

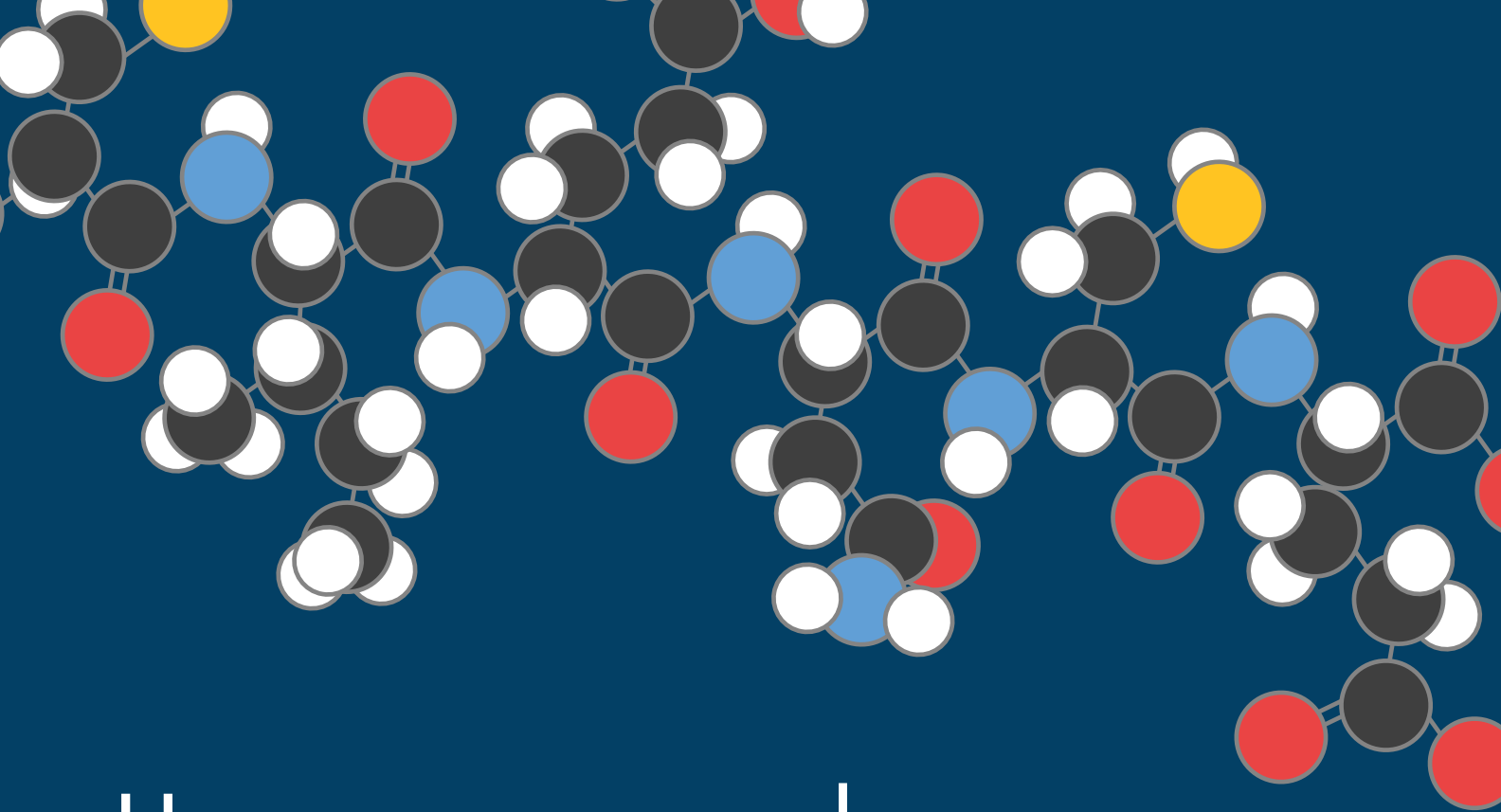
Vol. 18 / No. 9 / October 2019

ASBMB TODAY

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

Biochemistry OF A Burger





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ASBMB elects officers and council members

Committees welcome new members, name new chairs

By ASBMB Today Staff

Members of the American Society for Biochemistry and Molecular Biology have elected new officers and council members, and the society's committees have appointed new members and leaders.

Officers



Antalis

Toni Antalis is serving for one year, starting in August, as president-elect, followed by two years as president and then one year as past-president. She previously served two three-year terms as ASBMB treasurer and chaired the Publications Committee. Antalis is a professor of physiology at the University of Maryland School of Medicine, where she is also the associate director for training and education and the director of the program in molecular medicine and the graduate program in life sciences. Her lab's research is focused on signaling mechanisms involved in vascular disease and cancer.



Yang

Wei Yang is serving a three-year term, also beginning in August, as secretary. She received the society's Mildred Cohn Award in Biological Chemistry in 2017 and served as

co-chair of the 2016 ASBMB Annual Meeting. Yang is an investigator and section chief at the National Institutes of Health, where her lab focuses on the structural characterization of proteins involved in DNA mismatch repair and translesion DNA synthesis.

Council members

Three members have joined the society's governing council. Their three-year terms began in August.



Barbour

Suzanne Barbour, a past member of the Education and Professional Development Committee, is dean of the graduate school and a professor of biochemistry and biophysics and at the University of North Carolina at Chapel Hill. Barbour also has served on the Minority Affairs Committee.



Broderick

Joan Broderick, previously a member of the Nominating Committee, is a professor of chemistry and biochemistry at Montana State University. Her lab uses biochemical, spectroscopic and synthetic approaches to elucidate detailed chemical mechanisms for metal catalysis.



Gentry

Matthew Gentry, formerly chair of the Public Affairs Advisory Committee, is a professor of molecular and cellular biology at the University of Kentucky College of Medicine. His lab studies the role of signal transduction machinery, namely phosphatases and E3 ubiquitin ligases, in neurodegenerative disease and biofuels research.

Committees

Kevin Campbell of the University of Iowa College of Medicine was appointed to the Awards Committee.

Christopher Heinen of the University of Connecticut School of Medicine, **Margaret Kanipes** of North Carolina A&T State University and **Saumya Ramanathan** of Fisk University were named to the Education and Professional Development Committee.

Edward Eisenstein of the University of Maryland, a current member of the Membership Committee, has been named chair of that committee. He previously served on the outreach committee. **Peter Kennelly** of Virginia Polytechnic Institute and State University, a past member of the Education and Professional Development Committee, has become past chair of the Membership Committee.

Joseph Provost of the University of San Diego, also a past member of the EPD, has been appointed to the Membership Committee.

Celia Schiffer of the University of Massachusetts Medical School and **Nicholas Tonks** of Cold Spring Harbor Laboratory have been named to the Nominations Committee.

Terri Goss Kinzy of Western Michigan University has been named chair of the Public Affairs Advisory Committee. **Ronald Wek** of Indiana University School of Medicine was appointed to the committee.

Robert Haltiwanger of the University of Georgia, a co-chair of the 2020 ASBMB Annual Meeting, was elected to the Publications Committee.

Nicole Weitowich of Northwestern University was named chair of the Science Outreach and Communication Committee. **John Tansey** of Otterbein University, **Christina Marvin** of the University of Wisconsin–Madison and **Amy J. Hawkins** of University of Utah have been appointed to the committee.

Chad Park of the University of Arizona has been named to the Student Chapters Committee as the southwest regional director.

Chad Slawson of the University of Kansas Medical Center and **Blanton S. Tolbert** of Case Western Reserve University have been appointed to the Meetings Committee.

Vahe Bandarian of the University of Utah and **Ruma Banerjee** of the University of Michigan Medical School have been named to the Minority Affairs Committee.

ASBMB symposia program call for submissions

The ASBMB symposia program aims to provide niche segments of the scientific community with opportunities to present unique, cutting-edge science and engage in active networking opportunities. Help advance your field by planning an ASBMB symposium.

Proposal deadline: Nov. 1

www.asbmb.org/SpecialSymposia/Proposals/

Member update

By ASBMB Today Staff

Hartl wins Janssen award

Franz-Ulrich Hartl of the Max Planck Institute of Biochemistry won the 2019 Dr. Paul Janssen Award for Biomedical Research along with Arthur Horwich of Yale School of Medicine.

The pair, who were honored with the American Society for Biochemistry and Molecular Biology's Tabor Research Award in 2013 and the Albert Lasker Basic Medical Research Award in 2011, are known around the world for their pioneering studies of the cell's protein-folding machinery.

"Drs. Hartl and Horwich combined their brilliant insights and elegant approaches to overturn the dogma of their day about the process of protein folding," David Julius of the University of California, San Francisco, chairman of the selection committee, said in a statement. "Their studies revolutionized our understanding of how proteins achieve their shape

and revealed how defects in this process may contribute to a variety of disorders ranging from metabolic to neurodegenerative diseases."

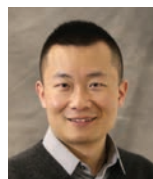
The late Paul Janssen had a hand in developing more than 80 medicines, four of which remain on the World Health Organization's list of essential drugs. Johnson & Johnson established the award in his name in 2004. ASBMB members who have won the Janssen award in the past include Nobel laureate Yoshinori Ohsumi (2016) and Emmanuelle Charpentier and Jennifer Doudna (2014).

Hartl was elected to the National Academy of Sciences in 2011 and is a member of the editorial board for the Proceedings of the National Academy of Sciences.



Hartl

Pew award for Zhang



Zhang

Xin Zhang, an assistant professor of chemistry and of biochemistry and molecular biology at Pennsylvania State University, has been chosen to join this year's class of Pew Biomedical Scholars.

The program, run by the Pew Charitable Trust, provides four years of funding for exploratory research by assistant professors. The aim is to support risky but potentially high-reward research inquiries.

Zhang's lab studies protein misfolding and aggregation during cellular stress, with special attention to intrinsically disordered proteins that contain prionlike domains. His team visualizes these proteins using tags whose fluorescence indicates aggregation. The work could help in understanding of neurodegenerative disorders driven by proteopathy, such as Huntington's or Alzheimer's disease.

Zhang, a chemical biologist, earned a Ph.D. in chemistry at the California Institute of Technology and pursued postdoctoral research at Scripps Research. He has been on the faculty at Penn State since 2015.

Sumter named dean at Winthrop



Sumter

Takita Felder Sumter, a professor of chemistry at Winthrop University in South Carolina, assumed the role of dean of the College of Arts and Sciences in July. Sumter has taught at the university since 2004; in 2017 she served as interim dean.

Sumter studies the chromatin binding high-mobility group A1, or HmgA1, proteins, which are overexpressed in cancer.

Sumter serves on the ASBMB's governing council and the National Science Foundation's advisory committee for biology. Deeply committed to education and mentorship, she co-founded the ASBMB's annual Interactive Mentoring Activities for Grantsmanship Enhancement, or IMAGE, grant writing workshop. She also contributes to biochemistry textbooks and has published on best practices in teaching chemistry and biochemistry.

"Takita is well respected by all who know and work with her," Winthrop University President Dan Mahony said. "She clearly made a positive impression on her colleagues during her time as interim dean."

Diamandis wins Canadian service award



Diamandis

Eleftherios P. Diamandis, head of clinical biochemistry at the Mount Sinai Hospital and University Health Network, has won the 2019 Canadian Academy of Clinical Biochemistry Award for Outstanding Service to the Profession of Clinical Biochemistry.

The award was established in 1993 to recognize those who have made “unique contributions in laboratory medicine and had a worldwide impact in clinical medicine.” Diamandis, who also leads the clinical biochemistry division at the University of Toronto, conducts translational research on cancer biomarkers using proteomics and genomics.

Diamandis will be recognized in a citation read at the annual conference of the CACB. He also will receive a certificate and a \$1,500 prize sponsored by Siemens Canada, the principal Canadian subsidiary of the multinational company Siemens.

Blanco concludes media fellowship



Blanco

Daniel Bastardo Blanco spent the summer as an intern at Discover Magazine through the American Association for the Advancement of Sciences' mass media fellowship.

The program allows undergraduate and graduate students in science, engineering, technology and math fields to spend 10 weeks learning the ropes of scientific communication in newsrooms around the country.

Blanco is a Ph.D. candidate in immunology at St. Jude's Children's Research Hospital/University of Tennessee Health Science Center. He was a 2019 ASBMB Hill Day advocacy trainee.

While interning at Discover, Blanco wrote about probiotics, 3D printing spacecraft, climate change, the microbiome and other topics.

Chewing gum project honored

Dan Dries of Juniata College presented an ASBMB Science Fair Award on May 10 to middle school students Gracie Hobbs, McKensie Klauss and Shaelyn McGinnis for their project Rinku Chewy, an eco-friendly solution to disposing of used chewing gum.

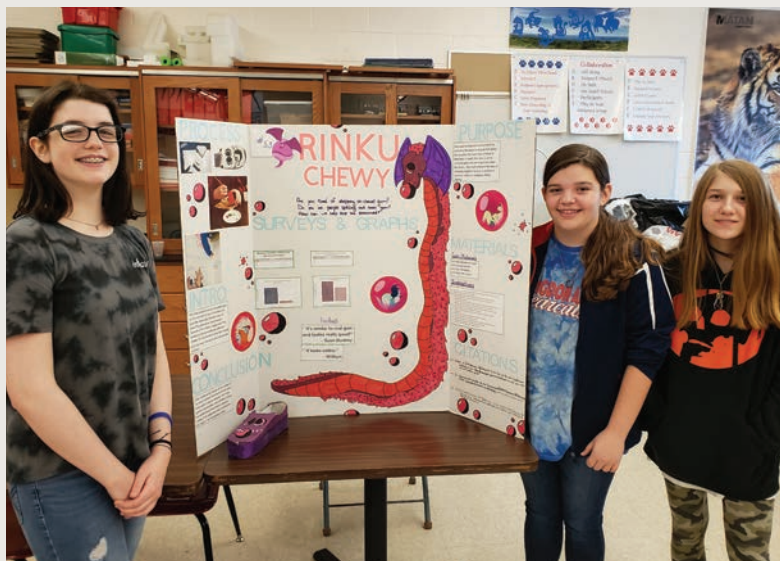
When tasked with developing a project for their local science, technology, engineering and mathematics fair, the team wanted to combine an ecologically responsible product with outreach to their community. Rinku Chewy is a homemade organic chewing gum that, when returned to the company, is repurposed as filler for shoe soles. These shoes, produced using the revenue of their

company, are distributed to the less fortunate.

The three students of Huntingdon Area Middle School in Huntingdon, Pennsylvania, wanted to appeal to their peers who, they noticed, often chew gum. The team also wrote and produced an anime ad to promote the product.

“It's so cool to win something this big!” Shaelyn said of the award.

Pictured with their winning poster are, left to right, Huntingdon Area Middle School students Shaelyn McGinnis, McKensie Klauss and Gracie Hobbs.



COURTESY OF DAN DRIES

IN MEMORIAM

Henry Koffler



Henry Koffler, president emeritus of the University of Arizona, died March 10 at age 95.

Koffler fled Nazi-occupied Austria in 1940, arriving in Arizona at age 17. He attended the University of Arizona, where he met fellow student Phyllis Pierson; they were married for 71 years.

Trained in biochemistry at the University of Wisconsin, Koffler joined the faculty at Purdue University, eventually becoming the head of the university's division of biological sciences. His award-winning microbiology research focused on flagella, structures important for bacterial motility. In one line of inquiry, Koffler and colleagues showed that flagellar enzymes from thermophilic bacteria are more heat-stable than flagella from their less heat-resistant relatives.

Beginning in 1975, Koffler took on increasingly senior administrative roles at the University of Minnesota and the University of Massachusetts Amherst. He then served a nine-year term as president of the University of Arizona, his alma mater. Colleagues say his leadership was key to expanding the faculty, enabling technology transfer and establishing the University of Arizona's reputation as a research university.

Among Koffler's many honors were recognition as one of Purdue University's Great Teachers, founding governorship in the American Academy of Microbiology, fellowship in the American Association for the Advancement of Sciences and knighthood in France's Ordre de Palmes Académiques.

John Tymoczko



John Tymoczko, an emeritus professor at Carleton College in Northfield, Minnesota, died May 26 of a heart attack.

Tymoczko taught at Carleton for 39 years starting in 1976 and is remembered warmly by generations of students. Laura Pogemiller Caron, a former student, wrote, "I think only John could make that intro material so engaging — and do it over and over. He really got a kick out of watching the lightbulb click every time a new class understood."

His teaching extended beyond the Carleton campus; along with Jeremy Berg and Gregory Gatto, Tymoczko co-authored five editions of the classic textbook "Biochemistry" by Lubert Stryer used by college students across the country. Berg called Tymoczko "a thoughtful scholar and a very hard worker, always ready with a bad pun to lighten a discussion."

Tymoczko is survived by his wife, Alison Unger, their son and daughter, and three grandchildren.

RETROSPECTIVES

We invite you to honor a recently deceased ASBMB member with a personal retrospective article in ASBMB Today. For details, email asbmbtoday@asbmb.org.

Leonard A. Sauer



Leonard A. Sauer, who spent most of his career as a research physician at the Mary Imogene Bassett Hospital in Cooperstown, New York, died April 15. He was 89.

Sauer attended high school in Schenectady, New York, but according to a published obituary, he is said to have skipped school often to play pool. He enlisted in the Army in 1948 and for almost four years was a member of the Signal Corps, which to this day manages communications and information systems.

When his military service ended, Sauer attended Cornell University and then earned his medical degree at the University of Rochester and his Ph.D. from the Rockefeller Institute in New York. He spent several years doing research at Yale University before joining Bassett in 1975.

During his career at Bassett, a teaching hospital now affiliated with Columbia University, Sauer published upward of 70 papers on cancer metabolism pathways and other topics.

He retired in 1996 and spent his later years fly fishing and woodworking at his home on the Bitterroot River in Montana, where he lived with his wife, Mimi, who survives him.



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RESEARCH

12 young scientists win PROLAB awards

Twelve emerging scientists will receive grants this year from the Promoting Research Opportunities for Latin American Biochemists program to advance their research by working directly with collaborators in laboratories in the United States, Canada and Spain.

Since 2012, the American Society for Biochemistry and Molecular Biology, the Pan-American Society

for Biochemistry and Molecular Biology, and the International Union for Biochemistry and Molecular Biology have given 71 biochemists these travel awards.

This year's PROLAB travel grants are going to Ph.D. students and postdoctoral fellows from Argentina, Brazil, Chile, Mexico, Spain and Uruguay. All but one will work in the United States.

The 2019 recipients are:



Barrachina

Ferran Barrachina, a Ph.D. student at the University of Barcelona in Spain, will go to the lab of Sylvie Breton, who is affiliated with the Massachusetts General Hospital and Harvard Medical School. Barrachina is studying the role of the extracellular vesicles in epididymal sperm maturation and function. "This great opportunity will allow me to expand my knowledge in reproductive biology, learn a sophisticated variety of techniques, such as high-resolution microscopy, and interact with outstanding researchers and physicians," Barrachina said.



Bonnet

Laura Bonnet, a Ph.D. student at the National University of Córdoba in Spain, will spend time in the lab of Anna Kashina at the University of Pennsylvania. Bonnet, who studies the role of post-translational arginylation of proteins, said of her plans: "I hope this project sheds light on the neuronal role of Ate1 during the autophagic degradation process. The identification of Ate1 as a regulator of this process in the central nervous system will open new avenues of investigation into the arginylated proteins involved in neuronal proteostasis regulation."



Figueroa

Alfredo Figueroa is a graduate student at the Center for Scientific Research and Higher Education at Ensenada in Mexico. He will be spending time in the lab of Mary Munson at the University of Massachusetts at Amherst to advance his studies of the C-terminus of the protein Sec10 in exocyst assembly in the bread mold *Neurospora crassa*. "This is a great chance to put my graduate research to the test and answer questions

that can only be answered with advanced experimental equipment," Figueroa said.



Lima-Filho

Ricardo Lima-Filho, a Ph.D. student at the Federal University of Rio de Janeiro in Brazil, will be hosted by the lab of Bruce McEwen at the Rockefeller University in New York. Lima-Filho studies the molecular mechanisms by which exercise regulates mood. "(R)esults from these experiments will extend the robustness and significance of our project and nourish an important collaboration to help unveil the effects of exercise-related molecules in the depressed brain," Lima-Filho said.



Oliveira

Carolina Oliveira, a Ph.D. student at the University of the Republic in Uruguay, will go to the lab of Thomas Kislinger at Princess Margaret Cancer Centre in Toronto. Oliveira studies the role of the noncoding RNA nc886 in prostate cancer progression. "I strongly believe that this is an excellent opportunity for me to learn about and (apply) advanced proteomic techniques to a very active field of noncoding RNA research," Oliveira said. "Also, I will have the opportunity to share and discuss our results and perspectives with scientists of one of the top cancer research centers in the world."



Pascual

María José Pascual is a graduate student at the National University of General San Martín in Buenos Aires, Argentina. She will travel to the Stowers Institute for Medical Research in Kansas City, Missouri, to advance her studies of how dengue infection affects tRNA repertoire

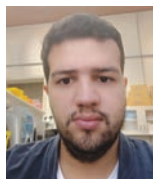
and mRNA stability of the host cell. Working in the lab of Ariel Bazzini “will be a completely different experience compared to my present work in Argentina,” she said. “I will be learning lots of new techniques and (have access to) facilities that will expand my horizons.”



Pineda

Margarita Jacaranda Rosendo

Pineda, a Ph.D. student at the National Autonomous University of Mexico, will work in the lab of Claudia Moreno at the University of Washington. In Mexico City, Pineda studies the modulation and localization of NMDA receptors during mitosis. Spending time at the Seattle campus “is a great opportunity for increasing my skills in electrophysiology and super-resolution techniques,” she said.



Ribeiro

Felipe Campos Ribeiro, a Ph.D.

student at the Federal University of Rio de Janeiro, Brazil, will work in the lab of Ottavio Arancio, a cellular neurobiologist at Columbia University. Ribeiro said he plans “to test if enhancement of proteasome activity could hold therapeutic potential on Alzheimer’s disease models” during his stint in New York.



Salazar

Paula Belen Salazar is a Ph.D.

student at the Instituto Superior de Investigaciones Biológicas in San Miguel de Tucumán, Argentina. She will work in Guillermo Altenberg’s lab at the Texas Tech University Health Sciences Center in Lubbock. Salazar studies inhibitors of the human enzyme acetylcholinesterase. Altenberg’s lab “has profound knowledge on membrane proteins,” Salazar said. “I’ll certainly learn state of the art biophysical techniques, which is quite exciting. Hopefully, the project will provide important insights into the mechanism of inhibition of acetylcholinesterase by polyphenols.”



Scilletta

Natalia Scilletta, a Ph.D. student at

the Institute of Nanoscience and Nanotechnology in Argentina, will work in the lab of Ali Khademhosseini at the University of California, Los Angeles. “I will study the biological processes that occur in eukaryotic cells while growing on the biomaterial coating I am developing,” she said of her plans in L.A. “In this way, this experience will allow me to learn

new molecular biology techniques and to deeply understand the nanosystem I am studying. Moreover, working with prestigious scientists will undoubtedly enrich my career and knowledge on the subject.”



Vago

Juliana Vago, a postdoctoral research-

er at the Federal University of Minas Gerais in Brazil, will travel to La Jolla, California, to work in Lindsey Miles’ lab at Scripps Research. Vago studies the plasminogen system and its role in the control of inflammatory/infectious diseases. “I believe this is a great opportunity to improve my professional and personal skills,” she said. “I hope that the interaction with prestigious scientists will enhance my network and allow me to further collaborate with them in the near future. Also, I hope to apply in my home institution what I will learn and improve the quality of my work.”



Valdés

Maira Rivera Valdés, a postdoctoral

researcher at the Pontifical Catholic University of Chile, will spend time in the lab of Elizabeth Komives at the University of California, San Diego. Rivera studies KaiB, a cyanobacterial metamorphic protein. “Dr. Komives’ lab has vast experience in the study of protein biophysics using mass spectrometry. Using this technique to analyze the refolding of the circadian clock protein KaiB, I will obtain promising results and also enrich my knowledge about this technique to implement it in our own instrument in Chile,” Rivera said.

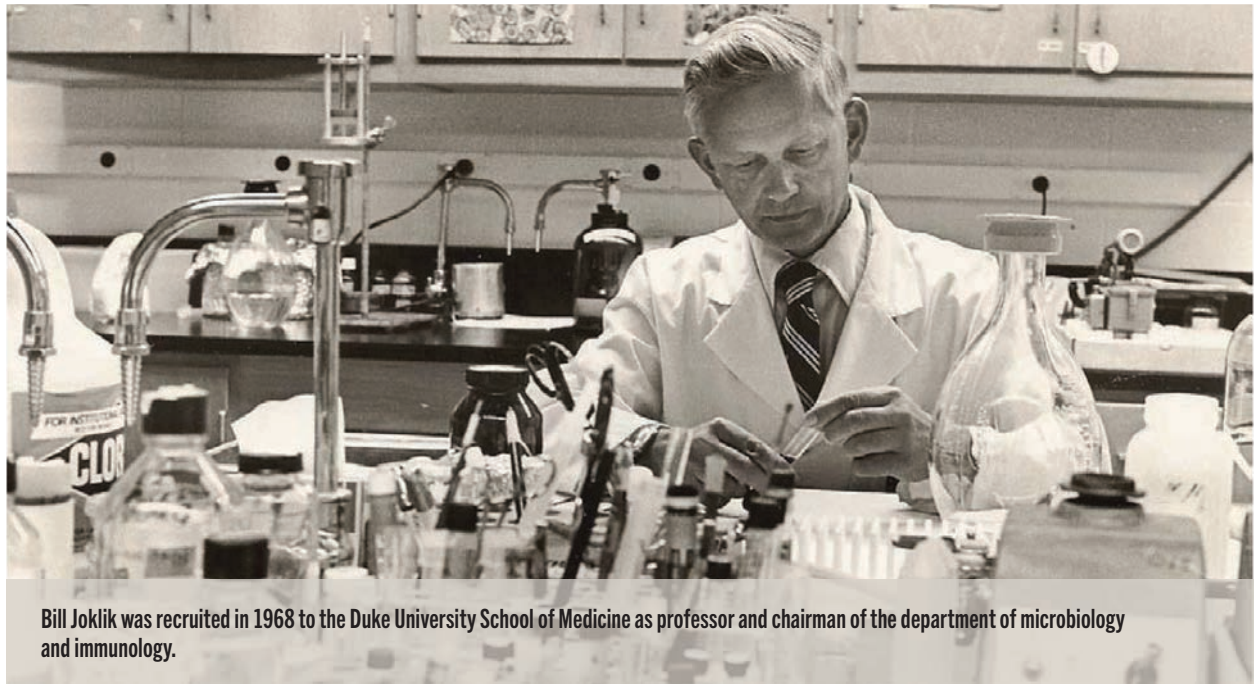
LEARN MORE

The ASBMB welcomes applications for PROLAB scholarships from trainees and new investigators (not more than five years past postdoctoral work) from all countries in the Pan-American Society for Biochemistry and Molecular Biology, including Spain and Portugal. The awards offset the costs of travel and living expenses for one to six months up to a maximum of \$5,000. The deadline for 2020 applications is May 1.

For more information, go to ASBMB.org/pabmb.

Wolfgang Karl Joklik (1926 – 2019)

By Jack D. Keene, Charles E. Samuel & John J. Skehel



DUKE UNIVERSITY

Bill Joklik was recruited in 1968 to the Duke University School of Medicine as professor and chairman of the department of microbiology and immunology.

Wolfgang Karl “Bill” Joklik, a molecular virologist who pioneered numerous contributions to science and our understanding of Poxviridae and Reoviridae, died July 7.

Bill Joklik’s research addressed fundamental problems of virus replication by investigating mechanisms of expression of viral genetic information, the function of virus-encoded proteins, host responses to infection and the actions of anti-virals. Bill was a superb mentor, a generous contributor and an outstanding leader both within his profession and in the wider community.

Early years and education

Wolfgang Joklik was born Nov. 16, 1926, in Vienna, Austria, where he received his initial schooling. When he was 11, his family moved to Sydney, Australia. There, he and his younger brother Günther assumed the English nicknames Bill and Frank, and the two attended Cranbrook School. Bill earned his Bachelor of Science with first class honors in 1947 and his Master of Science in biochemistry in 1948, both from the University of

Sydney. His initial research training was in enzymology, studying the hydrogenase from *Escherichia coli*. He then attended the Sir William Dunn School of Pathology at Oxford, U.K., as an Australian National University scholar to study virology using the T1 and T2 bacteriophages under the mentoring of Sir Paul Fildes. While working toward his Doctor of Philosophy from Oxford, he published several seminal papers, among them “The Influence of Cortisone on Cell Division,” co-authored with Howard W. Florey, who won a Nobel Prize for the development of penicillin.

Bill did postdoctoral work in Herman Kalckar’s laboratory at the University of Copenhagen. He and Paul Berg, later a Nobel laureate, discovered and characterized nucleoside diphosphokinase. Bill returned to Australia in 1953 as a member of the department of microbiology at the John Curtin School for Medical Research in Canberra, where he remained until 1962. There he initiated studies of animal viruses with Frank Fenner and others, focusing on laboratory models of smallpox virus, myxoma virus and vaccinia virus, and making novel discoveries on the reactivation of heat-inactivated poxviruses.

Research in the U.S.

During a sabbatical with Harry Eagle, a leader in the development of defined cell culture media at the National Institutes of Health, Bill developed the Joklik modification of Eagle's minimum essential medium, which permitted the growth of cells in suspension culture and purification of viruses. Upon returning to Australia in 1962, he devised methodologies for the purification of poxviruses that set the stage for his subsequent molecular studies. Within a year, Eagle recruited Bill back to the U.S. to work at the Albert Einstein College of Medicine, so Bill and his family moved to New York, where he joined the department of cell biology at Einstein as an associate professor. In 1965, he became the Siegfried Ullman professor of cell biology.

Bill's laboratory carried out innovative studies on poxvirus multiplication that led to landmark discoveries, largely using vaccinia and rabbitpox virus. These studies included work on the temporal regulation of poxvirus mRNA expression, early and late; the formation of polyribosomes containing viral RNA; the characterization of the replication and coating of poxvirus DNA; and the characterization of poxvirus enzymes and proteins synthesized during infection. Using vaccinia virus, Bill also studied the biochemical mechanism of the anti-viral action of interferon.

Bill was recruited in 1968 to the Duke University School of Medicine as professor and chairman of the department of microbiology and immunology. He became James B. Duke professor of microbiology in 1972, a position he held until becoming professor emeritus in 1996.

While Bill's interest in poxviruses continued at Duke, he increasingly focused on reovirus research initiated at Einstein. Among his lab's innovative findings in both locations were characterization of the reovirus segmented double-stranded RNA genome and its transcripts, identification and characterization of reovirion proteins and viral nonstructural proteins produced in infected cells, and elucidation of the functions of reovirus proteins during virus replication. Bill applied new technologies to his studies of reoviruses, including the molecular cloning of viral RNAs, the sequencing of viral RNAs and cDNA clones, and the isolation and characterization of hybridomas producing monoclonal antibodies against viral proteins.

Service and leadership

Bill was an extraordinary leader. He built a nationally

recognized department at Duke with strength across microbiology and immunology, increasing the faculty from 6 to 33. He also was a co-founder of the Duke Comprehensive Cancer Center in 1971 and founder and first president of the American Society for Virology in 1982. He served on numerous administrative and advisory committees in academic institutions and governmental agencies both nationally and internationally.

Bill was a leader at the journal *Virology* for 30 years as an associate editor, editor and finally as editor-in-chief from 1976 to 1994. He was an associate editor of the *Journal of Biological Chemistry* from 1978 to 1988 and editor-in-chief of *Microbiological Reviews* from 1991 to 1995.

Highly regarded as a dedicated teacher and mentor, Bill was a popular lecturer in both graduate and medical student courses at Duke. He trained nearly 100 graduate students and postdoctoral fellows in his research laboratory, many of whom went on to successful independent careers. He was the editor of multiple editions of



DUKE UNIVERSITY

While at Duke, Bill Joklik's research increasingly focused on reovirus.

“Zinsser’s Microbiology,” for several years a leading textbook for medical students.

Bill was elected to the National Academy of Sciences in 1981 and the Institute of Medicine of the NAS in 1982. He received the Senior U.S. Investigator Humboldt Prize in 1986, the International Chemical and Nuclear Pharmaceutical Corporation International Prize in Virology in 1991 and a Lifetime Achievement Award from Duke University in 2013.

Sports and lebensfreude

Bill was equally adept with a tennis racket in either his left or right hand. He enjoyed a round of golf and was a dedicated fan of Duke basketball but also followed cricket on the radio and television. He greatly enjoyed travel throughout his life both for science and for pleasure. He said he was “equally at home in two cultures,” Austrian/German and British/American, and he maintained an interest in global politics.

The impact of Bill Joklik as a scholar and as a leader is immense. He had a wonderful career and life that the three of us and many others are honored to have observed and shared.

On the web

The Duke University Medical Alumni Association produced a video about Bill Joklik in 2013 when they honored him with the William G. Anlyan Lifetime Achievement Award. To see the video, go to asbmb.org/asbmbtoday.



DUKE UNIVERSITY

Bill Joklik was a longtime member of the American Society for Biochemistry and Molecular Biology and an associate editor of the Journal of Biological Chemistry from 1978 to 1988.

CRANBROOK ACADEMY



The Joklik brothers, Bill and Frank, are pictured with their mother, Helene, in 1943, when both boys were students at Cranbrook Academy. Bill, born in 1926, was elected to the National Academy of Sciences and Frank, born in 1928, was elected to the National Academy of Engineering at approximately the same time. Frank presented a eulogy at Bill’s funeral.

Jack D. Keene (jack.keene@duke.edu) is the James B. Duke professor of molecular genetics and microbiology at the Duke University School of Medicine.

Charles E. Samuel (samuel@lifesci.ucsb.edu) is a research professor, C. A. Storke professor, and distinguished professor emeritus at the University of California, Santa Barbara.

John J. Skehel (John.Skehel@crick.ac.uk) is an emeritus scientist at the Francis Crick Institute, London, and former director of the National Institute for Medical Research, Mill Hill, London.



CALL FOR SUBMISSIONS

The wellness issue — January 2020

DEADLINE EXTENDED: OCT. 28

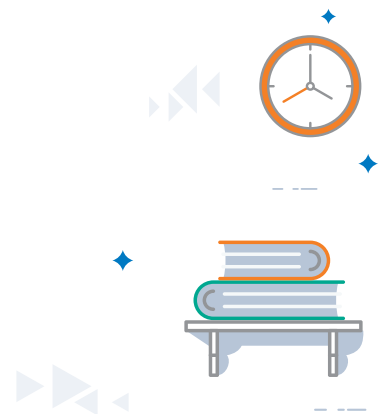
What keeps you well? Exercise? Sleep? Faith? Family? Pets? Something else? Tell us about what works for you and/or your wellness challenges.

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

ASBMBTODAY

Upcoming ASBMB events and deadlines

OCTOBER	1	ASBMB degree-program accreditation deadline
	6–11	Mental Illness Awareness Week
	7	Art of Science Communication fall course begins
	11	National Depression Screening Day
	15	Deadline for priority-consideration abstracts for 2020 annual meeting
	20–24	ASBMB–BSC Symposium on the Interplay Between Epigenetic Regulation and Genome Integrity
NOVEMBER	24–27	Emerging Roles in Nucleolus symposium
	25–26	Student Chapters northwest regional meeting
	1	Proposals for 2021 symposia due
	3	Student Chapters northeast regional meeting
	14	Deadline for abstracts for 2020 annual meeting
	16	Student Chapters Outreach Grant deadline
DECEMBER	18–24	U.S. Antibiotic Awareness Week
	20	Student Chapters renewal deadline
	27	Deadline for 2020 annual meeting travel award applications
	2–8	National Influenza Vaccination Week
	5	ASBMB–Deuel Conference on Lipids early registration deadline



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University of North Texas

Yiwei Ai,
Johns Hopkins University

Andrew Alpert, PolyLC Inc.

Mia Antinone,
West Virginia University

Takeshi Bamba,
Kyushu University

Brian Barth, University
of New Hampshire

John Beale, St. Louis
College of Pharmacy

Babatunde Bello,
Georgia State University

Agnes Berki,
Caldwell University

Grant Blouse,
Catalyst Biosciences

Lauren Boutz,
Arizona State University

Amber Bowman, College
of William and Mary

Shelby Bradford,
West Virginia University

Carson Bryant,
Yale University

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University of Pittsburgh

Brittany Carpenter, Van
Andel Research Institute

Joshua Chandler,
Plymouth State University

Godfrey Chukwuemeka,
Michael Okpara University
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Aedin Culhane, Dana–Farber
Cancer Institute, Harvard
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Lipoprotein (a): Many strides made, yet there is a long road ahead

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First tooth controls where and when the rest come in

By Karen Bascom

Whether it's a baby human, baby zebrafish or anything else with teeth, those first pearly whites form in an orderly fashion. They start with a single tooth, followed by its immediate neighbors, then their neighbors, creating neat streets of teeth.

This timing of teeth wasn't lost on A. Gordon Edmund, a paleontologist at the Royal Ontario Museum, who in 1960 proposed an idea as to why: that the first tooth controls the process by sending a message along the jaw that stimulates the formation of the other teeth.

Fifty-nine years later, a team of scientists demonstrated how this early tooth guides the rest of the dental formation process. Published in the *Proceedings of the Royal Society B* on June 12, the paper's lead author is Yann Gibert, associate professor of cell and molecular biology at the University of Mississippi Medical Center.

"In just about every species, development of the dental row starts with a single tooth or pair of teeth, and that tooth initiates a wave of new teeth proximally and distally," said Gibert, who joined UMMC and the Cancer Institute and Research Center in 2018.

In his research, Gibert uses zebrafish primarily to study new therapeutics for cancer and metabolic diseases such as diabetes and obesity. He also has a longstanding collaboration with colleagues at the University of Lyon in France and

Bowdoin College in Maine studying tooth formation in these tiny fish.

"It's more difficult to study development in mammals because they take so much longer to develop," Gibert said. "However, zebrafish grow from an embryo to free-feeding larva in five days."

Zebrafish embryos start to grow their first tooth, called 4V1 for its place along a row that sits in the eventual fish's throat, about 48 hours post-fertilization. Its neighbors, 3V1 and 5V1, begin to form in the following hours. To determine if 4V1 is responsible for the creation of the other teeth, Gibert and his collaborators designed a series of experiments that altered that first tooth's timing, location and biochemistry.

First, they used a chemical to block 4V1 from forming and observed that 3V1 and 5V1 didn't form either. However, even after the tooth's normal developmental win-

dow passed, they were able to induce the growth of a 4V1-like tooth, which was followed by 3V1 and 5V1, all in their regular locations.

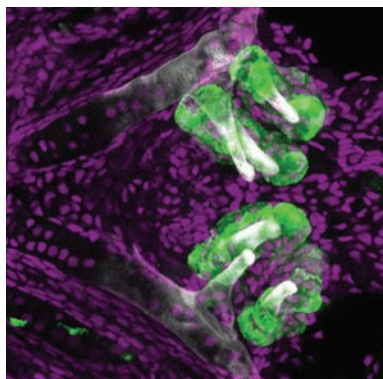
In another experiment, they used retinoic acid, a chemical signal used in growth and development, to make a 4V1 tooth form in an area of the throat where it doesn't usually grow. The neighbors soon followed.

"Our results show that by modifying the formation of the initiator tooth it is possible to control the formation of a dental row," Gibert said.

In terms of the actual signal that the initiator tooth used, Gibert and team showed that 4V1 produces a fibroblast growth factor, or FGF, another chemical signal used for growth and wound repair, during the time that 3V1 and 5V1 form. By blocking the embryo's ability to make FGF after 4V1 had formed, they were able to stop the subsequent teeth from developing.

Lacking the molecular tools available today, "Edmund based his idea of a signal coming from the tooth on anatomy and histology alone," Gibert said. "We expected to show that this first tooth was both necessary and sufficient for the other teeth to form but didn't think we would fully show that FGF is the likely transmitter."

"The fundamental question behind this research is 'How do teeth get organized into rows'?" said study co-author William Jackman, an associate professor of biology at Bowdoin



Zebrafish teeth (labeled with a green fluorescent protein) along the pharyngeal jaw about five days post-fertilization.

WILLIAM JACKMAN, BOWDOIN COLLEGE

College who studies organ formation in animals. “There’s this developmental clockwork that is instructing the cells to make teeth in a particular place, and we’re trying to understand the mechanism behind that.”

Jackman said that even though animal teeth display a great diversity in their number, size and ability to regenerate, teeth and their row patterning have been present in animals for hundreds of millions of years.

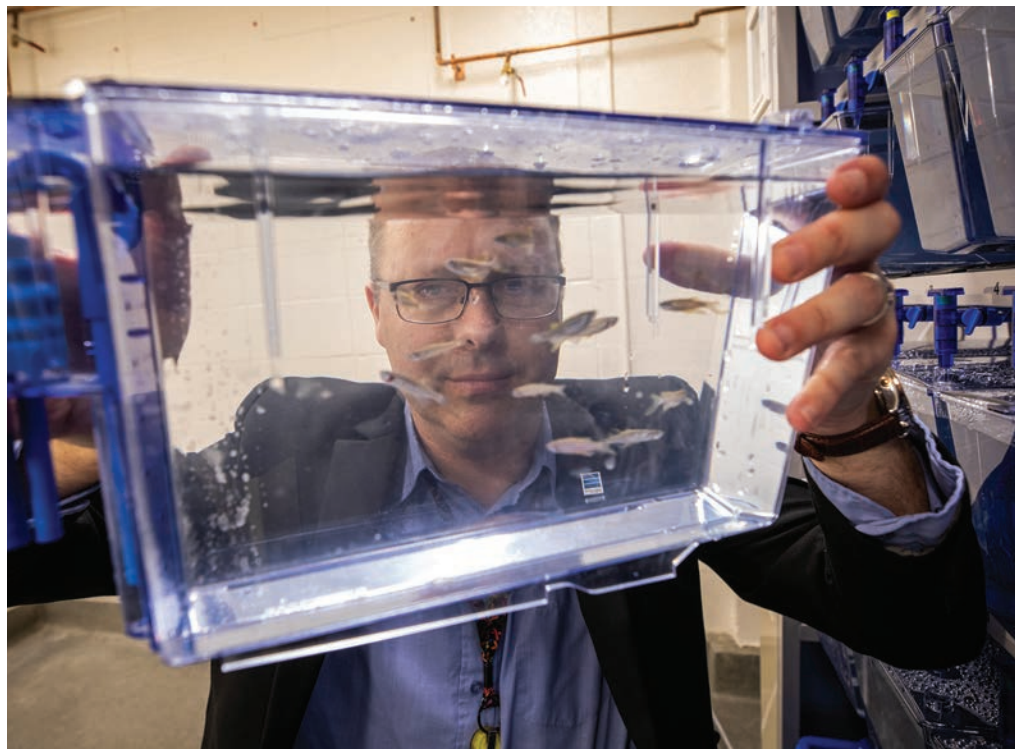
“If a system works, evolution will keep it around,” Gibert said. The same is true for other aspects of anatomy, physiology and biochemistry. “If you look at a zebrafish pancreas, you will see the same molecular and cellular mechanisms as a mammal pancreas.”

This tendency of distantly related species to share traits makes model organisms useful in biomedical research, whether it be studies aimed at treating cancer or tooth loss.

“Tooth development in fishes and reptiles is very efficient. Think of sharks, who can replace teeth continually throughout their lives,” Gibert said. But over the course of evolutionary time, “humans and most other mammals lost the ability to regenerate teeth.”

According to the Centers for Disease Control and Prevention, only half of adults aged 20 to 64 have a full set of non-wisdom, permanent teeth. Dental implants are made of ceramics and metal, and they break. Scientists at other universities are already looking

UMMC



Yann Gibert, associate professor of cell and molecular biology at the University of Mississippi Medical Center, uses zebrafish to study disease and development.

for ways to regrow teeth, using techniques including gum line-derived cells and lasers.

“What do we need to have in terms of genetic instruction in order to create new human teeth?” Gibert said. He laid out a scenario where scientists could run experiments using dental pulp-derived stem cells to test in vitro models of tooth regeneration, testing molecular switches that are analogous to the genes that allow teeth to form in our finned friends.

“If someone could figure out a way to regenerate teeth in humans,

they would be a billionaire,” Gibert said. “This is just step one.”

After all, he said, “It took 59 years to confirm Edmund’s idea. That’s how science works.”

DOI: 10.1098/rspb.2019.0401

This article was originally published on umc.edu.

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Peptides to the rescue

By Martin J. Spiering

Insulin and glucagon are well-known peptide hormones that keep our glucose levels within a healthy range. But they are only part of a complex network that controls concentrations of this ubiquitous sugar in blood and tissues. Other molecules regulate glucose by controlling insulin secretion from the pancreas or protecting pancreatic beta cells against stresses that lead to dysfunction or cell death.

One of these protective regulators is glucagonlike peptide 1, or GLP-1. It's 30 amino acids long and is produced in specialized epithelial cells of the intestine called L cells and also in the brain and other organs and tissues.

GLP-1 belongs to a group of peptides that mediate the incretin effect, an endocrine response to glucose arising from food digestion in the intestines. This response helps regulate food intake and the fate of dietary glucose. Specifically, GLP-1, which is released when food is ingested, binds to and activates the GLP-1 receptor, or GLP-1R, a G protein-coupled receptor on many cell types, including beta cells in which GLP-1R signaling stimulates insulin synthesis and secretion. The incretin effect stimulates insulin secretion from pancreatic beta cells more strongly than exposure to glucose alone.

A 2003 article published in the **Journal of Biological Chemistry** added to our understanding of the incretin effect by showing that GLP-1R signaling protects beta cells from cell death. This is significant for pre-

venting or managing type 2 diabetes, in which beta-cell apoptosis may contribute to insufficient pancreatic insulin production.

Yazhou Li and Daniel Drucker at Toronto General Hospital in Ontario, Canada, along with colleagues, exposed wild-type and GLP-1R-knockout mice to the compound streptozotocin, which induces beta-cell death, in the presence and absence of the specific GLP-1R agonist exendin-4. The authors then assessed the effect of the GLP-1R stimulation on glucose tolerance, blood and pancreatic insulin levels, and pancreatic cell viability and proliferation.

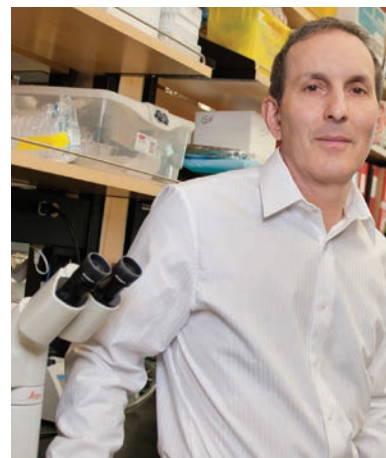
To find out what spurred this seminal paper and learn more about its findings, JBC reached out to Drucker, now at the Lunenfeld-Tanenbaum Research Institute, Mt. Sinai Hospital, in Toronto.

What prompted your investigation? In particular, what was unknown about GLP-1 and GLP-1R and their effects on beta-cell viability, and what motivated you to study these questions?

GLP-1 had previously been shown to expand beta-cell mass by stimulating beta-cell proliferation. We wondered whether GLP-1 might also contribute to the control of beta-cell mass by reducing cell death. We were also aware that cell survival pathways were activated by cAMP, an important downstream messenger that is increased by GLP-1R activation.

What were your main findings?

We made several interesting



LUNENFELD-TANENBAUM RESEARCH INSTITUTE

Daniel Drucker is the senior author on a seminal 2003 *Journal of Biological Chemistry* paper that showed that GLP-1R signaling protects beta cells from cell death.

discoveries. First, pharmacological activation of the GLP-1R with exendin-4 reduced beta-cell death that had been produced by experimental pancreatic injury in mice. We noted that this reduction in beta-cell apoptosis is associated with preservation of beta-cell function and glucose homeostasis in the mice.

Second, we found that basal GLP-1R signaling is physiologically essential for beta-cell survival, as the GLP-1R knockout mice exhibited enhanced beta-cell injury when challenged with streptozotocin.

Third, we saw that GLP-1's anti-apoptotic activities are direct, and we, that is, our collaborator Philippe Halban, could also demonstrate them *ex vivo* in purified rat beta cells exposed to cytotoxic cytokines, a model of tissue inflammation. We also discovered that GLP-1's

anti-apoptotic properties are not unique to beta cells and can be conferred to heterologous cells transfected with the gene encoding GLP-1R.

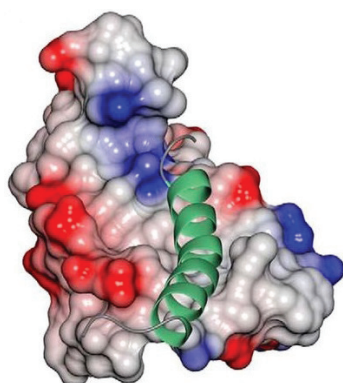
Why did you use exendin-4 rather than GLP-1 to stimulate GLP-1R?

We used exendin-4 because it's a highly stable, degradation-resistant GLP-1R agonist that is more biologically potent in animals and humans than GLP-1. It was also the lead GLP-1R agonist in clinical trials and became the first GLP-1 drug approved for management of diabetes.

Does repeated exendin-4 stimulation downregulate the receptor as is sometimes the case with repeated receptor stimulation?

In most tissues, there is little evidence that continuous GLP-1R activation by agonists downregulates this receptor. This fortuitous finding enables the development of long-acting GLP-1R agonists for managing diabetes and obesity.

As your JBC paper has shown, the GLP-1R stimulation prevents beta-cell apoptosis and increases pancreatic islet mass. Could this



The small peptide GLP-1 (green ribbon) binds to and activates the GLP-1R (gray, red and blue structure) on beta cells and thereby protects them against injury and death.

increase heighten the risk for uncontrolled cell growth/cancer?

This has always been a theoretical concern, but there's no evidence that would support it. The first GLP-1R agonist (exenatide, the common drug name for exendin-4, used in diabetes management) was approved for clinical use as an anti-diabetic medication in April 2005. After 14 years of clinical use, with multiple drugs and millions of patients taking the medication, we have not seen an increase in cancer rates due to exenatide or GLP-1R agonist use.

Is GLP-1 the major incretin hormone, or does it have some overlapping functions with other incretins, and do other incretin hormones also promote beta-cell mass?

Both GLP-1 and another peptide, gastric inhibitory polypeptide, or GIP, are important naturally occurring incretin hormones. GIP is likely the more important incretin under physiological conditions. And yes, most peptide ligands that, like GLP-1, increase cAMP levels in B cells — such as pituitary adenylate cyclase-activating polypeptide, GIP, and fatty acids — also reduce beta-cell apoptosis.

Were your findings expected, and how has your own work and the field progressed since your paper's publication?

Before our study, I don't think anyone had clearly addressed the question of whether GLP-1R signaling can inhibit beta-cell death. Since our JBC publication, GLP-1R signaling has been shown to reduce cell death in many cell types, from beta cells to neurons to endothelial cells and cardiomyocytes.

As for the field, research into both the basic science and clinical

relevance of GLP-1 has expanded tremendously since 2003. GLP-1R agonists are approved for treating patients with diabetes or obesity and under investigation for nonalcoholic steatohepatitis and neurological disorders. We continue to explore the mechanisms underlying GLP-1 action in numerous cells and tissues. In 2002, only 196 published studies of GLP-1 were listed in PubMed. In 2018 alone, there were 1,461, and the field continues to grow.

What was the impact of your paper on the field of diabetes and clinical research in general?

This is a little difficult to appreciate. The paper has been widely cited (author's note: at this writing, it has been cited 712 times in Google Scholar), and it was one of the first studies to highlight a cytoprotective role and not just an insulin-secretory role for GLP-1.

It's also noteworthy that GLP-1 has recently shown some promise in clinical trials investigating its therapeutic role in human neurodegenerative disorders such as Parkinson's disease and continues to be explored for therapeutic intervention in Alzheimer's disease. So the concept that GLP-1 might generally protect vulnerable cells continues to have high clinical relevance.

Drucker and Li's paper was nominated as a JBC Classic by JBC Associate Editor Eric Fearon at the University of Michigan Medical School. This article originally appeared in JBC. It has been edited for ASBMB Today. Read more JBC Classics at jbc.org.

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



Researchers link new protein to Parkinson's

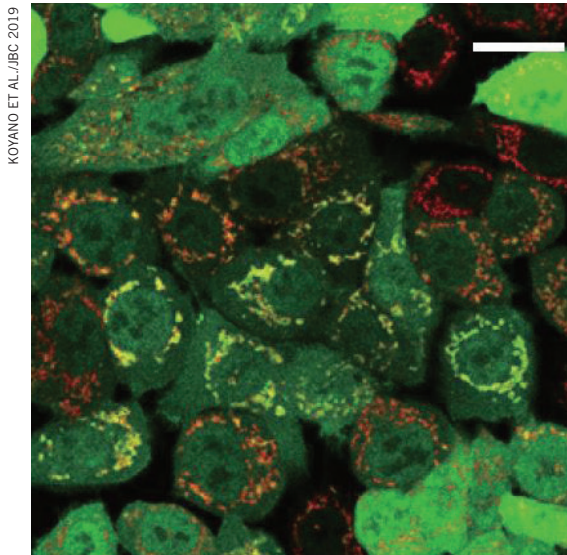
By Laurel Oldach

Researchers in Japan are reporting new insight into how the Parkinson's disease-associated protein parkin selects its targets. The finding might improve experimental therapies for Parkinson's that aim to boost parkin activity.

Cells depend on parkin to help get rid of damaged mitochondria. The research, published in the **Journal of Biological Chemistry**, suggests that parkin depends on other proteins, including one called MITOL that has not been linked previously to Parkinson's disease, to direct it to those damaged mitochondria.

Parkin adds a degradation tag called ubiquitin to proteins on the mitochondrial surface. In some patients with familial Parkinson's disease, parkin activity is disrupted and bad mitochondria cannot be destroyed. Harmful byproducts from those bad mitochondria can damage neurons. By understanding how parkin works and what goes wrong when it's mutated, researchers hope also to help patients with other forms of Parkinson's disease.

While other ubiquitin-tagging proteins, known as E3 ligases, recognize specific amino acid sequences on their substrates, parkin has many known substrates that don't seem to share a sequence in common. While studying how parkin chooses its substrates, researchers led by Fumika Koyano in Noriyuki Matsuda's lab at the Tokyo Metropolitan Institute of Medical Science discovered that parkin can tag any lysine-contain-



KOYANO ET AL./JBC 2019

This image of cells with damaged mitochondria shows overlap, in yellow, between parkin protein in green and the mitochondria, shown in red.

ing protein with ubiquitin — even a bacterial protein not ordinarily found in the cell — as long as it's present at the surface of the mitochondria.

“Parkin is not regulated by its substrate specificity,” Koyano said of the finding. Instead, control of parkin activity comes from how it is recruited and activated by other proteins.

The discovery that activated parkin is not terribly selective led Koyano and her colleagues to take a closer look at parkin's recruitment and activation. Some details of that process are well known; for example, a protein called PINK1 is known to boost parkin activity. But Koyano and colleagues discovered a new step that must happen before PINK1 can contribute to parkin activation. They found that parkin acts more rapidly when a first ubiquitin molecule is already present, acting as a seed for the

addition of more ubiquitins. In most cases, the researchers found, this seed ubiquitin is added by a protein called MITOL, which had not been linked previously to Parkinson's.

The research could contribute to the design of new drugs, some of which aim to boost parkin activity to slow the advance of Parkinson's disease.

“If we achieve upregulation of seed ubiquitylation on mitochondria,” Koyano said, “it might accelerate parkin recruitment and parkin activation to eliminate damaged mitochondria more efficiently.”

DOI: 10.1074/jbc.RA118.006302

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



JBC launches program for early-career scientists

Postdocs and new investigators invited to participate in peer review

By Angela Hopp

The **Journal of Biological Chemistry** has launched a program designed to involve scientists at early stages of their careers in peer review.

The JBC Early-Career Reviewer Board offers postdoctoral researchers and newly independent investigators a structured path for developing peer-review skills and learning about the scholarly publishing process. In addition, editors said, the program promises to diversify the community of peer reviewers and make use of untapped scientific expertise.

“Peer review is the cornerstone of the trust [scientists] place in each other,” JBC Editor-in-Chief Lila Gierasch of the University of Massachusetts Amherst wrote in a recent editorial. When a research group submits a paper to the JBC, an associate editor shepherds it through the review process. Historically, the associate editor has recruited professors from the journal’s editorial board and, if needed, external specialists to provide expert evaluations of the findings.

Now associate editors have the option of adding an early-career reviewer to that roster of reviewers. All of them will work together to assess the scientific approaches, results and conclusions of each manuscript submitted to the JBC to determine whether

it should be published or needs more work. Supplementary evaluations by early-career reviewers will be assessed by associate editors, who will work with the early-career reviewers to hone their recommendations for authors.

“By getting feedback on the clarity of their written reports and advice on the level of detail and emphasis in critiques, the ECRs will gain valuable information about how to constructively participate in the publishing process,” Gierasch wrote.

She emphasized that the initiative will provide emerging scientists with valuable training and provide the journal with fresh and diverse perspectives: “We anticipate that some of our ECRs will go on to serve as full editorial board members, further establishing their credentials as experts in the field.”

Learn more at jbc.org/site/ecr.

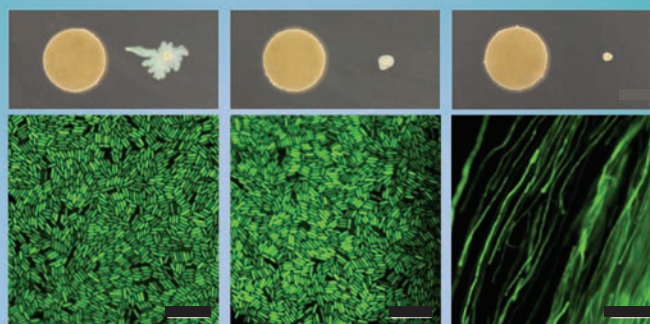
Angela Hopp (ahopp@asbmb.org) is the ASBMB’s communications director and executive editor of ASBMB Today. Follow her on Twitter [@angelahopp](https://twitter.com/angelahopp).



VIRTUAL ISSUE

Antibiotic activities and mechanisms of resistance

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jpc.org/site/vi/antibiotic_resistance

Better samples, better science

Study explores integrity of research specimens

By *Richard Harth*

Effective diagnosis and treatment of disease draw on painstaking research, which often relies on biological samples. The avalanche of studies used to better understand illnesses and design effective therapies cost billions of dollars and potentially affects millions of lives.

So it would seem reasonable to assume that the reliability of biological samples, on which accurate results depend, would be of paramount concern for the scientific community.

According to Chad Borges, a researcher in the Biodesign Institute's Virginia G. Piper Center for Personalized Diagnostics at Arizona State University, that assumption is often wrong.

"One of the major reasons that there are so many discoveries of biomarkers in the literature but so few positive validations that confirm those findings is the fact that in many cases, during the discovery, samples were used that have a history or an integrity that's simply unknown."

Biological samples can be susceptible to changes over time, which often occur when they are removed from deep refrigeration. Degraded samples can produce spurious results in research. To address these concerns, Borges and his colleagues have designed a sensitive test that can be used to establish the integrity of blood plasma and serum, the most common biosamples used in medical research.

Ensuring such samples have been

properly handled is the first step in careful research that meets the necessary high standards of reliability and reproducibility. The new test, which relies on accurate measurement of the relative proportions of two forms of the protein albumin present in blood, recently was described in the journal **Molecular & Cellular Proteomics**.

Houston, we have a problem

The immediacy of the issue of sample quality became apparent to Borges during his own research, which involved experiments on biological samples slated for distribution by the National Institutes of Health.

"We got a little suspicious that something wasn't quite right about the sample set," he said. Borges applied the newly designed test to the samples, with surprising results. "Lo and behold, there was a major difference between the cases and controls for this specimen integrity marker."

Borges found that the freezer in which the control samples were stored had lost power for several days during a natural disaster. "That information is really important with regard to the quality of the samples and the stability of the markers that were in them."

The implications of this discrepancy plainly went beyond his own research. "Who knows how many other markers are differentiated simply because of the way in which the cases and controls were handled," Borges said.

Biological samples are ground

zero in the quest for dependable science, yet researchers hoping to publish their work may have a disincentive to spend the time to probe the integrity of their specimens. Should they uncover a problem, it may throw their data into question and preclude publication—a serious setback, with little for the researcher to show for it. There is a danger of an ignorance-is-bliss mentality.

Addressing the problem requires two things, Borges noted. First, a regulatory body such as the NIH needs to issue strict guidelines that include detailed documentation of sample history and handling. Some scientific journals do require documentation of specimen storage conditions prior to publication, but such records are often inadequate for ensuring a high level of sample integrity. Secondly, researchers need reliable methods for testing their samples to ensure they meet exacting standards. The technique described in the current study is an important advance in this direction.

QC for blood

The new biomarker sets cutoff values for blood plasma and serum, allowing researchers easily to assess the quality of samples and their suitability for given experiments, even if a detailed record of sample handling and storage is unavailable. For the first time, plasma and serum—the most commonly used biospecimens for medical research—can be tracked with a reliable biomarker.

The biomarker, which relies on



relative proportions of two isoforms of albumin, requires only a low volume of plasma or serum and minimal sample preparation. (Different isoforms of this protein are functionally similar, but an oxygen-induced modification that occurs to an abnormal extent outside of the body is used to identify mishandled samples.)

Albumin is the most abundant protein in blood plasma and serum, constituting roughly half of all protein content in these biofluids. Outside the body, the natural unmodified form of albumin becomes oxidized with time. This can be detected by observing a change in protein mass using mass spectrometry.

By describing a chemical rate law for this protein oxidation reaction that takes place in plasma and serum,

the biomarker acts as a kind of molecular stopwatch that can gauge precisely the elapsed time a particular sample has remained in a thawed state.

The biomarker described is inexpensive, easy and rapid to use, and can be fully automated, making it a strong candidate to serve as the new gold standard for plasma and serum analysis. It is capable of detecting biospecimen exposure to room temperature conditions for as little as two hours, quickly and accurately identifying mishandled or poorly stored samples and preventing their inclusion in clinical research.

In addition to more conventional clinical research, the new biomarker is poised to make inroads in a variety of health-related investigations. It recently has been incorporated into

a project sponsored by the Defense Advanced Research Projects Agency, which uses epigenetic markers in blood to identify exposure to weapons of mass destruction or their precursor chemicals. The new biomarker will be used to ensure the quality of blood samples, further establishing the power and versatility of this approach.

DOI:10.1047/mcp.TIR119.001659

This article originally was published on biodesign.asu.edu. It has been edited for ASBMB Today.

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JLR virtual issue sheds light on a key risk factor for heart disease

By Jonathan Griffin

Because lipids such as cholesterol and triglycerides are hydrophobic and tend to clump up, rather than dissolve, in water, they need help getting around inside the body. Lipoproteins are complex assemblies with hydrophilic outer shells that package hydrophobic lipids in their core, allowing them to hitch a ride through the bloodstream. These delivery particles play an important role in the absorption of dietary lipids from the small intestine and also transport lipids to and from the liver.

High levels of one particular class of lipoprotein, known as lipoprotein (a), are associated with atherosclerosis, inflammation and thrombosis, but no treatments are available in the clinic that specifically lower Lp(a), and much of what governs Lp(a) assembly is still unknown.

A new virtual issue from the **Journal of Lipid Research** titled “Lipoprotein (a): Many strides made, yet there is a long road ahead” explores the past, present and future status of Lp(a) research and showcases researchers pushing this field forward. This issue was assembled by JLR Junior Associate Editor Gissette Reyes-Soffer from Columbia University Irving Medical Center in New York City.

Several papers collected in this issue offer insights into how various Lp(a)-reducing drugs work. In one of these studies, Enkhmaa Byambaa and colleagues at the University of California, Davis, and the University of Hong Kong demonstrated that

alirocumab — an inhibitor of the lipid-binding enzyme PCSK9 — could lower Lp(a) levels regardless of the isoform of proteins in Lp(a).

A study by Frederick Raal and an international team of researchers suggests that another PCSK9 inhibitor, evolocumab, reduces Lp(a) levels partly by increasing the expression of LDL receptors.

Elisa Waldmann and Klaus Parhofer at Ludwig Maximilian University of Munich wrote a review that discusses apheresis as an effective method of selectively clearing Lp(a) from the blood and reducing risk of

cardiovascular disease.

Another review, penned by George Thanassoulis at McGill University, describes the association of Lp(a) with aortic valve disease and outlines steps toward developing much-needed preventive and therapeutic strategies.

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The cover of the JLR virtual issue depicts the Lp(a) particle following the steps of a walking path, getting bigger as the road stretches into infinity.

Bacterial sphingolipids: Perhaps not as rare as we thought?

By Eric A. Klein

Among the ways cells adapt to changes in their environment, regulation of the lipidome is critical for maintaining cellular integrity. Species that lack temperature homeostasis adapt by modulating acyl chain saturation to resist changes in membrane fluidity. Bacteria such as *Escherichia coli* desaturate their fatty acids as temperatures decrease; the double bonds formed by acyl chain desaturation introduce kinks in the fatty acids that inhibit lipid packing and increase membrane fluidity to counteract the effects of lower temperature.

Temperature is not the only environmental variable that necessitates membrane remodeling. In many settings, nutrient availability can vary widely. For example, nutrient levels in fresh-water lakes fluctuate with the seasons, and plant decomposition affects soil. In particular, oscillations in phosphate concentration can limit bacterial growth.

When phosphates are limited, the synthesis of membrane phospholipids becomes an obvious challenge. Studies have shown that alphaproteobacteria, such as *Agrobacterium tumefaciens* and *Mesorhizobium loti*, adapt to phosphate starvation by increasing production of diacylglycerol-based glyceroglycolipids and ornithine lipids.

In our lab, we recently showed that the Gram-negative aquatic bacterium *Caulobacter crescentus* responds to phosphate limitation by synthesizing a novel hexosyl-hex-

uronosyl-ceramide glycosphingolipid, or GSL. Ceramide-based GSLs are ubiquitous in eukaryotic organisms, but in bacteria they had been observed previously only in the Sphingomonadaceae family, where they function as a substitute for outer-membrane lipopolysaccharides, or LPS. Unlike *Sphingomonas* species, *C. crescentus* produces LPS even during phosphate starvation; in this organism, the GSLs appear to play a role in resistance to phage-mediated killing.

Now that we know that bacterial GSLs are not limited to just the Sphingomonadaceae, just how widespread are these lipid species? The honest answer is that we simply don't know. While the lipidomes of many bacteria have been characterized, our findings in *C. crescentus* demonstrate that lipid abundance can vary with growth conditions. Indeed, previous characterizations in rich growth media did not identify GSLs in *C. crescentus*.

Another major challenge is that, unlike for eukaryotes, we do not know which enzymes are responsible for ceramide synthesis in prokaryotes. Only the enzyme that catalyzes the first step of ceramide synthesis, serine palmitoyltransferase, has clear homologues in bacteria as described in a recent review by Dominic Campopiano and colleagues. This implies that either (1) bacteria carry out the same synthetic chemistry as eukaryotes, but these enzymes diverged so long ago that the functionally



U.S. DEPARTMENT OF ENERGY/WIKIMEDIA COMMONS

Eric Klein's lab showed that the Gram-negative aquatic bacterium *Caulobacter crescentus* synthesizes a novel glycosphingolipid when phosphates in its environment are limited.

equivalent proteins cannot be identified by sequence homology or (2) bacterial ceramide synthesis evolved independently using novel enzymes and/or synthetic pathways. If the genes required for ceramide synthesis are identified, researchers will be able to take a bioinformatic approach to finding additional species that might produce these lipids.

A growing body of work demonstrates that bacterially produced sphingolipids may play an important role in aspects of human health such as gut homeostasis and oral pathology. Uncovering the mechanism of prokaryotic ceramide synthesis will help determine how widespread these lipids are in bacteria and also may provide a novel route for pharmacological intervention.

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From the journals

By Gelareh Abulwerdi, Jonathan Griffin & Elizabeth Stivison

Cholesterol transport disruption in Alzheimer's

Scientists know that cholesterol plays a role in Alzheimer's disease, but that role is not fully understood. In a recent study in the **Journal of Lipid Research**, Cinzia Marchi of the University of Parma and colleagues in Italy describe another piece of the cholesterol–Alzheimer's puzzle.

With a growing body of work linking disruption of cholesterol homeostasis to Alzheimer's disease, Marchi's team asked specifically whether efflux of high-density lipoproteinlike particles is disrupted in Alzheimer's. They examined the cerebrospinal fluid, or CSF, of Alzheimer's patients, non-Alzheimer's dementia patients and healthy control subjects, measuring the ability of the CSF to promote cholesterol efflux through membrane transporters. In the Alzheimer's patients' CSF, cholesterol efflux capacity was reduced dramatically; this was not true in the healthy controls or non-Alzheimer's dementia patients. Future research may shed light on the intricacies of the causal role of cholesterol homeostasis in Alzheimer's disease progression.

DOI: 10.1194/jlr.P091033

Refining the culprits behind Parkinson's

Amyloid inclusions primarily composed of alpha-synuclein protein, or alpha-syn, are a hallmark of Parkinson's disease. Different species of alpha-syn exist, but the relative contribution of each

conformation to neurodegeneration has not been characterized. Jessica Froula of the University of Alabama at Birmingham and an international team produced monomers, beta-sheet oligomers and fibril fragments of alpha-syn and injected them into mouse striatum. They found that while beta-sheet oligomers exhibited some toxicity, fibril fragments produced Parkinson's-like phenotypes, driving inclusion formation, loss of dopamine neurons and motor-behavior defects. These results, published in the **Journal of Biological Chemistry**, point toward alpha-syn fibrils as a potential target for Parkinson's disease treatment.

DOI: 10.1074/jbc.RA119.007743

Microbiota and obesity

Obesity and related conditions such as heart disease and type 2 diabetes are major public health problems, generating an estimated \$147 billion in medical costs annually in the United States. Diet-induced obesity, or DIO, is a form of obesity with a nongenetic cause. Hao Tran at Georgia State University and colleagues in Georgia and California set out to identify biomarkers indicating proneness to DIO in gut microbiota, the diverse community of microorganisms that inhabit the gastrointestinal tract.

In their recent paper in the journal **Molecular & Cellular Proteomics**, the researchers looked at correlation between microbial species and protein abundance. After feeding a high-fat diet to mice, they saw a shift in the mice's feces metaproteome.

Specifically, proteins derived from species of Clostridiales and Bacteroidales decreased, while proteins from Lactobacillales increased. However, they did not see this metaproteomic change when they looked at species number by fecal microbial analysis. This shows that fecal metaproteomics is a promising tool for identifying biomarkers to predict the risk of DIO after exposure to high-fat diet.

DOI: 10.1074/mcp.RA119.001623

New models for the study of sarcoma treatments

The genes encoding the RNA-binding proteins FUS and EWSR1 are prone to chromosomal translocation events that produce proteins that underpin liposarcoma and Ewing's sarcoma. Jeremy Ryan and a team of researchers at Washington University and the University of Pennsylvania report new yeast models that overexpress the aberrantly fused proteins and replicate the toxicity and aggregation patterns seen in sarcoma patients. In their study published in the **Journal of Biological Chemistry**, the researchers used the models to show that engineered potentiated Hsp104 proteins suppress the toxicity of the chromosomal translocations. The authors suggest that the yeast models could be useful platforms for studying both the underlying mechanisms of and treatments for sarcoma.

DOI: 10.1074/jbc.RA119.009494

New role for the farnesoid X receptor in adipocytes

The farnesoid X receptor, or

The role of ECM proteins in heart regeneration

The extracellular matrix provides a cell with mechanical and structural support and plays a role in biochemical signaling to neighboring cells. The ECM is composed of proteins including collagens, proteoglycans and glycoproteins (fibrillin and fibronectin). These ECM proteins play a role in tissue regeneration, the process by which injured tissue is restored to nearly normal function. In adult mammals, there is limited recovery of heart tissue after injury that results in a fibrotic scar, which may lead to reduced heart performance. Therefore, studying regenerative processes to design medicinal strategies is important. Nonmammalian vertebrates such as zebrafish can recover large portions of their hearts after amputation, so studying cardiomyocyte regeneration in zebra fish can help researchers design regenerative strategies for cardiovascular disease, a leading cause of death in humans.

Anna Garcia-Puig at the Center of Regenerative Medicine in Barcelona and colleagues in Spain studied the genomic and proteomic changes in ECM during heart regeneration in zebrafish. In a recent paper in the journal **Molecular & Cellular Proteomics**, they describe a novel method of decellularization of amputated adult zebrafish ventricles, using a detergent treatment to increase

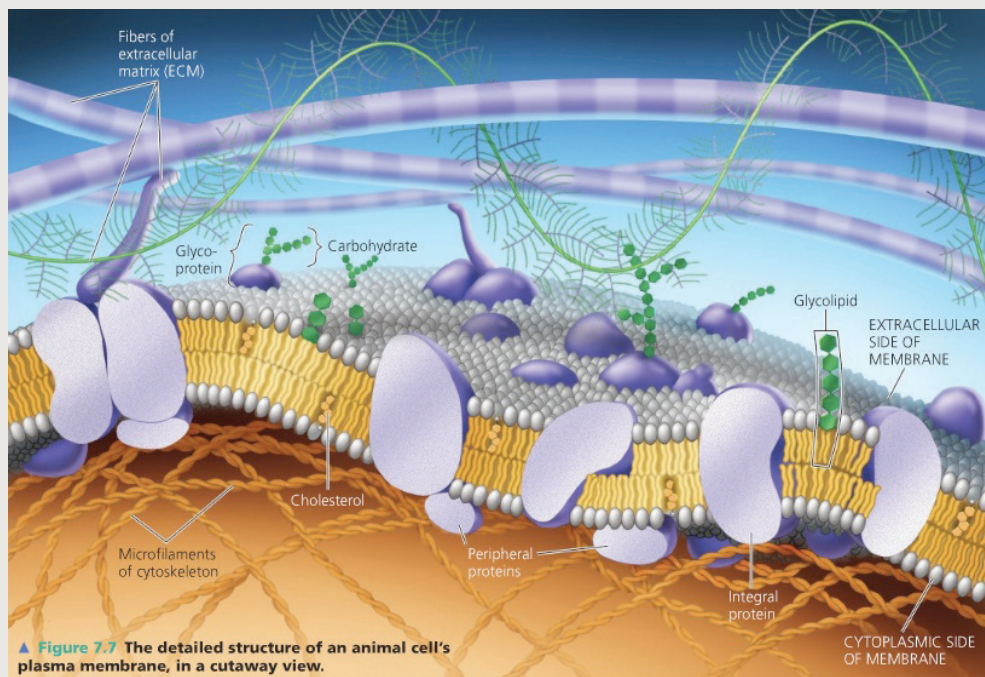
the number of ECM proteins. In comparison with older methods, this ECM protein isolation retains the integrity of ECM to provide a more robust panel of change. To identify changes in ECM proteins, the researchers decellularized zebrafish ventricles at seven, 14 and 30 days after amputation and analyzed the proteins with liquid chromatography-mass spectrometry, or LC-MS. The largest ECM protein profile changes between intact and amputated hearts occurred after seven days. Several ECM proteins — such as fibrinogen a, b and g; fibronectin 1b; and periostin b — increased after seven days, while levels of collagens and fibrillin 2b decreased.

A biomechanical property of ECM is its stiffness, which plays a role in cell proliferation, differentiation and regulation. Using atomic force microscopy, the researchers evaluated changes in zebrafish heart stiffness during regeneration. They saw a significant decrease in ventricular ECM stiffness after seven days, which returned to normal by 14 days. These data support the LC-MS findings that showed collagen was reduced after seven days; collagen concentration contributes to stiff myocardium.

DOI: 10.1074/mcp.RA118.001193

— Gelareh Abulwerdi

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▲ **Figure 7.7** The detailed structure of an animal cell's plasma membrane, in a cutaway view.

This image shows the plasma membrane with extracellular matrix components. The ECM helps maintain the integrity of the cell and plays a role in cellular communication and regeneration of organs.

FXR, is a nuclear receptor activated by bile acids. However, research has shown that its effects go beyond the intestine. FXR is moderately expressed in adipocytes, and a new study in the **Journal of Lipid Research** digs into what it might be doing there.

Tim van Zutphen of the University of Groningen and colleagues in Europe and the U.S. showed that when human FXR is expressed in mouse adipocytes, a number of metabolic disease–relevant phenotypes appear, from whole-body insulin resistance to increased adipocyte size to ectopic fat deposition. Metabolic disease is increasingly common in modern society, and understanding its biology is essential to finding treatments. This study gives new insight into the complex web of interactions in metabolic diseases such as diabetes.

DOI: 10.1194/jlr.M094508

An unexpected metabolic target in cancer

A dependence on glycolysis over oxidative phosphorylation is thought to be a hallmark of cancer cells, but recent work has demonstrated mitochondria still are functioning in most cancers. In a report in the **Journal of Biological Chemistry**, Ekta Agarwal and colleagues provide new evidence for the reliance of cancer cells on mitochondrial oxidative phosphorylation. Using multiple techniques and cancer cell lines, the team showed that two oncogenic proteins, c-Myc and N-Myc, control the expression of the mitochondrial chaperone TRAP1. Moreover, they found that Myc-mediated regulation enabled oxidative bioenergetics through pathways that, when shut down within an organism, suppressed primary

and metastatic tumor growth in a TRAP1-dependent fashion.

DOI: 10.1074/jbc.AC119.008656

A model system to study heart development

In cell signaling, information from the exterior of the cell is transmitted to the interior. The Notch signaling pathway, one of the many signaling pathways in a cell, is conserved in many cell types and has an important role in the development of organs such as the heart.

Notch signaling plays a role in the development of heart chambers and valves, and alterations in Notch signaling can lead to cardiac disease. Early in the development of heart tissue, the heart tube is formed through outer epithelial myocardium and the inner endocardial layer. Proper signaling between endocardium and myocardium is crucial for the development of heart structures. Studying the signaling mechanism involved can help researchers understand cardiac diseases and find therapeutic interventions.

In a recent paper in the journal **Molecular & Cellular Proteomics**, Rebeca Torregrosa–Carrion of the Centro Nacional de Investigaciones Cardiovasculares Carlos III and colleagues in the U.S. and Spain manipulated Notch activity in mouse embryonic endocardial cells followed by mass spectrometry–based proteomics to study Notch-dependent embryonic factors secreted by heart endocardium involved in heart development and disease.

DOI: 10.1074/mcp.RA119.001492

Bringing Alzheimer’s-associated proteins together

Recent reports indicate that tau protein, which forms aggregates

in Alzheimer’s disease, undergoes liquid-liquid phase separation, or LLPS, but the mechanism by which this happens remains mostly unknown. In a study in the **Journal of Biological Chemistry**, Solomiia Boyko and colleagues at Case Western Reserve University used polyethylene glycol to induce tau LLPS and characterized the resulting droplets with fluorescence recovery after photobleaching. The authors report that tau LLPS is driven largely by electrostatic interactions and does not require phosphorylation. This insight provides a foundation to better understand how post-translational modifications could influence tau LLPS in both normal and pathological states.

DOI: 10.1074/jbc.AC119.009198

Defining the birth of ribosomes

Ribosome assembly is a complex process that determines the rate of protein synthesis. Although precursor ribosomal particles, known as preribosomal complexes, have been detected in eukaryotes, their assembly remains poorly understood. Danysh Abetov and an international team of researchers present a new method to isolate and characterize preribosomes in mammalian cells. By optimizing nuclear lysis conditions, the authors preserved the complexes and characterized them with mass spectrometry and Northern blotting-based rRNA detection. They identified two new types of preribosomes and found that their formation was nutrient-dependent, elucidating a critical step in the process of ribosome assembly. The results were published in the **Journal of Biological Chemistry**.

DOI: 10.1074/jbc.AC119.008378

Whipping an acid into shape improves biofuel production

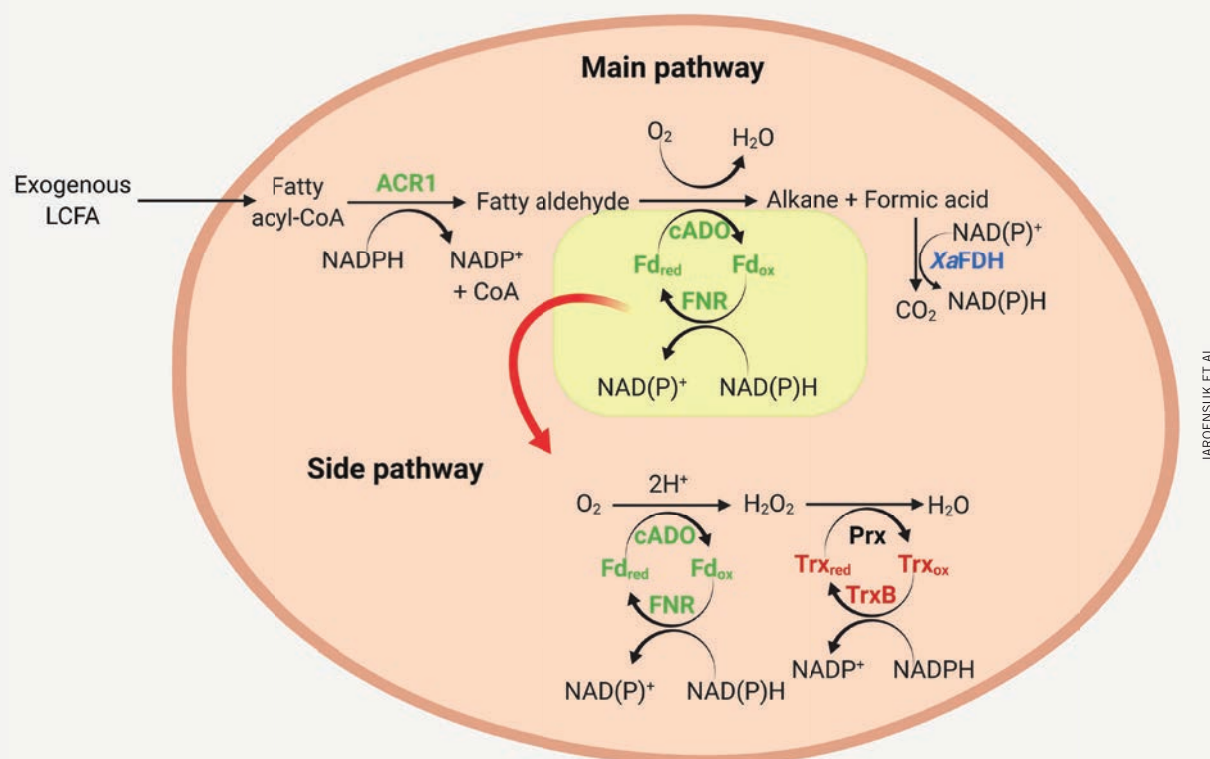
With fossil fuel shortages and carbon dioxide emissions, alternative energy sources are increasingly important. Biofuels converted from waste products like fat-rich feedstock are one alternative source, but their production is not yet efficient enough to meet the demands of many countries. Researchers in Thailand report in the **Journal of Biological Chemistry** that the enzyme formate dehydrogenase, or FDH, can significantly boost bacterial production of alkanes, which can be used as fuel for transportation, cooking and material synthesis.

Using synthetic biology approaches, researchers had previously designed a metabolic pathway that converts fatty acids into alkanes in bacteria. The yield of alkane from this pathway is about 35%, however, which is quite low. One reason is the limited activity of the enzyme aldehyde-deformylating oxygenase, or ADO, which carries out the final step of the process — the conversion of fatty aldehydes into alkanes with formic acid as a byproduct. If produced in excess, formic acid can decrease cellular

pH, creating an acidic environment that slows ADO activity. Juthamas Jaroensuk and Pattarawan Intasian of the Vidyasirimedhi Institute of Science and Technology and colleagues aimed to increase alkane production by converting formic acid into something more useful for ADO activity.

Through bioinformatics analysis, the researchers found that the enzyme FDH from the bacteria *Xanthobacter* sp. 91 potentially could benefit ADO activity in two ways. Their analysis showed that FDH can remove excess formate by oxidizing it into carbon dioxide. This conversion also results in the generation of NADPH, which ADO uses to convert aldehydes into alkanes. The authors found that inserting the gene for FDH into an alkane-producing pathway expressed in *Escherichia coli* brought cellular pH closer to neutral and increased concentrations of NADPH. Cells expressing FDH reached conversion yields of 50%, the best yield yet for alkane production by whole-cell bioconversion. DOI: 10.1074/jbc.RA119.008246

— Jonathan Griffin



A metabolic pathway refined for enhanced alkane production: Enzymes and proteins associated with alkane production, formic acid elimination and detoxification of reactive oxygen species are shown in green, blue and red, respectively.

New tools to study sphingolipid metabolism

Sphingolipid metabolism is essential to many cellular processes, and this becomes obvious when defects contribute to diseases that range from developmental disorders to cancer. In a recent paper in the **Journal of Lipid Research**, Wataru Sakamoto of Stony Brook University and colleagues in New York and Japan describe new tools for the study of sphingolipid metabolism.

Ceramides are a family of related lipids, and the researchers' work is framed by what they call the "many ceramides" hypothesis that the biological activity of each ceramide is determined by its localization, which is in turn determined by the localization of enzymes that metabolize ceramides. Sakamoto's team investigated this hypothesis by developing a system to target sphingomyelinase, or SMase, which converts sphingomyelin into ceramides, and ceramidase, or CDase, which degrades ceramides into free fatty acids, to different compartments in the cell. They

targeted these enzymes to the inner plasma membrane, nucleus, mitochondria, endoplasmic reticulum, Golgi and cytoplasm of HeLa cells and analyzed the lipids produced in each case.

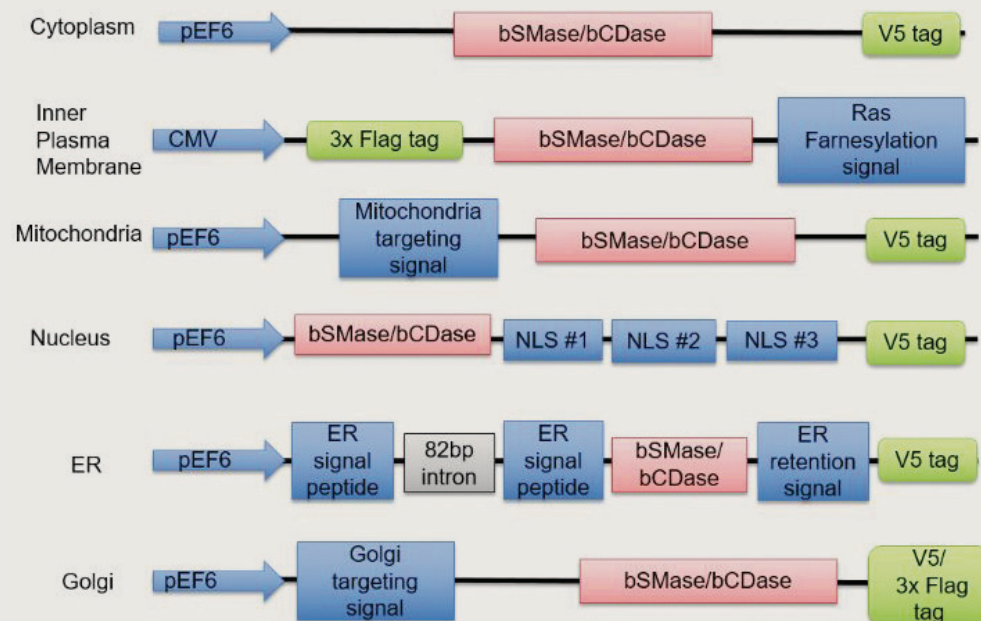
The researchers found that SMase expression consistently increases ceramides in the cell, but the type of ceramide produced varies based on the organelle. For example, SMase in the plasma membrane acted on long-chain sphingomyelin but not on very long-chain, while SMase in the endoplasmic reticulum acted on both. They also showed that CDase expression alone does not change ceramide levels but does so in conjunction with SMase expression, which warrants further investigation.

This work sheds light on the compartment-specific effects of sphingolipid metabolism and provides new tools that can be used for future studies.

DOI: 10.1194/jlr.M094722

— Elizabeth Stivison

SAKAMOTO ET AL./JLR



New tools created by Wataru Sakamoto and colleagues target sphingomyelinase and ceramidase to specific cellular compartments.

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For October, magnesium helps the leaves stay green

By Quira Zeidan

We mark the 150th anniversary of Dimitri Mendeleev's periodic table of chemical elements this year by highlighting elements with fundamental roles in biochemistry and molecular biology. So far, we've covered hydrogen, iron, sodium, potassium, chlorine, copper, calcium, phosphorus, carbon, nitrogen, oxygen and manganese.

October is the month for peak fall foliage in states across the northern and central U.S. Leaves turn yellow, orange and red as chlorophyll — the photosynthetic pigment that gives plants their green color — breaks down due to limited sunlight and cooler temperatures. Chlorophyll consists of a porphyrin ring — a molecule made of carbon, nitrogen and hydrogen — attached to a long hydrocarbon tail. At the center of the porphyrin ring, a magnesium ion stabilizes the chlorophyll molecule and transfers electrons down an electron transport chain to drive the photosynthetic process.

Magnesium — with symbol Mg and atomic number 12 — is a reactive alkaline earth metal that readily can lose two electrons to form a cation with charge +2. In nature, it occurs mostly in compounds with other elements such as carbon, sulfate, oxygen and chlorine.

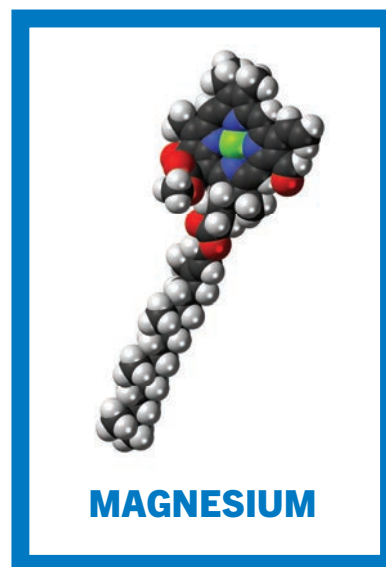
Magnesium is the ninth most abundant element in the known universe. It is produced in large stars when helium fuses with neon or in supernovas when three atoms of helium fuse sequentially with a

carbon nucleus. Supernova explosions disperse magnesium into space, where it falls onto the surface of planets, and into the interstellar medium, where it's recycled into other star systems.

On Earth, magnesium is the fourth most common element after iron, oxygen and silicon. It is the eighth most abundant element in the Earth's crust, where it forms large mineral deposits of magnesite, dolomite and other rocks. Magnesium salts easily dissolve in water, making oceans and rivers the most abundant source of biologically available magnesium.

In vertebrates, magnesium is the fourth most common metal ion and the second most abundant intracellular cation after potassium. Protein transporters that carry magnesium across biological membranes must recognize the cation's large hydration shell and deliver the naked ion. Examples of magnesium transporters are the XntAp protein in the freshwater ciliate Paramecium, the MgtA and MgtB system in the pathogenic bacteria Salmonella, and the SLC41A1 carrier in the plasma membrane of mammals.

Inside the cell, magnesium can be found in the cytosol or stored in intracellular compartments. Free cytosolic Mg⁺² alters the cell's electrical properties by regulating the function of voltage-dependent Ca⁺² and K⁺ channels. This has important consequences in excitable cells such as neurons and muscles, and it



The chemical structure of chlorophyll shows a magnesium ion in green sequestered at the center of a porphyrin ring, which is attached to a long hydrocarbon tail.

regulates processes like neurotransmitter release and muscle contraction and relaxation. Magnesium bound to protein plays a structural role as part of the protein's conformation or a regulatory role by activating or inhibiting enzyme activity. Magnesium within mitochondria affects the enzymes of energy metabolism and the process of programmed cell death, or apoptosis. And in the nucleus, most of the magnesium is associated with nucleic acids and free nucleotides, neutralizing the negative charge of phosphate groups.

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Biochemistry OF A Burger

Impossible Foods does science, makes food and tries to change the world *By Laurel Oldach*

In what has become a journalistic cliché, I took my boyfriend, a vegetarian for the past 10 years, to our local greasy spoon to try out an Impossible Burger.

He didn't care for it.

He had lost his taste for ground beef and found the experience of a plant-based, completely vegan yet beefy-tasting burger less than appealing. I, on the other hand, was a fan; his burger tasted better to me than my own, which was made the old-fashioned way, with beef.

People like me are exactly the people Impossible Burger is targeting: millennials who eat meat sometimes but fret about its impacts on a crowded, warming world.

David Welch is the director of science and technology at the Good Food Institute, a think tank promoting the burgeoning plant-based meat industry. He said one of the reasons Impossible Foods and its strongest competitor, Beyond Meat, have garnered so much interest from investors is their average customer.

"They're not targeting the vegan or vegetarian consumer," Welch said. "They're targeting the meat eater who is being more conscious about their decision."

Impossible Foods' second claim to fame is its scientific approach to imitating meat, which relies on reductionist biochemistry and an unusually sourced key ingredient. This it owes to its founder, Pat Brown, a biochemist and former Stanford University professor with a long history of shaking things up.

"We were approaching (meat) the same way you might approach figuring out the entire system for replicating genes," Brown said during an interview in June. "Basically, start looking at what are all the possible components that could be players ... and then deconstruct and reconstitute the biochemical system."

Market and mission

The world eats a lot of beef: 57 pounds per person per year in the U.S., with consumption increasing worldwide. Because

cattle are the least efficient livestock animal at converting feed into edible meat, environmentalists have argued for years that reducing beef consumption is an important conservation act.

Brown, who has been vegetarian for decades, says that those arguments have not been effective, even when made by parties as influential as the Chinese government. “That experiment has been done,” he told an audience of microbiologists during the American Society for Microbiology’s keynote lecture in June, which he delivered wearing a “no cows” T-shirt. “You don’t solve the problem by asking people to change their diets.”

Brown frames the problem instead as relying on an outdated technology — namely the cow — for beef production. He wants to solve the problem by making meat imitations so appealing that they’ll outcompete what he calls the legacy industry. Impossible Foods explicitly states that its mission is to eliminate all animals from the food production system by 2035.

Staffing with scientists

Becoming a CEO wasn’t in Brown’s original plan. Compared with being a professor, he thought a job in business would be dull. He first set out to eradicate animal agriculture while on sabbatical from Stanford in 2009 and thought he could do it by persuading someone else to take on disrupting the industry.

He anticipated that an established food producer would adopt the meat-alternative idea as enthusiastically as he had. “I went around to food industry conferences and gave a spiel to the effect that someone’s going to

make a killing if they are the first mover to replace animals in food production technology,” he said in 2017. “That was stupid.”

When the food industry didn’t bite and a workshop he organized at the National Academies resulted in no discernible policy change, Brown decided to do it himself.

“I was not a savvy business person, but I had the very good fortune of living in the epicenter of venture capital,” he said. The funding may have had less to do with Brown’s physical proximity to the venture capital firms of San Francisco than his track record of disrupting scientific fields (see box on page 34: A research career).

Early on, Brown hired mostly biochemists, many from his professional circles at

Impossible Foods approached meat “the same way you might approach figuring out the entire system for replicating genes.”

—Pat Brown



MARTY KATZ

Pat Brown, CEO of Impossible Foods, pictured in 2009.

A research career

Before launching Impossible Foods, Pat Brown was already well known for a 30-year career in research and scientific activism. Now, he's so famous as an entrepreneur that news articles sometimes mention that first life — during which he established the field of functional genomics and started rolling a rock that's now an avalanche of open-access publication in the life sciences — as an afterthought.

According to his colleagues, Brown always has excelled at coming up with creative solutions to difficult problems. Throughout his career, these problems have grown in scale and expanded in impact beyond the lab bench.

Brown learned the process of detailed biochemical investigation, which his team would later apply to the humble hamburger, from some of the most noted biochemists of the 20th century. As a graduate student at the University of Chicago, he trained with the late Nicholas Cozzarelli. After finishing a Ph.D. and a medical residency, Brown joined the lab of biochemist J. Michael Bishop at the University of California, San Francisco, as a postdoc, where he collaborated closely with members of Harold Varmus' lab to study HIV molecular biology.

Bruce Bowerman, who worked closely with Brown at UCSF, recollected a sign over Brown's lab bench "that said, in bold black letters, 'If I have seen farther, it is by standing on the shoulders of —' and instead of 'giants,' which is the Newton quote, he had written, 'idiots.'"

"Pat was not a modest person," he said. "But he wasn't unpleasant at all."

In 1988, Brown was hired as an assistant

professor at Stanford, where he would remain on the faculty for 25 years. The scientific work he's most famous for in that time is developing the DNA microarray, a technique that originally was envisioned for genetic mapping but became popular as the first method to measure changes to a whole transcriptome.

To interpret the data on regulation of thousands of genes produced by a microarray, Brown and his team hoped to mine the scientific literature, which was beginning to be available online. But they found that journals, which depended on subscriptions, weren't open to the idea. With Varmus and Michael Eisen, a postdoc in his lab, Brown embarked on an advocacy project for open access to the scientific literature that started with a proposal to expand PubMed and culminated in founding a new publisher, the Public Library of Science.

When Brown decided to run Impossible Foods full time, he left Stanford, giving up his status as a Howard Hughes Medical Institute investigator. J. Michael Bishop, a Nobel laureate who advised Brown as a postdoc, attended the HHMI meeting where Brown gave notice of his decision.

"Instead of giving a valedictory with his science, he gave a 20-minute talk on the ecological problem that he wanted to address," Bishop said. It wasn't a swan song; it was a presentation on his next big project.

"I think we were all surprised that someone as well situated as he was academically ... and who still had a passion for the science would make that change," Varmus said. "But I'd say it worked out pretty damn well for him."

Stanford — along with some of his closest relatives (see box: All in the family). “I knew a lot of talented students and postdocs, and a lot of my friends were scientists and they knew a lot of people,” he said. “Of course, there was no field of creating meat directly from plants, so they came from all kinds of backgrounds. All I really wanted was raw scientific talent.”

According to the Good Food Institute’s David Welch, staffing at Impossible Foods is unlike that at more established meat-alternative companies.

“At tech-focused companies like Impossible Foods and Beyond Meat, the R&D teams are full of biochemists,” he said. “A more traditional plant-based meat company may have had a different balance in terms of the scientific talent within that company, with much more focus on food science and culinary aspects of assembling ingredients.”

Brown said that he looked for scientists who were up for a challenge. “I had the most awesome recruiting tool, which is that I could tell them with a straight face that we are working on unequivocally the most important scientific problem in the world, and it’s really challenging. If you want to get great scientists to work for you, that’s pretty much what you need.”

For people like Laura Kliman, a senior flavor scientist at Impossible Foods, the company’s environmental mission was a selling point. In 2016, Kliman, an organic chemist by training, was working as a pastry chef. She had just left a job as a chemist at a company that once developed biofuels but was transitioning to natural gas. She heard about Impossible Foods from a news story on the radio.

“I couldn’t believe how exciting and perfect it was,” she said. “Obviously extremely focused on sustainability, while incorporating culinary (aspects) as well as chemistry.”

Eric Decker, head of the department of

food science at the University of Massachusetts at Amherst, said that Impossible Foods is not unique in hiring scientists with no food science training.

“There have been biochemists — and organic chemists, and analytical chemists — in the food sector for decades,” Decker said. “And flavor houses have been trying to replicate meat for a long time.”

Rather, he said, what sets Impossible Foods apart are its startup-style business model, which has allowed the company to invest tremendous resources in a single product, and its patented plant-based heme protein ingredients.

Flavor chemistry

The team at Impossible Foods set out to define a burger biochemically by heating grocery store ground beef and, with a gas chromatography system and a mass spectrometer, characterizing the products of the complex reactions that resulted as it cooked. Then, instead of trying to incorporate all the aromatic chemicals they identified into a veggie patty, Brown’s team used precursors to the final flavor compounds, letting the chemistry happen during cooking.

“One of the things that I think sets us apart,” Kliman said, “is that we really took the time to research meat on the molecular level and understand all the actual reactions that are happening and what the products are that are being created.”

According to most coverage of Impossible Foods, its scientists were the very first to take a reductionist approach to replicating the flavor of meat. The scientific literature tells a more complex story.

An industry report for the National Cattlemen’s Beef Association in 2006 summarizes a literature spanning decades of analytical chemistry work in numerous food science journals, most of which aimed to identify the most important flavor compounds in beef

All in the family

There’s plenty of science in Impossible Foods founder Pat Brown’s family; his wife, Sue Klapholz, whom he met at the University of Chicago, holds an M.D. and a Ph.D. and works as the company’s vice president of nutrition and health. One of Brown’s brothers, a neuroscientist, has worked at the company for about three years as a sensory perception expert. But the most startling team member is Brown’s daughter, Ariel Klapholz-Brown, who studied film in college before starting as an early employee in the labs of the company that would become Impossible Foods. Today she’s a senior research associate on Impossible Foods’ materials and texture team.

“I love working with my daughter,” Brown said, adding that she’d always been a talented math and science student. “She notices everything, which is just a great quality for the role that she’s in. There’s an art to creating new prototypes, and also there’s an incredibly important demand on observation. You have to pick up subtle things that you’re not looking for.”

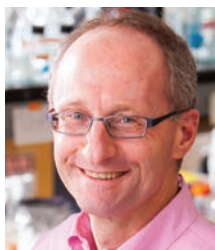
On working with family and friends, he added, “If you have people that you know are all-in on what you’re doing and talented, and you know for sure that you can tolerate them, that they’re going to be good colleagues, then that’s great.”



David Welch



Eric Decker



Mark O'Brian



Ruma Banerjee



Sharon Long

and determine what affected them; Brown and colleagues had a lot of background to work with.

That report focused on optimizing husbandry, meat handling and processing practices to improve the final flavor. But in other contexts, scientists have worked for years to develop additives based on a thorough understanding of meat chemistry. As early as the 1960s, food companies like Procter and Gamble patented precursors that could give bland protein isolates a beefy flavor upon heating.

Chemists working to recreate beef flavors have long focused on two major types of reactions that occur when a piece of meat hits a hot grill: lipid oxidation and Maillard reactions.

Lipid oxidation occurs when reactive oxygen species oxidize lipids, especially polyunsaturated fatty acids, at their double bonds. The reaction can generate low-molecular-weight fission products and, sometimes, short-lived epoxide compounds; some of these taste appealing, but most do not.

“Iron is the major problem in any (food) that undergoes oxidation,” Decker said. Either free or balanced in the aromatic, heterocyclic ring complex of heme, iron can catalyze oxidation of polyunsaturated fatty acids, resulting in a warmed-over flavor.

Maillard reactions, the second major reaction family driving beef flavor, happen when an amino acid and a sugar are mixed and heated. The reaction, an umbrella term for condensation between a nucleophilic amine and an electrophilic carbonyl, is important in cooking chemistry from browning pretzels to flavoring roasts. One of the best-studied Maillard reactions involved in flavoring meat takes place when ribose and cysteine are heated, creating a range of cyclic volatile compounds that contribute characteristic flavor notes to meat. Hydrogen sulfide derived from cysteine plays an important role in making some of those compounds, catalyzing addition of sulfhydryl groups to reaction products.

Inorganic iron was known to speed up Maillard reactions. But a key part of Impossible Foods’ story is its discovery of a new effect of heme iron, which the company calls its “magic ingredient,” on the flavor of meat.

The magic molecule

“How does it taste?” Brown said. “Basically, that’s just an assay — like radioactive thymidine incorporation in the early days of DNA replication. It’s just an assay that tells you whether what you’re trying to get to happen is actually happening. And then, you deconstruct and reconstitute the biochemical system.”

If a researcher heats a simple solution of cysteine and glucose, an Impossible Foods patent asserts, the product will have a faint rotten-egg smell. Should that researcher add ferrous gluconate, which contains an iron cation similar to the one in heme, again the product smells sulfurous. But replace the gluconate with a heme protein, and that unappetizing odor is replaced with smells that evoke chicken broth, burnt mushrooms and bread.

Biochemically, what’s so special about heme? Unsurprisingly, Impossible Foods has not volunteered chemical specifics. Given the odors mentioned in the patent, it’s tempting to speculate that the answer may have something to do with interaction between heme and hydrogen sulfide derived from cysteine.

According to Ruma Banerjee, whose lab at the University of Michigan Medical School studies hydrogen sulfide signaling, such speculation is not unreasonable. Banerjee’s lab discovered that hemoglobin in red blood cells, which lack normal hydrogen sulfide turnover pathways, can oxidize hydrogen sulfide to generate more complex sulfur-containing molecules.

“The biochemical evidence for this chemistry is very strong,” Banerjee said. “It’s not just reversible binding; the sulfide is actually transformed by the heme in air to oxidized products.”

Perhaps such catalysis is part of how

heme diminishes the off-putting odors and promotes more palatable flavors in the simple two-ingredient mixture. By adding additional molecules — ribose, thiamine, various amino acids and lipids — the researcher can make the product both more complex and more reminiscent of meat.

This, in essence, is the approach the Impossible Foods team took. A patent describes a mixture of amino acids, sugars and metabolites titrated to match meat tissue; when heated with leghemoglobin, it enables the key reactions that build a meat flavor profile. Meanwhile, according to Decker, levels of polyunsaturated fats are lower in the Impossible Burger than in meat, which may prevent the added heme from boosting unpleasant flavors.

But applying insights from a simple mixture of two or three ingredients to the complex chemical and material mixture in a vegetable patty is a difficult task.

“As an organic chemist, you have so much control over what’s in your reaction. And that’s just not the case with food,” Kliman said. “There are so many reactions that it’s hard to track them all and to know what products are being produced from what sort of precursors.”

Globins without animals

When characterizing meat, Brown said, “The thesis was that there’s absolutely nothing that was required that was specific to animals. That could have been wrong. It turned out to be right, which was good.”

Brown thought he knew a good place to harvest heme without killing an animal: the root nodules of legumes. Sharon Long, a colleague on the biochemistry faculty at Stanford, studied these tiny hotbeds of nitrogen fixation, and Brown was familiar with their iron-rich microecosystem (see box: Buffering oxygen).

“We spent quite a lot of money and quite a large fraction of our time in the first year and a half on this quest to figure out a way to harvest root nodules ... and creating all these

kind of Rube Goldberg contraptions,” Brown said in a podcast with the American Society for Microbiology’s Julie Wolf.

It turned out that harvesting and cleaning root nodules and extracting their leghemoglobin, while possible, was impractical at an industrial scale. Instead, the team pivoted to producing heme-binding proteins in yeast.

Constant optimization

Though heme as a magic molecule is key to the company’s brand narrative, Brown often stresses that there’s more to an Impossible Burger than that.

“If you’ve nailed the flavor chemistry and nothing else, well, you have beef broth,” he

ROWAN ADAMS/WIKIMEDIA COMMONS



Nodules on the roots of legumes, like these Wisteria roots, are home to symbiotic bacteria that fix nitrogen. Impossible Burgers contain a nodule protein called leghemoglobin, cloned from soy and produced in yeast.

Buffering oxygen

Legumes — plants like soy, pea and clover — are well known for converting atmospheric nitrogen into ammonia, which is a source of nutritional nitrogen. The reducing reaction called nitrogen fixation, for which the plants often get credit, is in fact carried out by symbiotic bacteria that live in specialized organs in the plants’ roots. Mark O’Brian, chair of the biochemistry department at the University at Buffalo, studies nitrogen fixation by *Bradyrhizobium japonicum*, which colonizes soy roots.

A *Bradyrhizobium* enzyme called nitrogenase breaks the bonds in atmospheric nitrogen, O’Brian explained. The process demands a tremendous amount of energy, which *Bradyrhizobium* supplies through aerobic respiration. But an appetite for oxygen, the ultimate oxidizer, is perilous for the nitrogenase. Plant tissue in root nodules express a high level of leghemoglobin, a protein that, like other heme proteins, coordinates oxygen cooperatively.

“You need oxygen for the bacteria to respire, but you can’t have a lot of free oxygen because it’s going to kill the nitrogenase. Leghemoglobin really resolves that paradox,” O’Brian said, by binding with high affinity to free oxygen and releasing it only when the concentration of oxygen is low. “Essentially, it’s facilitating oxygen diffusion, which is similar to what myoglobin does in the muscle of animals.”

Since Impossible Foods has become prominent, O’Brian said, he has found it easier to describe his research to nonscientists.

“If you say, ‘We work on ABCD,’ it’ll put people to sleep. But if you say, ‘This is being used for the Impossible Burger,’ people are interested.”

IMPOSSIBLE FOODS



This year, Impossible Foods introduced a new recipe and overcame a production shortage. Its scientists plan to continue testing new ingredients to optimize plant-based meat.

“Flavor houses have been trying to replicate meat for a long time.”

—Eric Decker

said. “And if you’ve nailed the texture, and you don’t have the flavor, you have crab cakes. ... Basically, the more progress we make on one dimension, the more we think, ‘Oh, we’ve gotta make more progress on the next.’”

The first prototype ranked somewhere below crab cakes or beef broth. Supertasters on staff compared it to “rancid polenta.” But, according to Brown, improvement was swift after that. This is part of the company’s mindset; a perfect reproduction of ground beef is not its end goal. If chemists can improve on the eating experience, producing something with fewer off flavors or a more palatable texture, then they will.

“In a certain sense, we’ll declare victory when the incumbent industry is in the rear-view mirror,” Brown said. “But, on the other hand, to the extent that we can make people happier and our product more affordable and versatile and food secure, we’re going to just keep working and working. I’m not sure whether it will ever end.”

Production problems

This year, Impossible Foods introduced a new formulation that chefs say is a better match for beef, but the company was also hindered by its own runaway success. After launching the new recipe, this spring the company became unable to keep up with accelerating demand for its products. The timing was unfortunate; the company was in the midst of a regional pilot partnership with Burger King.

Brown told *The New York Times* that the company’s efforts to scale up production had been “like changing the tires while driving down the freeway.”

Talking to *ASBMB Today*, he elaborated on their reaction to the shortage. “When we realized that manufacturing was limiting, I sent out a call to everybody in our R&D facility operation, basically saying, ‘OK, I need volunteers to work 12-hour shifts that either start or end at 3 a.m., just doing whatever it takes in a room that’s 37 Fahren-

heit. And it’s across the (San Francisco) Bay.’ And within 24 hours, a hundred people had volunteered.”

He tells the story with evident pride in his team’s dedication to the mission. On the website Glassdoor, where workers can post reviews of their employers, anonymous posts reveal mixed feelings about the company’s monthslong production sprint, and several note a lack of food industry know-how.

Others, however, like the challenge. Kliman, the flavor scientist, said, “In an academic lab — this is sort of a sweeping generalization — you have a lot of time, and you have almost no money. So you get creative about ways to solve problems. In an industry (lab), let’s say pharma, it’s very much about the bottom line, and time is money. Here at Impossible, it’s like the best of both worlds,” with a dual focus on optimizing the company’s products and contributing ideas for new ones. She cited periodic innovation weeks when the research and development team spends all its time trying new ideas or experiments.

In April, Impossible Foods hired Dennis Woodside, a lawyer by training with some 16 years of corporate leadership experience, into the newly created role of president. Having a president, Brown said in June, would free him up to focus on future innovations — as soon as the company caught up to its manufacturing shortfall. “I want to spend a lot more time on R&D, but even our R&D team are all hands on deck trying to get this manufacturing caught up,” he said.

In July, the company declared an end to the shortage and announced its plans to open a second production plant in Chicago.

Changing the meat industry

For the Impossible Foods plan to succeed, ranching needs to go from marginally profitable to losing money. This is not at all popular in the beef industry, which has lobbied for restrictions on marketing plant-based foods as meat. The product, on the other hand, is growing in popularity — and improving as a substitute.

According to market analyses, in 2019 plant-based meat is a \$12 billion industry, and it's expected to grow. Impossible Foods, which is privately owned, does not report its sales figures. But its closest competitor, Beyond Meat, reported that its revenues more than doubled from 2017 to 2018.

In light of that reality, more of the food industry is beginning to adopt plant-based protein production. This year, Tyson Foods, the largest meat company in the United States, appointed a vice president for alternative proteins and sustainability and announced a new brand that's set to launch this fall. Even legacy companies like Morningstar Farms, which has been making plant-based protein foods for 40 years, have introduced new faux meats that seek to compete more successfully against Impossible Foods and Beyond Meat.

Somewhat upstream from burger production, ingredient companies are aiming to catch the plant-based meat wave by providing pure protein and other ingredients. For example, Motif is a Boston startup that focuses on using biotechnology methods to produce components other food companies can use.

"Motif is somewhat unique in that they're taking a synthetic biology or recombinant biology approach to creating new ingredients," Welch said. The approach is similar to the way Impossible Foods generated a yeast strain to produce soy leghemoglobin at scale. Welch said that Motif is trying to do similar things with other possible ingredients, such as milk proteins.

There's also some evidence that the surge in popularity of plant-based meat is changing American crop fields. "We're starting to see some examples of it now," Welch said. "I think, in the future, we'll see more examples of crops being grown that are specifically bred for plant-based meat applications."

Protein foods for the future

With characteristic confidence, Brown has moved on to making plans to further redefine the food industry of the future.

"If the technology we develop is used to produce a significant fraction of the world's food supply and protein and so forth, it's a huge responsibility," he said in June. "Impossible Foods the company is not going to be responsible for all of that — but we're developing the technology to enable (it)."

The company has announced that prototypes of chicken, fish and even eggs, all made without animal products, are in hand. Meanwhile, a crop of smaller competitors also are developing and introducing their replicas of those foods.

Now, Brown is thinking about what plant ingredients to use as source material. One possibility that seems to have caught his imagination — lately he has volunteered it a lot in interviews — is to replace plant-derived protein from grains and legumes with protein from leaves. Impossible Foods has patented an approach to purify the protein rubisco in bulk from the leaves of alfalfa, a crop presently used for animal fodder, or other plants. But according to David Welch, the protein feedstocks of the future are as likely to be generated from bacteria, algae or fungi as from traditional crops.

"We're constantly screening things," Kliman said. "Anything you can think of to generate a plant-based protein, or other sorts of nutrients and ingredients, we're interested in looking at that and seeing if we can turn it into something amazing."

"People are always telling me, 'You've got to focus more,'" Brown said. "And I feel like being unfocused is incredibly valuable ... when you know where you want to go, but there's no road map, and you have to figure out how to get there."

"The last thing you want to do is say, 'I'm just going to go down this trail and I'm gonna keep going until I fall off a cliff.' No. I'm going to explore and wander."

And as a postscript: This fall, my vegetarian boyfriend gave the Impossible Whopper a try. He enjoyed it enough to order a second — Impossible Foods converts another customer.

As a scientist, "if you say, 'This is being used for the Impossible Burger,' people are interested."

—Mark O'Brian



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Under the skin out in the world



Elaine Fuchs' legacy of stem cells and love of exploration

By John Arnst

If Elaine Fuchs had been born a century earlier, she may have been a naturalist rather than one of the most decorated cell biologists of her generation.

“I grew up in a family of scientists. But ... I think what really inspired me was getting a butterfly net from my mother, who put it together and sent me out to the fields,” said Fuchs, who was raised outside of Chicago near Argonne National Laboratories, where her father worked as a geochemist. “That, and taking buckets and going out to the swamp and seeing what I could find.”

For more than four decades, Fuchs, now 69, has investigated the properties of adult stem cells that reside in skin. Much of what we know about human skin's capacity to heal and regenerate — and, in cases of mutation, to succumb to diseases like epidermolysis bullosa — has been made possible by Fuchs' work, from her first lab at the University of Chicago to her current position as the Rebecca C. Lancefield investigator at the Rockefeller University.

Landing in the lab

As an undergraduate, Fuchs had no plans to become a researcher — at least not immediately. During her senior year of college, she protested the Vietnam War and had

her eye on the Peace Corps. She hoped to teach chemistry in Chile, where Salvador Allende recently had become the first Marxist elected president in a Western liberal democracy.

“Growing up during the Cold War, I thought, ‘How can that happen, where people elected to have a Marxist government even though they had 100 years of democracy?’” Fuchs said.

She spent a year learning Spanish, studying Latin American history and writing papers on Chilean agrarian reform. But the Peace Corps had other plans.

“I got accepted to Uganda, and Idi Amin was in charge. He was a tyrant — he was killing his own people and just ruthless,” Fuchs said. “I thought about it, and I decided in the end to go to graduate school.”

Though the Peace Corps dream didn't pan out, Fuchs has been an ardent traveler since her days as a graduate student at Princeton University. Her work also has taken her across oceans. In 2018, she was appointed to the Pontifical Academy of Sciences, a papal think tank established in 1936 as a successor to the Accademia dei Lincei founded in 1603 under the stewardship of Galileo. In that role, and on occasion before she was appointed, Fuchs has attended scientific workshops at the Vatican to help keep



Elaine Fuchs established her lab at Rockefeller University in 2002. She has been a Howard Hughes Medical Institute investigator since 1988.

the Roman Catholic Church's highest leader apprised of the regenerative potential of stem cells derived from all areas of the body.

"They're excited by the prospect that different tissues harbor stem cells that have in some cases, like skin, considerable regenerative capabilities," she said. "They have a very broad base of scientists with different areas of expertise."

For Fuchs, that area of expertise is stem cells.

Building a field

When Fuchs started working on skin-derived stem cells during the field's nascency in 1978, the cells went by

a different name.

"Human epidermal keratinocytes. A very boring name," she said. "We now, of course, know that virtually every tissue of our body has long-lived stem cells that are able to regenerate tissue, both to repair dying cells and also to repair wounds, so it's virtually a universal property of the tissues of our body. But back then, there was very little known about it."

At that time, Fuchs was a postdoctoral fellow at the Massachusetts Institute of Technology in the lab of Howard Green, a cell biologist who pioneered skin grafting by growing human cells in culture. When Fuchs was a graduate student at Princeton working on bacterial spor-

ulation, she had attended a guest seminar by Green about culturing cells from human skin.

“I just immediately thought, ‘That’s what I want to work on for my postdoctoral work,’” Fuchs said. “It was at the time where a few people were starting to do mammalian cell culture, but they were all on transformed cells, cancer cells, or cells where people weren’t really studying their ability to regenerate tissue.”

In Green’s lab at MIT, she met Fiona Watt, another postdoc who had just finished her Ph.D. at Oxford University.

“I always describe her as the big sister that I never had,” said Watt, now the director of the Centre for Stem Cells & Regenerative Medicine at King’s College London. “If I needed to know how to do something, she would help me. But I think pretty soon after I got to the lab, she was learning to think about her independent career and where she would go next. You could really, I suppose, in hindsight, see the scientist she was going to become.”

In Green’s lab, Watt worked to culture cells from human skin, while Fuchs attempted to clone the keratin gene. “This was really cutting-edge molecular biology, nobody else in the lab knew how to do that,” Watt said. “So there was a sense that she was really pushing the boundaries.”

After finishing her postdoc in Green’s lab, Watt returned to the U.K. to start her own lab at the Kennedy Institute of Rheumatology in London; she has continued to investigate the role of stem cells in adult tissue maintenance. This overlaps with Fuchs’ research, so they have remained close colleagues over the years. They also have built a highly collegial field of study.

“More than 10 years ago ... we were at a conference in Toronto, and people from her lab invited people from my lab out for a meal,” Watt said. “And I remember saying to my lab, ‘Look, they’re just going to want to suck your brains out, know everything you’re doing, but remember you can probably drink more than they can.’ And that evening, I wasn’t there. I don’t think Elaine was either. But it was transformative for the field. Because the scientists in each of our labs at the time were some of the best we’ve ever trained. They got on really well with one another, and instead of feeling that you’re either in the Fuchs lab or the Watt lab, it was, ‘This is the field that we care about. And we have to help one another.’”

By their lab’s records, Fuchs and Watt collectively have trained more than 200 Ph.D. students and postdocs in the decades since they left Green’s lab at MIT.

“We may have started out with that with that big

sister–little sister dynamic,” Watts said. “But now we’ve founded these massive dynasties. And they all have these wonderful networks of relationships amongst each other.”

Female bonding

Fuchs’ knack for building supportive networks was especially useful at the University of Chicago, where she was the first woman hired at the department of biochemistry.

When she was setting up her laboratory, a technician from another lab asked her if she was Dr. Fuchs’ new technician. She replied, “I am Dr. Fuchs.”

Such interactions weren’t new to Fuchs; in her undergraduate physics class at the University of Illinois, she was one of three women in a lecture hall of 200.

“I would see, in retrospect, a tremendous amount of discrimination, but I didn’t recognize it as that,” she said. “I just took it as the need to do better. My adviser at Princeton didn’t think women belonged in science, and I just thought, ‘Well, that means I need to work that much harder.’”

“It was a little annoying (receiving) really derogatory comments made by some of my colleagues if they would get irritated over a remark I would make. On the other hand, you kind of take that as water off a duck’s back.”

By Fuchs’ account, a turning point at the University of Chicago came when she and her colleagues Janet Rowley and Susan Lindquist took advantage of a departmental reorganization to join the department of molecular genetics and cell biology.

“Each department had their token woman or two, and, when we organized and were allowed to join one department, we all decided to join the same department,” Fuchs said. “And it was really only then that I think it really did start to feel different, because I did have colleagues who thought the same way and weren’t derogatory.”

Within that new environment, she was able to stake out her support for equality at the university.

“It’s important to pick the battles that you have, and so I picked them with issues that were grossly unfair in terms of say, salary, or now, in terms of the importance of just having representation at scientific meetings.”

Fuchs’ camaraderie with women scientists cuts across fields. For Mina Bissell, former head of life sciences at Lawrence Berkeley National Laboratory, a galvanizing moment in their friendship came in the early 1990s at a large scientific meeting in Chicago.

At that meeting, Fuchs took the podium to present research findings that expressing a mutant keratin in mice

could make them display a skin-blistering phenotype identical to epidermolysis bullosa simplex, or EBS, in humans.

According to Bissell, who had met Fuchs a few years earlier when she had visited LBNL, Fuchs soon was assailed by a senior keratin researcher from Australia.

“I have never seen anything so arrogant,” Bissell said. “This man was so biting: ‘And you mean that this mouse is replicating human disease? That’s nonsense.’ I mean, he just went on and on.

“I got so mad that I stood up. I said, ‘Excuse me, what’s your problem? She very nicely has described her data; she’s made the mice imitate human disease. And you don’t believe it? Go to your own lab and do it. For crying out loud, do it yourself. What are you doing being so mean?’”

By Fuchs’ account, Bissell’s defense was the catalyst for the chair of dermatology at the University of Pennsylvania to corroborate Fuchs’ diagnosis of EBS. Eight months later, her work displaying mutant keratin overexpression as a cause of EBS in mice appeared in the journal *Cell*.

Leadership

Though Fuchs has been an active leader in the scientific community (see box: Awards and accomplishments), research and mentorship have remained priorities for most of her career.

“I’ve never chaired a department. I’ve never been a dean, I’ve never been the president of the university. I’ve never wanted to be any of those,” she said. “I really take the professor’s side very seriously. It’s not just the research that we do, it’s also important for me to mentor students as part of my professorship. So that’s where I funneled the bulk of my energy over my career.”

Julie Segre, now a senior investigator at the National Human Genome Research Institute who examines the composition of the human skin microbiome and tracks hospital-associated bacterial pathogens, joined Fuchs’ lab at the University of Chicago as a postdoctoral fellow in 1996.

Segre had been involved with the Human Genome Project at MIT while working on her Ph.D. and was interested in combining her genomic and technological skill set with biological questions regarding proliferation and differentiation in organ systems. In the Fuchs lab, she was able to explore those questions in a subgroup devoted to cell differentiation.

“Elaine is fiercely involved in every scientific project in her lab,” Segre said. “You had time to develop a



DAMON RUNYON CANCER RESEARCH FOUNDATION

Following in the footsteps of their postdoctoral mentor Elaine Fuchs, Shruti Naik (left) and Julie Segre (right) both received the Damon Runyon Postdoctoral Fellowship Award.



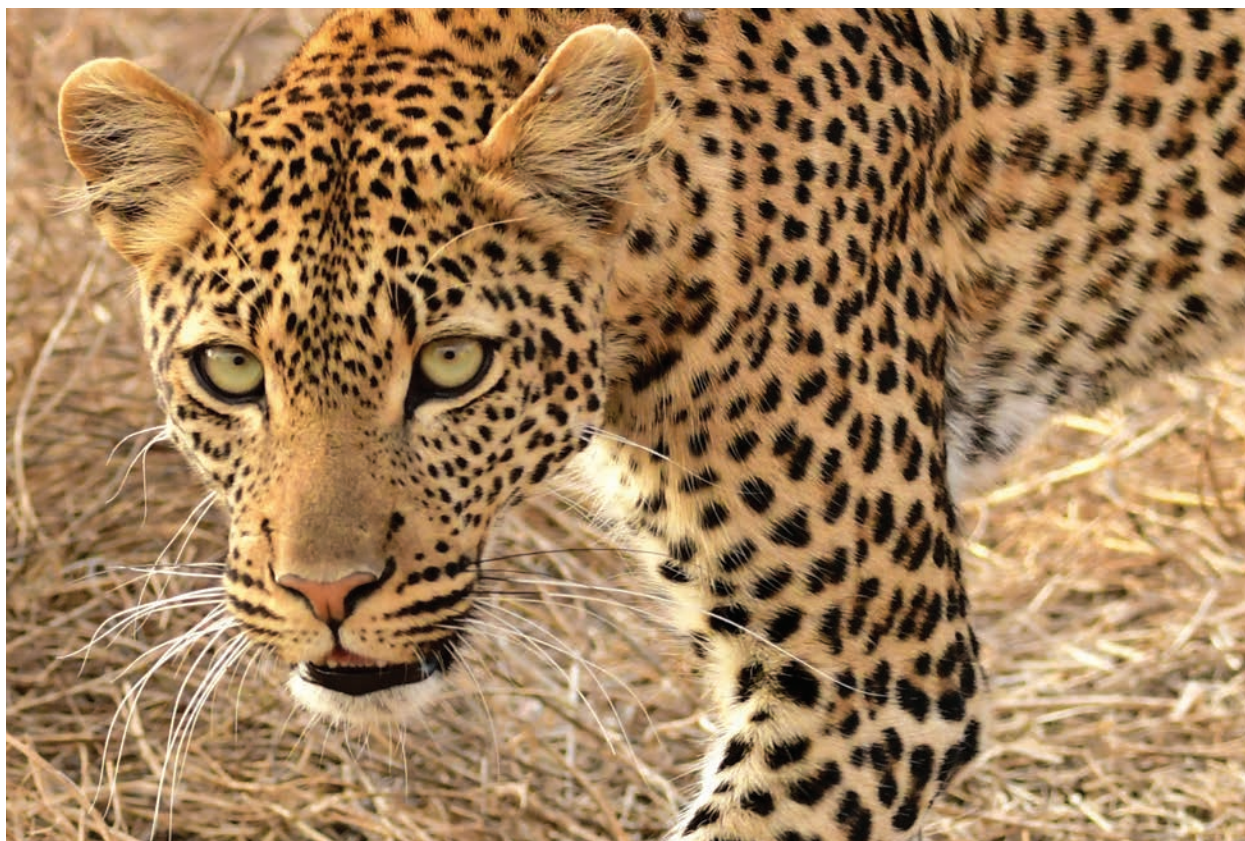
COURTESY OF ELAINE FUCHS

Fuchs with her friend Mina Bissell and her husband, David Hansen.

project, but then at a certain point, the project would capture Elaine’s imagination. She would decide that you were close to finishing, and then you would kind of go into overdrive ... she was pretty amazing at never having anything sit.”

After four years in Fuchs’ lab, Segre took a position at the NHGRI of the National Institutes of Health, where she was promoted to senior investigator in 2007.

“Elaine has continued to be engaged in my scientific development and scientific life, and I still consider her the mentor that I would go to for both scientific advice and (scientific) conversation,” Segre said. “It’s always nice when people say, ‘Oh, now we’re just colleagues.’ And I’m like, I would never give up being one of Elaine’s mentees, because she has so much to give that I still do want. I have a lot of colleagues, but I only have one postdoc adviser.”



Outside of the lab, Elaine Fuchs loves documenting her travels through photography. See more of her work at asbmb.org/asbmbtoday.

Traveling partners

During her semester breaks as a graduate student at Princeton, Fuchs made the most of the Spanish she'd honed for the Peace Corps, traveling to Guatemala, Mexico, Ecuador, Bolivia and Peru. Subsequent trips found her visiting Greece, Turkey, Egypt and Nepal.

A few years later at the University of Chicago, her colleague and close friend Susan Lindquist introduced her to David Hansen, a history buff and fellow academic who had done a stint with the Peace Corps in Sierra Leone. The two hit it off over their mutual interest in traveling and soon visited South Africa together.

"We just started traveling places that we hadn't been between the two of us," Fuchs said. "Our honeymoon was Zimbabwe and Botswana — Victoria Falls instead of Niagara Falls."

In recent years, Fuchs and Hansen have been to Indonesia, Laos, Tanzania and, on several occasions, Myanmar.

All that travel takes a toll; earlier this summer, Fuchs had hip replacement surgery, a procedure she took in stride.

"These days, it's basically like going down and getting an oil change for your car. It's fairly routine," she said of

the surgery. "(But), if you use it, it is going to wear down, and I tend to be active."

Fuchs' love of travel led to one of her favorite hobbies, photography.

"My favorite are pictures of people," she said. "But (recently) I've gotten really fascinated with leopards, and also with birds."

She and Hansen are planning a trip to the Galápagos Islands this winter, where she is excited to photograph the panoply of birds that call the archipelago home.

"In another life, I think I would want to be out with National Geographic," she said.

In this life, her professional evolution has stuck to science.

"I was a chemistry major at the University of Illinois, in Champaign–Urbana, and I was good at it. But I knew it wasn't my calling. And then at Princeton, I was doing biochemistry, seeing if I could find something more biomedically oriented. And that really wasn't it either. And then it was that spark of hearing Howard Green speak. And I knew then that that's really what I wanted to do. So I think it's a progressive maturation, honing our scientific star that's inside of us."

Awards & Accomplishments



SANDY SCHAEFFER/NSF

Elaine Fuchs received the National Medal of Science from President Barack Obama on Oct. 8, 2009.

Throughout her career, Elaine Fuchs has been an advocate for women in science; for this, in addition to her groundbreaking research, she received a L'Oréal–UNESCO Award for Women in Science in 2010. Her accolades also include a National Medal of Science in 2008 and, this year, the American Association for Cancer Research's Clowes Memorial Award.

Fuchs was elected to the American Academy of Arts and Sciences in 1994, the National Academy of Sciences in 1996, and the American Association for the Advancement of Science in 2008. She has served as president of the American Society for Cell Biology, the International Society for Stem Cell Research and the Harvey Society; has contributed to numerous scientific advisory boards and review panels; and has served on the board of governors for the New York Academy of Sciences and the board of directors for the Damon Runyon Cancer Foundation.



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MEET

Qi-Qun Tang

By John Arnst

The adipocyte expert and JBC associate editor wants to see better research papers from China

Brown fat generates heat and white fat increases our risk of metabolic disease, but what of the beige that lies between? At Fudan University Shanghai Medical College, Qi-Qun Tang and his colleagues are investigating the metabolic processes by which stem cells become white, brown or beige fat; the third of these exhibits some of the heat-generating, circulation-inducing characteristics of its brown counterpart.

After receiving a medical degree in 1990 and a Ph.D. in 1995 from Fudan University Shanghai Medical College, Tang did his postdoctoral research at Johns Hopkins University in the lab of M. Daniel Lane, a pioneer in understanding adipocyte differentiation. Tang became an as-

sistant professor at Hopkins in 2002. He returned to Fudan University in 2005, and he now divides his time between his lab in Shanghai and his family in Baltimore. He became the Journal of Biological Chemistry's first associate editor in China in late 2017 and now evaluates research papers on adipocyte development and function, carbohydrate metabolism, and cellular signaling related to liver metabolism.

As vice president of the Chinese Society for Biochemistry and Molecular Biology, Tang helped coordinate the society's annual meeting this month in Taiyuan; its close to 2,500 attendees will include a dozen JBC editorial board members. He also helped organize a joint symposium by the CSBMB and the ASBMB, "Epigenetic Control of the Epigenome," this month in Suzhou, near Shanghai.

Tang spoke with John Arnst, an ASBMB Today science writer, about his work. The interview has been edited for clarity and length.

What is your research group at Fudan University working on?

We originally worked on adipogenesis, which is how stem cells can become fat cells. These days, we mainly focus on adipose tissue as a whole, because it doesn't just consist

of adipocytes; it's also stem cells, immune cells and preadipocytes. We're also looking at angiogenesis of blood vessels. We're really interested in plasticity and how adipose tissue is remodeled.

We always think of adipose tissue as fairly important for storing energy that can be released when required. Normally, the adipose tissue itself is really healthy. But later, when it becomes chronically inflamed, this tissue becomes unhealthy, or there is a risk for metabolic diseases. So we're currently focused on subcutaneous, or white, fat because it accounts for most of the fat in bodies it can actually be induced to be beige, or brownlike, adipose tissue.

That beige fat has characteristics somewhere between white and brown fat, right?

Correct. During exposure to cold temperatures or exercise, those white adipocytes can actually be induced to become beige cells. And then later, after that stimulation is removed, they tend to turn back. That modeling and remodeling also stimulates angiogenesis, the generation of blood vessels, and induces change to the immune system's macrophages.

It's a whole host of changes, and

Since Qi-Qun Tang started as an assistant editor at the Journal of Biological Chemistry, more than a third of the papers he's edited have come from primary and senior authors based at institutions in China.

COURTESY OF QI-QUN TANG

we're trying to really unravel those physiological processes. It's an exciting area, because these beige cells were only identified around 10 years ago, but the field is now moving very fast.

One of the cytokines we've been working on is BMP4, which can induce the adipocytes to transform to beige cells. It also upregulates the production of M2 macrophages and activates them, and it induces angiogenesis. It's one of many factors we're looking at, and we're also trying to use some of the latest omics to identify new factors.

It seems like a burgeoning field.

The field is very hot right now. We're also using screens to test the ability of chemical compounds to induce white adipocytes to become beige. One is called artemisinin, which was originally used to treat malaria. It's a famous compound extracted from sweet wormwood (author's note: Chinese chemist Youyou Tu won a 2015 Nobel Prize in medicine for isolating and chemically identifying the compound, which had long been used in folk medicine). That's just one of the compounds that we are working on.

How did you find yourself involved in adipogenesis?

I was training for my M.D. in forensic medicine, but I didn't like it very much.

During my second year of medical training, in 1988, one of my supervisors saw this and let me know that molecular biology was booming and that it could be a really exciting career. So, once I wrapped up my M.D., I got started on my Ph.D.

I started with the adipocyte research after I got to Hopkins for my postdoctoral training. At the

time, we were trying to understand how a preadipocyte turns into an adipocyte. I mainly focused on C/EBP beta (author's note: CCAAT/enhancer-binding protein beta), which is an upstream transcription factor for the C/EBP alpha and PPAR gamma. They are really a master transcription regulator for adipocyte genes, and they are transcription factors that can turn on almost all the genes involved in the adipocyte differentiation. A few years back, I wrote a JBC review about how C/EBP beta regulates all of these genes.

“Right now, I'm really interested in helping to promote the journal in China.”

And you've been involved with subsequent JBC reviews. What has your work looked like with JBC in recent years?

I published my first of several papers in JBC in 2009 and was invited to become an editorial board member a few years later.

Right now, I'm really interested in helping to promote the journal in China.

The journal has always been helpful to young scientists who are trying to understand how to improve the quality of their papers. In China, the stakes for submission are very high, but JBC's acceptance rate is low. I think at least part of the reason is the quality. So I think that we can work with the journal to have a lot of impact on the societies within the CSBMB society.

I'm glad you mentioned the Chinese Society for Biochemistry and Molecular Biology. I was wondering

how you divide your time between China and the United States.

I spend most of my time in China right now. We have a summer break and a winter break, and I sometimes come back here for meetings during the middle, like ASBMB's annual meeting. I probably spend eight or nine months of the year in China.

That's an impressive balancing act. Do you have advice for early-career scientists about balancing life in the lab and life outside of the lab?

Keeping some outside activity is really important. These days, I go to the gym a lot, and I've hired a personal trainer. I was diagnosed as being prediabetic in 2004, and because I work in understanding metabolism, I wanted to be on top of dealing with it.

I think another good outlet for when you get really stressed out, especially early on, is going swimming for a while. Then, you can totally forget about stress, you can refresh your mind to start working again. I used to go in the afternoon, and after I'd come back, I'd feel refreshed.

There is definitely something unique to swimming in that regard. The only thing you have to focus on is the bottom of the pool, and maybe the upcoming wall.

You can just let your brain completely relax and go wherever it needs to. And then when you come back, your mind is crystal clear to do your work.

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Q&A

Sandhya Visweswariah does a balancing act between science and her society

By Isha Dey



COURTESY OF SANDHYA VISWESWARIAH

In addition to her study of the implications of cyclic nucleotides in diarrhea, Sandhya Visweswariah works to remove roadblocks for women in science in India.

While the global scientific community still leans toward patriarchy, Sandhya Visweswariah has made a mark for herself as one of the most prominent women in science in India.

Visweswariah chairs the department of molecular reproduction, development and genetics at the Indian Institute of Science in Bangalore, India, and co-chairs the institute's Center for BioSystems Science and Engineering, which she helped establish in 2015. She has won international recognition for her work on watery diarrhea and cyclic nucleotides in the form of grants and awards from the likes of the Royal Society and the Bill and Melinda Gates Foundation.

Born in India, Visweswariah did her early schooling in England and then Zambia. At the age of 17, she returned to India and earned a bachelor's degree in botany, chemistry and zoology from Osmania University followed by a master's in chemistry from the Indian Institute of Technology, Kanpur. She went on to earn a Ph.D. in biochemistry from the IISc.

Over the years, Visweswariah has explored scientific interests in industry as well as in academia; she worked at AstraZeneca before joining the faculty at the IISc. Her initiatives to improve translational research in India earned her the Margadarshi fellowship from the Wellcome Trust/DBT India Alliance in 2017, which provides biomedical scientists with an opportunity to lead cutting-edge interdisciplinary research programs. She was elected a fellow of the World Academy of Sciences in 2018. In addition to her research work, she constantly strives to remove roadblocks for women in science in India; in one notable step, she worked to modify the rules at the IISc to extend the tenure assessment period for women on the faculty by one year per child.



This cartoon by Tejeswani Padma, a former project assistant in Visweswariah's laboratory, depicts the lab's research interests.

Q&A

“Looking back, I feel things worked out the way they should, because I realize that I am more of a scientist than an artist.”

Visweswariah spoke with ASBMB Today contributor Isha Dey about her research and addressed questions about scientific advancement in India and women’s representation in science. The interview has been edited for length and style.

Tell us about the research in your lab.

My lab is interested in looking at old-fashioned cyclic nucleotides like cAMP and cGMP and their implications in diarrhea. Being a biochemist by training, what interests me is how protein structure and function are coupled to cellular physiology like cell-to-cell and cell-to-environment communication. So I look at receptor proteins, which transmit signals from other cells or the environment to elicit a response within a cell.

We study guanylyl cyclase C, a receptor expressed in the gut, which has an extremely complex structure with multiple domains, and try to understand how these domains communicate with each other. We, along with clinicians in Europe, were the first to report that mutations in this receptor cause congenital secretory diarrhea. We have received funding from the Bill and Melinda Gates Foundation to make relevant mouse models to better study this disease.

One of my former students some years ago wanted to look at cAMP in microbes, so we picked up *Mycobacterium tuberculosis* as a model system. We soon realized that there was little information on the enzymes that regulate cAMP levels in *Mycobacteria*. So that project has also been a major focus in my lab for the past decade.

How did you become interested in science?

My first interest during my schooling in England was the arts. I was interested in Western music, literature and languages. I was learning German, French, Russian and Latin. However, when I moved to Zambia with my parents at the age of 16, the only subject options given to me in school were physics, chemistry, biology and mathematics.

When I came back to India for college, I continued with my scientific pursuits. Looking back, I feel things worked out the way they should, because I realize that I am more of a scientist than an artist.

Who would you consider to be your mentor/influencer?

Growing up, I won’t say I had a vision of one day becoming a scientist. However, if there is any one person who inspired me to do science, it was Srinivasan Chandrasekaran, an organic chemistry professor at the Indian Institute of Technology, Kanpur, where I did my master’s.

During this time, I realized what it was to do real research. Before that, I never felt that there was any magic in scientific discovery; it was more like memorizing what is written in the textbook. But his approach to science and the way he ran his laboratory inspired me and continue to influence me even now.

Being a graduate student and now a professor at the IISc, how do you think funding and opportunities for translational research in India have changed over the years?

A lot. Resources and funding at my time as a Ph.D. student were in no way comparable to international standards. We had to think of research ideas that were smart but not resource intensive. Funding and interdisciplinary research have dramatically increased in the last decade because of initiatives from the government of India as well as international research collaborations between governments like India and France or India and the U.K.

The biggest game changer has been the Wellcome Trust/DBT funding supporting basic and translational research. Through this initiative, we have set up a collaboration with Christian Medical College in Vellore for an M.D.–Ph.D. program and closer interactions with faculty in IISc. This is to encourage M.D. students in India to become clinician-researchers, which are rare in this country.

What are your thoughts on gender bias against women in science?

What we call bias against women need not be correlated to any kind of harassment; neither is there any conscious prejudice against women by men in science. It is just that men are not sensitized to understand the needs of women during decision making, because they may not be aware that women may have a different view on things. Given my current position in the institute, I have become acutely conscious of this in the last five or six years. For example, ensuring that the tenure process is sensitive to motherhood and that instances of sexual harassment are dealt with sensitively and promptly. That's when I realized that unless you have women in decision-making positions in leading institutions, you cannot bring in change for the next generation of women.

Because India is a patriarchal society, men are brought up without sensitization toward women's needs. It is not that they want to exclude women, but there is no positive desire to include them. In the West, over the past decade or so, men have become aware that there are things that women can bring to the table and have made very conscious efforts to include women at all levels in decision making. Unfortunately, in India, we have a long way to go before we reach that level of inclusion.

Fewer than 14% of researchers in India and fewer than 30% of researchers worldwide are women. What can be done to increase women's representation in science?

All of this comes from a perceived bias as to what a woman can and can't do. Women are told from an early age that they are not good in science and engineering. So this is an upbringing problem coupled with the fact that there aren't enough women in every sphere of activity. Consider teaching, for example; men in general do not consider teaching in elementary school as a good profession, because they are hardly ever taught by men at that stage. Girls in this country might aspire



COURTESY OF SANDHYA VISWESWARIAH

Students at the Indian Institute of Science explain basic science to younger school children during an IISc Open Day.

to become movie stars just because they see successful female movie stars. Women should be allowed to choose their career paths and see more varied role models so that we have more women represented in every sphere of activity, not just science.

Talk about your work as a fellow of the World Academy of Sciences in advancing science in developing countries.

We go to local schools and colleges all over the country and communicate our research and scientific thoughts and ideas to the students in a language that they can comprehend. Last year, I attended the first induction meeting of the World Academy of Sciences, and I was absolutely inspired by

“Unless you have women in decision-making positions in leading institutions, you cannot bring in change for the next generation of women.”

Q&A

Sandhya Visweswariah earned her Ph.D. at the Indian Institute of Science in Bangalore, India, (right) where she now chairs the department of molecular reproduction, development and genetics.



IISC ALUMNI

young scientists from countries where there is so much turmoil, like Sudan, Iraq, Iran, Syria, Zimbabwe and Palestine, coming and talking about science. I realized how lucky we are to be in India.

How can we tackle prejudices against scientific development, such as religious superstitions and avoiding vaccination?

We need to educate people about basic science and scientific advancement. In parts of India, people marry members of their own families, which sometimes results in transmission of genetic diseases. But they consider the illness a curse of God or fate without being aware of the dominant and recessive gene pool. Visiting a temple and worshipping a deity cannot cure a disease. Unless science is a part of human life, it is difficult to tackle this. This education has to happen in school and also at home in our microenvironment. There has to be better scientific communication across all spheres. We all have the tools — almost everyone has a smartphone — but we do not use them to educate ourselves on issues like this.

What advice would you give to current and prospective women scientists?

Growing up, women are cautioned at different steps about what they can do in a world run by men, and this affects our thought process. We are constantly questioning ourselves: Can I have a family and do science? Can I

have a child and still succeed? Can I disagree with my mother-in-law and come in to work?

I was fortunate in being brought up by parents who never made a distinction between my brother and me and never told me there were things I could not do. Therefore, any questions I had along these lines were those that I myself raised after having a child, but I had the confidence given to me by my parents, especially my mother, that I could do it all. The minute we doubt ourselves, we are ready to give up. So women just have to believe that they can do as well if not better than their male colleagues.

What does it take to be a good scientist?

Honestly, I think to be a good scientist, you need to be a decent human being. You have to show empathy. You need broad-mindedness and a liberal way of looking at things — you should be ready to accept that your hypothesis may not be correct. You need to be curious about the world around you and why things are the way they are. We need to have an inherent interest in the field of science coupled with good communication skills to put our ideas across to everyone.

Isha Dey (ishaadey@gmail.com) is a scientist at Thermo Fisher Scientific in India.





T-SHIRT CONTEST

All ASBMB members are eligible to submit a T-shirt design related to biochemistry and molecular biology.

The winning T-shirt will be sold at the 2020 ASBMB Annual Meeting in San Diego.

Submit your shirt design by Jan. 27.

For more details visit asbmb.org/meeting2020/tshirt/

 **ASBMB**
American Society for Biochemistry and Molecular Biology

How science took over the town at the tip of California

By Ana Maria Barral

San Diego's history as a research hub makes it a great place for scientists to gather.

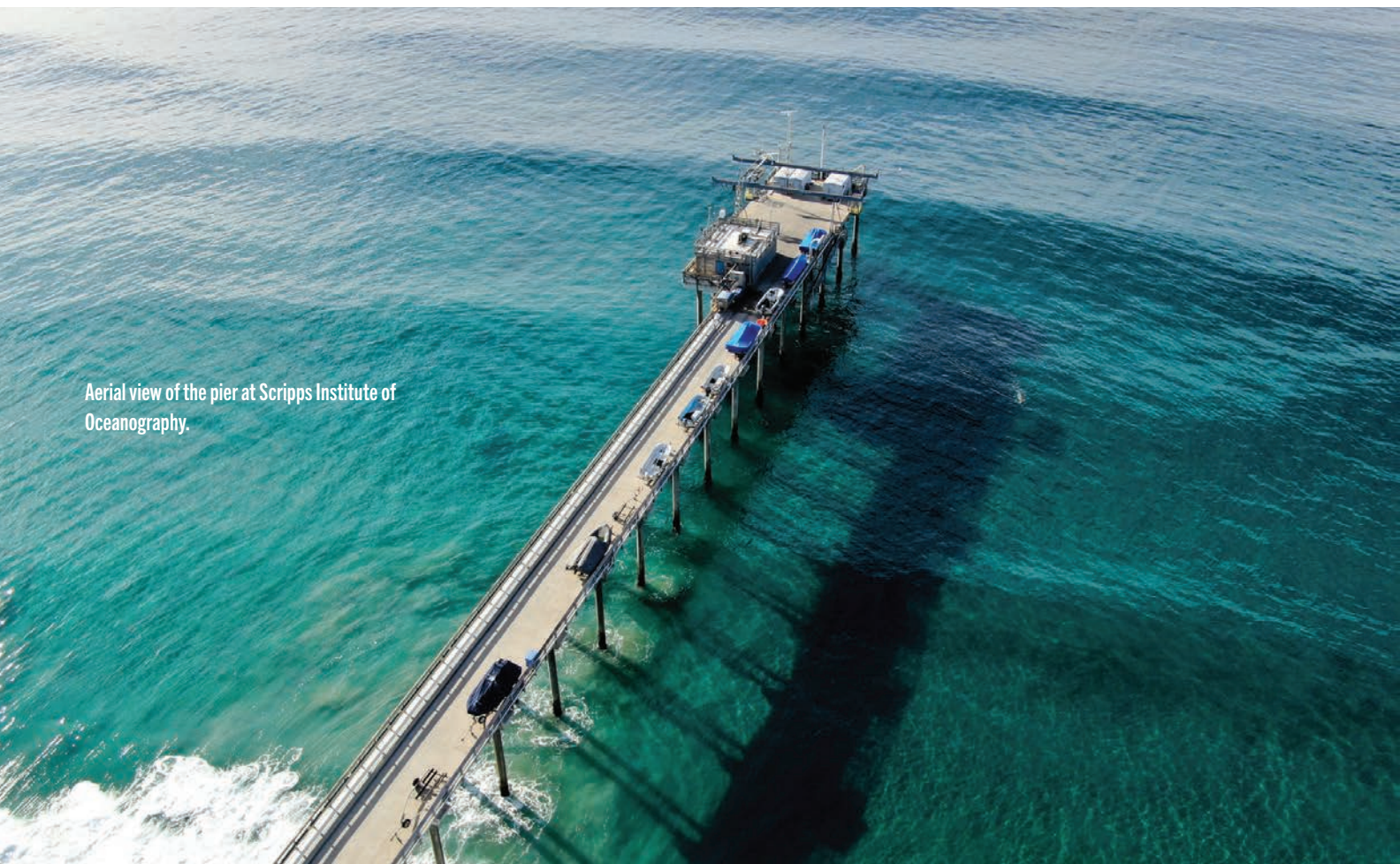
Blue skies touching the immense waters of the Pacific Ocean. Warm sunshine bathing long stretches of sand. Surfers. Palm trees. Glorious sunsets. These are the postcard images of San Diego.

For scientists, particularly in biomedical fields, San Diego can be a different kind of dream destination as a conference site or a place to complete postdoctoral training or find a biotech job. In Genetic Engineering and Biotechnology News' 2018 list of the top biopharma clusters, San Diego ranked second in California (behind the San Francisco Bay

Area) and fifth in the nation. The ranking was based on factors such as National Institutes of Health and venture capital funding, lab space, and job opportunities.

Indeed, choices abound: From large public institutions such as the University of California, San Diego, and San Diego State University to renowned private institutions such as Scripps Research and the Sanford–Burnham–Prebys Medical Discovery Institute, from industrial behemoths such as Illumina to this year's red-hot startups, plenty of opportunities exist for scientists looking for a new phase in their careers.

Aerial view of the pier at Scripps Institute of Oceanography.





San Diego's Balboa Park at twilight.

However, it is not always sunny in San Diego; many coastal transplants experience what's known as the "May gray, June gloom" period of fogginess due to the heavy marine layer. And the city only became a beacon for science after a long and winding history. San Diego's status in the scientific community has as much to do with wars and cunning politicians as with visionaries and generous philanthropists.

Much has been written about the many social paradoxes of Southern California, particularly San Diego, and it is not the goal of this article to discuss them. Instead, we will focus on some key moments that transformed the isolated village on a spectacular bay into a booming science and technology powerhouse.

Balboa Park and the rise of the military metropolis

As home to the San Diego Zoo and many

museums and events, Balboa Park is now a popular destination for residents and visitors. It began as City Park, 1,400 acres set aside by San Diego civic leaders in 1868.

In the early 1900s, city officials were intensely courting the U.S. Navy to open a base in San Diego and bring with it federal dollars that could boost urban development. Capitalizing on excitement about the 1914 opening of the Panama Canal, those officials decided to showcase their city in what became the 1915 Panama-California Exposition. Most of the arts organizations along Balboa Park's famous El Prado pedestrian walkway are housed in Spanish Renaissance-style buildings made especially for that occasion. The exposition contributed to San Diego's success in becoming a military metropolis. Naval Base San Diego was founded in 1922, and with military funding came other industries, including aerospace and engineering,

As home to the San Diego Zoo and many museums and events, Balboa Park is now a popular destination for residents and visitors.



A boat approaching the naval base in San Diego.

providing the first major reinvention of the city's character.

War industries

San Diego is a Navy town. In and around the city are 14 major Navy and Marine Corps installations, and San Diego is home to 60% of the ships in the U.S. Navy fleet. More than 100,000 active-duty members of the military call the city home. San Diego can thank both its geography and the intense lobbying of local politicians and civic leaders over the last century for its outsized military presence.

We may not think the defense industry is related to the booming bioscience scene in San Diego, but federal investments in military installations, especially during World War II and the Cold War, supported tremendous growth in research and development. During World War II, the federal government increased its investments in basic research to support technology development. The Scripps Institution of Oceanography, or SIO, started as a marine biology research station at the turn of the 20th century. In 1938, Robert Gordon Sproul, president of the University of California system, created a UC Division of War Research that supported strong scientific and military collaborations. SIO scientists were instrumental in the R&D of naval warfare technologies, and after the war, Scripps became a powerhouse of scientific research, playing an important role in the establishment of UCSD.

Philanthropists

The Scripps name is ubiquitous in San Diego. The family, particularly the newspa-

perman E.W. Scripps and his half-sister Ellen Scripps, established and supported multiple scientific and civic institutions from the 1890s to 1930s, including the Marine Biology Institute (later the SIO), the Metabolic Clinic (now Scripps Research), the San Diego Zoo and the Scripps Memorial Hospital. Anyone enjoying a hike in the Torrey Pines State Park can also thank Ellen Scripps. Other philanthropists followed her example of donating to scientific endeavors, including Joan and Irwin Jacobs, Debra Turner and Conrad Prebys and Malin Burnham. Their names often appear in the names of institutions their generosity supports.

Postwar and UCSD

The city reinvented itself after World War II as a major center for advanced R&D. This development was largely tied to industries closely aligned with the military, such as aerospace and nuclear technologies, including major players General Dynamics Corp. and General Atomics, respectively.

The strength of the SIO's research relationship with the Navy gave the institute leverage to press for the creation of a new general campus of the University of California in San Diego, something local leaders had been advocating for since the 1920s. Planning of the campus was not devoid of controversies, however. Industry leaders such as John Jay Hopkins of General Dynamics wanted a technical research institute, while city voters preferred a broad-based school that included undergraduates as well. In 1956, the regents approved a "graduate program in science and technology" that included undergraduate programs, a compromise accepted by all.

The new campus hired world-class experts, and by 1963, the 80 faculty (mostly scientists) included two Nobel laureates and 13 members of the National Academy of Sciences. Luminaries such as Harold Urey, David Bonner, Jim Arnold and Sol Penner were early UCSD recruits. Excellent collaborative research brought funding and expansion of the university, including the opening of its medical school in 1968.

READ MORE

"Invention & Reinvention: The Evolution of San Diego's Innovation Economy"

by Walshok, Mary Lindenstein, and Shragge, Abraham J. Stanford, California: Stanford University Press, 2014.

"2017 Biocom California Economic Impact Report Databook"

prepared by TClower & Associates

Biotech City

While San Diego benefitted enormously from military R&D, city leaders sought to diversify the economy after the Cold War. The Scripps Metabolic Clinic originally was founded by Ellen Scripps in 1924 to diagnose, treat and research diabetes. Over time, the clinic became more focused on research, and in 1956 it was renamed the Scripps Clinic and Research Foundation. A number of high-profile researchers were hired in the 1950s, headed by Frank Dixon from the University of Pittsburgh. This development coincided with other advances in the biomedical sciences, including the founding of the Salk Institute and the opening of the UCSD School of Medicine.

All these institutions (and many more to come) settled in the Torrey Pines Mesa, part of pueblo lands that were acquired by the city after the Mexican War and more than a century later were sold cheaply to institutions and companies to attract investment in R&D. The city rezoned the area to attract light industry, and San Diego's first biotech company, Hybritech, known for developing the prostate-specific antigen test for prostate cancer, also moved to the Mesa. After the sale of Hybritech in 1986, one of its founders, Howard Birndorf, helped found a string of biotech companies, including Neurocrine and Ligand, which are still in operation. Many other companies in San Diego can trace their origins to Hybritech alumni.

The third reinvention of San Diego started in the mid-1980s as developers and investors aimed to commercialize the products and services created by the R&D community. Along with established institutions such as General Atomics, Scripps Research, the SIO and UCSD, new players arrived, both research institutions and biotech companies. To help these organizations work together, a program called CONNECT was established in 1985. In addition to assisting startups, CONNECT is credited with developing San Diego's business culture. A number of organizations now support various technology sectors, including BIOCUM for life sciences



A sign at the University of California, San Diego Scripps Institution of Oceanography.

and San Diego Biotechnology Network, or SDBN, for biotech.

Still going strong

San Diego's life sciences engine still hums along. New institutions have joined the existing ones, among them the San Diego Zoo Conservation Research Institute, the La Jolla Institute for Immunology, the Sanford Consortium for Regenerative Medicine, the J. Craig Venter Institute, and the UCSD Clinical and Translational Research Institute. Some biotech companies have expanded, others have been bought, some have disappeared and new ones keep springing up.

When attending the 2020 American Society for Biochemistry and Molecular Biology annual meeting, you can look out from the convention center and see many signs of the city's military past and present. If you have a chance, visit the area of the SIO and the Birch Aquarium; from there you can see both the magnificent beaches of the city and UCSD. Beyond lies the Torrey Pines Mesa, the "Hispanic dowry" of 48,000 pueblo acres that helped San Diego to become a R&D success story. This convoluted and fascinating history befits what was dubbed in 1972 by then-Mayor Pete Wilson "America's finest city."



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Searching for drugs on the ocean floor

By Kerri Beth Slaughter

Growing up in New York City, Paul Jensen watched the famous undersea explorer Jacques Cousteau on television and dreamed of studying the ocean.

“I wanted to explore the water even though I couldn’t get in it very often,” Jensen said.

No one in Jensen’s family ever had graduated from college, but he was determined to learn more about science and the sea. He took a leap of faith after high school and some community college, moving south to pursue a bachelor’s degree in marine biology at the Florida Institute of Technology.

Now, decades later, the first-generation college student and East Coast city kid is a professor at Scripps Institution of Oceanography in San Diego. Jensen’s nontraditional career path equipped him with tools to mentor future scientists and to study marine microbes for drug discovery.

He initially thought earning an undergraduate degree was all that mattered, and he received little guidance about what would come next.

“I didn’t understand what was needed to advance in a career in science,” he said.

Getting hooked

After graduation, he found a job at Harbor Branch, an oceanographic research institute in Florida. Around that time, Harbor Branch started Seapharm, one of the first programs to search the ocean for potential drugs produced by microbes as biologically active secondary metabolites. It was Jensen’s first exposure to the field of natural products, and he was hooked. The institute was small, so he was able to lead projects and publish first-author papers.

When an outside company withdrew funding for Seapharm, Jensen faced a choice. He could take another position within Harbor Branch or move to San Diego to work as a technician at Scripps under the organic chemist William Fenical.

San Diego is a great location for the ASBMB annual meeting because, as Ana Maria Barral points out in the preceding pages, it is home to so many life scientists. Here’s the story of how one researcher made his way to “the town at the tip of California.”

Jensen elected to take the position at Scripps and used his Harbor Branch experience to help Fenical establish a program in marine microbial natural products. In 2003, Jensen, Fenical and others discovered salinosporamide A, a small molecule produced by the marine microbe *Salinispora tropica*. After years of work by many scientists, the biopharmaceutical company Celgene now is developing the discovery for cancer treatment.

Jensen enjoyed making discoveries with Fenical, but he quickly realized a graduate degree was key to advancing professionally in marine science.

“If you have ambitions about exploring your own ideas and doing creative science, then you have to go to graduate school,” he said.

Jensen earned a master’s from San Diego State University and returned to Scripps to complete his doctorate in marine biology. He worked at Scripps for 13 years as a non-tenure track faculty member before becoming a professor.

Marathon training

After many years doing research at Scripps, Jensen said the part of the work he most values is the students.

“We get many of the brightest and most enthusiastic minds from around the world that want to come here for graduate studies,” he said. “Their energy, dedication and effort lead to discoveries that put our institution at the forefront of so many areas of marine science.”

Graduate school is about learning how to think independently and solve problems, he said, and the students who do the best at Scripps are the ones who embrace this independence. Jensen encourages the students in his lab to decide the direction of their thesis research and offers them wisdom from his own career path.

“I tell my students it’s a marathon, not a sprint,” he said. “If you’re doing research you really like, then there’s value in staying in it even if it takes some time for your

GREG ROUSE



Paul Jensen and graduate student Nastassia Patin collect sediment samples in 2014 at the Smithsonian field station in Carrie Bow Cay, Belize.

career path to develop.”

His students’ research today looks very different from the work Jensen did when he started at Scripps. Advances in molecular genetics have transformed the way scientists study natural product synthesis.

Random isolation and culturing of marine microbes has been streamlined with high-throughput DNA sequencing to identify strains of bacteria with new or interesting gene patterns. This method, known as genome mining, helps Jensen and other scientists understand what genes look like and how they make enzymes to build natural products.

Jensen does less hands-on work now than when he first came to Scripps, but he still loves getting in the water for field work. About twice a year, he and members of his lab visit marine labs in places such as California’s Channel Islands, Fiji, Belize and the island of Moorea in French Polynesia to collect samples for research.

“Two weeks in the field can generate two years’ worth of work in the lab,” he said.

Buried resins

Back on shore, Jensen’s lab screens samples from various habitats to identify genes that appear relevant for making natural products. With advances in sequencing, they can examine ocean environments at a DNA level and predict where interesting natural products are synthesized.

His lab also uses absorbent resins to study natural product synthesis at its source.

“We are looking to see if we can detect molecules directly in the habitats in which they are produced,” he said.

COURTESY OF PAUL JENSEN



Paul Jensen, center, and members of his lab collect samples at the Channel Islands.

The resins are buried in ocean sediments to capture molecules made by microbes in the environment. In the lab, the molecules are removed from the resin with an organic solvent and analyzed to learn about how and why they are made. Jensen believes these techniques will lead to findings about marine microbe interactions with hosts and chemical competition among bacteria.

Changes in the field have broadened the scope of Jensen’s research. With access to DNA sequence data, his researchers can study the evolution of natural products in marine microbes. Jensen’s lab looks at closely related microbial species to see how they make different versions of similar molecules. Their analysis gives his team a chance to see how nature works to generate chemical diversity.

“We could identify the microbes before,” Jensen said, “but we could never understand the relationships between the microbes and the molecules they produced.”

Jensen’s work has evolved with time to harness the wealth of microbes produced beneath the ocean’s surface. His career path, though unclear early on, taught him the importance of running the slow and steady race for science. Today, he continues to use what he learned along the way to make breakthroughs in marine microbiology.

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The journal Molecular & Cellular Proteomics (MCP) fosters the development and applications of proteomics in both basic and translational research. It showcases cutting-edge advances in proteomics, metabolomics and informatics. The American Society for Biochemistry and Molecular Biology publishes MCP. The artwork above is from the MCP Special Collection: Multi-Omics Data Integration.



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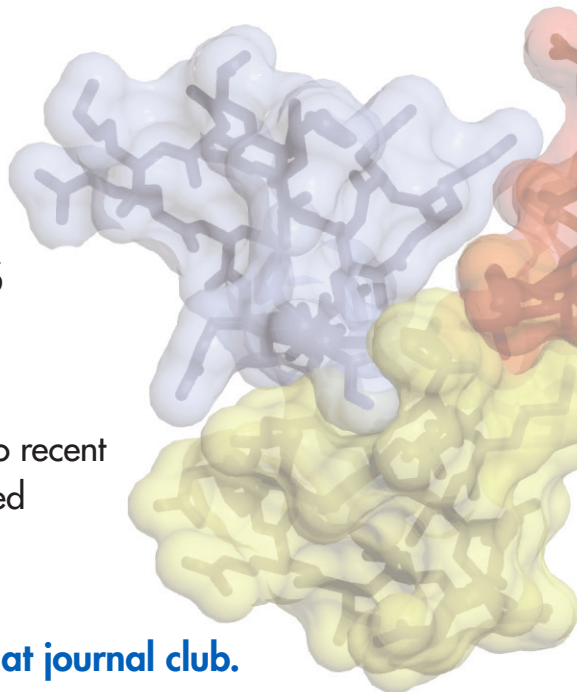
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A professor among prisoners

By Ruma Banerjee

It was 1981. As a student at Delhi University, I had spent the fall licking postage stamps and envelopes and mailing applications, pregnant with expectations for admission to graduate schools in the U.S. Across oceans, A.B. (whose initials have been changed to protect her privacy) had entered prison in Michigan, sentenced to serve the balance of her life without the possibility of parole. We were both 20 years old. Our paths were to cross many decades later.

Since that time, my life has unfolded in a kaleidoscope of opportunities and experiences. I meandered through institutions of higher learning, flitting from botany to biochemistry to biophysics, and then settled into a life of scholarship at a land-grant institution in the prairies. I upped the ante on the academic stress track by having children pretenure in a departmental home where for a long time I was the lone woman. My growing academic family added to my personal one with two children and a spouse who was a fellow biochemist. Yet something was missing.

Advocating for criminal justice reform

When I was growing up, my mother deftly modeled community service in our family. She found causes to champion and institutions to serve, even as she relocated constantly as the wife of an army officer who rose to be a lieutenant general. She assembled bandages for veterans, helped Mother Teresa's Missionaries of Charity, supported a cottage industry for rural women who wove

dreams into rugs and volunteered at a nonprofit that delivered ophthalmic care to the indigent. In contrast, my interest in social causes found only limited expression. In those early years, we occasionally volunteered as a family at a soup kitchen that was a stone's throw from my lab.

Fast forward to 2013. I had relocated to the University of Michigan, where, reading a campus rag one day, I found myself drawn to a story about a colleague who had introduced the Inside-Out Prison Exchange Program, in which students from the outside study with inmates serving time inside correctional facilities. On a whim, I reached out to her. That, in turn, led me to the National Lifers of America chapter at the Women's Huron Valley Correctional Facility, the only women's prison in the state of Michigan, where prisons outnumber public universities 2 to 1. The NLA is an advocacy group comprising prisoners serving long indeterminate or life sentences and volunteers who support their work.

Before stepping into the WHVCF for the first time, I had no prior experience with prisons and generally subscribed to the stereotypical view that they held dangerous individuals who needed to be separated from society. In retrospect, I had been prepared subconsciously by my daughter's activism as an undergraduate with Students Organizing Against Prisons to abolish the prison industrial complex and with a nonprofit to help the formerly incarcerated with reentry. Although I

remember wishing that my daughter would direct her activism to a safer issue, I admired her for her interest in a marginalized community and her commitment to criminal justice reform long before it had started to percolate up into political and media consciousness.

As a novice, I have struggled to grapple with our criminal justice system. With less than 5% of the world's population, the U.S. is home to about 20% of the world's incarcerated, according to 2018 statistics from the online World Prison Brief hosted by the Institute for Criminal Policy Research. Over 2.1 million of our citizens languish behind bars. Our imprisonment rate (655 per 100,000) surpasses that of repressive regimes like the Russian Federation (402) and China (118, though numbers for China are incomplete), and is staggering compared to that of India (33), the world's largest democracy.

Prison demographics reveal that we disproportionately punish people of color and the poor. As Michelle Alexander notes in "The New Jim Crow," it was projected in the 1970s that investments in U.S. prisons would decline, as research indicated that punitive approaches were less effective for reducing crime than providing economic and educational opportunities and access to health care. Few people anticipated that the politicization of crime to monger fear and fuel mass incarceration would prove to be a hugely successful campaign strategy used by everyone from all-powerful county prosecutors



The Women's Huron Valley Correctional Facility near Ypsilanti is the only women's prison in the state of Michigan.

to presidential candidates.

Crossing the sally port

Barbed wire curls around the perimeter fences, and a sense of desolation hangs over the WHVCF. Its overcrowded interior, however, bustles with life. After checking in with (usually burly) armed guards and surrendering my driver's license, I traverse the sally port where security guards, in addition to the routine pat down, inspect the nape of my neck and beneath my tongue and feet for contraband. It is an uncomfortable experience that invariably imbues me with a sense of foreboding, although I always enter with nothing but the authorized notebook (without metal ring binders) and a pen with a clear barrel. I figure that the guards are trained to be expressionless. Though I have been a regular visitor to the facility for half a dozen years and more, it is the rare person who admits familiarity.

The program building is a short

distance from the main entrance across a central yard, which I cross as vigilant eyes stare down from watchtowers that have been radioed about my presence. I have been instructed to walk but never run. Double doors open into a corridor lined by rooms and lead to a large auditorium designed for reverberation and to drown out communication. One of the rooms is an often-busy library. At the end of the corridor sits another guard. I must check in with him too before I can finally turn to my work as a volunteer.

On the first Monday of each month, we meet in one of the drab rooms with the NLA leaders who run the various committees advocating for sentencing reform, medical commutations for the frail, changes in aiding and abetting laws, and other initiatives, and we plan programs for the larger NLA meetings, whimsically referred to as the Saturday soirees. They invite speakers

such as domestic violence scholars, legislators, or advocates of prison reform working for nonprofits. At other times, they organize workshops for writing or parole readiness. As volunteers, we support and enable these activities.

I am deeply touched by the resilience of women who are locked up for life. In them, I see altruism, humanity and hope despite the dehumanizing circumstances that conspire constantly to instill despair. I also see their largesse; many earn about 84 cents a day yet contribute generously to breast cancer research or to shelters by organizing walks in the prison yard.

I have had powerful experiences with the women at the WHVCF using the restorative justice practice of peace circles for learning and healing through a collective process. The circle-keeping approach is one of several that we use to help women articulate personal responsibility



Another approach is writing. The NLA newsletter is the only one authorized for circulation outside the walls of the WHVCF. As its volunteer editor, I help women use the newsletter as an instrument of self-expression.

and empathy to repair harm and to prepare for parole hearings, which can be a brutal experience.

Another approach is writing. The NLA newsletter is the only one authorized for circulation outside the walls of the WHVCF. As its volunteer editor, I help women use the newsletter as an instrument of self-expression. Some articles are newsy and describe visitors (such as Abdul El-Sayed, who ran for governor) or bills that the NLA supports. Others are introspective, with titles like “What would I like my victim to know.”

Parallel paths

A.B.’s path and mine crossed a few years ago when she decided to rejoin the NLA chapter, which she had, in fact, founded at the WHVCF. Entering prison with a fourth-grade education, A.B. picked up the broken thread from a childhood stamped by poverty and instability. She earned her GED in prison and later trained as a paralegal. A.B. is quiet and has a matriarchal air. I noticed that peers looked to her for her legal expertise and historical knowledge about NLA procedural issues.

As the years passed, I worried that A.B. looked puffier and more ashen every time I saw her. On a diet that is estimated to cost less than \$2 per person per day for three meals, healthy eating is not an option. Obesity is rampant at the WHVCF.

At a soiree that we organized last fall, A.B. learned that Rick Snyder, the outgoing governor of Michigan,

was interested in felons like her who had been sentenced under the state’s common law felony murder rule, which broadened the crime such that accomplices and co-conspirators could be found guilty of murder. Six weeks after A.B.’s 1981 sentencing, the state’s Supreme Court, in *People v. Aaron* had deemed the rule “fundamentally unfair.” The ruling was applied to trials in progress but was not grandfathered. A.B.’s life sentence was thus unaffected.

I was in the prison on Dec. 21, and A.B. seemed despondent as we talked. The governor’s term would run out at the end of the year, and there had been no word on her appeal. Later that evening, we heard that Snyder had signed her commutation order.

On Feb. 12, 2019, A.B. was released on a 48-month parole. A week before her release, A.B. penned her final article for the newsletter, “My praise report.” As a volunteer, I am forbidden to maintain contact with her. I have heard through the grapevine that she is thriving and has enrolled in a graduate program in criminology. I smile as I realize that we remain connected on parallel

Ruma Banerjee (rbanerje@umich.edu) is the Vincent Massey collegiate professor of biological chemistry at the University of Michigan and a *Journal of Biological Chemistry* associate editor. She received the 2019 ASBMB–Merck Award.



What I wish people understood about being a trans scientist

By TL Jordan

Every morning I wake up wondering: *How many times will I be misgendered today? How many times will people call me something I am not? How many times will I be called a girl? How many times will I have to correct people awkwardly when they say “she” instead of using “they”?*

How many times will my identity be invalidated today?

I’ve been out as a queer, non-binary trans person for almost two years. I realized I was nonbinary my senior year of undergrad and came out my first year of graduate school in a place where there were no other trans people for support and very few LGBTQ people. My entire life I have dreamed of being a scientist, exploring the world and spending my time learning. Being nonbinary has changed many of my interactions within science and academia. Coming out as a trans scientist immediately isolated me and made the simplest tasks hostile and full of fear. A day in the lab wasn’t just spent learning and working but also questioning how much invalidation I would endure.

Questions of identity and identity invalidation plague many members of the trans community. I know I’m not alone. Many of us are scared and have to spend time assessing if a space is safe before we enter it, trying to determine if we are welcome. But being a trans scientist seems to make these questions more common.

Academia lags far behind in becoming an inclusive environment

for many marginalized communities, but there is a particular isolation that comes with being a trans nonbinary scientist. I look around my institution and I don’t think I can name more than one other transgender individual working as a scientist. I certainly can’t name a trans member of the faculty. In my entire Ph.D. training, I will never have a mentor who shares my identity and my experiences.

And that is one of the most isolating truths that I have to endure every day.

Most of the faculty and students I work with still struggle to use my pronouns (they/them) on a regular basis. On top of my normal lab duties, grant writing and planning for qualifying exams, I have to go through each day being beaten down and invalidated. People I’ve met many times refer to me in emails as “she” and “her.” On an average day, at least five people will misgender me (if not more). I don’t always have enough energy to correct them. If my day is filled with meetings, by afternoon I’ve had to affirm my gender in my head about 30 times after others have projected an incorrect gender on me. I try to spend most of my time in the safe haven of my lab or my desk. At least the cells I’m culturing won’t misgender me; at least the few people in my lab understand and make an effort to use my correct pronouns.

I experience gender dysphoria if I go out in public without binding

my chest, but then some days I have to stay home because my body is sore from binding my chest, and it is too dysphoric for me to go out in public without wearing my binder. I’m not trying to skip out on being productive, but this is difficult for me to explain to my colleagues. I feel tired and degraded, and all of this affects my ability to do science. While most graduate students are worrying about their Western blots or their qualifying exams, I’m also worrying about whether insurance will cover the services I need, gritting my teeth at having to gender myself on forms and struggling to breathe in my chest binder.

I also question my safety. In bathrooms I get yelled at or catch people giving me side eye. I have to remember where the nearest gender-neutral bathroom is on campus; there isn’t one on any of the research floors in my building. Walking around the city or in the halls of my institution, people stare at me. I hear cat calls and slurs from passing cars.

Every time I reach out to someone to start a new collaboration or get advice on a project, I wonder if they will refuse to work with me because I am trans. Will my science be impeded because someone believes that I shouldn’t exist? It’s a fear that I have to live with constantly, every time that I branch out and meet someone new. I have yet to experience this level of discrimination, but when I see headlines every day about another trans person being shot or

With the confidence of feeling comfortable in my own skin, I have improved my speaking skills, and I am more willing to be a champion and speak for those LGBTQ people who aren't out or aren't comfortable speaking out against the injustices in STEM.

courtrooms determining whether my identity exists, it keeps the fear alive in the back of my head.

The idea of presenting my work at a conference is both thrilling and terrifying, because there's a good chance I'll be the only trans person there — the only person who has scratched their pronouns on their name badge. I wonder if people will judge my science differently because of my identity.

Existing as a trans scientist means compartmentalizing that fear whenever I meet new people, hoping and praying that I won't have to answer dehumanizing questions like “When is the surgery?” or “Are you a boy or a girl?” or “Why does it matter if I use they/them when referring to you?”

Being a trans person in science means bearing the weight of ignorance. I work overtime to advocate for myself at my institution. I'm trying to teach my department and institution how to create an environment that is safe for me and other trans people. I find myself doing an incredible amount of uncompensated work with the diversity departments in my institution just because of my trans identity.

Some days, being a trans Ph.D. student feels like getting an education in hard mode.

Despite all this, I am incredibly proud of my identity. I am loud and

outspoken about being nonbinary and trans. Coming out turned me into a more confident person, and I really enjoy the person that I have become. I am more comfortable in my own skin than I have ever been. I can dress in the way that I feel comfortable, and I have become less apologetic about doing so. I like to wear T-shirts that say things like “Nonbinary Icon” or “No TERFs” (trans-exclusionary radical feminists) because I feel affirmed in my gender and my beliefs. Unfortunately, being out and proud as a trans person comes with the baggage of misgendering and discrimination. That's the price I have to pay to be myself.

With the confidence of feeling comfortable in my own skin, I have improved my speaking skills, and I am more willing to be a champion and speak for those LGBTQ people who aren't out or aren't comfortable speaking out against the injustices in STEM. Being isolated from my graduate school peers makes me want to work harder to be the nonbinary mentor in science that I've never had.

I am connected to many LGBTQ scientists through Twitter. They have helped me navigate some of the ins and outs of being trans in science and commiserated with me about identity-related pressures that pile up on my already stressful plate as a Ph.D. candidate. We've

discussed what it's like to have to come out every time I meet someone new in school — or decide whether coming out is the smart thing to do. In addition to relating to another trans person about day-to-day struggles, it's incredible to be affirmed and see that other trans scientists are doing wonderful work. I don't get to see them doing their science in person, but Twitter helps me feel less isolated.

I am proud to be a trans nonbinary scientist. Despite the difficulty and isolation, I will continue to be myself in every way. Some days are better than others; I don't always have the support of allies around me. But I will never be able to do science successfully if I don't put every ounce of my own identity forward. To push the forefront of science to be more inclusive and diverse, I must make academia a better place for up-and-coming trans scientists.

My name is TL Jordan. I am trans. I am nonbinary. And I am proud of who I am.

TL Jordan (Jordan.Torri@mayo.edu) is a predoctoral student at the Mayo Clinic and an ASBMB Advocacy Training Program delegate. Follow them on Twitter @TLJordanScience.



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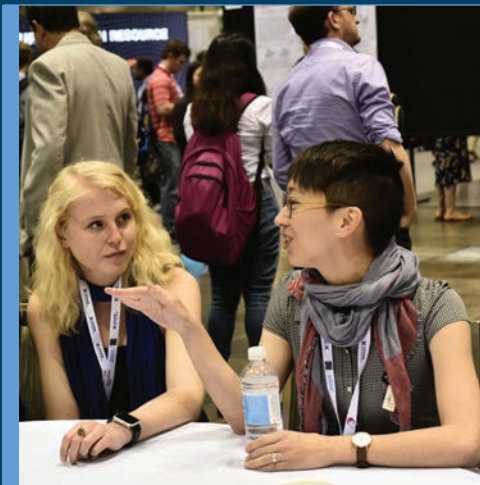
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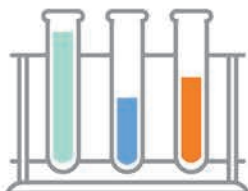


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