display for epitope mapping, they mostly have presented variants on a known target protein rather than random peptides.)

"The beauty of phage display is the protein sequence and the coding sequence are linked together," Tao said. Therefore, after biochemically extracting phages that bind to an antibody of interest, the team quickly could identify these phages through next-generation sequencing. By comparing all of the phage peptides that bound to each antibody, they detected common protein motifs. This let them establish a consensus binding sequence for each antibody — without any preconceptions about what it would be.

Sometimes the epitope they determined matched the protein or peptide against which the antibody was raised. In other cases, the consensus epitope sequence was not found in the protein an antibody was raised against. According to Tao, this makes sense when you think about antibod-

ies and their targets binding in three dimensions.

"How antibodies are generated is not always based on the linear sequence," Tao said. "Sometimes it's based on conformational structure."

Because of the nooks and crannies folded into any protein's structure, amino acids that are not adjacent in its linear structure often are found next to each other on its surface. While the technique is quite useful for finding linear epitopes, the authors said, it cannot detect conformational epitopes; they hope to find new computational approaches that will bridge the gap.

Still, the research has clear scientific and commercial potential. Since the paper was published, Tao said, the team has improved the speed and efficiency of their technique. The lab has struck up a partnership with a reagent supply company to map the epitopes of 10,000 of its antibodies and anticipates using the resulting data set to learn more about the relationships among antibody, antigen and epitope. They're also considering other applications, such as identifying potential off-target binders that could cause unexpected side effects in antibody-based drugs.

DOI: 10.1074/mcp.RA120.002314

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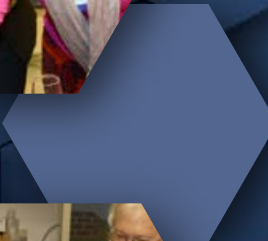


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From the journals

By *Caleigh Findley, Nivedita Uday Hegdekar & Anand Rao*

We offer summaries of papers recently published in the **Journal of Biological Chemistry**, the **Journal of Lipid Research** and **Molecular & Cellular Proteomics**.

Sorting out the role of Serinics in HIV–host fusion

Human immunodeficiency virus reduces an infected individual's abil-

ity to ward off infections and, left untreated, can lead to AIDS. Prior to infection, HIV must enter a host cell by fusing its lipid envelope with the cell's plasma membrane. This process happens so rapidly that researchers have difficulty identifying its intermediate steps.

In a recent paper published in the **Journal of Biological Chemistry**, Amanda Ward of the University of

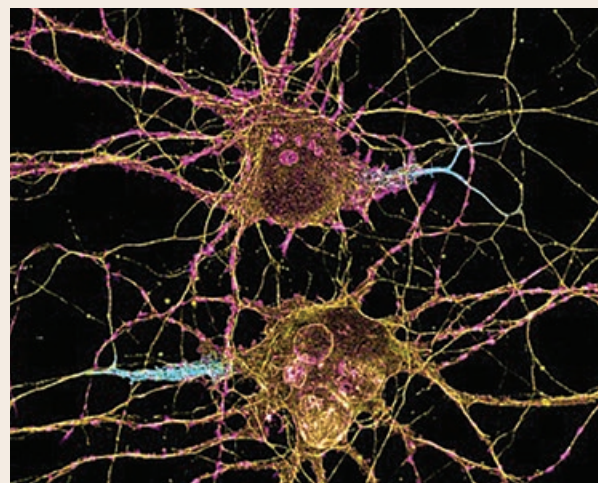
Virginia School of Medicine and colleagues used cryo-electron tomography and total internal reflection fluorescence microscopy to visualize HIV–membrane fusion and unravel the role of Serinics proteins in viral infection. The researchers adapted giant plasma membrane vesicles from cell membranes that were modified to express the appropriate receptors as targets for fusion with HIV envelope

Membrane organization in nerve cells

Nerve cells, or neurons, are the primary communication cells in your brain. Projections from these cells' bodies, called neurites, mediate all incoming and outgoing messages. Researchers know that the plasma membrane enclosing neurites is especially important for communication, with specialized sections in different areas of the cell. But how, exactly, do neurons establish these distinct sections?

Hideaki Kuge and colleagues at Kochi University in Japan describe their efforts to answer this question in their recent paper published in the **Journal of Lipid Research**. This group's prior work focused on 1-oleoyl-2-palmitoyl-phosphatidylcholine, or OPPC, a rare phospholipid species produced by acyl chain remodeling of phosphatidylcholine. Acyl chain remodeling occurs when enzymes in the phospholipase A1 or A2, or PLA1/2 families cut a phospholipid acyl chain to attach a different fatty acid group. This team previously showed that OPPC localized at neurite tips after stimulation with nerve growth factor, or NGF, highlighting PLA1 activity as a mediating factor. These results led to further investigation into the potential role of local acyl-chain remodeling in membrane organization.

The researchers stained neurite tips for several known PLA1 enzymes and found pancreatic lipase-related protein 2, or PLRP2, expressed at the tips and colocalizing with OPPC. Moreover, stimulation of the neuron by NGF induced changes to the expression of PLRP2. Using the gene-editing technique CRISPR–Cas9 to silence PLRP2 expression, the researchers found that loss of PLRP2 decreased expression of OPPC at the neurite tips. Loss of PLRP2 also reduced the surface expression of an impor-



LETTEREN/NEUROCYTO LAB, INP

This image, captured at the Institute of NeuroPhysiopathology in Marseille, France, shows two neurons with neurite projections from the cell body.

tant membrane protein called the dopamine transporter, or DAT. This membrane component allows the reuptake of dopamine back into the cell, an important process for neuronal homeostasis and communication.

They also saw that syntaxin 4, or Stx4, a protein involved in vesicle trafficking to the membrane, interacts with OPPC domains, dependent on PLRP2 expression. Silencing of Stx4 through the same gene-editing method showed that surface expression of DAT also requires Stx4. Vesicle immunoprecipitation assays confirmed the presence of PLRP2, Stx4 and DAT in the same transport vesicles. Together, these findings show the essential role of a local acyl-chain remodeling factor, PLRP2, in mediating neuronal membrane specialization.

DOI: 10.1194/jlr.RA120001087

— Caleigh Findley

glycoprotein-expressing pseudovirus particles. By controlling whether the particles included Serinc host restriction factors, the investigators showed with unprecedented clarity how Serinc proteins, specifically Serincs 3 and 5, can interrupt membrane fusion.

DOI: 10.1074/jbc.RA120.014466

Novel fungal protease improves proteomic coverage

Enzymatic digestion of protein into shorter peptides by sequence-specific proteases is a key step in mass spectrometry-based shotgun proteomics experiments. Trypsin has been used predominantly due to its high specificity (it cleaves exclusively after the amino acids arginine and lysine), widespread availability and ease of use.

Diana Samodova and a team at the University of Copenhagen characterized another protease, ProAlanase, isolated from the fungus *Aspergillus niger*, that cleaves primarily on the C-terminal side of proline and alanine amino acid residues of proteins. Compared to trypsin-only digestion, a combination of ProAlanase and tryptic digestions showed improved proteome coverage. The researchers also demonstrated ProAlanase's broad utility in other proteomics applications in a recent paper published in the journal **Molecular & Cellular Proteomics**.

This study highlights the importance of investigating alternative proteases for proteomic experiments. Alternatives to trypsin will be beneficial in cases where digestion by trypsin is not ideal, such as when the content of arginine and lysine in the protein is low. Moreover, as proteases with different cleavage sites will generate different sets of peptides for the same proteome, combination digestion will yield improved results for various applications, such as identification of

proteins, protein-protein interactions and post-translational modifications in various biological systems.

DOI: 10.1074/mcp.TIR120.002129

Targeting lipids in liver disease

Lipids, including fatty acids, steroids, and other molecules, are essential for maintaining the structure and function of cells. These metabolic building blocks are deposited into each cell as an organelle called a lipid droplet. The 17-beta hydroxysteroid dehydrogenase 13, or HSD17B13, gene encodes a liver lipid droplet enzyme important for fat storage. While researchers know little about the composition and function of HSD17B13, mutations that impair the function of this gene can prevent liver injury, disease or cancer.

Yanling Ma of the National Institute of Diabetes and Digestive and Kidney Diseases and a team of U.S. colleagues sought to better understand the inner workings of HSD17B13 in their study published in the **Journal of Lipid Research**. Results showed that targeting the HSD17B13 enzyme to the lipid droplet requires three specific N-terminal fragments. One of the fragments also may factor in the proper protein folding of HSD17B13 in the endoplasmic reticulum. The team then used a similar gene, HSD17B11, to successfully predict and verify important residues for HSD17B13's enzymatic activity. These findings offer clues about the functional role of HSD17B13 in disease and provide potential targets for drug development.

DOI: 10.1194/jlr.RA120000907

Exosites mark the spot for factor X activation

The interplay between active sites and exosites, secondary binding sites located far from active sites, is crucial for protease specificity. Researchers have been unable to define the balance

between these sites for serine proteases that act as coagulation factors in the blood.

Manjunath Goolyam Basavaraj and Sriram Krishnaswamy of the Children's Hospital of Philadelphia found a new mechanism by which coagulation factor X, which plays a key role in the coagulation cascade, is activated. Using biochemical, pharmacological and fluorescence studies, the scientists demonstrated that this activation, mediated by an intrinsic Xase complex, requires exosite binding.

These results, published in the **Journal of Biological Chemistry**, may help with future inhibitor development that will aid in the treatment of coagulation disorders such as hemophilia.

DOI: 10.1074/jbc.RA120.015325

Expression of HLA-II shows promise for immunotherapy

When the immune system is suppressed, glioblastoma, or GBM, develops into an aggressive cancer in the brain or spinal cord, with poor prognosis. Understanding the interaction between the T-cell receptor on CD4+ T cells and HLA-II cancer-specific epitopes on GBM cells is vital for the development of immunotherapies. However, HLA-II complexes almost never are expressed naturally in GBM cells, and scientists believe their absence contributes to the poor anti-tumor immune response commonly seen in GBM.

In a recent paper in the journal **Molecular & Cellular Proteomics**, Greta Forlani and a team of Swiss researchers write that they discovered how to induce HLA-II expression by inserting the gene histocompatibility complex transactivator, or CIITA, into various GBM cell lines. They then used a number of techniques to uncover more than 30,000 unique HLA-II peptides in those cell lines.

If HLA-II expression can be

induced successfully, it has promising therapeutic implications for HLA-II–negative tumors such as GBM. For example, mice with tumor cells injected with CIITA (which causes increased HLA-II expression) have been shown to produce robust anti-cancer immune responses. Furthermore, CIITA-expressing tumor cells will be useful for discovering antigens that can be used to develop immunotherapies.

DOI: 10.1074/mcp.RA120.002201

Balancing longevity and starvation resistance

The human body regulates its energy reserve according to how much food it receives over a given period. Many factors contribute to this balance whether the body gets plenty of fuel (food) or none at all. Among the metabolic proteins involved in regulating this process are lipins. Under fasting conditions, lipins move to the cell's nucleus to change gene expression in response to reduced energy intake.

In a study published in the **Journal of Lipid Research**, Stephanie E. Hood and a team at the University of Arkansas explored how lipin migration to the nucleus and enzymatic activity affect life expectancy and starvation resistance. Researchers created a fruit fly mutant model that lacked the correct signal to move lipins into the nucleus. When fed properly, these flies were healthier and had a longer life expectancy. Yet this came at a cost, as the mutant flies were also less resilient against starvation-induced death. Results showed changes to several genes involved in metabolism, feeding behaviors and immunity in response to contrasting levels of food availability. This study highlights the diverse roles of lipins in modulating genome-wide responses to energy intake and the importance of lipins in starvation resistance.

DOI: 10.1194/jlr.RA120001051

New insights into Duchenne muscular dystrophy

Duchenne muscular dystrophy, or DMD, is characterized by progressive muscle degeneration and weakness due to the alterations of the dystrophin protein that keeps muscles intact. Development of effective treatments for DMD has been challenging because researchers do not understand completely the pathological consequences resulting from loss of dystrophin.

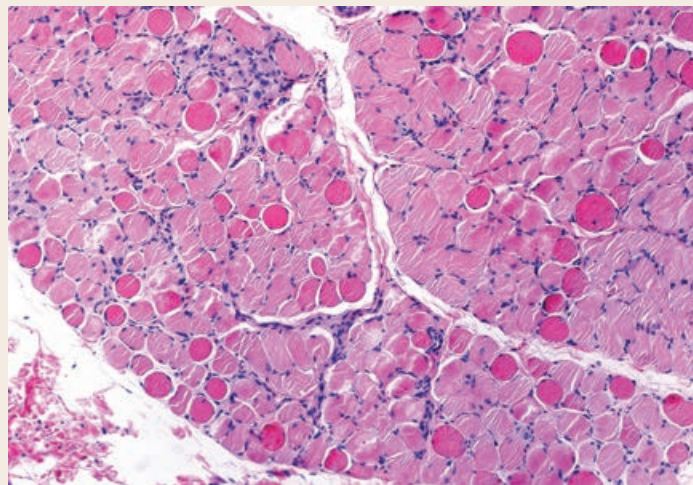
In a recent paper in the journal **Molecular & Cellular Proteomics**, Tirsia L.E. van Westering and researchers at the University of Oxford used mass spectrometry to identify differential protein expression in muscles at three different ages (representing the different stages of DMD pathology) from two strains of mice with genetically altered DMD and one strain of unaltered mice (control).

The protein profiles of the two types of DMD mice were found to be similar; however, numerous proteins were differentially expressed between DMD mice and unaltered mice at each of three stages of DMD pathology. These included proteins associated with the extracellular matrix and muscle function, many of which had not been reported in previous studies. Further analysis showed that the dystrophic condition is characterized by multiple perturbed pathways and crosstalk among inflammatory, metabolic and muscle growth pathways.

The researchers created a publicly available data set that reports the quantification of 4,974 proteins across the DMD mice and control mice at various disease time points — the highest number of quantified proteins in dystrophic muscle described to date. It will offer many researchers a wider perspective into the proteomic signatures characteristic of DMD and potential therapeutic targets and also will be useful for researchers studying the effects of aging on the muscle proteome.

DOI: 10.1074/mcp.RA120.002345

— Nivedita Uday Hegdekar



Necrotic muscle fibers are characteristic of Duchenne muscular dystrophy.

Iron sensing in *E. coli*

The bacterial ferric uptake regulator, or Fur, transcriptionally modulates genes to regulate iron uptake, storage and use in response to changes in ferrous iron. However, researchers have not identified the mechanisms underpinning the iron-sensing ability of Fur.

Using Fur purified from *E. coli*, Chelsey R. Fontenot of Louisiana State University and collaborators at the University of St. Thomas showed that Fur binds an all-Cys-coordinated [2Fe-2S] cluster via conserved cysteine residues. However, depletion of intracellular free iron using a membrane-permeable iron chelator removed the [2Fe-2S] from Fur in *E. coli* cells.

These findings, published in the **Journal of Biological Chemistry**, provide new mechanistic information on how the regulator responds to changes in iron.

DOI: 10.1074/jbc.RA120.014814

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Sphingosine, spike protein and SARS-CoV-2

As global COVID-19 cases continue to surge, researchers race to identify new treatments that will expand clinicians' therapeutic arsenal. Both groups are keenly interested in developing a prophylactic treatment that can guard hosts against infection by SARS-CoV-2, the virus that causes COVID-19, or least prevent infections from taking the most severe course of disease that potentially could lead to death and disability.

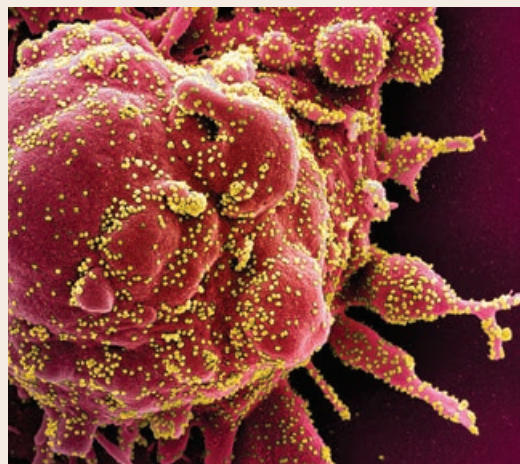
SARS-CoV-2 infects cells through an interaction of the viral spike glycoprotein with its cellular receptor angiotensin-converting enzyme 2, or ACE2. Association of these two proteins leads the virus to enter its cellular host, where it goes on to replicate. Identifying ways of interrupting this interaction could lead to new strategies for preventing SARS-CoV-2 infection.

Sphingosine, a primary component of sphingolipids, has the demonstrated ability to protect against bacterial respiratory tract infections, but researchers don't know if it also can prevent and eliminate viral infections. Michael J. Edwards of the University of Cincinnati Medical School and collaborators investigated the ability of sphingosine to modulate the infection of human epithelial cells by pseudovirus particles expressing the SARS-CoV-2 spike glycoprotein. The team showed that pretreatment of cultured epithelial cells from African green monkeys or freshly isolated nasal epithelial cells with sphingosine (suspended in 0.9% sodium chloride solution) can prevent infection by SARS-CoV-2 pseudovirus particles. They went on to identify the mechanism responsible for this result, showing that sphingosine binds to ACE2, thus blocking its interaction with the viral spike protein.

These findings, published in the **Journal of Biological Chemistry**, suggest that sphingosine may have therapeutic potential for prevention of infections by viruses, including SARS-CoV-2.

DOI: 10.1074/jbc.RA120.015249

— Anand Rao



This image, captured by scanning electron microscopy and colorized, shows an apoptotic cell (red) heavily infected by SARS-CoV-2 virus particles (yellow), isolated from a patient sample.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NIH

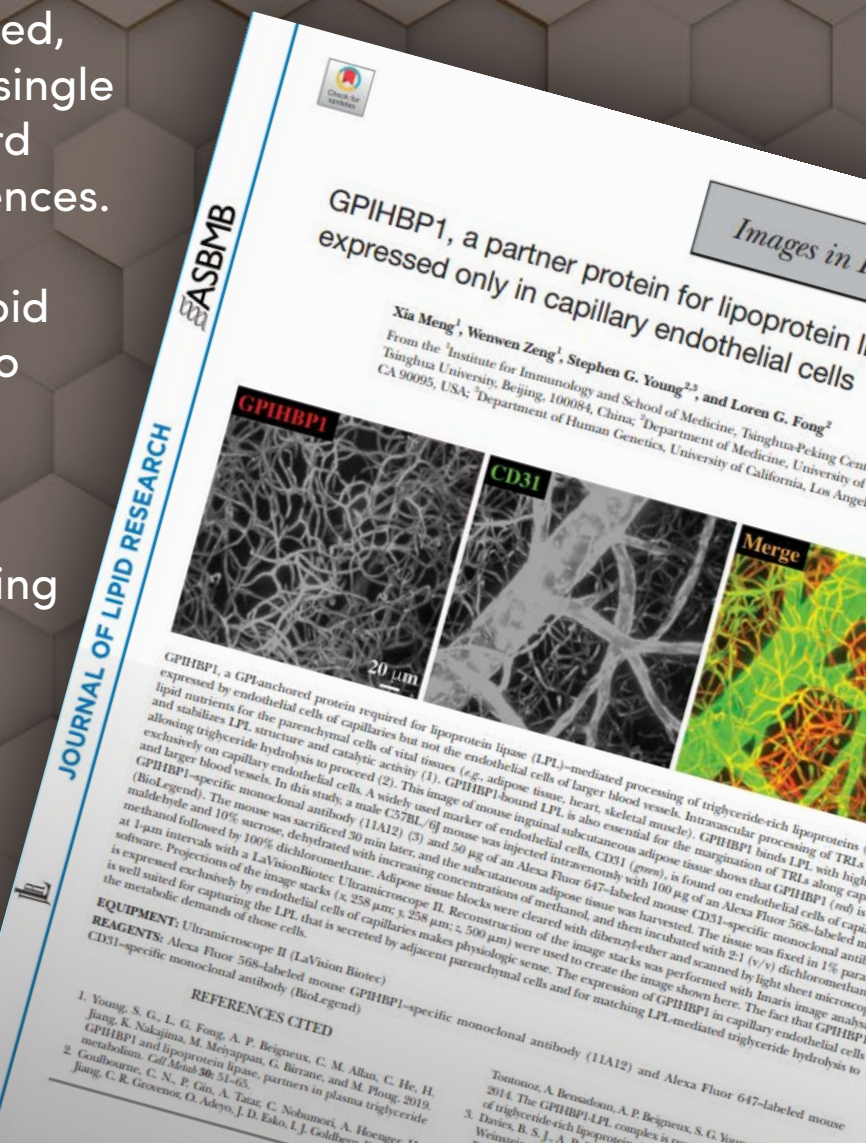
Images in Lipid Research

A new article format in the
Journal of Lipid Research

The editors of the Journal of Lipid Research are pleased to announce the adoption of a new article format: "Images in Lipid Research." Each peer-reviewed, one-page article contains a single horizontal image, a 400-word caption and up to four references.

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Scratching away



The complexities of chronic itch

By Katherine Harmon Courage

It seems hard to believe that a basic human sensation — one that can be evoked by a simple mosquito bite — still has scientists scratching their heads. Yet despite centuries of study, understanding itching is still fraught.

Itch, write two scientists in a review in the journal *Immunity*, “has been described as one of the most diabolical sensations. In Dante’s *Inferno*, falsifiers were eternally punished by ‘the burning rage of fierce itching that nothing could relieve.’” Yet, the researchers note, “There have been very few advances in itch treatment in over 360 years.”

That’s finally starting to change. In the past decade, scientists have made strides toward understanding this infuriating sensation. They are untangling itchiness from other noxious stimuli, such as pain. They are even starting to distinguish one type of itch from another, by poking study participants with itch-inducing plant spikes or deleting itch-related genes from mice.

This wide-ranging research is gradually going beyond an understanding of familiar acute histamine-driven itch — the mosquito or poison ivy variety — to reveal the complicated mechanisms and players involved in the often debilitating type of itching that lasts for weeks and sometimes years. Chronic itch, as it’s termed, can be generated by a multitude of factors, from chemicals secreted within the body to nerves gone haywire, and in many cases, has no known cause or cure.

This inquiry is more than an academic exercise (or a quest to make mosquito welts recede faster). While acute itch is fleeting, chronic itch may plague some 7 percent of people each year, and one in five people will experience it at some time in their lives. Beyond a maddening persistent urge to scratch, the condition can lead to depression, sleep deprivation and a drastic decrease in the quality of life. “It can be as devastating as chronic pain,” says Robert LaMotte, an itch researcher at the Yale School of Medicine.

And pain is actually where the itch story starts.

Itching has myriad causes and mechanisms, many of which remain elusive. Scientists are making headway on parsing its biological underpinnings, in hope of better treatments.



GUSTAVE DORE/WIKIMEDIA COMMONS

Chronic itching is so brutal that it is one of the punishments suffered by souls in Hell who have committed fraud or treachery in Dante’s “Divine Comedy,” shown here in an 1892 illustration by Gustave Doré.

Revealing itch as a sensation in its own right with a dedicated pathway was a crucial step forward in understanding it.

Identifying itch

For much of the last century, itch was considered a lower-tiered version of pain. In the early 1920s, for example, Austrian-German physiologist and pain researcher Max von Frey documented in an influential study that a slight skin prick gave research participants the aftersensation of itch. This conceptual model continued to feed the field of itch for decades.

But eventually, the idea that itch was simply a subset of pain began to crumble. Scientists determined, for example, that they could not reliably turn a pain into an itch just by decreasing the pain's intensity — or turn an itch to a pain by increasing the itch's intensity. Yet the nerves and pathways of pain and itch appeared to be so similar and deeply intertwined that for years scientists lacked a clear understanding of how the two responses were wired into the body.

Then, in 2007, the sensation of itching finally crawled out from under the shadow of pain and into its own light.

That year, a seminal paper in *Nature* reported the first dedicated itch receptor — a protein on nerve cells in the central nervous system that responds specifically to itch but not pain, indicating that the sensation might travel its own separate pathway to the brain. Zhou-Feng Chen, at Washington University School of Medicine in St. Louis, and colleagues showed that mice engineered to lack genes for this receptor — called the gastrin-releasing peptide receptor — could still feel pain but barely felt itch, no matter what the researchers tried.

“This changed the paradigm,” says Brian Kim, a dermatologist and codirector of the medical school's Center for the Study of Itch, who now works with Chen. Revealing itch as a sensation in its own right with a dedicated pathway was a crucial step forward in

understanding it, he says.

Since the discovery of this first itch receptor, researchers have discovered more cellular players involved in chronic itch, separating it out from acute itch. They have learned, for example, that chronic and acute itch are relayed by different sets of neurons that send signals along their own dedicated tracks in the nervous system. When researchers have simulated chronic itch in experiments with healthy volunteers, MRI scans reveal that the two itch types spur different patterns of brain activity.

These most foundational observations reveal just how much more we have to learn about itch. But they also help create a path to bringing relief to those who experience debilitating chronic cases. The sensation can be so bad that, for instance, some people with liver disease receive transplants precisely because of their itching. Others choose to go off of essential cancer medications because of the itching the drugs can cause.

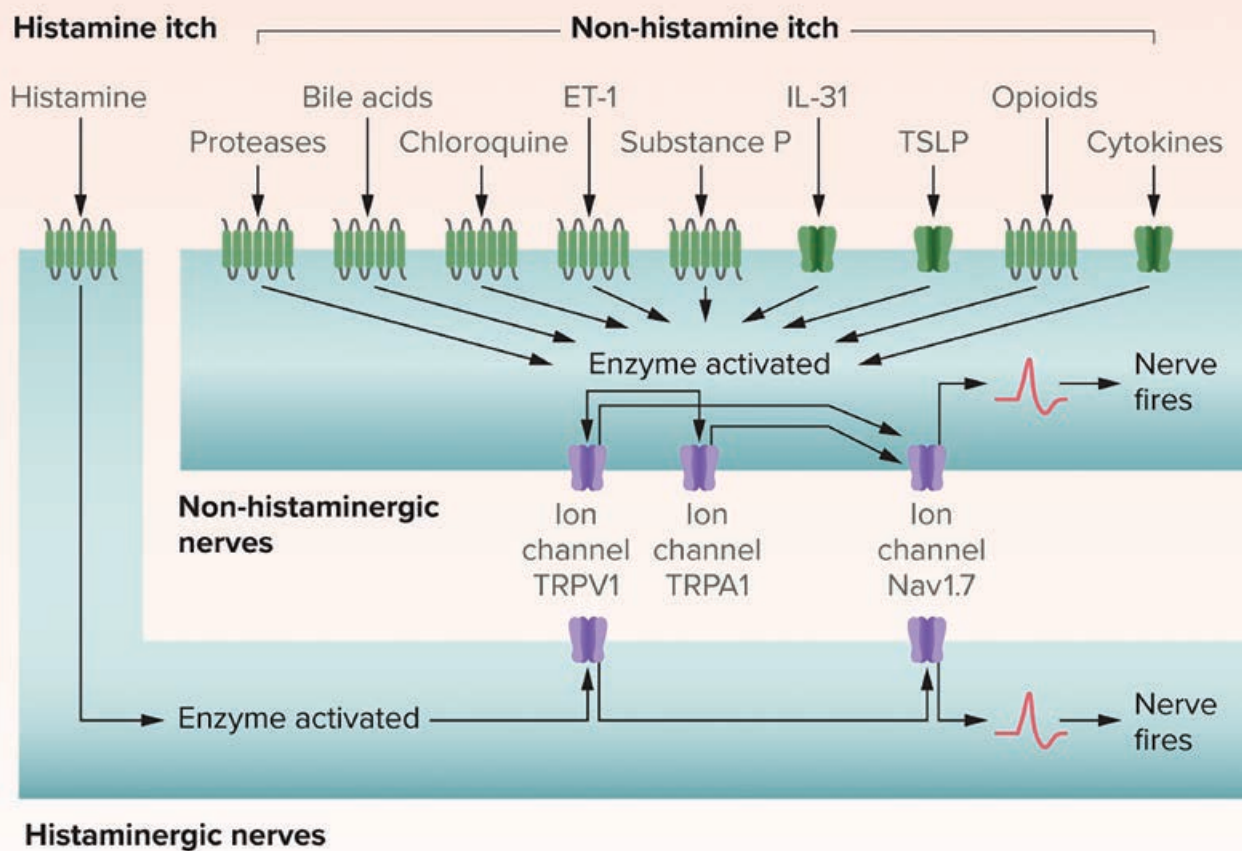
And for years, researchers were focused on the low-hanging fruit of histamine-driven itch, which is easier to study, in part because it is being driven by a single chemical compound. Experimenters could spread or inject known irritants on or into the skin, cuing the body to make histamines, producing that familiar welty reaction that can be soothed by antihistamines like cortisone. But most chronic itch (technically, itchinness that lasts more than six weeks) doesn't involve histamines. And the routes — there are many — to chronic itch are far more complicated.

Now, as scientists refocus their investigations on chronic non-histamine itch, they're doing much of the research the old-fashioned way: by making people and animals itchy.

Itch by itch

Initiating an itch is not as simple as it seems. One approach that's been especially fruitful for zeroing in on

Many pathways of itch



non-histamine itch is to poke people with tiny hairs (or spicules) from a tropical plant called cowhage, or velvet bean.

In a key series of experiments, LaMotte and his colleagues took about 10 of these spicules, which are a few microns wide at the tip, and inserted them about 0.2 millimeters into the skin of study participants. Every 30 seconds, for up to 20 minutes, the thus-pricked people reported sensations they felt, such as pricking, burning or itching, as well as the intensity. The studies confirmed that an unusual compound within the minute hairs, called mucunain, rapidly causes itchiness but — unlike many plant-based itch-prompting compounds — doesn't activate histamines. That makes cowhage spicules a powerful way to investigate the circuitry of non-histamine itch and

possibly provide insight into mechanisms for chronic itch.

Next, LaMotte and his colleagues incubated human cells with mucunain in lab dishes to tease apart which receptor proteins might be receiving and responding to the incoming itch. They found responses in two types of such receptors — known as PAR2 and PAR4. Identifying itch-related receptors like these can help get medicine closer to a potential treatment.

To more fully understand the basics of itch and help disentangle it from pain, LaMotte and colleagues took a deep dive into the subtleties of the scratching behavior of mice. They learned where on the mouse body to inject their various irritants so as to reliably distinguish itchy types of scratching from pain types of scratching.

There are many routes to itch, but scientists have uncovered two, independent subtypes of neurons that relay the itch message to the spinal cord and brain. The histamine pathway (left), which is involved primarily in acute itch, is engaged when a trigger such as a mosquito bite spurs the release of histamines by the body's immune system, which activate histamine receptors. Non-histamine itch (right) can be set off by a wide range of internal and external triggers, including immune system molecules such as cytokines, enzymes called proteases that cut up proteins and the antimalarial drug chloroquine. After a trigger activates receptors in either pathway, enzymes are kicked into gear that spur the opening of ion channels, prompting the nerve to fire and send the itch signal to the spinal cord and brain.

Basic nervous system malfunctions like a pinched or damaged nerve can generate pain in some people but itch in others.

More than a decade on, the researchers can take advantage of the many biological mechanisms underlying itch — such as receptors and nerve pathways — that are similar in mice and people. That means they can now move back and forth between the two, injecting similar chemicals, for example, and tracking behavior (self-reports for humans, actions for mice) for intensity and duration.

Meanwhile, the lab of Xinzhong Dong, an itch researcher at Johns Hopkins University, has used mice to pinpoint nerve endings that are truly itch-specific. “You can activate those nerves, and you’ve got an itch sensation; you don’t feel pain,” he says. When he and his colleagues inactivated these dedicated itch neurons, mice were immune to itchy stimuli but still felt pain, the researchers reported in 2012 in *Nature Neuroscience*.

Other researchers aim to unlock itch’s secrets with a more pure form of laboratory itch.

Dermatology researcher Akihiko Ikoma, then of Kyoto University, and colleagues took a mechanical approach to the problem. Instead of relying on chemical compounds, the team developed a small wire loop that vibrates at a specific frequency. As the team described in 2013 in the journal *PAIN*, when the loop is touched to the fine hairs on people’s faces, it creates an itch that takes more than 10 minutes to completely dissipate. This work has helped scientists to pinpoint itch-specific neurons around the skin that work independently of histamines or various other chemicals that stimulate itching.

The hope, for both methods, is to identify neurons and pathways specific to different kinds of itch. This will eventually help scientists investigate drugs that could relieve chronic itch in long-time sufferers.

But there remains more to untangle about itching’s complex circuitry, with new receptors and nerve cells still being uncovered.

A partnership with pain

Despite all these advances — and despite the fact that itch is found throughout the animal kingdom, from fish to primates — “much of itch perception is still a mystery,” Dong and Hopkins colleague Mark Lay note in the 2020 *Annual Review of Neuroscience*.

For one thing, even though there’s been progress, the intertwined nature of itch and pain is still difficult to untangle. One reason may be that both originated as self-protection. Just as pain sends the signal to withdraw from something dangerous, itch prompts scratching, which could, for example, prevent infections by shooing away parasites. Scratching also appears to help recruit local immune cells that can fend off infection.





Itch and pain also have a peculiar overlap that even occasional scratchers are familiar with: Scratching can generate mild pain, which can often override the sensation of itch. Some researchers have proposed that when groups of neurons are activated — some of them itch-specific and some of them pain-specific — the pain stimulus, if strong enough, can mask the itch signals.

And despite the new itch-only discoveries, many nerves do seem to be involved in communicating both painful and itchy stimuli. The confusing overlap is exemplified in people with chronic conditions like atopic dermatitis. In these cases, nerves in the skin become hyper-sensitive to itch, and perceive as itchy stimuli that are normally painful — or simply mechanical or thermal. This is similar to what's experienced by some people with chronic pain, where light touch can actually hurt. And basic nervous system malfunctions like a pinched

or damaged nerve can generate pain in some people but itch in others.

The overlap with pain is also present in the ways — still poorly understood — in which itch travels from the peripheral nerves in the skin to the spinal cord and up to the brain, Dong says.

All of these lingering mysteries mean that itch — especially chronic itch — has been extremely difficult to effectively treat. “Like in pain, there’s not just one painkiller that destroys all types of pain,” says Gil Yosipovitch, a dermatologist at the University of Miami and founder of the International Forum for the Study of Itch.

“I have patients who have a lot of complexities, and they require more than one pill or one cream, similar to patients who have chronic pain. And it requires a lot of time and patience.”

For most of the population, itch is still a passing irritant, perhaps from bug bites in the summer or dry

skin in the winter. But as a clinician and a research scientist, Kim says all of the suffering he sees from chronic itch keeps him working harder in the lab to understand this torturous sensation and correct too many years of inattention.

“It’s just this cascade of neglect,” he says.

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FROM ANNUAL REVIEWS

This article is republished from *Knowable Magazine*, an independent journalistic endeavor from Annual Reviews.

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Taking the spit test

By Laurel Oldach

How at-home SARS-CoV-2 tests work — practically and biochemically

LAUREL OLDACH/ASBMB TODAY

For months, over a million tests for COVID-19 have been administered each day in the United States.

These spit tests are gaining traction because they can be done by the person being tested and don't require a potentially risky contact with a healthcare worker. Some — like the one I took in October — even allow a person to collect a sample at home.

At the neighborhood grocery store's pharmacy counter, a pharmacist opened the small, tidy box and showed me the contents: a collection tube into which I was to deposit a milliliter of saliva (the enclosed instruction sheet had tips on how to get things flowing), a set of labels to fill out with my name and date of birth, a zip-close bio-hazard bag, and an express shipping envelope. The pharmacist instructed me not to collect a saliva sample on Friday or Saturday; it would be good only for 56 hours.

I was surprised that intact viral RNA can last for more than two days in saliva. It was difficult to imagine trying to carry out qPCR with such a sample; although it has been a few years, my experience with the technique involved flash-frozen tissues, buckets and buckets of ice, and a near-pathological fear of RNase. But experts like RNA biologist Joan Steitz, a professor at Yale School of Medicine and the

Saliva and buffer, mixed and shaken, fill a sample collection tube.

Howard Hughes Medical Institute, suggest those concerns may have been overblown.

“You don’t need very much intact in order to get something that you can PCR that’s about 100 (nucleotides) long,” Steitz said, pointing out that 20 years ago, researchers succeeded in reconstructing the genome of the 1918 influenza virus from just wisps of RNA. “I think that’s what’s being taken advantage of in these tests.”

Buffered stability

In the grocery store parking lot, after a solid two minutes of hunching over the collection tube and drooling, I finally reached the vial’s fill line. Next, the instructions said, snap the cap closed. Doing so broke a seal that released a milliliter of stabilizing solution.

Scott Rabuka is the senior director of molecular products at DNA Genotek, the company that manufactured my saliva collection kit and owns the combination funnel-plus-snap-cap technology. The solution involves “lytic chemistry and stabilization chemistry,” he said.

That is, the mixture lyses any cells and inactivates any virus without damaging the RNA in the sample. Rabuka was cagey about the exact chemicals involved, but according to a preprint from an academic group with a competing approach, they are familiar to biochemists: The preprint states that it’s an aqueous solution of Tris buffer and ethanol.

DNA Genotek initially manufactured these saliva collection kits for genetic tests as well as genomics, microbiome and other mail-away consumer or clinical assays. The device I used was marked for DNA collection, although the company lately has rolled out comparable devices optimized for RNA stabilization that preserve RNA molecules for longer. Each one costs about \$28.

But a more significant competitor

in the COVID-19 testing arena may be no stabilization at all. A testing strategy pioneered at Yale involves simply sending raw saliva at ambient temperatures to be tested at a lab. They estimate that, per test, reagents should cost only about \$5.

SalivaDirect

Yale researcher Anne Wyllie co-developed a saliva test for SARS-CoV-2, the virus that causes COVID-19, that now is used in 49 labs in 24 states across the country and is still in the process of rolling out. It received emergency-use authorization from the Food and Drug Administration in mid-August, the cheapest of a wave of saliva-based tests.



ANNE WYLLIE

Before COVID-19 hit, Wyllie focused on the difference between saliva and nasopharyngeal samples for diagnosing another pathogen altogether. She got involved in coronavirus testing in March, when Nathan Grubaugh, an assistant professor at the Yale School of Public Health who was helping to set up a research program to track the pandemic, asked for training on an RNA extraction kit that Wyllie was working with.

Saliva is a more challenging sample than nasal swabs, which are dunked into viral transport media and always come in the same format. Saliva varies in viscosity; it may be contaminated with sputum or with food particles. Still, based on her earlier research, which had shown that saliva can be a more sensitive sample than nasopharyngeal swabs in patients with pneumococcal infections, Wyllie suggested that the lab try it. In a study they published in the *New England Journal of Medicine*, the

Testing basics

The FDA has issued emergency use authorizations for 32 molecular tests that detect the SARS-CoV-2 genome. Most use reverse transcription polymerase chain reaction, or RT-PCR, but a few are based on other nucleic acid amplification techniques such as loop-mediated isothermal amplification, known as LAMP, or transcription-mediated amplification, or TMA.

RT-PCR is considered the gold standard for diagnosing a SARS-CoV-2 infection, and according to the COVID Tracking Project, a nonprofit organization that collects and reports national data on the pandemic, a majority of states and territories only report on the number and results of PCR tests they conduct. But there are other methods as well.

Eleven antigen tests, which detect proteins from SARS-CoV-2, have emergency authorization. Some also test for antigens from other respiratory pathogens, such as the influenza virus.

Sixty-three antibody tests designed to detect antibodies the immune system produces in response to a SARS-CoV-2 infection have emergency authorization. These are more likely than other types to miss an active infection but can tell whether a patient previously was infected.

PHOTO SERIES: LAUREL OLDEN/ASBMB TODAY



The test kit comes with a saliva collection funnel. When closed, the lid releases stabilizing buffer.



Step-by-step graphical instructions show the user how to collect and stabilize a sample.

team compared saliva and nasopharyngeal swab samples from hospitalized COVID-19 patients and found that, over time, saliva samples yielded fewer false negatives than the swabs.

Although she joined the project as an RNA extraction expert, Wyllie later found that RNA extraction was not necessary for SARS-CoV-2 detection. After reading that other labs were running PCR assays on swab media with no further processing, she decided to try a similar protocol.

“I was setting up a qPCR, and I was like, ‘Got some raw saliva here; we’ll just put some into it and see what happens,’” Wyllie said, leaning into her New Zealand accent. “The results weren’t perfect, by any means, to begin with — but it was enough to be promising.”

After optimizing the protocol, which calls for a lengthy vortex step in lieu of traditional RNA extraction, the team applied for the emergency use authorization the FDA approved in August. Since then, Wyllie said, she’s been busy

helping other labs set up the test protocol, which is branded as SalivaDirect but not marketed for profit.

Unbuffered stability

Why does testing raw saliva work so well? RNA is famously unstable, prone to hydrolyzing its own backbone; how is it possible that in raw saliva, left at ambient temperatures for hours at a time, it can persist?

“We don’t know,” Wyllie said. “And remarkably, it seems quite specific to (viral RNA fragment) N1. We’ve actually heard that others have not found the same stability as we see.” When other labs tried the protocol using other regions of the viral genome as qPCR targets, the E or ORF regions, they observed much more degradation.

Rhiju Das, an associate professor in Stanford University’s biochemistry department, studies RNA structure and has worked on modeling the SARS-CoV-2 genome in three

dimensions.

“The RNA of coronaviruses ... appear to fold into highly stable secondary structures,” Das said. Coronaviruses have unusually long genomes, some 30 kilobases of RNA; scientists hypothesize that those structures may protect from the types of self-cleavage that RNA is prone to and perhaps also from recognition by innate immune proteins in the host cell. The nucleocapsid-coding region, Das said, seems to be especially rich in these structural regions.

Even when the viral genome is synthesized in a cell-free environment, “big chunks of the genome are protected from chemical reagents that would normally modify single-stranded RNA — including the self-cleavage reaction,” Das said. “That may be the answer to why the Yale diagnostic or other saliva diagnostics have a chance.”

Researchers also don’t know exactly where the RNA SalivaDirect detects is coming from. Based on the facts that raw viral RNA spiked into



The sample collection tube and a patient information form are shipped in a biohazard bag.



The kit comes with a shipping envelope pre-addressed to Phosphorus' Secaucus, New Jersey, laboratory.

saliva degrades rapidly and that a vigorous vortex is required to make the protocol work, Wyllie said it's unlikely that the viral RNA is floating freely in saliva. But is it in cells or in viral particles? Frankly, she said, finding out is not a priority for clinical use of the test, which has been her focus.

"The protocol's there; it's pretty easy," she said. "Have a go and let us know. If you find a better version, we're all for it!"

PCR testing

After some hours in a FedEx drop box and in transit, my saliva arrived at a genomics startup called Phosphorus based in Secaucus, New Jersey. Before the COVID-19 pandemic, CEO Alexander Bisignano said, the company used its qPCR machines for quality control to make certain that DNA samples had not degraded before processing them for next-generation sequencing. When the pandemic began, scientists at Phosphorus began trying

to conduct tests for SARS-CoV-2 and received emergency FDA approval in June — the second lab approved for testing saliva at home. They now run several thousand tests a week.

Sharply aware of supply-chain concerns, Phosphorus researchers tested a number of different RNA extraction kits, giving them some flexibility in case reagent supplies were interrupted.

Phosphorus' test order process includes an option to consent to research. According to Bisignano, this work is carried out in partnership with academic researchers. Using demographic and medical information combined with viral testing, researchers aggregate and de-identify data for further use. In some cases, when patients consent to DNA testing, researchers may map transcriptomic and genetic information to patients' clinical outcomes in order to investigate relationships between potential biomarkers and disease severity.

While the opt-in process gives

little information about what research might be carried out, Phosphorus is acutely sensitive to privacy concerns. In a statement, a Phosphorus spokesperson wrote, "patient data are de-identified according to HIPAA standards and current industry-wide best practices," and added that the company never collects genome information unless a patient specifically has consented.

Lacking those assurances when I was submitting my test, I had taken a pass on the research question. I put my saliva sample in a FedEx drop box on a Sunday; it was shipped on Monday, and my results came in by email and text on Thursday. I'd tested negative, and I had learned a lot.

Laurel Oldach (loldach@asbmb.org) is a science writer for the ASBMB. Follow her on Twitter @LaurelOld.



The Wellness Issue





A pandemic-proof mindset

How three scientists at different levels are coping

By *Caleigh Findley*

I first heard about COVID-19 when our Chinese New Year celebration was canceled in late January. News about the coronavirus in Wuhan had spread, and one of the organizing committee members recently had returned from a trip there. I remember thinking it was a freak thing, an outbreak happening overseas that we just needed to make sure didn't cross over. As the weeks passed, however, I began to see that this virus was a real threat. Before I knew it, the grocery stores were out of toilet paper, and the governor was announcing a lockdown.

The first months of the pandemic were the most stressful. My lab went on a restricted schedule, with only essential workers allowed to carry on their experiments. I had to perform my work as quickly as possible and then work remotely for the rest of the day. With little flexibility in my on-site schedule, my anxiety grew at the thought of how this lockdown could impact my graduation date. I did my best to remain calm, maintain a regular schedule and lean on my support system to take care of my mental health.

I knew I wasn't the only person with these feelings. According to a recent survey at public research universities, twice as many students reported suffering from major depression and 1½ times more said they had generalized anxiety disorder in 2020 than in 2019. I wondered how others around me were coping. I talked to three people at the university about their experiences.



The grad student: Be logical

Jesika Colomer-Saucedo, a fellow graduate student in my department, said the lockdown left her feeling anxious and unsure of the future. “I was just going to the lab like normal, but it was weird because no one was around,” she said. “But it was like, what’s the point? Nobody knows what’s going to happen.”

Colomer-Saucedo faced major challenges with living alone and having reduced contact with her support system. Before the pandemic, she could walk into her PI’s office to talk about her projects. The lockdown forced many professors to work from home, leaving grad students to troubleshoot and move forward with less oversight. Colomer-Saucedo now sees this as a period of professional

growth. “It forced me to be even more independent as a researcher,” she said.

Her “student mentality,” as Colomer-Saucedo calls it, allowed her to adjust better to changes in work-life balance. Many students are accustomed to working from home, and graduate students are certainly adept at learning as they go.

To combat pandemic anxiety while living alone, Colomer-Saucedo maintained a regular workout schedule, minimized her doom scrolling and news intake, and just tried to be “as logical as you can about things.”

The lab coordinator: Go with the flow

I live with my boyfriend and our two dogs that we treat as our children. But I knew that people with

families faced greater challenges than I did when daycare centers closed and school-age children had to switch to remote learning at home.

Sam McFadden is a laboratory coordinator, managing several aging projects and the logistics of a large lab. He found that juggling a shift-work schedule with a 2-year-old no longer in daycare and his wife still working on-site left him stretched thin.

“I had to come in (to the lab) on weekends, which threw off my life schedule,” he said. Aging projects have strict timelines for data collection, negating any flexibility for pandemic shift work. “It was necessary but unfortunate because I got less time with my family.”

While his work–life balance was being tested, McFadden found that adapting to his new normal meant taking things day by day. “I went with the flow of it, and the only way I could keep my sanity was to understand that I couldn’t control any of it.”

“I just took every day one day at a time and said, ‘Alright, that was today, and who knows what tomorrow will be, so just go to sleep and wait for the next day.’”

The PI: A marathon sprint

Kevin Hascup, an assistant professor and early-career principal investigator, works in tandem with his wife, Erin Hascup, director of the university’s Alzheimer’s center and an associ-

ate professor, studying Alzheimer’s disease pathology in several animal models. The onset of the pandemic left Kevin Hascup feeling anxious about the possibility of the lab shutting down and overwhelmed by the constant influx of new information as the virus spread.

“We’re an aging lab,” he said. “Some of the mice we use are aged out to a year or longer. If we have to cull the entire colony, that sets us back at least a year just to get back to the point we were at.”

With a large laboratory, a 9-year-old and a 5-year-old at home, and a publishing quota to reach, Hascup knew the pressure was on to find a way through the lockdown. He chose to face these challenges head-on, determined to make the most of an uncertain situation.

“I adapted by understanding more about the virus and then trying to adapt that to our research,” he said. “We both believed that there were going to be two scenarios that come out of this. You either come out stronger, or you fall behind. And we didn’t want to fall behind.”

Hascup refocused on various writing projects and research ideas that had been in the back of his mind. His efforts produced forward momentum in his work, with the publication of two editorials and successful application for additional funding toward COVID-19 and Alzheimer’s research.

Yet he felt the strain of finding a work–life balance as he and his wife attempted to continue their work while homeschooling their children. The children’s school was slow to adapt from hands-on teaching to virtual learning techniques, leaving the responsibility on parents to teach from home. No easy feat — even as a husband-and-wife team.

Hascup said he knew coping with the virus would be a long process, a marathon of sorts. But meeting the ever-growing demands of early pandemic life left him feeling like he was sprinting from one thing to the next, he said. “You’re able to sustain that for only so long before it mentally and physically wears on you.”

In facing these challenges, Hascup learned to take things in stride and place greater value on balancing his home and work life. He also relied on his tried-and-true technique for mental health — consistent exercise with his Peloton bike.

Now (somewhat) adjusted to pandemic life, Hascup said he realizes something that rings true for many of us — we are more resilient than we thought.

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From grief to healing in the year of COVID-19

By Nivedita Uday Hegdekar

When COVID-19 news began circulating, I was not overly concerned. I recall chatting with my family and friends, convincing them that the situation was under control and the U.S. government and health professionals would nip the virus in the bud. My friends and I continued to make plans for what we referred to as “the best summer ever.”

However, my concerns grew as the pandemic moved to the forefront of our lives. I was at the University of Maryland, 8,000 miles away from my family in India. My parents both have preexisting conditions that put them at higher risk for COVID-19. My father, a doctor, was in regular contact with geriatric COVID-19 patients.

I was particularly concerned for my maternal grandmother. She and I had always been extremely close: Ever since I was an infant, my mom and I visited her almost every weekend. We grew even closer after my grandfather died in 2003. My undergraduate university was near her house, and I often ran errands for her after class, followed by enjoyable evening chats. We shared a love for cooking, good literature and British period TV shows.

In mid-February, my grandmother suffered a major cardiovascular stroke, her third in two years. Thankfully, she was able to leave the hospital before the lockdown in India came into effect.

Before COVID-19, I had plans to visit home during the summer of 2020. However, when the international travel ban went into effect, I resigned myself to the fact that there



Nivedita Uday Hegdekar poses on her grandmother's lap in 1993. When she was very young, the author visited her grandmother every weekend.

was little I could do to help my loved ones in India. The last time I had seen my family was in April 2019.

Meanwhile, in Maryland, the first university employee tested positive for COVID-19; our campus completely shut down for in-person instruction, and all research ground to a halt. My lab euthanized most of its mice colony, and just like that, three months of experiments were obliterated.

As a senior Ph.D. student, I had a 12-month timeline to complete

my degree and find a job. As an international student on an F1 visa, my life revolved around organization and deadlines. The university's work-from-home order sent me into a panic. To do my work, I had to be in my research lab. I was in a constant state of anxiety, feeling sometimes as if I had lost my purpose.

Beginning in May, my grandmother's health began taking a turn for the worse. She lost the ability to walk independently, and she forgot



Nivedita Uday Hegdekar's undergraduate university was near her grandmother's house, and the two, shown here in 2016, shared a love for cooking, good literature and British period TV shows.

how to read and write. Relatives hired helpers to take care of her, but she was traumatized by the absence of her family during this trying time. Most of her children lived overseas, and even my mother was unable to go to her due to travel restrictions. When India relaxed its restrictions in July, my mom was finally able to go take care of her. However, my grandmother's health had crossed to the point of no return, and in August, she passed away quietly in her sleep.

My grandmother meant the world to me. Nothing could have prepared me for her death or the anger I directed at myself for being unable to help her during her final months. I withdrew from other people and retreated into my shell. Grieving is always a lonely journey, but the thousands of miles separating me from my family compounded the isolation.

My grandmother's death coincided with the phased reopening of research at my university. Initially, I threw myself into work, thinking that this distraction would keep the grief at bay. After a few torturous weeks, I

realized that this was an unhealthy coping mechanism. I took a few days off work to catch up on sleep and take care of myself.

Since August, the healing process has been uphill, but I see light at the end of the climb. I think wellness is an active process of making choices toward a healthy and fulfilling life. More than being free from illness, for me it has been a dynamic process of change and growth. (See the author's "Steps to survival and wellness" on page 39.)

Striving for wellness this year has been tough, but my struggles with anxiety and loss have made me kinder and more empathetic. I believe these experiences will help me face the uncertainties of the future.

Nivedita Uday Hegdekar (nivedita.hegdekar@gmail.com) is a graduate student at the University of Maryland working toward a Ph.D. in biochemistry and molecular biology and an M.S. in patent law. Follow her on Twitter @NiveditaHegdek1.



Steps to survival and wellness

During these months of loss, I realized that I needed to train myself to focus on controlling those things that were under my control and to seek the help I needed. Many of us are enduring losses. Here are some actions I found helpful.

TO COPE WITH THE PANDEMIC:

- 1. Stress limits.** I took note of everything that caused stress in my daily life, and then I limited my intake of the news and social media to one hour per day.
- 2. New hobbies.** Working from home blessed me with extra hours of free time. I finally read several books from my ever-growing to-read list. I also took up meditation and brisk 15-minute early morning walks (with a mask!). I discovered a passion for baking.
- 3. Connections.** My friends and I missed our regular hangouts and made a pledge to keep in touch. I kept a weekly schedule of virtual meetings with friends and loved ones and also made sure to check up regularly on friends who lived alone and those who had lost a job or whose graduation had been delayed.
- 4. Shared anxiety.** I reminded myself that many people I knew also were suffering from loneliness and anxiety. During low moments, we reached out to each other. When we communicated our hopes and fears and listened to each other, we shared the burden and increased our connection.

TO ENDURE GRIEF:

- 1. Take time.** I learned that healing can't be forced or hurried, and there is no normal timetable for grieving. I had to be patient with myself and allow the process to unfold.
- 2. Routine.** Once I came to terms with the fact that life moves on, I began reintroducing normalcy to my routine. I planned my day in chunks of time, including meals, exercise and time to grieve. This helped me make the transition back to my work routine. At the same time, I had to forgive myself for lapses and remind myself that progress comes slowly.
- 3. Seek support.** I learned that unresolved grief and prolonged sadness can lead to emotional damage, health problems and depression. When other people confided in me that they were coping with personal loss, this knowledge that I was not alone provided a lot of comfort. Eventually I sought professional help from my university's telecounseling services as well as an online support group.

— Nivedita Uday Hegdekar



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A lonely introvert in a pandemic

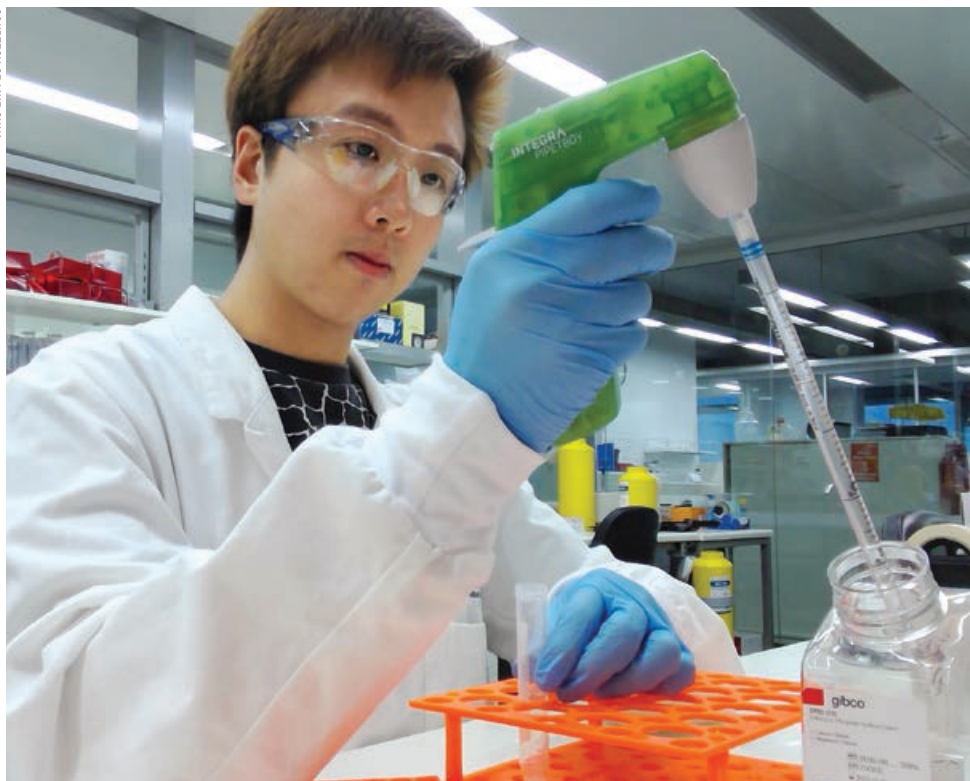
By Ngee Kiat (Jake) Chua

I am an introvert, so I need quiet personal time to recharge after a day with other people. In the lab, I prefer meaningful conversations to small talk. Since I started a new postdoc during the pandemic, I've been looking for a deeper purpose to my research life and trying to figure out how to find satisfaction in my simpler, socially distanced home life.

My dissertation was passed, and I graduated with a Ph.D. in February. I moved to Melbourne, Australia, in March to start my postdoc, leaving the city of Sydney where I had lived for seven years. Before the move, I knew I'd need to find support groups at my new workplace and in my personal life. Why does an introvert need a social circle? Don't misunderstand: I am delighted at the thought of spending time away from the lab and avoiding the current rocky state of the world, but I also knew I needed real human connections in my life.

At the start of the pandemic, I was indifferent to my life of isolation. But over time, my satisfaction with my new position deteriorated, living alone in Melbourne. I couldn't shake off the feeling I had just started a postdoc without knowing how a research career in science works. My visa was set to expire soon, and as a citizen of Malaysia, I feared deportation. I needed to complete several publications with my former Ph.D. advisor with tight timelines. Without companions to talk to, I found it difficult to be in a vibrant mood most of the time.

Eventually, I figured out that I



COURTESY OF JAKE CHUA

Jake Chua works as a postdoc in the lab in Melbourne.

needed to create new routines for my new life.

I had started blogging in January, months before my move and the peak of the pandemic. As a grad student, I had grown more confident and better at making decisions after hearing the stories of experienced postdocs and grad students. I wanted to do the same, to help newer grad students, through my blog "Walking in My Science Shoes." As research for the blog, I started reading uplifting articles about personal and career development in my spare time. Along the way, I connected with other bloggers and even ended up hosting a Zoom session on bloggers in science.

Through blogging, I became more mindful of my feelings and reactions, which helped me keep my emotional distress in check. Being a science communicator as a blogger fulfilled my desire to be in a quiet space where I could dive into the silent world of my mind. It gave me time to think and communicate freely in the comfort of home.

I always have been slow to warm up to others and reluctant to initiate contact, but I became frustrated; my routine of doing experiments and finishing desk work was just not enough. A week after I started my postdoc, I was told to work from home. When I was allowed back two months later,

I thought returning to the lab and meeting colleagues would alleviate my frustrations, but it was difficult to familiarize myself with the people and atmosphere of my new workplace. So I made the first move to sign up as a presenter for two series of weekly online events to make other connections. One of these developed into a community of Malaysian scientists, and another flourished as a community of grad students and postdocs from different parts of the world. We did a bit of show and tell about our research each week. Hearing about the lives of other scientists in these tighter circles has been comforting as I face the unknowns of my postdoc journey. These virtual communities contributed to what became daily positive affirmations that I have now to keep me going to the bench.

One new routine I initially loathed but then became strangely devoted to.

Every week, I teach an online class at the University of New South Wales in Sydney, where I had my Ph.D. training. At first, I just wanted to help maintain the university's reputation during the pandemic, but after the initial stress, I became infatuated with online teaching.

On the weekends, I worked at developing creative teaching resources and learning about how humans interact in the virtual world. I learned to make full use of the online realm for science, and that made me a better teacher. I began to enjoy meeting my students every Wednesday. I was excited to see how they learned to like molecular biology even without hands-on lab experience. Their words of appreciation continuously brighten my day. After class, I walk to my research bench empowered as a scientist, knowing that I've helped nurture the scientists of tomorrow.

I do enjoy my alone time, but introverts can get lonely. I realized that no matter how introverted I am, I still wanted contact with people who support and understand me. The difficulties of starting a post-doc, worrying about my visa status, taking care of unfinished business with my former Ph.D. advisor and living alone in a pandemic made that contact necessary. Taking time away from the research bench to set new routines and find online support communities helped me gain a better sense of belonging and satisfaction in my new life.

Ngee Kiat (Jake) Chua (chua.n@wehi.edu.au) is a postdoctoral research officer in the Feltham research lab, Ubiquitin Signalling Division, Walter and Eliza Hall Institute of Medical Research. Follow him on Twitter @mediocre_jake and read his blog at walkingscienceshoes.wordpress.com.



The poster features a background of colorful, abstract shapes resembling leaves and protein structures. The text is overlaid on the left side.

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Celebrating together, apart

By Courtney Chandler

Throughout the upheaval caused by the COVID-19 pandemic, I've been fortunate to keep my postdoctoral fellowship and remain surrounded by my supportive lab mates and mentor. Yet while we prioritize safety, social distancing takes its toll. We've all felt disappointed about canceled conferences, graduations, ceremonies and gatherings.

This rang true for me when my former roommate and best friend won a prominent award from our graduate school program for her thesis work. Normally, this honor is the occasion for a ceremony and reception with awardees surrounded by proud faculty, friends and family. This year, that wasn't possible.

It seemed like a small sacrifice to ensure everyone's safety. At the same time, it felt like her accomplishment (and all the work she put into earning it) was diminished. And the ceremony would have been a chance for us to reunite with close friends who had defended and graduated this year, then moved away to start new careers across the country.

I found it hard to reconcile feeling disappointed by something like a canceled awards ceremony with knowing people everywhere faced more immediate and dire problems. I was at a loss. I couldn't reunite with my closest friends, and I felt overwhelmed with guilt for even being sad. I felt powerless, unable to end the pandemic and just wanting to have something that felt normal.

For months, I'd pushed all the canceled celebrations out of my mind. I worked on adjusting, processing and rationalizing the idea that it's OK to celebrate anything in a pandemic.

COURTESY OF COURTNEY CHANDLER



Courtney Chandler and her friends created this image for their online celebration.

That brought me to the fall, around the usual date for presentation of the aforementioned awards. Just because the school wasn't hosting a ceremony, that didn't mean we couldn't celebrate.

And that's what we did — my friend (the awardee), our other friend (we're a trio) and I set a date for our own virtual celebration. Invitations were made (think black background, glitter and an unnecessary level of formality) and sent out, although the entire guest list was the three of us and significant others. An emcee was hired (just kidding — it was me), and a presentation was prepared. We were

set. We just had to count down the days to our custom-designed celebration/reunion.

When the night of the ceremony arrived, we each grabbed a glass of wine, logged onto Zoom (this time without the dread of yet another online meeting), and the self-made award presentation began. We talked about the award itself and its history as well as the awardee, her thesis work and why she was a deserving recipient. There was a toast, we all said "Cheers!" and the ceremony was over. It was fun, short and safe.

The evening progressed to our version of the reception, across time



zones, which included catching up (and glimpses of one particularly curious and mischievous cat friend). For me, this was a much-needed mental boost I didn't know I needed. I ended the call feeling more connected to my friends and less stressed than I had been all week, maybe longer.

It lacked the fanfare of a typical ceremony. But the important elements remained — we recognized our friend's hard work to earn the award, reunited after moving to different parts of the country and even saw the awardee blush as she reveled in our words and support. It wasn't what we expected for this year, but it was better than doing nothing.

Things are weird right now. A canceled in-person award ceremony is an understandable (and encouraged) consequence of the pandemic. But the lack of normalcy doesn't mean we can't celebrate.

People still put in the work, and their work should be acknowledged. Not in a way that puts anyone's health at risk or minimizes the terrible effects of COVID-19 but in a

way that provides the recognition and connections of an in-person ceremony.

We all have different approaches to protecting our mental health. This type of virtual ceremony may not be your cup of tea. For me, acknowledging that I wanted to connect with faraway friends for a few moments helped me find balance and mental well-being.

And you don't need to wait for a canceled event. Grab your favorite drink (tea, wine, whatever it may be) and send a quick email to your favorite fellow scientists. Did you meet that grant deadline? Celebrate. Did you manage to make it through the week? Celebrate.

Take a little extra time just to be together.

Courtney Chandler (courtneyec19@gmail.com) is a postdoctoral researcher at the department of biochemistry and molecular biology at the Johns Hopkins University School of Public Health and an industry careers columnist for ASBMB Today. Follow her on Twitter @CourtneyCPhD.




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New-ish adventures help me reconnect

By Jessica Desamero

In early October, I received an email from my home campus: “We are very happy to start our seminar series this Fall.” I was ecstatic. For the first time in a very long time I would be able to see people from my department. And I was thrilled to learn more about the cancer-related research being done at my school — cancer research in general piques my interest.

The day approached, and the seminar started; I was excited and eager to learn. But as it went on, my excitement faded, and I started to get sad. I couldn’t concentrate on the words, and I was left wondering: Out of all the seminars I’ve attended via Zoom, why is this one having this effect on me?

I felt this same sadness the first time I did other familiar tasks during quarantine. From analyzing data and writing reports at home to having virtual lab meetings with my research mentor and online recitation classes with my students, all was not as it used to be.

One day in April while working from home during the first peak COVID-19 surge in New York City, I was feeling particularly down, and every negative thought weighed on me all at once. To counter this feeling, I thought, “Hey, what if I try something different and new?”

By new, I didn’t mean completely divergent from my usual activities, but rather a different version of what I already do. I didn’t want to overwhelm myself. For example, I usually listen to music while grading assignments and doing household



During the pandemic, Jessica Desamero has branched out from her usual science-centric reading to books about racial injustice and mental health, including those pictured here.

tasks, but what if I tried listening to podcasts? I usually read journal articles related to my thesis project or other life sciences research, but what about nonscience literature?

Besides research reports and thesis proposals, I write articles for a cancer research blog called OncoBites about topics in cancer research based on published journal papers. To try something different, I wrote a few articles for BioBus, a science outreach organization I volunteer with. These articles were aimed at a middle school audience, and the topics were birdsong and snail venom — far from what I’m used to writing about. These were a challenge, but it felt great that I still was able to teach children science. Then I wrote an OncoBites article about an organization called

Black in Cancer, whose goals are to “strengthen networks and highlight Black excellence in cancer research and medicine.” I interviewed the organization’s co-founders, even though I hadn’t done an interview article since I was an undergrad.

Pre-pandemic, I attended chemistry, biology and biochemistry seminars on my home campus and at one other university. Now I can attend online biochemistry seminars from campuses around the country and the world. I even have listened to seminars in other fields.

At first, my main goal was to try something new for a positive change. But I eventually found another common theme — I was trying to reconnect with myself and with others around me in new ways.

The nonscience literature I've read, nonscience seminars I've attended and podcasts I've listened to mainly revolve around either racial justice or self-love and mental health. One of the more memorable talks I've heard was about an initiative dedicated to breaking the stigma around anxiety and depression. Talking points ranged from using journaling as a therapeutic tool to protecting ourselves from triggers on social media. Another talk was about how economic inequality extends to public school education. From this, I've learned the extent of the impact a lack of adequate resources can have on students.

In a time when tensions and anxieties are high, it is important to take care of my mental health, appreciate myself for who I am, and be as good

of an ally of the Black Lives Matter movement as I can be.

By writing a variety of articles and listening to science communication talks, I've connected in new ways with my passion for writing and sharing knowledge. And by attending the biochemistry seminars of a sister campus, I'm able to, in a way, connect with more of my school community rather than just with my home campus.

All these changes inspired me to reconnect with a good friend from undergrad whom I hadn't really spoken to since graduation. Over the years, every so often, I had contemplated getting in touch with her again. But because of all the time that has passed, I always felt too embarrassed and shy to do it. One night,

I decided to message her, and she quickly responded, to my pleasant surprise. Since then, we've had a number of conversations.

As the months go on, it's become easier to adjust to the new normal and proceed as I did before, albeit in a more virtual fashion. What has helped me the most is my reestablished relationship with myself and with others both directly and indirectly around me.

Jessica Desamero
(jdesamero@gradcenter.cuny.edu) is a sixth-year graduate student in the City University of New York's biochemistry Ph.D. program and a BioBus volunteer. Follow her on Twitter @JessicaDesamero



Upcoming ASBMB events and deadlines

JAN.

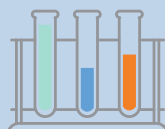
JANUARY	Cervical Health Awareness Month
1	ASBMB journals become open access
4	Deadline to submit ASBMB fellows nominations
7	Abstract deadline for the ASBMB Annual Meeting held in conjunction with Experimental Biology
11	Abstract deadline for Proteinases and their inhibitors
14	Deadline to apply for ASBMB Annual Meeting grants and awards
24	International Day of Education

FEB.

FEBRUARY	Black History Month
1	Early registration deadline for Proteinases and their inhibitors
1	Deadline to submit an ASBMB Annual Meeting interest group proposal
7	Periodic Table Day
11	International Day of Women and Girls in Science
14	Cancer testis antigens virtual event
22	Regular registration deadline for Proteinases and their inhibitors
24–26	Proteinases and their inhibitors
27	National Protein Day
28	Rare Disease Day



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To stay productive, ask for help

By *Brandon G. Roy*

Starting graduate school during a pandemic has presented some challenges, including scheduling lab time, traveling to and from classes in person and virtually, and lack of access to buildings. I joined the plant pathology and plant microbe biology Ph.D. program at Cornell University this fall. My university has tightened restrictions on using public spaces unless absolutely necessary — forcing students like myself to stay in our apartments most days. Living off campus, I sometimes feel disconnected from lab culture and the grad school experience.

What have universities been doing to combat the antagonists of student well-being? COVID-19 is challenging mental and physical health around the globe, and most grad students are under more stress than we have encountered in our whole lives. The short answer is that the resources are on campus; it's up to students to find and use them at our respective schools and take control of our wellness. In my program, the university urges us to use these resources without restraint and take care of ourselves to ensure success.

It took time to find all the resources I needed. I reached out to mindfulness groups, clubs and counseling services that would support me during graduate school. Asking was difficult. Knowing my mental state was difficult. Establishing my support system got easier over time, and it was one of the best decisions I made entering this program. Here are the people that I ask for help in grad school.

Ask your PI

It may be unusual that I can share struggles, successes and everything in between with my advisor since I just entered into this program. Graduate school is a time full of obstacles, frustration and chaos — all for the purpose of learning how to be a better scientist. Having someone to talk to and act as a mentor through this is critical to success. Others within my cohort have similar relationships with their PIs, but I know some grad students who have strictly professional relationships with their mentors. No matter what boundaries are in place, I believe that attempting a heartfelt conversation with your boss about COVID-19 and well-being is warranted.

To the extent that my PI knows I'm struggling, they have been able to help me through or guide me to the right resources. I was nervous when I started this conversation, but I was reassured by the end that I had picked the right advisor for me — and if I'd had any concerns, I would have taken them to the head of the department.

Other professors at my university have offered students time to talk if we need it. In October, I tweeted about my struggles feeling distant from home, and several professors reached out to me, saying they were here to talk if I needed it. This meant the world to me, and it made me feel supported in my education. I wish all grad students could experience this type of environment. I understand this is not always the case, but there are always

caring individuals on the administrative staff or elsewhere within the department, so search them out.

Two people in my cohort had their fellowship funding delayed, causing financial and emotional stress. Their respective PIs, once they became aware of this, showed great compassion — offering money for food or gas until the paycheck came and blasting the finance department via Twitter and email. This was a simple mix-up in another department, but it showed the compelling empathy of my cohort's advisors. The unity of my department was showcased through this mishap.

Ask your lab mates

All of us in the lab, postdocs and grad students, experience the same stressors day to day. While balancing classes, seminars, conference abstracts and lab meetings, we lean on each other for support and share our concerns. Talking with others in my lab has helped me to feel less isolated in my feelings of self-doubt and anxiety. I know that I am not alone in my struggles, thanks to the people around me — it's okay to be vulnerable with them.

We share the same failed experiments, the months spent trying to figure out a bioinformatics program, or the seemingly endless time spent trying to produce a worthy result. After commiserating with my lab mates about our collective problems, I have a sense of bonding that helps me overcome the obstacles. It boosts my morale and helps me keep going.



COURTESY OF BRANDON ROY

In summer 2019, Brandon Roy, third from right, joined members of the Fuchs lab at Cornell for a visit to a vineyard in Dundee, New York. At the time he was an intern with the lab, which he joined as a grad student in fall 2020.

Ask professionals

Every university and college has at least one licensed psychiatrist. My university has several dozen. After an initial evaluation, you have opportunities to continue one-on-one counseling or venture into group sessions since students often face parallel problems during graduate school. Group session topics at my university include mindfulness, procrastination, anxiety, imposter syndrome, depression and unpacking our complex feelings about COVID-19. Counseling professionals lead these sessions via Zoom. It may not be quite the same as in person, but it is nearly the same relieving outcome. I have taken advantage of plenty of mindfulness sessions, and I did this when I was an undergrad too. The online format just makes participating that much easier, with no hustling around campus required.

Our campus health centers are keen to provide information about resources to all students. They send email reminders on topics such as building a routine for productivity or

getting out of a depressed state. I've benefited from mindfulness practices during my most stressful times. I use the Koru Mindfulness App to keep it a habit. This program is targeted toward young adults and academics. Finding what worked for me personally took some navigating; it's important to try different avenues.

Ask family or friends

My family and old friends might not understand what I do every day or see the biggest issues in my life, but they provide a more holistic view of the world. I rely on my friends and family, and I support them in the same way with their struggles during this time. Sometimes when I get home from lab and I don't want to talk about the specifics of the day, I call my mom just to hear how my family and dog are. It brings a balance to my life as a scientist, because our work is important — but it's not everything.

I put family and friends as the last point because they aren't counselors,

colleagues or mentors; these are give-and-take relationships. I eventually realized that the people closest to me would prefer to hear fewer rants about how difficult lab was and more about the optimistic side of each day. This positive perspective took shape over time, and these cheerful relationships are essential to my overall well-being. It helps me to have that same attitude toward my friends and family that they show to me.

We are all dealing with COVID-19 in our own ways. Some days I hit the ground running while others my feet drag behind me. But I am learning how to be a better student by taking care of myself and trusting the people around me.

Brandon G. Roy (broy1117@gmail.com) is a graduate student at Cornell University. He earned his B.S. in biochemistry and molecular biology from Lebanon Valley College. Follow him on Twitter @_brandon_roy_.



Redirecting my COVID-19 anxiety into service

By Alison (Allie) Smith

The first time I heard the term COVID-19, I didn't think about getting sick or what would happen if we were quarantined — let alone still masked and distancing after more than 300 days and counting. As I felt anxiety bubble up inside me like too much yeast paste added to the tube, I thought about my students and whether or not they'd be OK.

I am all too familiar with this feeling; I live with generalized anxiety disorder. As soon as the pandemic led to a quarantine, I could feel my anxiety roar from inside of me as I worried about my every move. This is when I realized that I needed to start redirecting this anxiety.

For the last five semesters, I've been an associate instructor for an introductory biology laboratory course at Indiana University Bloomington. Last spring, my 25 students ranged from first-years to seniors. As the pandemic began, we thought we would be online for a week, which then became a month, then the rest of the semester. As soon as I realized I wouldn't be able to see my students and check in with them in person, I was concerned. I decided to proactively redirect this paralyzing concern. I often use this redirection strategy in my day-to-day life to lessen my anxiety; I delve into the thing in life that I love as much as science: service.

I started by contacting all my students on Canvas each week with a little message. I'd remind them what would be due over the next week and ask them what they were doing at home to take care of themselves



Even as her anxiety rose, Allie Smith knew that she would be OK in the pandemic. She could take care of herself and do most of her work from home, and she realized she was privileged to have the resources to do so.

physically, mentally and spiritually. I'd end by telling them something I had been doing (usually an update on how my Animal Crossing island was progressing).

Immediately, I started getting messages from students with updates on their Animal Crossing islands, recipes for new desserts they were cooking, suggestions for TV shows or podcasts they were using to decompress, updates on learning to rollerblade (being sure to say they were wearing pads and a helmet) and so on.

What really caught me off guard was that the students thanked me for checking in on them and asked what other students in the class were

doing to take care of themselves; they wanted suggestions for things they also could try. With this in mind, I shared everyone's self-care activities in an announcement called "How Allie's Section of L113 is Surviving COVID-19." This document included our amazing recipes, cautionary rollerblading tales and Animal Crossing: New Horizons tips.

I knew that I would be OK — I had people checking in on me. I was able to take care of myself and do most of my work from home, and I was privileged to have the resources to do so. As our fully in-person laboratory course switched into a fully online laboratory course, however, I learned

I had students who did not have the technology required to complete their assignments.

One student emailed me referring to himself as a “burden” for his professors because he didn’t have access to a computer with word processing or Wi-Fi. He wanted to know if he could handwrite the assignments, take a picture of the handwritten document and submit that image. I was sad that this was a concern for my student, and more than that, I was enraged that in 2020 there was not a way for the university to help my student with his technology needs.

Another associate instructor and I were inspired by this to create the IUcycle program. With sponsorship from the biology department and the Center of Excellence for Women & Technology at IUB, we started a program where students, staff and faculty can donate used but functional technology that can be upcycled to students, staff and faculty who may not have the means to obtain the technology they need. We did this with the hope that no student ever again would feel the need to refer to themselves as a burden. Since the program launched in November, we have received 10 functional laptops to upcycle.

In the time of COVID-19, when we all already are concerned about the survival of ourselves and our loved ones, the last thing someone should be worried about is whether they have the technology to write a story as I did today.

Since we started IUcycle, my anxiety no longer bubbles so intensely that it roars inside me; now it bubbles ever so slightly, saying, “What is our next adventure?”

Alison (Allie) Smith
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Finding ‘ikigai’ during a pandemic

By Deboleena M. Guharay

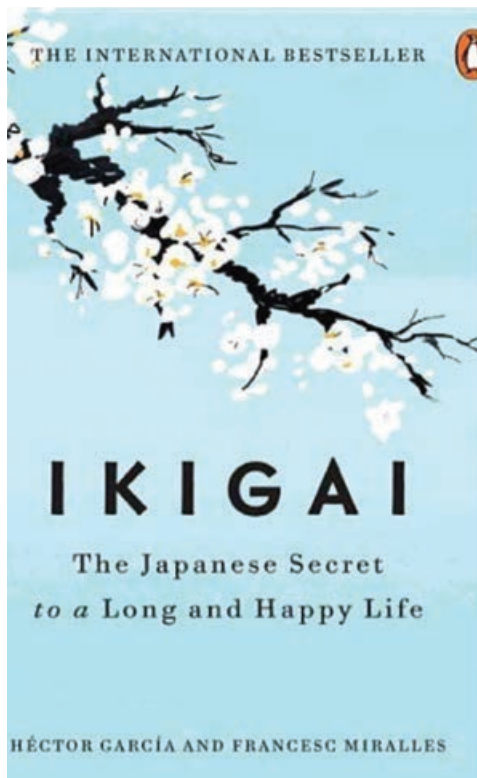
When COVID-19 upended everything around me, I took refuge in reading — something I enjoy but never invested much time in. Reading transports me to a place where I don’t have to think much about the pandemic. I read mostly at night after putting my toddler-age daughter in bed. Reading helps me relax, and it also means less screen time.

I borrowed a book called “Ikigai: The Japanese Secret to a Long and Happy Life” by Hector Garcia and Francesc Miralles from my mother-in-law’s collection. The Japanese word “ikigai” means finding a purpose to live. Many of the oldest living people on earth are from Japan. In this book, the authors write about these elders’ lifestyles, food habits and passions.

I was struck by their daily practice of habits that take care of their mental and physical health. Their diet is extremely healthy, they exercise daily, and they are connected with their communities. This is exactly what we need right now to get through the pandemic, I thought. Good diet, exercise and social connection can help us get through.

Diet and exercise

To fight any viral infection, we need a strong immune system. My husband and I have focused on diet very seriously. We know daily intake of green leafy vegetables, fish, healthy fat like avocado, fruits, nuts, and foods rich in vitamins C and D will



COURTESY OF DEBOLEENA GUHARAY

Reading “Ikigai: The Japanese Secret to a Long and Happy Life” confirmed the importance of purposeful changes in several aspects of Deboleena Guharay’s life, including cooking and eating.

boost our immunity. We enjoy creating our breakfast, lunch and dinner menu. We’ve tried new recipes.

To make cooking more fun, I started a family chat group called “Quarantine Food 2020.” We share recipes, cooking videos and pictures. Seeing the picture of a simple sautéed vegetable dish cooked by my mother-in-law motivated me to make something with vegetables the very next day. Her dish looked colorful, vibrant, healthy and very appetizing. Food brings people together, as did this virtual group with much

joy, delight and excitement.

My husband and I have cheat days once in a while when we eat something spicier or with more calories for a little change. Some of our favorite cheats have been fries, chocolate cake or an Indian yogurt-based dessert called mishti doi. This would help us get back to the healthy eating cycle the very next day.

Physical exercise is key to both mental and physical health. Staying at home means less movement, and we needed to incorporate some exercise in our daily routine. Some of my friends

go cycling or for long walks, practice yoga, or do gardening. My husband and I go for walks and enjoy the fresh air and nature. I also burn many calories running after my toddler.

Community

The greatest challenge we've faced is social disconnection: not meeting with friends and family, not visiting a local grocery store or a coffee shop. As the pandemic wore on, I began to appreciate the importance of human interaction in our lives.

My husband and I decided to make the best use of technology to stay connected with our extended family. We started doing regular video calls with friends and family, which soon became an integral part of our lives. These sessions bubbled oxygen into our systems that helped us breathe through the next few days.

We giggled, laughed and shared our anxieties. We celebrated my mother's birthday virtually in November. My daughter sang "Happy Birthday" for her, and I could see clearly from my mother's face that this moment made her day. We wished we were together, but we made the most of a virtual birthday celebration and enjoyed it immensely. We also celebrated anniversaries, festivals and Halloween virtually.

During this pandemic, I derive inspiration from people around me. My friends, family and neighbors are all inspiring in their own ways. Some have to work full time and also look after their children. It's been tough, but they pursue it with such zest and enthusiasm. And they also find time to follow their passions and do fun activities with their kids. A friend of mine started a food drive to help the needy. She used social media to spread

the word and had a great response from the community. One of my other friends started an online painting session and donated her earnings from it to a charity. She did it while holding a full-time job and managing her two kids. Whether it's a painting or a craft or a delicious meal or a little sign in the neighborhood saying "Thank you, frontline workers," each of these is an inspiring act, an act that gives life purpose.

The people around me inspire me in finding my "ikigai." My friends help me believe that the world will soon get better.

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earned her Ph.D. in chemistry from Virginia Commonwealth University. She is very enthusiastic and passionate about science communication.



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Walking through this pandemic

By Howard Chang

This year my movements have been restricted more than any other time in my life. Physical distancing mandates have made it challenging to exercise.

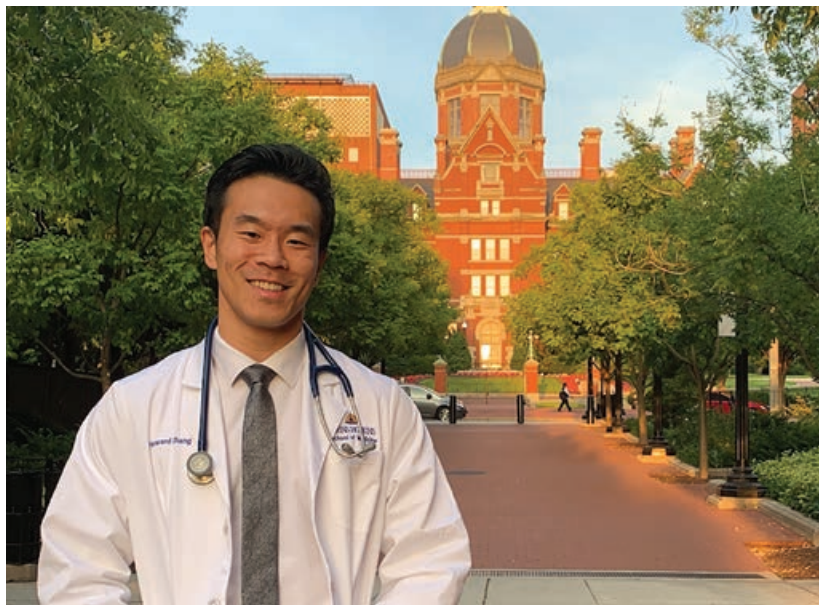
When the gyms shut down, I quickly adopted a resistance band workout routine at home that has been a sufficient substitute for strength training with weights. But I worried about finding a form of cardiovascular exercise that was both sustainable and enjoyable. Years ago, I tried high-intensity interval training, but I could only keep it up for a few months. I usually play basketball.

I noticed that the pandemic seemed to spare outdoor runners and walkers. I have never enjoyed outdoor running, so I decided to try regular walking. I was hesitant at first. I prefer working up a sweat to burn calories more efficiently, so I thought walking was a waste of time. Nothing was further from the truth. Since I started walking regularly in the summer, I have found that this simple form of exercise offers unique benefits.

1. It's easy to do, and to stick with.

I can walk virtually anywhere: outdoors, indoors and even in my home. It is affordable, requiring no memberships or special equipment other than a comfortable pair of shoes. And it takes little physical and mental discipline to get up and take a walk — for my science friends, the activation energy required to get out and walk is one of the lowest among exercises.

Arguably, the most important component of exercise is consistency. A strenuous regimen that quickly burns



Howard Chang, in his white coat, stands outside the Johns Hopkins Hospital on Sept. 10, 2019.

calories does little good in the long term if it is too challenging to maintain. Consistency is easier to achieve with exercises such as walking that do not overtax the central nervous system or impair muscle recovery.

Walking is also safer than running, an important consideration for those who have preexisting injuries or who must take precautions when exercising. Few things are more demoralizing to athletes and exercisers than injuries that stop them from doing what they enjoy. Preventing injuries is crucial to long-term exercise success.

2. It's effective for fat loss, cardiovascular health and appetite control.

I'll be frank: I used to look down on walking as a form of exercise because I didn't think it was effective enough. From my days as a high school athlete, I bought fully into the mantra "No pain, no gain."

Walking may not build stamina and endurance as well as strenuous cardio, but don't underestimate its benefits for fat loss and cardiovascular health. Again, sustained consistent walking is a powerful way to achieve favorable long-term health outcomes.

An immediate benefit I noticed was that regular walking did not ramp up my appetite. Strenuous cardio tended to deplete my energy, so I would compensate by overeating. I was also prone to rewarding myself with unhealthy foods after intense exercise. Walking is quality exercise that doesn't stoke the flames of hunger — the Achilles' heel of most arduous exercise plans.

3. Its possibilities are limitless.

Within reason, walking knows no bounds — mentally and geographically.

Mindful walking, particularly when implemented within the immersion

COURTESY OF HOWARD CHANG

in the natural world known as forest bathing, is a meditative practice that brings physical, mental and emotional health benefits.

This summer, I walked around my neighborhood several times each week while listening to podcasts or talks. I began to see these walks as incredibly efficient uses of my time — I was simultaneously learning and benefiting from my listening material, resting and relaxing due to the sights and sounds around me and, obviously, exercising.

Walking has led me to some beautiful sights that I never would have experienced if I only exercised in the confines of my local gym. I spent a day walking through the incredible Huntington Botanical Gardens in California near my hometown, and I recently hiked in Patapsco Valley State Park in Maryland for the first time.

I also never realized until my long summer walks how beautiful my Baltimore neighborhood truly is.

Walking has helped me see what I've been missing both around me and within me. Since I started walking, I have developed a healthier relationship with exercise. I am now less attached to immediate results and more interested in enjoying the experience. With walking, the results come in time — through consistency — and I am already beginning to gather the fruits.

This essay was adapted from an entry on Biomedical Odyssey, a blog about life at the Johns Hopkins School of Medicine.

Howard Chang (hchang68@jhmi.edu) is a second-year medical student at Johns Hopkins University School of Medicine.

COURTESY OF HOWARD CHANG



Howard Chang writes that walking has led him to beautiful sights he never would have experienced if he only exercised at the gym.



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Hell, heaven, a whale and me

Literary lessons for pandemic times

By Binks Wattenberg

My advice for staying sane in our unique circumstances is to read long and impenetrable books that you were supposed to read in college. Recently a poet and a toxicologist (different people, but it would make a good combination) suggested that I read “Paradise Lost” by John Milton and “Moby Dick” by Herman Melville, respectively.

Now you might think I am being snooty, and dear Lord, you would not be the first, but one of the limited number of advantages of aging is that sometimes books like these get transformed into instruction manuals for life. And perhaps they will for you as well.

My strategy for reading them, because I had the time, was to approach them as I would an important but dense manuscript, taking my time to understand every passage. After all, the devil (literally in the case of “Paradise Lost”) is in the details. Here are some tidbits for your consideration.

Responding to setbacks

“Paradise Lost,” Milton’s luscious and extravagantly trippy epic poem, describes Adam and Eve’s fall from God’s grace. You may recall that their fall results from Adam and Eve being seduced by Satan to eat an apple from the Tree of Knowledge after being expressly forbidden to do so by God. I am by no means the first to notice that at times “Paradise Lost” seems like a coded love letter to Satan. With that in mind, since we are now going through hell, why not get some expert advice?

The poem opens in the aftermath

of Satan’s failed rebellion. He and his minions wake up in a lake of fire. Who among us has not felt this way after a two-week experiment yields error bars the height of Mount Olympus? Yet Satan gets himself up, brushes off the lava and successfully exhorts his legions to make God pay for dooming them to everlasting suffering. Not the plan that I would have chosen, but still, you have to admire his moxie.

So, first piece of advice: To recover from failure, plot revenge.

We are all in this together

Many of you may know that “Moby Dick” is based in part on the cursed voyage of the Essex, a whaling ship out of Nantucket. The Essex was rammed and sunk by a whale who was annoyed by the sailors’ refusal to turn down their infernal hornpipes. After the sinking of the Essex in the middle of the Pacific Ocean, the sailors escaped in their small whaleboats with few supplies. Eventually, succumbing to starvation, the survivors resorted to cannibalism.

The captain of the voyage, George Pollard, had brought his sister’s son along on the voyage and promised to take care of him. You probably know where this is going. Pollard made sure that his nephew was in his whaleboat after the sinking of the Essex. Pollard survived, but there was nothing left of his nephew when they were rescued. Which no doubt led to a rather awkward conversation between Pollard and his sister on his return to Nantucket. “I loved your son, especially with a touch of aioli.”

So here, before even getting into “Moby Dick” itself, is my first take-away relating to the Melville classic: During these trying times, while we are all in this lifeboat together, let’s not eat each other. Unless absolutely necessary.

Forging a path through uncertain times

We need to transit from our previous world to the new post-COVID-19 one. In “Paradise Lost,” Satan presents a plan to the assembled mass of fallen angels to corrupt God’s newly created Earth. But to get to Earth from hell, a terrifying and shapeless void must be crossed. He asks for volunteers, but the newly appointed demons look at each other, shrug, and answer, “Sorry, busy torturing telemarketers.” So Satan declares he will undertake the perilous journey himself. This is what he encounters:

*“The secrets of the hoary deep,
a dark
Illimitable ocean without bound,
Without dimension, where length,
breadth, and highth,
And time and place are lost; where
eldest Night
And Chaos, ancestors of Nature, hold
Eternal anarchy, amidst the noise
Of endless wars, and by confusion
stand.”*

Yikes! Satan has wandered into a faculty meeting.

How does Satan make his way through this frightening, uncharted territory?



MUSEUM OF FINE ARTS, HOUSTON/WIKIMEDIA COMMONS

This illustration of Satan tempting Eve is a mezzotint plate by artist John Martin from a 19th century edition of John Milton's "Paradise Lost."

*"O'er bog or steep, through straight,
rough, dense, or rare,
With head, hands, wings, or feet
pursues his way,
And swims or sinks, or wades, or
creeps, or flies."*

So, two things here. Say what you want about Satan, but in taking on the journey through Chaos himself, he shows true leadership skills. Secondly, to make it through, he will do whatever it takes; he will creep if creeping will get him where he wants to go.

Maintaining one's appearance

At one point in "Moby Dick," the narrator, Ishmael, is enumerating the uses of whale oil to emphasize how essential the products of these whaling

voyages were at the time. He lands on the use of whale oil in anointing the heads of royalty:

"Much might be ruminated here, concerning the essential dignity of this regal process, because in common life we esteem but meanly and contemptibly a fellow who anoints his hair, and palpably smells of that anointing. In truth, a mature man who uses hair-oil, unless medicinally, that man has probably got a quoggy spot in him somewhere. As a general rule, he can't amount to much in his totality."

Melville's advice: Be careful with hair products; avoid quoginess.

Seeking knowledge

There is no getting around that "Paradise Lost" is relentlessly misogynistic, at least superficially. Although

the poem rails against the incautious and seductive nature of women, Eve is far more interesting than Adam, who comes off as rather dim. At one point, in his despair, Adam suggests to Eve that it would be unfair to pass their cursed sin on to their offspring. He suggests that they should refrain from what Milton delicately terms "connubial love." To which Eve, wise as always, replies, "You're kidding, right?"

After the couple gets word that evil is afoot (or, in this case, aslither), Adam insists that Eve stay within his sight. Eve will have none of it, and off she goes to enjoy some alone time. She encounters Satan (in the form of a snake) without that killjoy Adam getting into the middle of things. Satan easily convinces Eve to eat from the forbidden tree, because why should she be denied knowledge?

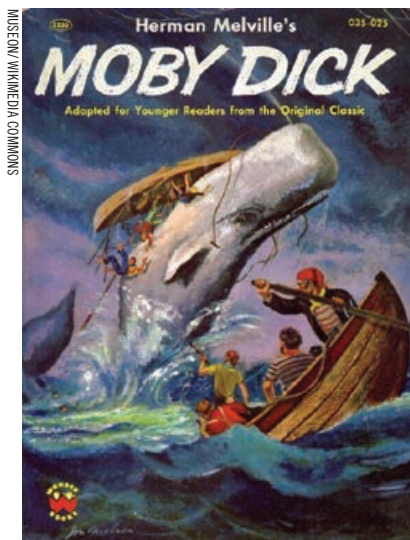
*“That whoso eats thereof, forthwith
attains
Wisdom without their leave? And
wherein lies
Th’ offence, that man should thus
attain to know?”*

I am with Eve and Satan on this one. It is our business to seek knowledge. We not only would have eaten the apple from the Tree of Knowledge but also would have dissected it; fractionated it into skin, seed and flesh; and performed lipidomics, proteomics, genomics, glycomics, epigenomics, metabolomics, and good-and-evil-omics on it till it yielded enough preliminary data for an R01 application. Adam is a nice enough guy, but I would not want him in our graduate program. Give Eve a fellowship.

Focusing on a goal and finding a team

As you no doubt know, “Moby Dick” is about how Ahab, the captain of the whaling ship Pequod, is focused maniacally on hunting down and killing the monstrous, homicidal white whale, Moby Dick. Students have been hounded mercilessly for eons to identify metaphors in the story. Am I Ahab, flogging my lab members in pursuit of Moby Dick in the guise of a Cell paper? If so, why does it keep swimming away? Well, whatever it all means, we can look to Melville to describe how it feels to be in the grip of a goal and whom you should pick to help you attain it:

*“Ahab had cherished a wild
vindictiveness against the whale,
all the more fell for that in his
frantic morbidness he at last came
to identify with him, not only all
his bodily woes, but all his intel-
lectual and spiritual exasperations.*



Cover image from a 1969 abridged version of *Moby Dick* by Herman Melville, adapted for younger readers.

*The White Whale swam before him
as the monomaniac incarnation of all
those malicious agencies which some
deep men feel eating in them, till they
are left living on with half a heart
and half a lung. Here, then, was this
grey-headed, ungodly old man, chas-
ing with curses a Job’s whale round
the world, at the head of a crew, too,
chiefly made up of mongrel renegades,
and castaways, and cannibals.”*

I guess the lesson here is that when you pick a project, go at it with half a heart and half a lung. And for your crew? Speaking as a gray-headed, ungodly old(ish) man, my favorite colleagues are mongrel renegades, castaways and cannibals. I would welcome them into my lab any day.

Paradise is what you make it

Let’s talk about Adam and Eve’s expulsion from Eden. One of my children once wrote that when they came to the lab, they saw that it was in my lab that I was truly home (too late for parenting advice, but

thanks for your concern). So, to spell it out, the lab is my Paradise. When my institution announced that our labs were going to be shut down, I knew how Adam felt when the archangel Michael told him that he would be expelled from Eden:

*“Adam at the news
Heart-strook with chilling gripe of
sorrow stood,
That all his senses bound.”*

Capturing my reaction exactly when I was exiled from the comforting piles of papers composting on my office desk and the wonderful cast of renegades and castaways that constitute my colleagues and lab mates.

My point here is that in March of 2020 we were cast out of paradise. Our world has been changed irrevocably. But Milton has some guidance for us in the form of Adam and Eve’s final response:

*“Some natural tears they dropped, but
wiped them soon;
The world was all before them, where
to choose
Their place of rest, and Providence
their guide:
They hand in hand with wand’ring
steps and slow,
Through Eden took their solitary
way.”*

Unlike Adam and Eve, we are being readmitted carefully to Paradise. So here is what I think is the most important lesson from this poem:

If you are back in the lab, or will be soon, cherish your favorite vortex mixer. After months of silence, it hums with delight at your return.

Binks Wattenberg
(Brian.Wattenberg@vcuhealth.org) is a professor in the department of biochemistry and molecular biology at Virginia Commonwealth University and a member of the ASBMB Today editorial advisory board.



The language gap: Hidden struggles of the non-native speaker

By Saurja DasGupta

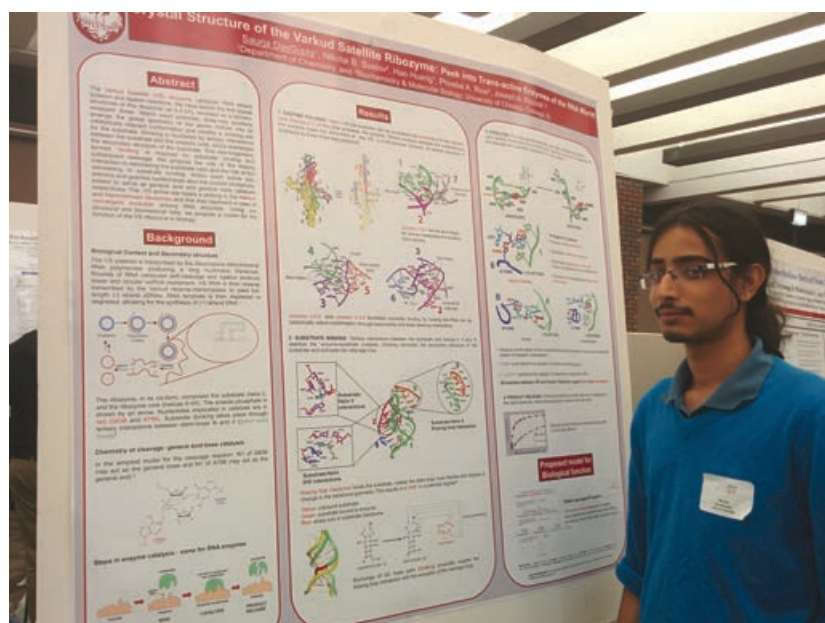
My first experience of education in the U.S. was a two-week English as a second language course at the University of Chicago. There I learned that “clothes” was pronounced “close” and squash is a kind of vegetable. I was told that I use too many redundant words that are hardly necessary (yes, like that). After two weeks, our international cohort was informed that we were good to go. But were we?

Every year, about half a million students travel to the U.S. to study science, technology, engineering and math subjects. An overwhelming majority of these students are non-native speakers of English, the lingua franca of the scientific enterprise. This is the same group that ultimately will comprise half of the country’s postdoc pool and one-fourth of the STEM faculty in a few years’ time. These favorable outcomes suggest that the system really works for international students, but does it?

Concerns about the gender gap, race gap and wealth gap in STEM have permeated public consciousness in recent years thanks to efforts by universities, funding agencies and scientific bodies, but the language gap for non-native speakers hardly is discussed.

Louder than actions

Classes were taught in English in my school back in India, but all my



The author presents his work at the 2016 Midwest Enzyme Chemistry Conference in Chicago. After writing his first paper, he found new communication challenges in sharing his research at a poster session.

interactions outside those few hours in school were in my mother tongue, Bengali. When I got to the University of Chicago to work on a Ph.D. in chemistry, my adviser’s job was to train me in scientific research; I was expected to be proficient in English. In my early years in grad school, I had a hard time penetrating the dense scientific literature I had to read for my research.

When it came time for my first research paper, I realized how difficult scientific writing could be. The research was done, and we were satisfied with our results, but preparing the manuscript took close to a year. Like most Ph.D. students, I had

no training in technical writing, so my first draft was a mess. Because English is not my first language, I had a hard time finding the right words to describe my results, and my sentences were awkward and long-winded. My adviser, busy with other priorities, edited the draft heavily. The edited manuscript read better, but I didn’t know why. Even when I finally could bask in the glory of my publication — we had discovered the structure of an RNA molecule that also behaves as an enzyme — a nagging inner voice reminded me that the process would be almost as tedious the next time around.

With my paper submitted, I reg-

PRAMASH SHEE

ESSAY

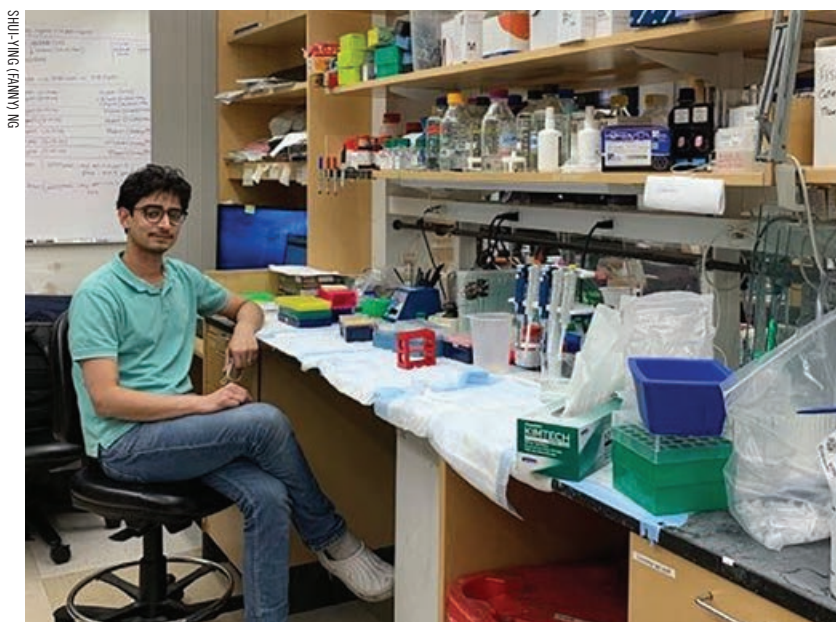
istered for my first scientific conference. While preparing, I soon realized that, unlike writing, my talk would not be edited. In my first poster presentation, my interactions with others were less spontaneous than the American presenters', even after considerable preparation. I have become a more confident speaker since then, but at every conference I attend I meet non-native presenters struggling to convey their hard-earned results.

Student talks rarely last more than 15 minutes, which calls for precise communication. As a listener, I don't know how many times I've given up on a talk because I couldn't understand the speaker's words or I found their monotone soporific. Though I use a script, I aim to write a talk that sounds spontaneous by using short, direct sentences, pausing to emphasize important points and keeping my tone conversational. I also have found that using questions as segues increases audience engagement.

Bridging the gap

Like most non-native speakers who join the U.S. academic workforce, I was aware of the language gap before I came here. And I don't think the solution lies in critiquing the linguistic hegemony of English over the sciences. It lies in rethinking graduate training.

Universities should offer a semester-long course on science communication to first-year grad students, with special attention to non-native speakers. The writing component should include exercises in summarizing scientific findings or reviewing scientific literature. Students should be introduced to the phrases and terminology commonly used in scientific writing, taught how to synthesize related ideas into concise sentences, and provided with a primer on technical writing. Impromptu group discussions, flash presentations and practice talks could be included in the oral component. Through mutual



SHULI YING (FANWY) NG

The author is pictured in 2020 in his lab at Massachusetts General Hospital where he is now a postdoctoral researcher.

critique and suggestions, all new grad students soon would gain the confidence to approach scientific communication with excitement instead of unease.

Of the six courses I took in graduate school, only two were even remotely related to my Ph.D. work, whereas a communication course would have been useful to the entire entering class, irrespective of their field of research. Such courses probably don't exist because university administrators are unaware of the difficulties I've outlined. After joining a lab, most students have little communication with the department administration. We don't like to complain, so our struggles remain siloed.

From the student's perspective, I can see how fitting such a course into an already packed first year might be difficult. In most schools, including mine, teaching assistant duties take up most of the week. My primary concern in the first year was to find a suitable research group. Busy students may not consider such a course a priority, but I think this initial time investment would

pay high dividends in a few years.

A course would be an excellent starting point, but I have found that self-improvement is the only way to level the playing field. A healthy reading habit has done wonders for my language skills. I have benefited especially from science writers such as Richard Dawkins and Paul Davies. When my busy schedule does not permit additional reading, I find that listening to narrative podcasts, even those that have nothing to do with science, is a great way to learn effective sentence construction. I suggest podcasts by the Parcast network as examples of effective storytelling.

Non-native speakers have been and continue to be successful because we power through uncomfortable experiences. That's what learning is. I present my story as an example of countless stories. I believe universities can do much more to empower one of the most productive groups in American science and technology.

Saurja DasGupta (saurjadg@gmail.com) earned his Ph.D. at the University of Chicago and is now a postdoctoral researcher at Massachusetts General Hospital. Follow him on Twitter @SaurjaDasGupta.

“Besides getting sweat on me at times, I have enjoyed the experience”

By Laurel Oldach

Shyretha Brown had an academic postdoc lined up prior to attending Experimental Biology 2017. In the EB exhibit hall, she came across a postdoc opportunity at the Gatorade Sports Science Institute and learned that it takes a lot of physiology research to make a good workout recovery drink. Now a senior scientist at PepsiCo, Brown works on products like a wearable sweat sensor that gives athletes personalized hydration instructions. Reached by phone, Brown told ASBMB Today about her career path and her educational outreach. This interview has been condensed.

1 What did you study in graduate school?

I studied how environmental contaminants, such as butyltins, affect immune cell function — specifically interleukins IL-1 β and IL-6. I didn't know that my graduate school work could be applied to industry. Now that I think back on it, I wish that more opportunities related to science and how applicable it is to industry had been discussed in grad school.

2 What did a normal day look like for you pre-COVID-19?

I conduct human clinical trials with athletes. On a normal day, I would monitor the athlete during a stationary bike ride or treadmill run, collect sweat samples and analyze those samples in our biochemistry lab. Besides getting sweat on me at times, I have enjoyed the experience.

My normal day without scrubs involved paperwork around those

trials. I also work on a few innovation and education related projects.

3 You also founded an education nonprofit?

I founded a nonprofit called Building Bridges Inc. to expose, equip and empower young girls to pursue STEM through self-awareness education. The main goal is to fill in gaps by building bridges that will empower young girls to embrace creative thinking and endless possibilities. Our most popular program pre-COVID-19 was “The Science Behind Hair.” Students learned the hair growth cycle and then made their own conditioner and shampoo.

4 Why is education important to you?

Growing up, my mind was first set on becoming a nurse, then a medical doctor. Those things didn't happen. It was through education that I got exposed to research in undergrad, which led to other opportunities. Opportunity after opportunity has exposed me to what else is out there that I didn't know about previously. If you don't know, you just don't know!

I'm very passionate about mentoring and exposing youth to different opportunities so they can spend less time jumping the hurdles. If I can be a stepping stone to help someone get there quicker than I did, then I'm OK with that.

5 Any advice you wish you'd gotten?

Enjoy the ride; however, know the destination. Meaning, set the pace



Shyretha Brown

CURRENT POSITION

Senior Scientist, PepsiCo

DEGREE

Ph.D., biological sciences, Tennessee State University, 2017

POSTDOC

Gatorade Sports Science Institute

FAVORITE PROTEIN

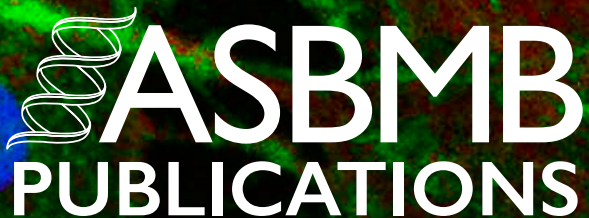
Interleukin-6

and enjoy the journey, but know exactly what you're trying to accomplish.

Would you like to suggest an ASBMB member who works in industry for a Five Questions interview? Send an email to asbmbtoday@asbmb.com.

Laurel Oldach (loldach@asbmb.org) is a science writer for the ASBMB. Follow her on Twitter @LaurelOld.





ASBMB
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JBC

JOURNAL OF
BIOLOGICAL
CHEMISTRY

JLR

JOURNAL
OF LIPID
RESEARCH

MCP

MOLECULAR
& CELLULAR
PROTEOMICS

CLASSIFIEDS

Postdoctoral Position Available

Department of Tropical Medicine at Tulane University

A NIH-funded postdoctoral position is immediately available to join the Scaraffia research group. Scaraffia's lab is particularly interested in unraveling the physiological, biochemical, and molecular basis underlying the regulation of nitrogen and carbon metabolism in mosquitoes, as well as in discovering new metabolic targets that can be used for the design of better mosquito-control strategies. The successful candidate will apply traditional and modern biochemical approaches to investigate the mechanistic regulation of ammonia metabolism in *Aedes aegypti* mosquitoes.



Requirements

- PhD degree in biochemistry or related discipline with a strong background in protein biochemistry, and metabolic signaling
- Research experience in metabolic studies
- Documented experience in biochemical techniques including western blotting, immunoprecipitation and immunofluorescence microscopy
- Excellent communication skills and ability to work independently as well as part of a team

To apply, submit a single PDF file to mmobilliot@tulane.edu with the subject Postdoc Application and include:

- (1) a cover letter describing research interests (no more than 1 page);
- (2) your curriculum vitae; and
- (3) contact information for three references.

Assistant Professor, School of Chemistry and Materials Science

Rochester Institute of Technology

The School of Chemistry and Materials Science (SCMS) at the Rochester Institute of Technology



(RIT) invites applications for a tenure-track Assistant Professor faculty position, beginning in August 2021.

We are seeking an individual who has the ability and interest in contributing to a community committed to access, equity, diversity, and inclusion, student-centeredness, professional development and scholarship, integrity and ethics, innovation and flexibility, and teamwork and collaboration.

To receive full consideration all application materials should be received by February 15th, 2021. The position will be kept open until a suitable candidate is found. <https://sjobs.brassring.com/>

<https://careers.asbmb.org/job/assistant-professor-school-of-chemistry-and-materials-science/55439884/>

Tenured/Tenure-track faculty position

University of Massachusetts Medical School

The Department of Biochemistry & Molecular Pharmacology at the University of Massachusetts Medical School seeks applicants for a tenured or tenure track faculty position in biochemistry.

With research programs spanning a broad range of subjects, our faculty is committed to tackling fundamental biological questions at a molecular level. We are an interactive group that encourages the development of enabling technologies, research at the interface of multiple disciplines, and team science. More information about the department can be found on our website (<https://www.umassmed.edu/bmp>).

Applicants should submit a cover letter, curriculum vitae, statement of research interests, diversity statement, and contact information for three references to <https://academicjobsonline.org/ajo/jobs/17755>. Inquiries, but not application materials, should be directed to the Chair of the Faculty Search Committee, Dr. Sean Ryder. Evaluation of applications will begin as soon as they are received, and will continue until the position is filled.

<https://careers.asbmb.org/job/tenuredtenure-track-faculty-position/55389764/>



Research Biologist I

Biocryst Pharmaceuticals

BioCryst Pharmaceuticals discovers novel, oral, small-molecule medicines that treat rare diseases in which significant unmet medical needs exist and an enzyme plays a key role in the biological pathway of the disease. Biocryst Pharmaceuticals is seeking a highly motivated Research Biologist to contribute to our exciting drug discovery program.



Some responsibilities include:

- Design, validate, and conduct in vitro biological and immunological assays for the pharmacological characterization of new small molecule drug candidates for multiple research programs. Screen compounds in single concentration and concentration-response schemes, analyze and report data.
- Conduct cell-based assays to enable drug discovery efforts. Conduct cell-based assays to measure the functional consequences of inhibition of diverse targets, including signaling pathways, enzyme activities, and protein and mRNA levels; assays include ELISA, Western blot analysis, real-time PCR, etc.
- Conduct in vivo studies or models for analyzing new drug candidates and current investigational drugs for efficacy and pharmacokinetics in rodents – would include disease models in rodents.

<https://careers.asbmb.org/job/research-biologist-i/55274411/>

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

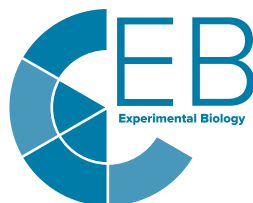


The 2021 ASBMB Annual Meeting will be virtual!

Join us April 27–30

Advance registration deadline: April 12

Learn more at asbmb.org/annual-meeting



The ASBMB annual meeting is held in conjunction with Experimental Biology.