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ASBMB TODAY

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

6 questions *for* 3 PRESIDENTS

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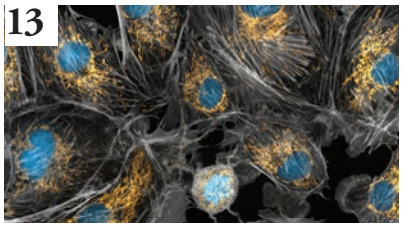

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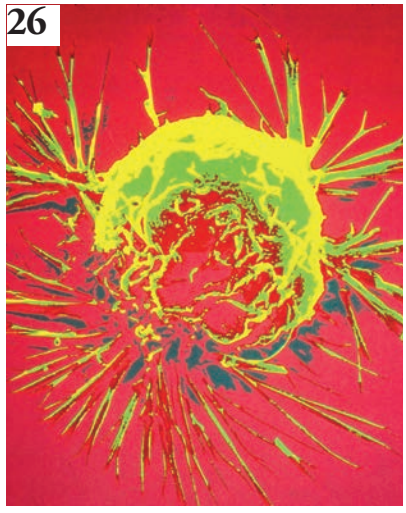

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Reclaim inspiration

By Comfort Dorn

Back when Juliette Bell was a chemistry professor, she shared her concerns about a lack of research support with the new president of her university. "That president told me that if I wanted things to change, I had to be willing to take a leadership role and not just stand by and complain," she said. And Bell did just that. She became an interim dean, a dean and then a provost. Now she is president of the University of Maryland Eastern Shore.

After earning an undergraduate degree and working in analytical chemistry for a few years, Ashley Warfield Oyirifi realized it was time to face the distance and detachment she felt as a black woman in the field of biochemistry. She wrestled with this question in graduate school and began to find answers in, of all places, an elective anthropology class. She is now a passionate advocate for scientific investigation situated in a larger societal context.

I recently heard the writer Ta-Nehisi Coates say in a podcast that, no matter what they say, no white person would ever really want to be black. I thought back a decade to when Barack Obama was on his way to becoming president and Michele Obama said she was proud of her country for the first time. Though I knew that was a harsh and problematic thing to say, it made sense. I was proud too, but I wished I could share the pride that was in her heart. At that moment, I thought, it must feel so good to be a black American.

Now it's 2018 and Donald Trump is in the White House, and it feels like all the progress that's been made in my lifetime and the century that preceded my birth is in danger of imploding with each morning's presidential tweet. And I have to admit that Coates is right. It's a perilous thing to be an American of color.

You wouldn't know that talking to Juliette Bell and Ashley Oyirifi and the other African American scientists and educators featured in this issue. As we enter Black History Month in this most peculiar era, we need to balance all the awfulness of the last year with some inspiration. So in this issue, we question three college and university presidents about how their lives as black Americans and scientists have shaped the way they administer institutions of higher learning. That's quite the crucible for leadership, yet they wear their legacy and responsibility with grace and humility. "I learned by making a lot of mistakes," says Roy Wilson of Wayne State University, "and learning from mistakes."

We also talk to experts tackling the tough issues of health disparities among people of color in this country, asking them about the role of basic researchers in what seems to be overwhelmingly an issue of poverty and inequality in the delivery of health care.

And we bring you Oyirifi's imaginative and inspiring essay on diversifying educational content to attract and keep more underrepresented minorities in scientific research. This piece was submitted to us back in August, and I've been itching to share it since then. I'd love to hear your responses. And it may sound corny, but please — keep the faith.

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

The NIH is cruising — now let's boost the NSF

By Benjamin Corb

Since fiscal 2015, the National Institutes of Health budget has increased 13 percent, from $30.3 billion to $34.1 billion. We are thrilled to see NIH funding on the rise, especially after nearly a decade of flat budgets that, when adjusted for inflation, eroded the NIH's purchasing power by 25 percent. Current proposals for fiscal 2018 will likely lead to another 3 percent increase, so we are cautiously optimistic that members of Congress from both parties recognize the need for robust and sustained investment in the NIH.

Sometimes, though, we wonder if Congress realizes how the research enterprise works. While the NIH wins support, other critically important science agencies in the government don't receive the same attention and are in need of funding increases.

The National Science Foundation funds basic biological research, work that often builds a foundation for the groundbreaking, lifesaving discoveries made at the NIH. The NSF is also the second highest funder of our members (after the NIH) according to recent surveys of the American Society for Biochemistry and Molecular Biology membership. And while the NIH budget has grown significantly, the NSF budget has not. Since fiscal 2015, the NSF budget only has risen from $7.3 billion to $7.4 billion, a 4 percent increase. It is a mistake not to fund the two agencies proportionally.

Partnerships between the NIH and the NSF include the BRAIN Initiative and the Precision Medicine Initiative. Many NIH-funded investigators have received grants by building off NSF-funded basic research. For example, the CRISPR-Cas9 gene editing technology that is breaking ground in the life sciences has its roots in NSF-funded research.

As Congress receives the fiscal 2019 budget from President Donald Trump and begins its appropriations process, the ASBMB will host a Capitol Hill briefing to educate lawmakers on the NSF's important role in supporting and advancing life science research. This is part of our ongoing work to influence the funding process to benefit all our members.

In advocating for the NSF, the ASBMB remains committed to fighting for a diverse, sustainable and successful American research enterprise.

Hill Day

It's that time of year again. The Public Affairs Advisory Committee is preparing for its annual day of Capitol Hill visits, when scientists from across the country come to Washington, D.C., to receive training from the ASBMB's public affairs staff and take part in meetings with congressional representatives to talk about the importance of robust federal investments in science. This year's Hill Day will be April 12. We are accepting applications for participants at asbmb.org/advocacy/HillDay.

Advocacy opportunities

As we prepare for the release of President Trump's fiscal 2019 budget, the Public Affairs Advisory Committee is launching our first 2018 grassroots advocacy campaign. In February and March, we ask our members to take to social media to tell your elected representatives how the president's budget proposal would affect your science and your lab. In addition to tweets and Facebook posts, we'll create and circulate a petition calling on Congress and the president to provide the scientific community with the investments we need to keep the United States the global leader in biomedical research and innovation. Details are at policy.asbmb.org.

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

Member update

By Erik Chaulk

Three members named Breakthrough Prize winners

CLEVELAND

MORI

WALTER

Don W. Cleveland, Kazutoshi Mori and Peter Walter are among the winners of the 2018 Breakthrough Prize in Life Sciences.

The prize was established by a group of technology entrepreneurs, including Google co-founder Sergey Brin and Facebook co-founder Mark Zuckerberg, to honor outstanding scientific achievement in the life sciences, fundamental physics and mathematics.

The Breakthrough Prize in Life Sciences has been awarded since 2013 and honors contributions to understanding living systems and extending human life, including one prize that specifically acknowledges research on neurological diseases.

Don W. Cleveland, professor of cellular and molecular medicine at the Ludwig Institute for Cancer research, is being recognized "for elucidating the molecular pathogenesis of a type of inherited ALS (amyotrophic lateral sclerosis), including the role of glia in neurodegeneration, and for establishing antisense oligonucleotide therapy in animal models of ALS and Huntington disease."

Kazutoshi Mori, professor at Kyoto University, and Peter Walter, professor in the department of biochemistry and biophysics at the University of California, San Francisco, both are being honored "for elucidating the unfolded protein response, a cellular quality-control system that detects disease-causing unfolded proteins and directs cells to take corrective measures."

Each of the winners will receive a $3 million prize, the largest individual monetary award in science.

Oppenheimer wins FASEB BioArt prize

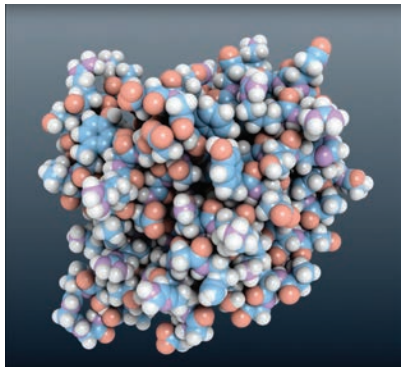
OPPENHEIMER

David Oppenheimer is a winner in the 2017 BioArt contest, sponsored by the Federation of American Societies for Experimental Biology. Oppenheimer's winning entry is a video showing the protein profilin twisting and wiggling.

Oppenheimer, a cell biologist and geneticist, is an associate professor in the department of biology at the University of Florida. He is also a creator of the Undergrad in the Lab blog, where he writes in his biography, "My current research interests are focused on the proteins that control cytoskeleton dynamics, and how this influences plant cell shape." Profilin, found in many organisms, regulates the assembly of structural proteins that form a cell's cytoskeleton.

Through the BioArt competition, FASEB aims to share the beauty and breadth of biological research with the public. Contestants include investigators, contractors or trainees with federal research funding and members of FASEB societies, including the American Society for Biochemistry and Molecular Biology.

Oppenheimer's video and the other winning BioArt entries can be seen at faseb.org.



COURTESY OF FASEB

David Oppenheimer's winning video shows the protein profilin twisting and wiggling.

Kinzy now VP for research at Western Michigan

KINZY

Terri Goss Kinzy has been appointed as the new vice president for research at Western Michigan University.

Kinzy was most recently vice president for research at Rutgers, where she oversaw the offices responsible for research and sponsored programs. In her new role, she will help main-

COURTESY OF THE BUFFALO ARTS STUDIO

An artist as well as a scientist, Milton M. Weiser painted this self-portrait.

In memoriam: Milton M. Weiser

Milton M. Weiser, former chair of the gastroenterology department at Buffalo General Medical Center, passed away in December at age 87. He had Parkinson's disease.

Weiser was born in Detroit, the son of eastern European immigrants. He earned his undergraduate degree in chemistry from Wayne State University before attending the University of Michigan Medical School, where he met his wife, Helen Freedman.

Weiser completed a fellowship in molecular biology at Albert Einstein College of Medicine. He then worked at Massachusetts General Hospital in Boston and led the Harvard-Massachusetts Institute of Technology Health Sciences Program.

In 1978, Weiser joined the University of Buffalo as a professor of medicine and biochemistry. He also served as head of research at Buffalo General.

A talented artist, Weiser became one of the first tenants in the Buffalo Arts Studio after he retired in 1998.

Weiser is survived by his wife, two sons, a daughter, a brother and five grandchildren.

tain and develop WMU's research initiatives.

In 1995, Kinzy joined the faculty at Rutgers, where she was a professor of biochemistry and molecular biology and pediatrics. Her research specializes in the areas of gene expression, protein synthesis and drug development.

Kinzy is a member of the American Society for Biochemistry and Molecular Biology's political affairs advisory committee.

She assumes her new role at WMU in the spring 2018 semester.

Rochester's Maquat wins Vanderbilt Prize

MAQUAT

Lynne Maquat, professor of biochemistry and biophysics at the University of Rochester School of Medicine and Dentistry, has received the 2017 Vanderbilt Prize in biomedical science.

Established in 2006, the Vanderbilt Prize recognizes female scientists who have contributed significant research as well as served as mentors to other women in science. Winners receive an honorarium, and Maquat will deliver a lecture and be a mentor to Vanderbilt Prize Scholars.

Maquat is highly regarded for her research on RNA metabolism in human disease. She is the founding director of the Center for RNA Biology at the University of Rochester.

In 2003, Maquat founded and has since served as chair of the Graduate Women in Science program, which provides professional aid and development for all graduate women at the university.

Maquat will be honored in November and will speak as part of the Flexner Discovery Lecture Series.

In memoriam: David Burrad Smith

SMITH

David Burrad Smith, a former professor in the department of biochemistry at the University of Western Ontario, passed away in July at the age of 100.

Born Dec. 6, 1916, in Kidderminster, England, Smith moved to Canada after World War I. He attended the University of British Columbia, obtaining his undergraduate degree in 1939 and his graduate degree in 1941. In 1950, Smith earned his Ph.D. in biochemistry from the University of Toronto.

Smith worked at Defense Industries Limited from 1941 to 1945. He later served as a lecturer in the department of chemical engineering at the University of Toronto and worked at Canada's National Research Council.

In 1966, Smith joined the University of Western Ontario as a professor in the biochemistry department. He remained at the university until retiring in 1982 as a professor emeritus.

Smith spent much of his career studying proteins, including significant research on the structure of hemoglobin.

Smith and his wife, Dorothy Westlake, were married for nearly 64 years before she passed away in 2005. They had three children, Stephanie, Janet and Duncan.

In memoriam: David Millhorn

MILLHORN

David Millhorn, senior vice president emeritus at the University of Tennessee, passed away in December. He was 72.

A native of Chattanooga, Millhorn received his bachelor's degree from the University of Tennessee at Chattanooga. He later earned his doctoral degree from the Ohio State University.

Millhorn was a professor in the department of physiology at the University of North Carolina at Chapel Hill and then served as director of the Genome Research Institute at the University of Cincinnati before returning to the University of Tennessee in 2005.

Millhorn joined UT as vice president for research and later assumed the additional role of executive vice president; he was instrumental in developing the university's research initiatives. He oversaw the university's contract to manage Oak Ridge National Laboratory and helped plan and develop the UT Cherokee Farm Innovation Campus.

He is survived by his wife, Sherry, and his three daughters, Amy, Emily and Lauren.

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

Send us your news

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

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Back to the (poly)basics — lipin enzyme phosphoregulation

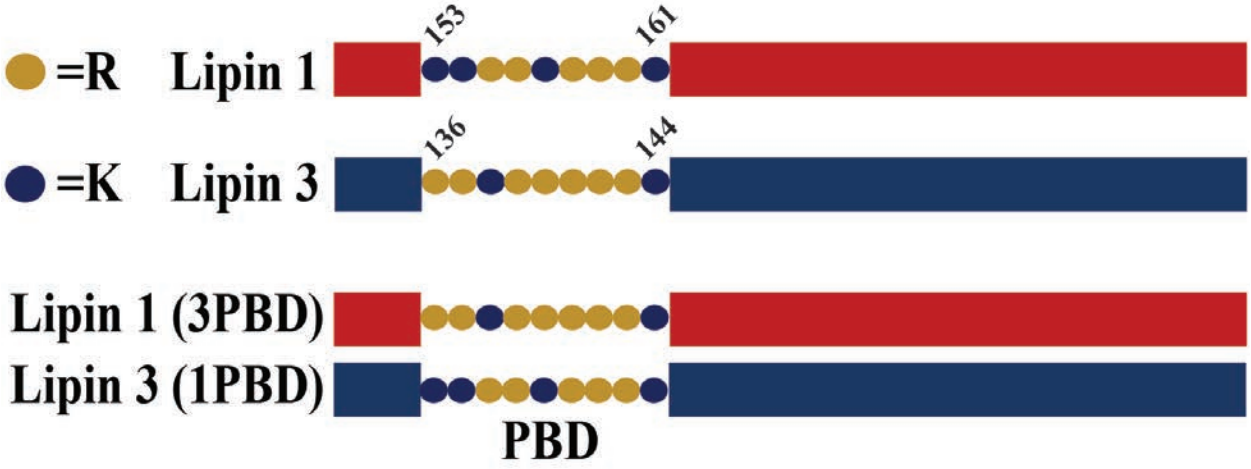
By Salome Boroda & Thurl Harris

Glycerolipid synthesis occurs largely in the endoplasmic reticulum, or ER. Almost all the enzymes involved in making glycerolipids are embedded in the membranes of the ER. The exception is a family of enzymes called lipins, which dephosphorylate phosphatidic acid, or PA, to generate diacylglycerol in the penultimate step of glycerolipid synthesis.

Lipins are soluble proteins that can be found in the cell cytosol but can move to the ER membrane to perform their function. This family of enzymes consists of three members known as lipins 1-3. Genetic studies have shown that increased levels of lipin 1 in the fat tissue of transgenic mice can improve glucose homeostasis, and genetic mutations in human lipins 1 and 2 have been associated with diseases such as rhabdomyolysis, a rapid destruction of skeletal muscle cells, and Majeed syndrome, a rare condition characterized by recurrent episodes of fever and inflammation in the bones and skin. At the molecular level, a series of studies has demonstrated a complex regulation of the lipin family that is tied intimately to their phosphorylation state and the chemical properties of PA (1-4).

The substrate of lipins can exist in two electrostatic forms: it is either monoanionic (-1 charged) or dianionic (-2 charged) (5). When the membrane pH rises or when PA is in proximity to hydrogen bond donors — such as phosphatidylethanolamine (PE) — it exists as a dianionic compound. All lipin family members preferentially associate with dianionic PA; this can be observed as an increase in lipin activity and association with PA in the presence of PE (2-5). And while it has been known that the lipins are highly phosphorylated, it is now becoming clear how phosphorylation might affect lipin enzymatic activity (2-4). Specifically, phosphorylation negatively regulates the ability of lipin 1 to associate with, and act against, dianionic PA (2). However, the activities of lipins 2 and 3 are not affected by their phosphorylation state (3, 4). Why such a stark difference in molecular regulation of enzymes that catalyze the same reaction? Perhaps the answer lies within lipins themselves.

All lipins contain a polybasic domain, or PBD, a short nine-amino acid sequence composed of lysines and arginines that is responsible for lipin association with PA (6). The precise sequence and number of lysines versus arginines varies between the lipins. Recent work has revealed that the unique PBD of lipin 1 may be the reason it is subject to regulation by its phosphorylation (phosphoregulation) (4). The evidence for this came from studies where the lipin 1 PBD was replaced with the PBD from lipin 3. When the activity of this mutant lipin was measured, it was found that the presence of the lipin 3 PBD



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A schematic of lipin polybasic domain exchange mutants.

eliminated the phosphoregulation of the lipin 1 enzyme. Conversely, the specific activity of the lipin 3 mutant containing the lipin 1 PBD showed potent inhibition by phosphorylation. While it is possible that the mutant lipin proteins became dysregulated, phosphoproteomic analysis found no significant changes compared to their wild-type counterparts.

To date, there is no structural information available for lipins. As such, the mechanisms whereby lipin 1 phosphorylation interferes with the ability of the lipin 1 PBD to recognize dianionic PA are a matter of speculation. However, the variation in the molecular regulation of lipins suggests that each has a unique role in specific cellular stimuli and physiological conditions, and perhaps the field is just beginning to elucidate the true complexity behind the function of these enzymes. Further work is needed to probe exactly how these enzymes may be regulated post-translationally. In particular, the exact residues and molecular pathways involved in the negative phosphoregulation of lipin 1 are still unknown and could provide insight into its physiological role.

REFERENCES

1. Harris, T.E. *et al. J. Biol. Chem.* **282**, 277-286 (2007).
2. Eaton, J.M. *et al. J. Biol. Chem.* **288**, 9933-9945 (2013).
3. Eaton, J.M. *et al. J. Biol. Chem*. **289**, 18055-18066 (2014).
4. Boroda, S. *et al. J. Biol. Chem.* **292**, 20481-20493 (2017).
5. Shin, J.J. & Loewen, C.J. *BMC Biol.* **9**, 85-7007-9-85 (2011).
6. Ren, H., *et al. Mol. Biol. Cell.* **21**, 3171-3181 (2010).

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Upcoming ASBMB events and deadlines

FEB

5: Art of Science Communication course begins
12: Outreach poster deadline for ASBMB annual meeting
16: Outstanding Student Chapter Award deadline for ASBMB annual meeting
16: PROLAB application deadline
27: Late-breaking abstract-submission deadline for ASBMB annual meeting
27: ASBMB annual meeting early registration deadline

MAR

6 – 9: ASBMB-Deuel Conference on Lipids
15: Accreditation application deadline

APR

12: Hill Day
13: IMAGE grant writing workshop nomination deadline
16: Outreach Student Chapters grant deadline
21–25: ASBMB annual meeting, San Diego
30: Spring Art of Communication course applications open

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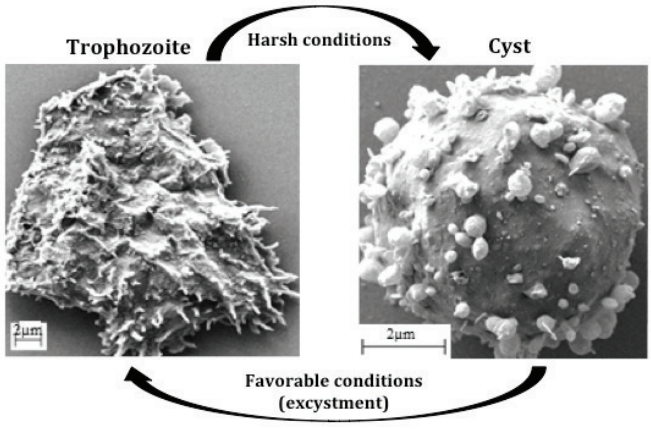
New insights into treating amoebic keratitis

By Isha Dey

The human body provides a hospitable environment for many micro-organisms that are essential to our survival. At the same time, it also attracts a host of parasites that, if not treated properly or eradicated, can be extremely harmful to our health. One such class of parasite is the infective amoeba, which causes rare and sometimes fatal diseases in humans. The Acanthamoeba species, found worldwide, mostly in water and soil, causes amoebic keratitis, or AK — an eye infection of the cornea that can result in permanent blindness. In the USA, 85 percent of AK cases occur in soft contact lens users. Although AK is potentially life-threatening, its treatment is not yet promising, owing to drug resistance and the absence of species-specific drugs. Hence, we need to identify specific drug targets to better fight these parasites.



COURTESY OF THE W. DAVID NES LABORATORY

Electron micrographs show the two stages in the life cycle of Acanthamoeba castellani.

Designing species-specific drugs requires an understanding of the unique evolutionary differences among species, especially with respect to biochemical pathways responsible for the survival of the parasite within the host. The Acanthamoeba life cycle has two stages — cyst and trophozoite. The trophozoite is the active form that infects humans, while the cyst is the dormant form that can survive harsh conditions such as stress and lack of nutrients. When conditions become favorable, the cyst transforms to a trophozoite via a process called excystment. Both forms can enter the human body through wounds, nostrils or contact with water.

Certain metabolic pathways cause the Acanthamoeba to cycle between stages and help the infective trophozoites survive and proliferate in humans. Thus, targeting these specific pathways could prove to be an efficient strategy to treat Acanthamoeba infections. W. David Nes and his group at Texas Tech University have investigated such pathways and reported sterol C24-methyltransferases, or SMTs, synthesized only in amoebae, as novel druggable targets. Their findings were published in the **Journal of Lipid Research**.

Sterols are amphipathic molecules that, by virtue of their lipid-based properties, act as membrane inserts to control overall growth and development. Ergosterol biosynthesis has been established as essential for the survival of many amoebae in humans, and SMTs are critical enzymes in the ergosterol biosynthesis pathway. SMTs catalyze a crucial step in the ergosterol pathway that maintains trophozoite growth. Interestingly, SMTs are absent in humans. Thus, the researchers found that inhibiting these enzymes with transition-state analogs that blocked the catalytic site on the enzyme, or with suicide substrates that irreversibly bound covalently to the enzyme, stopped the growth of trophozoites but had no effect on normal cholesterol biosynthesis in human cells. So this approach could treat specifically Acanthamoeba infections without harming us. This is the highlight of Nes' published work.

The work has been quite challenging, especially because differences in sterol biochemistry and life-cycle events among amoeba species make it hard to identify common drug targets. Moreover, Nes' group required an extensive collaboration to integrate a multidisciplinary approach so as to provide "the most effective drugs, which would escape mechanisms that otherwise could compromise their therapeutic longevity," Nes said.

Having used keratitis-causing Acanthamoeba castellanii as the model system in their published study, Nes and his group now want to test their hypothesis in mouse models. They also plan to extend their inhibitor studies to Naegleria fowlerii, a "brain-eating amoeba" that can cross the blood-brain barrier and destroy brain tissue, resulting in a disease called primary amoebic meningoencephalitis, or PAM. Further down the road, they hope to develop high-throughput screening techniques to repurpose existing drugs as novel SMT catalysis inhibitors to cure amoebic infections.

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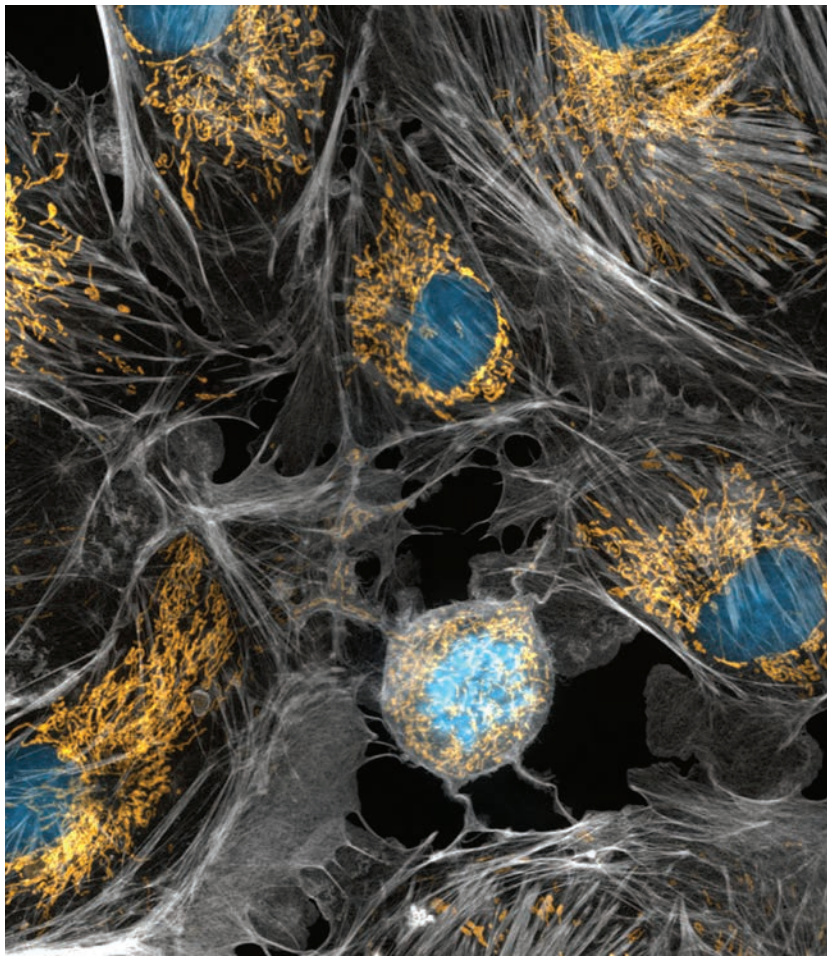
When mitochondria make B cells go bad

By John Arnst

B-cell chronic lymphocytic leukemia, or B-CLL, is the most common type of leukemia in adults and primarily affects elderly patients. The disease results from a patient's bone marrow overproducing immature lymphocytes, a form of white blood cells that fight infections less effectively than their healthy counterparts but survive longer, ultimately overwhelming them and spreading unchecked. Unlike acute leukemia, B-CLL can take several years to cause problems for a patient, but it is less responsive to chemotherapy.

While novel treatments have been developed in recent years, they only target the B cells once they've mutated to an immature, cancerous state. To develop treatments for B-CLL that might prevent B cells from becoming cancerous in the first place, researchers led by Christopher Gerner at the University of Vienna and Vienna Metabolomics Center have performed a comprehensive proteomics analysis of B-CLL cells and mature B cells in young and elderly patients. They described their work in a paper in the journal **Molecular & Cellular Proteomics.**



COURTESY OF TORSTEN WITTMANN, UNIVERSITY OF SAN FRANCISCO

When mitochondria, highlighted here in cow cells, suffer age-related oxidative damage, they can give rise to chronic lymphocytic leukemia.

"It could be nice to not only target the cancer cells, but those cells prone to becoming cancer cells," Gerner said. "What we actually saw when we compared the young and the elderly donors was a very clear signature of mitochondrial stress and metabolic stress."

Gerner and colleagues found that B-CLL cells have an increased expression of stem cell-associated molecules and a reduced expression of tumor-suppressing molecules and stress-related serotonin transporters as well as an observed increase in glutamine consumption and beta-oxidation of fatty acid.

This indicated that reactive oxidative species, which are carcinogenic and cause damage to cells, were being upregulated, Gerner said, which would explain why the incidence of mutations that lead to B-CLL increases with age. The researchers hope that the alterations in regulation also may provide a proteomic signature for immunosenescence, the immune system's natural weakening with age.

Gerner and his fellow researchers plan to continue this research by performing their proteomic analysis on blood samples taken from greater numbers of healthy elderly people and B-CLL patients to ultimatelybe able to test when mitochondria have become predisposed for the disease.

"The pressure on those cells was simply different … and this pressure is something I would like to detect and measure in patients," Gerner said. "That would be the ultimate aim."

John Arnst (jarnst@asbmb.org) is ASBMB Today's science writer. Follow him on Twitter at twitter.com/arnstjohn.

Sugary secrets of a cancer-related protein

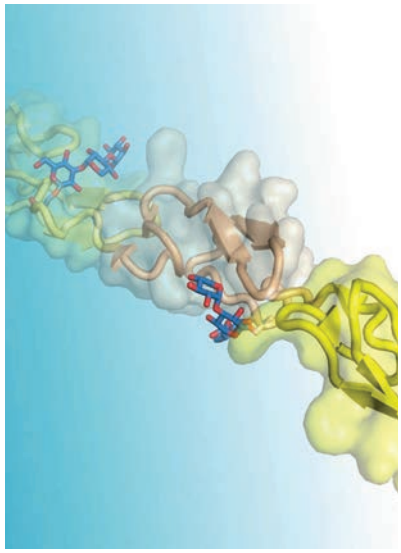
By Sasha Mushegian

The proteins in human cells are extensively decorated with different types of sugars, a phenomenon called glycosylation. These modifications greatly increase the diversity of protein structure and function, affecting how proteins fold, how they behave, and where they go in cells. New research published in the **Journal of Biological Chemistry** (1) demonstrates that a rare type of glycosylation profoundly affects the function of a protein that is important for human development and cancer progression.

Protein glycosylation is either called N-linked or O-linked, depending on whether the sugar is attached to nitrogen- or oxygen-containing sites, respectively. O-linked modifications typically involve the sugar N-acetylgalactosamine being attached to the amino acids serine or threonine, called "mucin-type" glycosylation because they are commonly found in proteins in mucus membranes; together with N-linked sugars, these "canonical" modifications modify thousands of types of proteins.

For over 20 years, Robert Haltiwanger's research group, now at the University of Georgia, has studied a rarer type of O-linked modification: attachment of the sugars glucose or fucose to serine or threonine, a modification that affects just a few hundred types of proteins. One of these proteins is Notch, a signaling receptor that is essential for cell development and differentiation and is dysregulated in cancers such as leukemia, breast cancer, and prostate cancer.

"The fact that we found these sugars on Notch was intriguing because Notch is a very important molecule," Haltiwanger said. "So we've been curious about how these sugars affect [Notch's] stability and activity."



COURTESY OF ROBERT HALTIWANGER, UNIVERSITY OF GEORGIA

Sugars fill the "notches" in the Notch receptor. The glycan stabilizes the Notch EGF repeats and thereby regulates Notch trafficking in cells.

The enzymes responsible for modifying Notch with glucose and fucose are called POFUT1 and POGLUT1. Haltiwanger's team, led by Hideyuki Takeuchi, wanted to know exactly why POFUT1 and POGLUT1 were attaching glucose and fucose to Notch in cells.

If you genetically engineer a fly or mouse without POFUT1 or POGLUT1, Haltiwanger said, "you get a dead fly or a dead mouse. You completely disrupt the Notch pathway; Notch is not functional if you don't add those sugars. There's been a lot of work over the years on: Why is that? What is [the sugar] doing?"

Haltiwanger's new work shows that the fucose and glucose modifications serve as quality-control markers that allow Notch to be transported to its final destination in the cell membrane. When the researchers knocked out POFUT1 or POGLUT1 in cell cultures using CRISPR/Cas technology, cells displayed much less Notch on the cell surface. When both enzymes were knocked out, Notch was almost completely absent. Using additional biochemical methods, the researchers found that POFUT1 and POGLUT1 attached glucose and fucose to portions of Notch only after they fold in a specific way.

"It's like a stamp of approval," Haltiwanger said. "This part's folded? Boom, you put a fucose on it. And somehow that tells the cell: Don't mess with this anymore. Leave it alone. If you don't add the sugar, [the Notch proteins] get stuck inside the endoplasmic reticulum, get degraded, and don't get secreted."

Knowing that these sugars are essential for Notch activity makes the enzymes that control them, POFUT1 and POGLUT1, potential targets for cancer treatments. Depending on whether Notch is overactive or insufficiently active in a particular cancer, manipulating the sugars that are added to Notch could help correct the dysregulation. Haltiwanger's team is working on finding chemical compounds that would inhibit POFUT1 and POGLUT1, thus stopping Notch from embedding in the cell membrane and carrying out its signaling functions. They're also attempting to unravel how the glucose and fucose modifications work together to fine-tune Notch activity.

"That'll keep us busy," Haltiwanger said.

REFERENCES

1. Takeuchi, H. *et al. J Biol Chem.* **292:38**, 15964-15973 (2017).

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Scientists find cellular backup plan for keeping iron levels just right

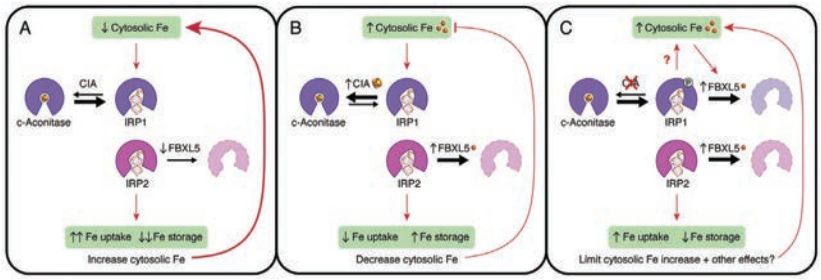
By Sasha Mushegian

Iron is essential for cell function, but excess iron can damage cells, so cells have sophisticated molecular mechanisms to sense and adjust iron levels. Disorders of cellular iron metabolism may affect more than a third of the world's population. In addition disorders like anemia, caused by overall insufficient iron levels, iron deficiency can impair brain function in the young and reduce muscle strength in adults. Iron may be dysregulated at the cellular level in neurological disorders such as Parkinson's disease, and disordered iron metabolism contributes to congenital conditions such as Friedrich's ataxia.

Researchers in the nutritional sciences department at the University of Wisconsin have uncovered a connection in the network of checks and balances underlying cellular iron regulation. Their research was published in the **Journal of Biological Chemistry** (1).

When iron levels in mammalian cells are low, iron regulatory proteins, or IRPs, spring into action. IRPs prevent iron that enters cells from being improperly stored, allowing the cell to produce essential iron-containing proteins. When there is excess iron, IRPs are inactive, leading to increased iron storage, lowering potential toxicity and reserving it for when iron availability is reduced. Too much or too little IRP activity can endanger cells.

Richard Eisenstein's research group at Wisconsin studies what controls IRP activity. Scientists have long thought the main method by which IRP-1 is inactivated involves essential compounds called iron-sulfur clusters.



COURTESY OF CARYN OUTTEN, UNIVERSITY OF SOUTH CAROLINA

CIA, FBXL5, IRP1 and IRP2 coordinate in control of iron metabolism. Protein degradation and iron-sulfur cluster production can suppress the activity of iron regulatory proteins, maintaining the correct iron levels in the cell.

When there is sufficient iron in the cell, an iron-sulfur cluster is inserted into IRP-1, inactivating it. Thus, the activation or suppression of IRP-1 relates to how much iron is available to produce iron-sulfur clusters.

However, there was some evidence of another method by which IRP-1 could be stopped when it was not needed: namely, that a protein called FBXL5 could add molecular tags to IRP-1 to tell the cell to degrade the protein altogether.

"The idea that IRP1 is also regulated by protein degradation was controversial when it was first discovered by others," Eisenstein said. "There's been a belief that IRP-1 was really regulated by this iron-sulfur cluster mechanism, and that the protein degradation mechanism wasn't so important."

To test whether this was the case, Eisenstein's team suppressed the production of iron-sulfur clusters. Even when this production was reduced, IRP-1 activity could still be suppressed. The team confirmed that this was due to the activity of FBXL5. This supported the idea that protein degradation was a backup mechanism that reduced IRP-1 action in cells with high iron.

The results have implications for understanding how iron is sensed, used and regulated in tissues. Different tissues have different levels of oxygen, but the iron-sulfur cluster production system functions best at low oxygen whereas FBXL5 functions best at high oxygen. Therefore, these two systems may trade off taking the lead in controlling IRP-1 in different parts of the body. Because iron-sulfur clusters and FBXL5 play many important roles in cell growth, this balance between these functions could help different types of cells control how they use iron.

"Diseases of iron metabolism caused by diet or by genetic perturbations are major public health issues," Eisenstein said. "To combat such diseases and develop effective treatments for those afflicted with them, it is essential to understand iron-sensing and iron-regulatory pathways."

Sasha Mushegian (amushegian@asbmb.org) is scientific communicator for the Journal of Biological Chemistry.

REFERENCES

1. Johnson, N.B. *et al. J Biol Chem.* **292:38,** 15976-15989 (2017).

From the journals

By Sasha Mushegian, Angela Hopp & Saddiq Zahari

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

Metabolites predict insulin resistance

Insulin resistance leading to high blood sugar, a hallmark of pre-diabetes, is a complex condition with many genetic and environmental determinants. Jacqueline Stöckli and colleagues from the University of Sydney carried out a comprehensive machine learning-enabled metabolomic analysis of three mouse strains fed high-fat or standard diets. The analysis showed that, despite individual environmental and genetic variation, a combination of three unrelated metabolites (C22:1-CoA, C2-carnitine and C16-ceramide) together formed an accurate signature for predicting insulin resistance. The study, published in the **Journal of Biological Chemistry**, is a step forward in creating precision medicine approaches to diabetes prevention and treatment.
doi: 10.1074/jbc.M117.818351

Unclogging the plaques

Heart disease kills 18 million people in the world every year. The underlying pathophysiology of heart disease is often atherosclerosis, a progressive buildup of plaques within the arteries. While some components of the atherosclerotic plaques have been studied, a comprehensive picture of the changes that occur during development of the plaques is still lacking. Investigators at the Max Planck Institute of Biochemistry led by Matthias Mann aimed to capture this picture by using a sensitive and in-depth mass spectrometry approach to profile the aortas of atherosclerotic mice over the development of the disease. The researchers quantified 5,117 proteins from this profiling strategy and found that 182 of them changed significantly in response to vessel maturation and plaque development. These include novel factors that were not known to be involved in atherosclerosis, including matrilin-2, peroxidasin and MAM domain-containing 2. The study, published in **Molecular & Cellular Proteomics**, provides the vascular disease research community with a valuable resource of time- and compartment-resolved proteomic changes during atherogenesis.
doi:10.1074/mcp.RA117.000315

Fatty acid metabolism and the migration of endothelial cells

Endothelial cells lining blood vessels help keep what belongs in and what doesn't belong out. These cells move around as needed — during, for example, development and wound healing. Abnormal endothelial cell migration is seen in various diseases, including rheumatoid arthritis, cancer and macular degeneration. Researchers suspect that manipulation of vascular endothelial cell migration could be a useful therapeutic approach for those and other conditions. The enzyme known as ACC, meanwhile, catalyzes the first and rate-limiting step in the biosynthesis of fatty acids. This enzyme, formally acetyl-CoA carboxylase, is of interest to researchers developing therapies for metabolic diseases such as obesity and diabetes and for certain cancers in which ACC is upregulated.

So what do vascular endothelial cells and ACC have to do with one another? That's the question that motivated a new study published in the **Journal of Lipid Research**. A research team led by Robert Fürst of Goethe University found that, in fact, ACC regulates endothelial cell migration. The study also underscored that manipulating ACC may be a worthwhile avenue for treating cell migration-related diseases. The researchers used human umbilical vein endothelial cells and human microvascular endothelial cells for the study. They interfered with ACC activities by administering a compound known as soraphen A. Originally isolated from slime bacteria, soraphen A has been used by scientists as an ACC inhibitor for some time. In this case, soraphen A's inhibition of ACC changed the lipid composition of the endothelial cell membranes and had other effects that ultimately prevented the cells from migrating as usual.

"Our findings show for the first time that (the enzyme) regulates endothelial filopodia formation and, most importantly, endothelial cell migration by rearranging the cells' phospholipid composition," the authors report. "The present study fills a gap in the literature by showing the relationship between the fatty acid metabolism and the migration of endothelial cells." In addition, the team noted that soraphen A could be a useful chemical tool for studying fatty acid metabolism in endothelial cells.
doi: 10.1194/jlr.M080101

Trypsin trips up

Alternative splicing has been shown to occur in up to 94 percent of human genes, resulting in expression of different splice forms for each gene. While this phenomenon is known to increase complexity at the transcrip-

CONTINUED ON PAGE 18

Two amino acids determine cells' response to warming

As the climate changes, we will have to adjust at many levels. In fruit flies, an enzyme called DESAT1, a delta-9-desaturase, is a key player in responses to temperature changes at both the cellular level, where it influences membrane fluidity by synthesizing monounsaturated fatty acids, and at the whole-organism level, where it controls temperature-influenced behaviors like mating.

Delta-9-desaturases are found in all organisms, from bacteria to humans. DESAT1 in fruit flies is transcribed at a constant rate, but the rate at which the protein degrades determines its overall expression level. Masato Umeda's research team at Kyoto University was interested in understanding how the degradation of DESAT1 is regulated in the fruit fly Drosophila melanogaster in order to better understand thermal regulation in diverse organisms. The results of their research were reported in the **Journal of Biological Chemistry**.

The team discovered that DESAT1 is degraded by calpains, calcium-dependent cysteine proteases, in the presence of unsaturated fatty acids and that this degradation is enabled by a diproline motif at DESAT1's N-terminus.

"It was surprising that it is regulated by only two amino acids," Umeda said. "A very small portion is responsible for expression of the protein."

Now, the team is going back a step further in the pathway leading to DESAT1 degradation, trying to understand how temperature changes are sensed inside the cell to lead to changes in fatty acid composition and consequent effects on the whole organism.

"Our ongoing project aims to elucidate how cells recognize temperature or cellular events caused by the temperature changes and control the expression of DESAT1 to adapt the cellular processes and behaviors," Umeda said. "We hope our study will lead to an alternative approach that could potentially circumvent the biological crisis due to global warming."

doi: 10.1074/jbc.M117.80193

— Sasha Mushegian

COURTESY OF MUHAMMAD MAHDI KARIM/WIKIMEDIA COMMONS

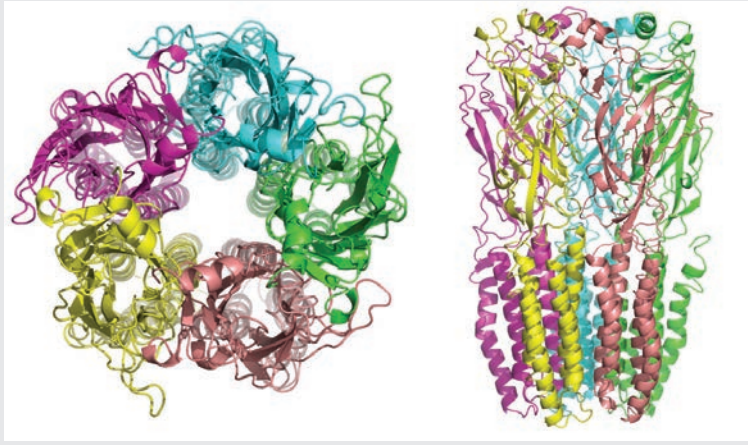
Drosophila, photographed in Dar es Salaam, Tanzania.

CONTINUED FROM PAGE 16

tome level, the effect of alternative splicing on the complexity at the proteomic level remains controversial. In a recent study in **Molecular & Cellular Proteomics**, researchers at Baylor College of Medicine and Vanderbilt University led by Bing Zhang showed why there has been a lack of evidence of exon–exon junction-spanning peptides in published proteomic data sets. They found that the ends of exons in the genome are enriched with codons coding for lysine and arginine amino acids. This occurrence could have hindered the detection of junction-spanning peptides, since most mass spectrometry experiments involve digesting proteins with the enzyme trypsin, which cuts peptide chains exclusively after arginine and lysine residues. The researchers further showed that combining chymotrypsin and trypsin during sample preparation increased the detection of junction-spanning peptides by 37 percent. The study demonstrates the importance of using complementary digestion schemes in research where identifying different splice forms of proteins is a priority.
doi:10.1074/mcp.RA117.000155

How nicotine affects receptor localization

Nicotinic acetylcholine receptors, or nAChRs, are the main receptors in neuromuscular junctions. Observations suggest that nicotine exposure affects the ratio of these receptors on the surface versus those in the endoplasmic reticulum of the cell and thus the cells' sensitivity to these receptors' natural ligands. To understand how nicotine affects nAChR localization, Ashley M. Fox–Loe and colleagues at the University of Kentucky developed sensitive, organelle-specific single-molecule imaging methods to quantify precisely changes in the stoichiometry of nicotinic receptors. Publishing the research in the **Journal of Biological Chemistry**, the team concluded that nicotine exposure affects receptor distribution through combined effects on both receptor assembly and trafficking, which eventually could help explain the effects of drugs like nicotine on neuromuscular functioning.
doi: 10.1074/jbc.M117.801431



COURTESY OF ATALY/WIKIMEDIA COMMONS

This illustration shows two views of a nicotinic acetylcholine receptor.

Mitochondrial signals through micro-RNAs

Communication between the nucleus and mitochondria is required for cells to function. While signaling from the nucleus to the mitochondria is most obvious, signals from the mitochondria to the nucleus are also crucial. In particular, mitochondrial-nuclear signaling regulates metabolic stress responses, and misregulation of this signaling has been observed in breast cancers. Trevor Carden and colleagues at the University of Alabama showed the first evidence of a micro-RNA's role in mitochondrial-nuclear signaling and tumor suppression. The expression of micro-RNA miR-663 was induced by mitochondrial reactive oxygen species production, an apoptotic signal and oxidative stress response, and miR-663 induced the expression of nuclear-encoded mitochondrial respiratory chain subunits. Correlative and experimental observations of breast cancer tumors also suggested that miR-663 has a tumor-suppressive effect. These observations, published in the **Journal of Biological Chemistry**, suggest that micro-RNAs could be important players in mitochondrial-nuclear signaling in normal and cancerous cells.
doi: 10.1074/jbc.M117.797001

Investigating the genetic basis of bile acid diarrhea

Bile acid malabsorption, which can accompany gastrointestinal disease or manifest alone, causes chronic diarrhea. Primary bile acid diarrhea, or BAD, in humans has been shown to be related to the hormone known as fibroblast growth factor 19. FGF19 is secreted in the intestine and downregulates the synthesis of bile acids in the liver. Researchers at the David Geffen School of Medicine at the University of California, Los Angeles, recently reported in the **Journal of Lipid Research** that they have identified a gene variant that affects FGF19 secretion and thus may affect bile acid metabolism in both sickness and health. Led by Karen Reue, the research team first used a mouse model that they had identified previously as having a spontane-

ous deletion in the Diet1 gene. A deficiency in Diet1 results in reduced FGF15 (the mouse equivalent of FGF19). The team characterized the effects of the gene deletion and found that the mice had symptoms similar to those experienced by patients with BAD. Next, they looked at how Diet1 expression in more than six dozen mouse strains correlates with the expression of FGFF15 and bile acid levels. Finally, they zeroed in on a variant in the DIET1 gene in humans that influences FGF19 secretion from cultured cells and is associated with FGF19 levels in BAD cases. "Our findings raise the possibility that the (variant) could contribute to the seven-fold variation in plasma FGF19 levels that have been observed in healthy individuals," the authors wrote. "Resequencing DIET1 in additional subjects will be required to reveal whether DIET1 rare mutations or additional common variants contribute to variations in bile acid metabolism.

doi: 10.1194/jlr.M078279

Do-it-yourself custom chromatin

In the nucleus, DNA is packaged with proteins in a form called chromatin. Chromatin's complex structure regulates gene expression, DNA repair and epigenetic inheritance. Building customized chromatin for molecular studies remains a challenge because of its multidimensionality. Mai T. Khuong and colleagues at the University of California, San Diego, developed a method to synthesize chromatin in vitro using histone chaperone proteins and an adenosine triphosphate-driven motor protein derived by a simple purification from Drosophila, template DNA and histones from the researchers' species of choice, and ATP. This simplified system then was used to assemble chromatin with desired DNA sequences and proteins from diverse organisms. The researchers hope that this method, published in the **Journal of Biological Chemistry**, becomes a user-friendly approach for a variety of chromatin-related experiments.

doi: 10.1074/jbc.M117.815365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Saddiq Zahari (szahari@asbmb.org) is the editor for manuscript integrity at Molecular & Cellular Proteomics.

6 questions *for* 3 PRESIDENTS

College and university leaders from underrepresented groups talk about how a background in science serves them at the academic helm

By Takita F. Sumter, Adela Cota-Gomez & Kayunta Johnson-Winters

COURTESY OF KENYON COLLEGE

Sean Decatur, president of Kenyon College in Ohio, and students gathered around his dining room table in spring 2016 for a seminar, "Case Studies in Protein Structure, Dynamics and Function." He plans to teach another seminar, on bioluminescence, this year.

All life scientists navigate academia, at least in the early stages of their careers. These encounters evolve in commitment and complexity depending on whether they occur as undergraduates, graduate students, postdoctoral fellows, faculty or — for a few — administrators.

Life sciences faculty at times assume leadership positions in academia that make good use of their background and skills as they face such issues as enrollment challenges, funding and the need to diversify certain disciplines. These administrative roles allow scientists to have a positive impact on the future of education, particularly training young biochemists and molecular biologists who ultimately will work to advance science and improve human health.

Biochemists and molecular biologists who move from the bench to college and university presidencies do so from a variety of backgrounds. Here, we present the views of three such presidents who are also from underrepresented groups: Juliette Bell of the University of Maryland Eastern Shore, Sean Decatur of Kenyon College in Ohio and Roy Wilson of Wayne State University of Michigan. Their schools and their academic backgrounds vary, but these three share certain key traits, including adaptability, a knack for picking up multiple skills and a unique ability to serve as role models for the next generation of scientists.

Describe your science background and discuss how it benefited you on your path. In your current role, how do you convey your passion for biochemistry and molecular biology or the scientific enterprise to burgeoning scientists?

BELL: I have a B.A. in chemistry from Talladega College and a Ph.D. in chemistry with a biochemistry concentration from Atlanta University. I also completed three and a half years as a postdoctoral fellow in biochemistry at the University of North Carolina at Chapel Hill. I am currently president of the University of Maryland Eastern Shore, an 1890 land-grant historically black university with a strong focus on science, technology, engineering and mathematics, or STEM, as well as agriculture and the health sciences. My science background was a great match for the priority on STEM at UMES, the University System of Maryland, and the state of Maryland. I convey my passion for science and research by actively and personally participating in and supporting undergraduate, graduate and faculty research activities. I also mentor students, work with professional organizations and work to strengthen the infrastructure for the sciences on my campus.

DECATUR: I majored in chemistry (with a minor in biology) as an undergraduate at Swarthmore College; then I went on to complete a Ph.D. at Stanford University in biophysical chemistry. My interests since graduate school have focused on spectroscopic approaches to studying protein structure, dynamics and folding, and for about 20 years (until I became president at Kenyon College), my research was supported by the National Science Foundation (including a CAREER award), National Institutes of Health and private foundations.

In my current role, I value the opportunities I have to teach and advise students (I am teaching a seminar in spring 2018, and I regularly advise students at Kenyon). In addition, I am pleased to support efforts of my faculty colleagues in the natural sciences to expand opportunities for research to students underrepresented

COURTESY OF KENYON COLLEGE

Sean Decatur, president of Kenyon College, started out as an assistant professor of chemistry at Mount Holyoke College, then was dean of the College of Arts and Sciences at Oberlin College.

COURTESY OF THE UNIVERSITY OF MARYLAND EASTERN SHORE

Juliette Bell, president of the University of Maryland Eastern Shore, previously served as a director of biomedical research, dean of the college of science, and provost/vice president/chancellor at three institutions.

in the sciences and to make the pedagogical approaches more inclusive. I am very proud of Kenyon's successes in this area over the past year, including an initiative funded by the Howard Hughes Medical Institute's inclusive excellence program, an NSF Scholarships in STEM program and a Clare Booth Luce grant to support undergraduate women to pursue research.

WILSON: I have a bachelor's degree in biology and pursued extra training in epidemiology/biostatics while I was in medical school. Later, when I was a faculty member, I pursued a Master of Science in epidemiology. I have collaborated extensively with trainees and junior colleagues in research work leading to publications.

What additional experience qualified you for the position of president (for example, were you a department chair or dean)? How did those experiences help prepare you to be president?

BELL: Before becoming president, I served as director of biomedical research, dean of the college of science and as provost and vice president/chancellor at three institutions. These experiences taught me leadership and management skills, which are essential in the presidential role. I also learned financial management, fundraising/friend raising, government relations, athletics and other areas essential to the presidency. Serving as a faculty member and in these various roles also increased my credibility with faculty, since I could relate firsthand to the challenges faculty face.

DECATUR: I rose up through the traditional faculty ranks, beginning my career as an assistant professor at Mount Holyoke College. Soon after I received tenure, I became chair of my department, and after that I took on responsibility for a number of institutional grant projects, becoming an associate dean of faculty. I moved from Mount Holyoke to Oberlin College, where I took on the role of dean of the College of Arts and Sciences, the chief academic officer for the college.

In this way, my career has been a gradual rise in administrative responsibilities. But my administrative work has roots in my scientific work. It was in my research program that I learned how to manage a budget, set out a plan for work and supervise a staff, all of which have served me well in my later work.

WILSON: I came up through a traditional academic system by first becoming a department chair in ophthalmology and then dean of the medical school (Charles Drew University of Medicine and Science), then dean of another medical school and vice president for health sciences (Creighton University), then president of a free-standing health science enterprise (Texas Tech University of Medicine and Science), then chancellor of the University of Colorado Denver (consisting of the general academic and health science campus). I then did a short stint at the NIH before coming to Wayne State.

Part of leadership is being able to bring people together and to resolve conflict. What experiences do you have that enable you to do this effectively?

BELL: As president, one must respond to many constituents. These include students, parents, faculty, staff, boards, legislators, partners, col-

leagues, accrediting bodies, business and community leaders, funders, and the list goes on. One must be a good listener, a good communicator and a consensus builder. It is also essential that you have good analytical skills and the ability to solve problems. These are skills well-suited to scientists and researchers. I often say that I use the scientific method every day as president. Learning how to arrive at win-win solutions to problems and conflicts is an ongoing learning process.

DECATUR: Managing people and relationships was an important component of running a research program, and the skills I learned in that work formed a valuable foundation for managing larger teams and eventually for my work as president. In all of this, listening is probably the most important skill I have needed to practice and hone; often what is most important for resolving conflict is to make sure that all voices are heard and respected.

WILSON: No specific experiences come to mind. I learned by making a lot of mistakes and learning from mistakes.

How did being an underrepresented minority help to shape your experiences and how you serve your institution?

BELL: As an African-American female biochemist, I was often characterized as a "double minority" in many of the professional environments I worked in prior to entering academia. Having overcome many challenges in achieving my goal of a career in science and research, I chose to use my experience, skills and passion to encourage and support other underrepresented minorities in achieving their dreams. This is what led me to devote my career to teaching, research and service at historically black institutions. Leading an HBCU is the ultimate opportunity for service to my community.

DECATUR: I am the first African-American, and first person of color, to lead Kenyon College. While the work of building a diverse and inclusive community should not (and does not) fall exclusively to leaders who are also members of underrepresented groups, I do feel that it is important that I keep issues of diversity and inclusion as key institutional priorities.

WILSON: I experienced a lot of what minority students experience in higher education today, so I can identify with their challenges and struggles. I believe these experiences have made me empathetic, and I try to influence policy that will positively impact all students.

Most aspiring young biochemists/molecular biologists do not plan a path toward leadership, and many do not pursue a high-ranking leadership position. Did any specific experience(s) lead you toward that goal?

BELL: For the first 12 years of my academic career, I was content teaching, conducting my research and serving as the director of several training programs. I increasingly became dissatisfied with the level of support for research at my university. I had the opportunity to share my concerns and suggestions for change

COURTESY OF WAYNE STATE UNIVERSITY

Before he was named president of Wayne State University, Roy Wilson earned an M.D., was dean of two medical schools, held administrative positions at two universities and worked at the National Institutes of Health.

with a new president. That president told me that if I wanted things to change, I had to be willing to take a leadership role and not just stand by and complain. I took her up on that advice and accepted an interim dean's position. I subsequently applied for and won the dean's job, then provost, and the rest is history.

DECATUR: I have always been interested in educational leadership, since I was an undergraduate (my Ph.D. adviser recently reminded me that I mentioned this in my graduate school application). But, over time, my view on how I could influence the educational experience of students gradually expanded from a focus on a specific classroom experience to the departmental level to the institutional level.

WILSON: I did not have an "aha" moment. I was thrown into leadership roles from the very beginning of my career, and I performed other faculty roles, such as teaching and research, concurrently. I knew there was no turning back when I became dean of medicine at Creighton.

How have the events of the past year (demonstrations in Charlottesville and by NFL players, actions by President Trump and congressional leaders) been reflected on your campus?

BELL: As HBCU students, my students are very aware of issues impacting diversity and inclusion, equity and social justice. The events of the past year have further increased awareness, especially as it relates to events in Baltimore, home to many of my students. This has sparked discussions and social and political action among UMES students.

DECATUR: Our nation has been burdened with deep-rooted legacies of racism for a long time, and the events of the past few years (not just 2017 but dating back to the tragic deaths of Trayvon Martin in 2013 and Michael Brown in 2014) have made the struggle for racial justice more visible and more urgent. College campuses are places where the nature and impact of discrimination can be examined with rigor and are often on the front lines of positive change. At Kenyon, the events of the past few years have provoked important discussion, led to reflection about our own practices as an institution and catalyzed the process of change.

WILSON: Like many other universities, we've had to confront a number of problematic issues this past year, including the immigration ban, overt racism, the assault on science, etc. We've tried to be true to our mission and our values during these times. We've communicated frequently with our entire university community and have sponsored many discussion sessions where people can express their feelings and concerns.


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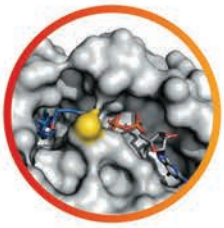
Adela Cota-Gomez (adela.cota-gomez@ucdenver.edu) is an associate professor of medicine in the division of pulmonary sciences and critical care at the University of Colorado Denver–Anschutz Medical Campus.


Kayunta Johnson-Winters (kayunta@uta.edu) is an associate professor in the department of chemistry and biochemistry at the University of Texas-Arlington.

2018 ASBMB Special Symposia Series



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Transcriptional Regulation by Chromatin and RNA Polymerase II

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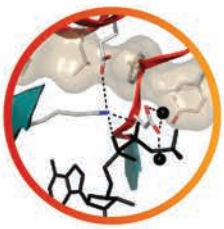

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Reminder: ASBMB members save on meeting registration.

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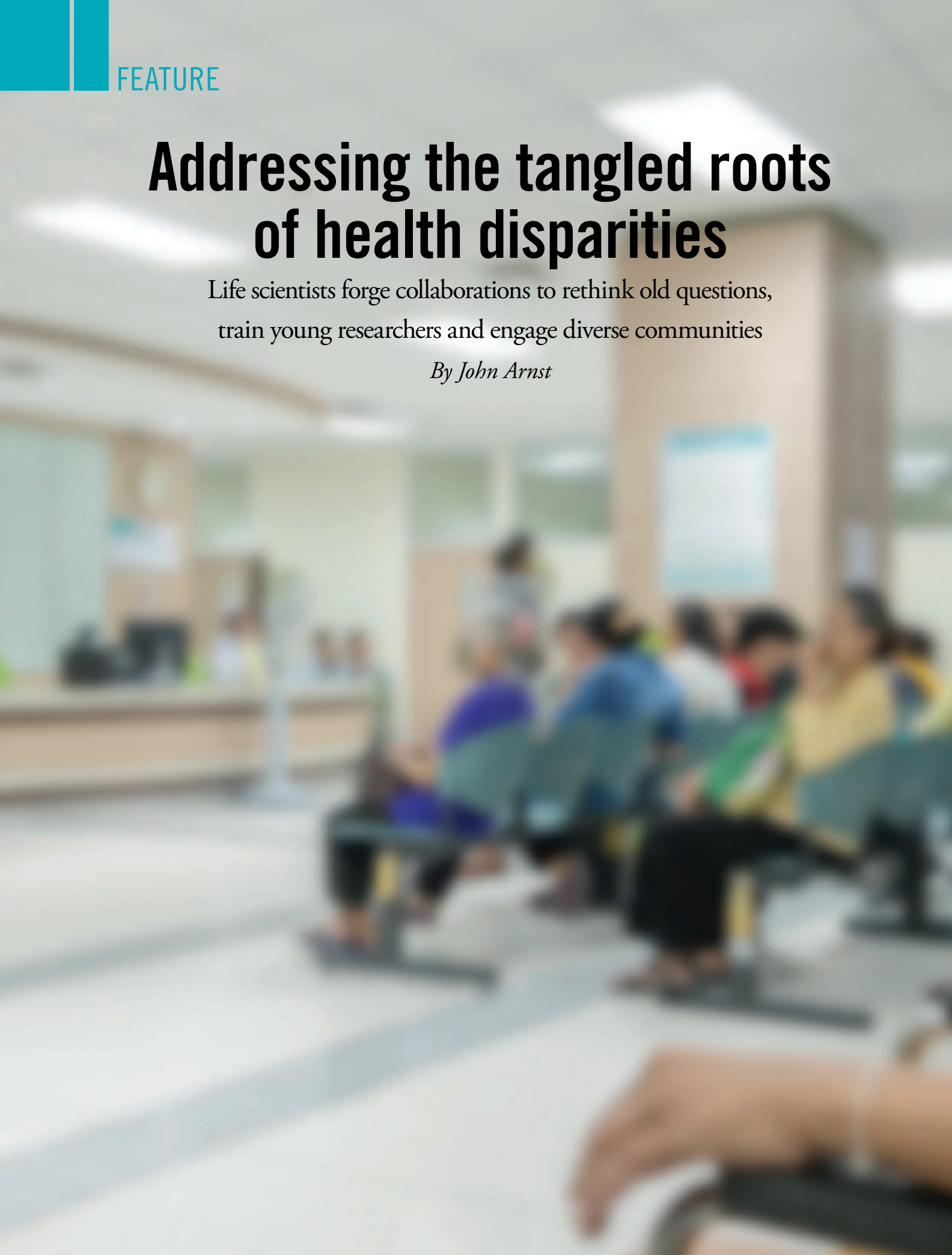
Addressing the tangled roots of health disparities

Life scientists forge collaborations to rethink old questions, train young researchers and engage diverse communities

By John Arnst



In the United States, black babies die during birth at more than twice the rate of white babies.

As adults, black men and women die from strokes and heart disease at higher rates than Americans of other races and ethnicities.

While advances in breast cancer screening and treatments have reduced the death rate for all women in the U.S., the death rate has decreased more slowly for black women than for white women, resulting in a significant disparity. For example, from 1999 to 2013, the most recent period for which there are data, black women in Houston were 72 percent more likely to die from breast cancer than white women.

The study of health disparities, which includes any condition disproportionately affecting one racial, ethnic or gender group, is a burgeoning, relatively young research field. The National Institutes of Health established the National Center on Minority Health and Health Disparities in just 2000 and then redesignated it as the National Institute on Minority Health and Health Disparities in 2010 as part of the Patient Protection and Affordable Care Act.

A product primarily of poverty and unequal access to health care, health disparities are a staggering challenge. The problem is as entrenched as the wealth gap — due to the strong correlation of income and life expectancy in the U.S., the richest 1 percent of American women and men live an average of 10 and 15 years longer, respectively, than the poorest 1 percent.

However, the problem goes deeper than income. The chronic stress caused by economic insecurity, discrimination and systematic racism is understood to have negative effects on the health of millions. Additionally, a growing body of evidence suggests the cellular stress caused by systemic trauma can have epigenetic-based detriments to the health of future generations. For a small number of diseases — including prostate cancer, triple-negative breast cancer and pre-eclampsia — biological predispositions (such as an elevated number of disease-associated alleles) may play roles.

Clayton Yates, professor of biology and director of Tuskegee University's Center for Biomedical Research, studies the biological mechanisms responsible for the increased mortality rate of prostate cancer in black men.

"If we're not understanding the disparities and the different mechanisms that are occurring at a biochemical level in different populations, it's no wonder that a large percent of our drugs that get to market are failing in a general population," he said, "because we're not even considering that in the discovery process."

In 2017, Yates and his colleagues received a five-year NIHMD grant of nearly $8.5 million to help train minority scientists involved in health disparities research. The grant is one of seven that the NIMHD announced last year for research centers in minority institutions, or RCMIs, in Alabama, Florida, Tennessee, North Carolina, Arizona, Puerto Rico and Hawaii. The NIMHD plans to disburse $122 million over five years for the institutions to train early-career investigators involved in health disparities and minority health research and to improve research infrastructure.

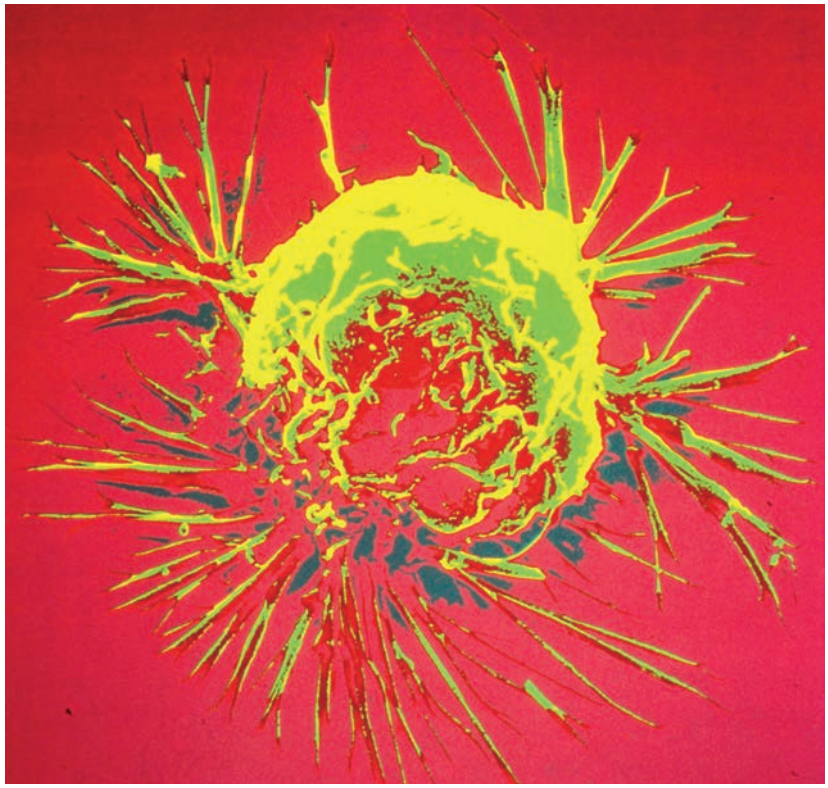
In addition, last year the NIMHD announced it would direct $82 million in funding over five years to 12 Centers of Excellence focused on multidisciplinary research and community-engagement activities.

Together, these grants made up around 15 percent of the NIMHD's $281 million budget for 2017.

In addition to advocating for the elimination of policies that give rise to social inequality, health disparities experts say basic researchers can help address health disparities by question-

COURTESY OF CHRISTOPHER RENEGAR

Clayton Yates has been a faculty member at Tuskegee University for 11 years.



COURTESY OF BRUCE WETZEL AND HARRY SCHAEFER, NATIONAL CANCER INSTITUTE, NATIONAL INSTITUTES OF HEALTH

A breast cancer cell, photographed by a scanning electron microscope. The disparity between breast cancer survival rates in black and white women has widened in recent years, despite decreases for both groups.

ing the established canon of biomedical research, building interdisciplinary collaborations, training scientists from underrepresented communities and enhancing community involvement through participatory research.

New frameworks for questions

How does inequity affect people at the molecular level? And how do those effects influence, for example, the rate of colorectal cancer in black men in Chicago? These are the types of questions being asked by researchers at the Chicago Center for Health Equity Research, or CHER.

There, Robert Winn and Karriem Watson are part of a multidisciplinary team of investigators from the University of Illinois at Chicago aiming to minimize disparities by examining the effects that continual violence and harassment have on the health of minority populations. The center, which is led jointly by Winn; Martha Daviglus, a cardiovascular researcher focused on health disparities; and Jesus Ramirez-Valles, a chair of the Division of Community Health Sciences at the university's School of Public Health, was established last year after the university received a $6.75 million five-year grant from the NIMHD to develop a center of excellence on minority health and health disparities.

"We want to strengthen health-equity scholars and produce research activities that can expand the understanding of structural inequality in order to identify the differential risks and vulnerabilities of racial, ethnic, and sexual minority groups," said Watson, who is also director of community engaged research and implementation science at the university's cancer center.

The team has three projects that investigate health and structural violence. One examines the factors associated with disparities in mental health among Asian immigrant populations. Another examines the relationship between cardiovascular disease outcomes in Latino families and stress due to racial discrimination. The third examines colorectal cancer and the epigenetic impacts that structural violence has on black populations in Chicago.

"When you think of colorectal disparities on the south side of Chicago, you think about that as an issue that spans translational research," said Winn, who is also the associate vice chancellor for community-based practice at the university. "That issue starts at the cellular-molecular level, with the actual testing and the understanding that biologists have of the pathology of colorectal cancer and diagnosis of colorectal cancer, all the way to the community uptake of that screening."

The colorectal cancer project employs a mouse model that the researchers established with the help of Paul Grippo, an associate professor specializing in animal models of

gastroenterology. They can use the model to simulate food insecurity and stressful situations perpetuated by aspects of structural violence, such as social isolation, stress and trauma.

"We can mimic those situations in animal models to demonstrate how certain biochemical markers, such as cortisol, may be elevated in those animals and that may also be elevated in our human population," which may illustrate environmentally induced epigenetic changes that cause an elevated risk of colorectal cancer, Winn said.

"That's just an example, to me, of where we now have tools that we didn't have (before) to study these really big issues of our society that actually do have a component that needs to be answered at the bench to be able to make any inroads," Winn said.

Disparities in cancer

While health disparities are primarily a consequence of economic inequity and unequal access to health care, certain types of cancers — prostate cancer in black men and triple-negative breast cancer in black women are two examples — are believed to occur disproportionately due to higher frequencies of predisposed alleles.

At City of Hope Cancer Center in Duarte, California, Rick Kittles is exploring the link between ancestry-informative genetic markers and disease risk and outcomes, with a special emphasis on prostate cancer.

"The bulk of health disparities really doesn't have any strong sort of biological component to it, it's more social, cultural, behavioral differences across populations that are contributing to disparities," said Kittles, the founding director of the Division of Health Equities at City of Hope. "But, there's a subset — for instance, prostate cancer — which has a strong genetic component to it that might account for some of the differences that we see when we compare black men and white men and Hispanic men."

While the overall death rates for cancer in black men and women have fallen by more than 34 and 19 percent, respectively, over the past two decades, they are still higher than the rates for the white population. Black men in the United States still have nearly twice the lifetime probability of dying from prostate cancer as white men.

"We've identified across all populations a region on chromosome 8 that increases risk (for prostate cancer)," Kittles said. "The interesting thing is that the frequency of these risk alleles, these risk variants, are much greater in African-descent populations. When we do the math, because of the higher frequency, they can account for the higher frequency we see in prostate cancer in African-descent populations."

The next generation

At the University of Hawaii at Manoa, Dean Jerris Hedges, Noreen Mokuau, Marla Berry and their colleagues are mentoring new and early-stage scientists to investigate health disparities in native Hawaiian and Filipino communities on the islands.

"We feel that if we can improve the health in those who have a gap in their overall lifespan and general wellness, then we can raise the health of all of the population," said Hedges. "We've been doing this in a translational manner, trying to do bench-to-bedside-to-community (work)."

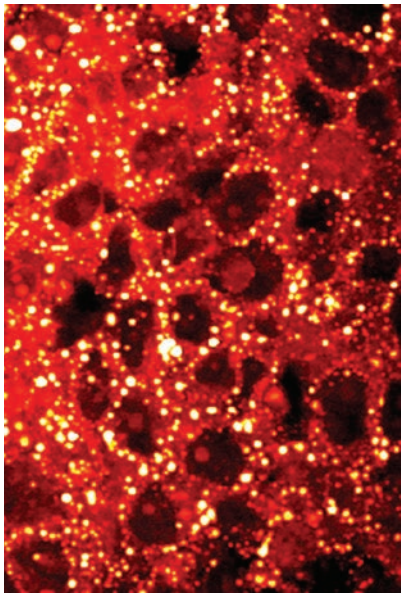
Hedges and Mokuau's team received an RCMI grant from the NIMHD for nearly $5 million in its first year to facilitate research on the causes of and most effective interventions for health disparities on the islands related to diabetes, cancer, glucose metabolism, cardiovascular disease and strokes. "There are elements of the current grant that focus not only on community, behavioral

COURTESY OF THE UNIVERSITY OF ILLINOIS AT CHICAGO

At the University of Illinois Cancer Center, Karriem Watson has helped create community-based programs for screening, preventiing and navigating breast, colorectal, cervical, prostate and lung cancer.

COURTESY OF THE UNIVERSITY OF ILLINOIS AT CHICAGO

In addition to his role at Chicago Center for Health Equity Research, Robert Winn is the primary investigator in a lab at the University of Illinois at Chicago that explores signaling pathways in lung cancer.



COURTESY OF JI-XIN CHENG, PURDUE UNIVERSITY CENTER FOR CANCER RESEARCH, NATIONAL CANCER INSTITUTE

Altered lipid metabolism, shown in yellow, may be a key signature of prostate cancer.

COURTESY OF TINA SHELTON

Prior to his current role at the University of Hawaii at Manoa, Jerris Hedges served as professor and department chair in emergency medicine at Oregon Health & Science University's School of Medicine.

and public health aspects, but also are looking at the epigenetics that may affect certain populations to a greater extent than others," Hedges said.

Part of the program focuses on introducing young scientists to experts in adjacent fields.

"(Each young investigator) has a partner or a collaborator or a mentor, or both, from a different discipline," Berry said. These pairings tend to include basic research scientists partnered with clinical or community-based researchers or cross-disciplinary pairings such as biologists and engineers.

At Tuskegee University's Center for Biomedical Research, Yates is using the NIMHD grant to train minority biomedical scientists who are examining disparities in HIV, obesity and prostate cancer.

"This grant has been a culmination of over 10 years of work through multiple other discoveries and papers, where we've identified that there are molecular and genetic differences, particularly in cell-signaling pathways that are associated with an aggressive (prostate cancer) tumor in an African-American patient versus a European-descended patient," Yates said.

The funding will allow Yates and colleagues to expand the center's research capacity by developing new laboratories and furnishing them with cutting-edge equipment. The program will operate adjacently with the center's pre-existing National Cancer Institute-funded mentoring programs.

Tuskegee's program pairs senior health disparities experts with new faculty members. The mentorship helps prepare the young investigators to answer disparities questions in their careers, Yates said.

They're asking these questions, he said: "How do you address this population? How do you transform what you are currently doing to address a specific population that you see has a disproportionate outcome or incidence of disease?"

Lovell Jones is a retired molecular endocrinologist who has received numerous awards for his leadership in minority health disparities, including the American Society for Biochemistry and Molecular Biology's Ruth Kirchstein Diversity in Science Award. Jones said he believes that these types of interdisciplinary partnerships are key to ensuring that the progress made in the laboratory ultimately has an effect outside of it.

"It's not that (basic researchers) have to become experts in psychology or experts in sociology, experts in urban planning, but they need to have an array of colleagues that can advise them in terms of direction," said Jones. "What has been asked before? What hasn't been asked before? What has it done?"

These partnerships are particularly important at the University of Hawaii, where the nearest major academic institution is more than 2,500 miles away, Berry said. "The university plays a unique role in training local scientists to address health disparities within their own communities," she said, "which makes developing these junior investigators particularly crucial."

Community-based research

Helping train minority scientists to study disparities in their own communities is an approach that Kittles and his colleagues at City of Hope also favor.

"One of the goals, obviously, is to increase not only disparities research but also diversity among the researchers," Kittles said. "For the most part, scientists study themselves, and so the more scientists of color we have, the more questions and opportunities to really explore this issue of disparity in the scientific community."

In Belcourt, North Dakota, Native American geneticist Krystal Tsosie is working simultaneously as a co-inves-

tigator for a study involving genetic determinants of pregnancy-related high blood pressure, or pre-eclampsia, in the Turtle Mountain band of Chippewa Indians and wrapping up her Ph.D. in genomics and health disparities at Vanderbilt University.

"I find that people within these interdisciplinary fields tend to come from their communities of interest, so researchers have their own firsthand experience with what it's like to grow up in these diverse, underrepresented communities," Tsosie said. "Being a Native American scientist, particularly a Native American geneticist, you have to wear many hats, and, because there are so few of us, our expertise gets called upon collectively and individually at earlier stages in our training than maybe other traditional students."

Prior to her work in Belcourt, Tsosie was using Vanderbilt's BioVU database of more than 225,000 de-identified genetic samples to study genetic determinants of uterine fibroids in black women.

The pre-eclampsia project at Turtle Mountain Community College involves a research cohort of local residents who have been working with the institution for more than 15 years.

Pre-eclampsia occurs in about 6 percent of pregnancies and can result in premature birth and death for either, or both, the mother and child. Tsosie's co-investigator, Lyle Best, is a family practitioner who has worked with the Indian Health Service in the Belcourt area since 1977.

While no genetic determinants have been found yet for pre-eclampsia, risk factors including mutations in DNA have been identified. By incorporating clinical data from electronic health records at the Belcourt-area Indian Health Service clinic, the researchers are able to examine potential environmental and sociocultural factors specific to women of the Turtle Mountain Chippewa Nation that may affect pre-eclampsia rates.

"In studies of diverse populations, Native Americans in the U.S. are very much ignored," Tsosie said. "Part of it is, the population is so small to begin with. Another challenge is having an informed process that not only educates American Indians about the potential benefits of engaging in genomics research, but then having the cultural competency of researchers to engage a community to have more equitable research."

Tsosie and colleagues have had a variety of research questions about the tribes' saliva and blood samples and have kept tribe members abreast of the results that come from their samples through newsletters or radio programs. Additionally, they train tribal students in the lab and work with a Tribal Institutional Review Board, which reviews and approves their projects.

This community-based participatory research, which involves community engagement at every step of the scientific process, is how most of the genomics research within Native American communities has trended since a 2004 lawsuit in which the Havasupai Tribe, in a remote part of the Grand Canyon, sued the Arizona Board of Regents and researchers at Arizona State University for misusing their DNA samples.

"We're really hoping that encouraging community-engaged research, in not just Native American communities but in all diverse ethnic populations, as a broad agenda, will not only change how researchers interact with potential participants but also make research more equitable for all diverse and nondiverse populations," Tsosie said.

At Tuskegee University, Yates and colleagues are involved in outreach programs led by campus investigators in venues such as town hall forums, where the researchers can tell community members about the elevated risk for prostate and breast cancers

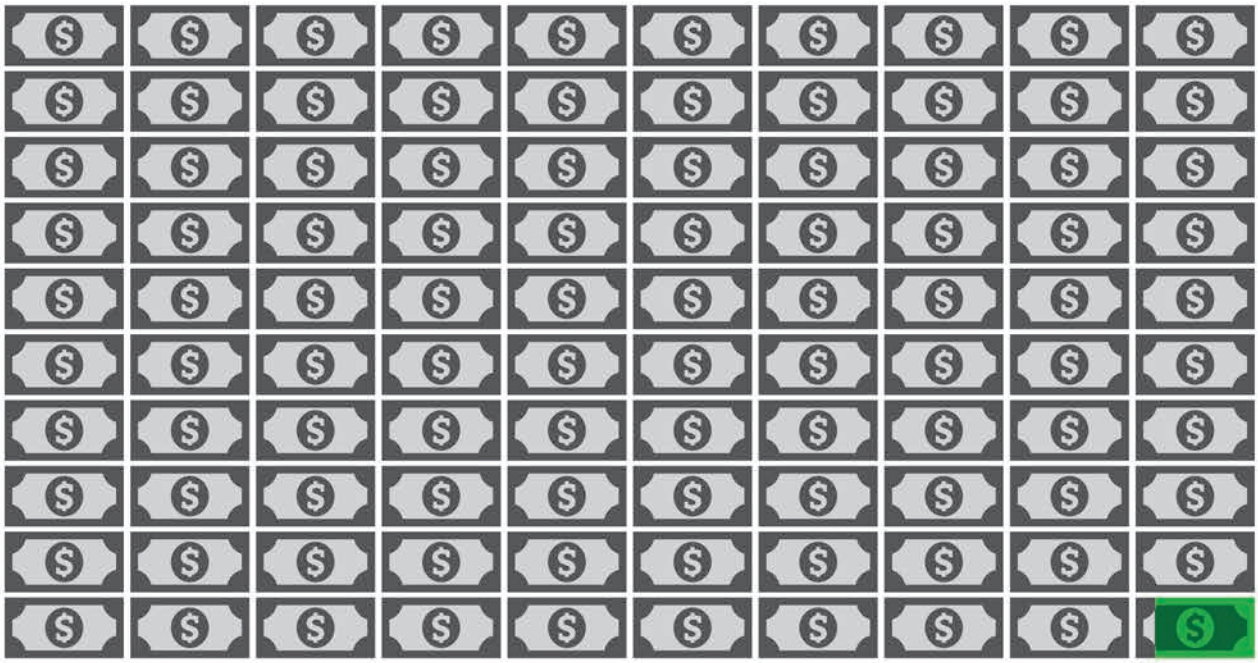
COURTESY OF JESTON MORRIS

At Vanderbilt University, Krystal Tsosie used the BioVU database to longitudinally examine whether genetic determinants contributed to black women's risk of developing uterine fibroids.

COURTESY OF THE UNIVERSITY OF CHICAGO

Rick Kittles has been researching ancestry-informative genetic markers and how they can be utilizes in genomic studies on disease risk and outcomes for more than 20 years.

In **2017**, the budget for all the National Institutes of Health was **$33 billion**, of which **0.8%** went to NIMHD.



These are the NIH centers and institutes that received the **most** and **least** amount of that funding.

TOP 5

- **$5.98 billion** National Cancer Institute
- **$4.72 billion** National Institute of Allergy and Infectious Diseases
- **$3.11 billion** National Heart, Lung and Blood Institute
- **$2. 51 billion** National Institute of General Medical Sciences
- **$1.97 billion** National Institute of Diabetes and Digestive and Kidney Diseases

BOTTOM 5

- **$281 million National Institute on Minority Health and Health Disparities**
- **$146 million** National Institute of Nursing Research
- **$130 million** National Center for Complementary and Integrative Health
- **$77 million** National Institute of Environmental Health Sciences: Interior Appropriation
- **$70 million** Fogarty International Center

COURTESY OF DEBORAH MANOG

One project funded by the University of Hawaii's NIMHD grant is an aquaponics pilot project at the Waimānalo Learning Center to promote healthy diets.

and how best to communicate that information with their doctors. The researchers partner with the Southern Christian Leadership network, a long-established presence in the community, to help disseminate this information and hold conferences across the state.

It can make a difference, for example, if community members know that tumors may be more aggressive in certain populations. "(That affects) how they have that conversation with the physician (and) how they stay on top of the clinical management and care of their own cancer tumors," Yates said.

'A national concern'

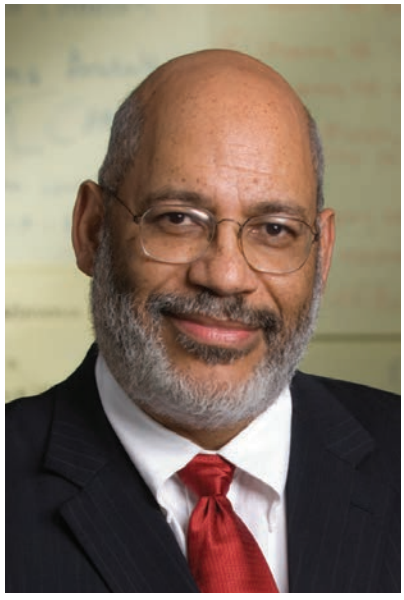
As the demographic makeup of the country changes each year, disparities affect a larger percent of the population, which both the health care system and the researchers who make treatments possible need to reckon with.

In 2017, the NIMHD's annual budget came in 22nd out of the NIH's 27 institutes and centers at $281 million, making up less than 1 percent of the NIH's total budget for the year. At $33.1 billion, the NIH's budget is just 3 percent of the federal government's $1.07 trillion budget for discretionary spending.

Jones, who was the founding director of the Health Disparities, Education, Awareness, Research and Training Consortium, is bullish on addressing health disparities on a societal level.

"Yes, the stock market is going up. Yes, unemployment rates are going down. But how long is that going to last when the population of your nation becomes less healthy as the demographics change and you do not address this population with these demographic health issues?" Jones said. "Ten, 20 years ago, it was a community concern. It was a population concern. But today it's a national concern."

John Arnst (jarnst@asbmb.org) is ASBMB Today's science writer. Follow him on Twitter at twitter.com/arnstjohn.



COURTESY OF LOVELL JONES

Lovell Jones is the founding co-chair of the Intercultural Cancer Council, the nation's largest multicultural health policy group focused on minorities.

ASBMB to host symposium on transcriptional regulation

The RNA polymerase II enzyme transcribes all protein-coding genes and many noncoding RNAs in eukaryotic genomes. Regulation of RNA polymerase II activity requires a host of protein and nucleic acid factors, including genomic DNA itself, which is assembled into chromatin. Precise regulation of RNA polymerase II function, including processing of its RNA transcripts, is essential for cell differentiation and development, and defects in these regulatory mechanisms underlie many human diseases. Recent advances in biochemical, cellular and biophysical methods have allowed for unprecedented insights about RNA polymerase II transcription and its regulation by chromatin and other factors.

Given the importance of RNA polymerase II in biology and human health, the American Society for Biochemistry and Molecular Biology has hosted a biennial symposium on chromatin and RNA polymerase II since 2004. The 2018 symposium, titled "Transcriptional Regulation: Chromatin and RNA Polymerase II," will be held in early October at the Snowbird Ski and Summer Resort, about 35 minutes from the Salt Lake City International Airport. The beautiful and intimate setting of the resort and the conference facilities provide extensive opportunities for scientific discussions and networking.

Attendance at the symposium will be capped at 200 participants, which will include principal investigators, postdoctoral fellows, students, and scientists from the pharmaceutical and biotech industries. Sessions will cover recent findings in RNA polymerase II regulation, including the contributions of noncoding RNAs, chromatin structure and post-translational modifications, and other factors that regulate gene expression. Dr. Eva Nogales of the University of California, Berkeley, will present the keynote address on her work on the structure and function of the RNA polymerase II transcriptional apparatus.

Students and postdoctoral fellows are encouraged to attend and will be eligible for poster awards; the winners will be given an opportunity to present their work as a short talk toward the end of the meeting. We look forward to seeing you in Snowbird for an exciting and enlightening symposium.

Transcriptional Regulation: Chromatin and RNA Polymerase II

Dates: Oct. 4–8
Location: Snowbird Ski and Summer Resort, Snowbird, Utah

Organizers:


ARNDT


REESE


TAATJES

Karen Arndt, University of Pittsburgh
Joseph Reese, Pennsylvania State University
Dylan Taatjes, University of Colorado–Boulder

Deadlines

Abstracts for platform presentations: **March 16**
Abstract submission for short oral presentations: **July 19**
Discounted registration: **Aug. 14**
Poster abstract submission: **Aug. 30**
Symposium registration: **Sept. 12**

The status of all submitted abstracts will be posted on the Meetings page at **asbmb.org**.

From a personal disease to a personal research project

By Eleftherios P. Diamandis

In 1964, I was an energetic 12-year-old living in my homeland, the island of Cyprus. Every August, our village filled with workers from other parts of the island who helped collect carobs, then the most valuable agricultural product of the island. My family owned thousands of trees, and I worked alongside my parents and our hired workers at least 12 hours a day for about a month. Tough labor, but well taken by a healthy young boy.

One evening, after one of those days of hard work, I woke up abruptly in the middle of the night, vomiting hard. I became very ill with a high fever and chills. My parents suspected a bad flu or food poisoning. The next day I went to the family doctor, who found nothing and also thought it was a flu. But the malaise, fever and chills did not subside, and after a week there was no diagnosis or improvement. I was desperate, and my parents thought I was going to die. I was admitted to the local hospital, where chest X-rays revealed two 10-centimeter symmetric masses, one in each lung lobe. There was calcification around them, and the specialist made the diagnosis of Echinococcus granulosus, or EG infection, with cysts in the lungs.

EG is a parasite that infects and lives in the gut of its definitive host, usually a dog or other carnivore. Intermediate hosts include farm animals, such as sheep and goats. Humans and sheep are infected through ingestion of unwashed vegetables or other products contaminated with eggs of the parasite from dogs' stool or through direct contact. After infection, the parasites form cysts containing larvae, usually in the liver and lungs of humans. Patients may be asymptomatic for years but get sick when a cyst ruptures or mechanically interferes with the organs. This disease was endemic in Cyprus in the 1960s and '70s, largely because household sheep were sacrificed in unauthorised places and their EG-infected organs, such as lungs and livers, were thrown to stray dogs, which were then infected. This is the EG cycle: from sheep to dogs to humans. Cyprus eradicated the disease in the 1980s by eliminating stray dogs and mandating animals be sacrificed only in government-controlled slaughterhouses.

COURTESY OF ELEFTHERIOS P. DIAMANDIS

Eleftherios P. Diamandis researched the effects of a parasitic infection he suffered during his boyhood.

Instead of going back to school that September, I had an operation to remove one of the cysts, which had partially ruptured and caused the anaphylactic reaction. The surgery included removal of some ribs and part of the lung. The same operation was repeated on the other lung a year later. These big operations hampered my physical development and my athletic performance. People at the beach were curious about big scars on my chest, but I did not look back. The EG chapter seemed closed.

I went to the University of Illinois at Urbana-Champaign in 1981 for a brief postdoc training. The compulsory medical screen included chest and abdominal X-rays. I was a bit worried when the university medical officer asked to discuss my results. They had found a big, calcified mass in the liver and thought it was a tumor. I reassured them it was another Echinococcus cyst that I knew about. My doctors suggested it should not be removed since the larvae, after all these years, were likely dead. As they put it, it was a garbage basket in my liver that was better left alone.

I did not think much about my disease for 40 years, but about five years ago, the emergence of immunotherapy for cancer gave me the idea of examining the possible relationship between EG infection and cancer. Based on existing literature, the expectation was that a chronic infection could protect against cancer due to the intensified immune surveillance. In published examples, some parasitic and other infectious diseases confer protection against cancer development. Also, a Turkish group

had hinted that patients who have surgery for EG are never found to have concomitant cancer.

I chose to do this research for the following reasons:

I was curious whether my old infection was increasing or decreasing my cancer risk. This information could be useful to others and lead to some practical benefits, such as vaccination against EG antigens to reduce cancer risk.

COURTESY OF ELEFTHERIOS P. DIAMANDIS

The author, second from left, looking at the camera, grew up on the island of Cyprus, where at age 12 he contracted a parasitic infection that caused large cysts to develop in his lungs and liver. Cyprus eradicated the disease in the 1980s.

It was a good time to do the study; 40 years had elapsed since my infection (enough for cancer development) and, as mentioned, the infection became extinct in Cyprus after 1980.

I found a retired collaborator in Cyprus who worked with the Ministry of Health in the 1960s and had records on who developed EG infection between 1960 and 1980, along with their contact info. At that time, there were no electronic records or e-mails, Tweeter or Facebook, or even personal phones.

My plan included placing a postdoc in Cyprus who was responsible for the whole project. The postdoc recruited 6 to 8 volunteers to help with the interviews. Each patient had to be located and interviewed at his or her home to verify the EG infection and the patient's current state of health, including diagnosis of cancer. At the same time, we recruited control subjects (age and gender-matched siblings or neighbors) for comparison. Many of the patients were dead, and we had to interview their relatives.

I won't detail all the difficulties we encountered, but some lessons are listed below. All in all, this study was a logistical and financial nightmare.

After three years of hard work, we ended up recruiting 249 patients and 753 controls (we hoped for a lot more but could not find them). Our study was underpowered, especially when we broke down the cancers according to organs affected. Our results were equivocal, and we ended up publishing them in a small journal as preliminary evidence. The reviewers killed us with criticisms, mostly justified. Our overall finding was an approximate 25 percent increase in cancer risk in EG-infected patients.

This exercise taught me some tough (but obvious to the specialist) lessons:

• Sentimentally motivated projects based on subjective criteria may cost a lot and carry increased risks of failure.

• Epidemiological studies linking diseases with candidate causative factors need to be planned carefully and powered appropriately. Better not to do an underpowered study than to start a study and then realize that recruitment is much smaller than expected.

• There may be a myriad of hidden biases with such studies, which could lead to wrong conclusions.

In the end, I learned that I should stick to what I do best and leave the epidemiological studies to the experts. Our results showed the exact opposite of my original hypothesis. My dream of finding a condition (such as EG infection) that prevents cancer development was shattered, and my anxiety about developing cancer in the future not only did not decrease but increased by about 25 percent.

I paid dearly for my sentimentally motivated mistake.

Eleftherios P. Diamandis (eleftherios.diamandis@sinaihealthsystem.ca) is the chair in prostate cancer biomarkers and head of clinical biochemistry, Mount Sinai Hospital, and head of the division of clinical biochemistry in the department of laboratory medicine and pathobiology, University of Toronto.

ESSAY

Raising a rainbow of scientists

Situating biochemistry and molecular biology in their social context to retain students of color

By Ashley Warfield–Oyirifi

I studied biochemistry as an undergraduate at the University of Missouri. As a freshman, I was immediately interested in the chemical processes that make biology go. However, as one of the only black students among more than 200 biochemistry undergrads, I found the culture within this major to be isolating. The concepts and applications presented never seemed to touch my person or my experience, and I failed to understand how a discipline that I found so profound and intriguing also felt distant and detaching. I perceived an excitement and sense of fulfillment among my white biochemistry peers that was paralleled in black peers only if they were enrolled in majors like social work, psychology or sometimes business.

Of course, I cannot assert that none of my white biochemistry peers longed for more meaning from their coursework or that all the biochemistry students of color sensed a gap between our academic and real lives. However, I can mention anecdotally that most black students feel responsibility and satisfaction in connecting their higher education to their loved ones or communities. Some of our relatives discuss academic topics, but many of us have living grandparents who, despite academic prowess, could not lawfully or reasonably attend the institutions we graduated from. Black and other underrepresented biochemistry students of color often want to take our university learning home to such talented yet disenfranchised relatives in a meaningful way. To do so, biochemistry must matter not just in a cell, organism or clinic but also at a dinner table and in life.

Although an understanding of how my biochemistry studies mattered around the dinner table eluded me, the work remained intriguing, and I completed my undergraduate studies in biochemistry. Like many in my cohort, I easily secured employment after graduation, working in analytical chemistry. The work was well paid and interesting, and this career seemed like a mark of success. However, I soon found myself pondering whether my career had any meaning. It had to matter beyond investigating molecular structures of compounds and active sites of proteins and helping my company generate revenue. Of what societal utility was the work I was doing? "Maybe, I'll find the answer in graduate school," I thought.

I didn't know it then, but I was not alone. Jeremy, another MU biochemistry graduate, recently said, after working five years in oil and polymer science industries, "I look around and think 'Does anybody care about this (work) beyond the economic value?' … When I see things around me, I try to consider it at the molecular level. I don't think other people are doing that. We are just making money." He paused to think. "Will graduate school make this mean more? Will I be able to do more meaningful stuff?"

An answer in anthropology

I could not answer Jeremy's question. Graduate school helped me find more meaning in biochemistry, but indirectly. I found the answer in an elective course taught by an anthropologist where we faced the question, "Is race a biological reality or a socially constructed phenomenon?" My classmates were students of many disciplines, from archeology to education. I was the resident life-scientist. As such, I was impelled to contribute a biochemical rationale to the class inquiry. In my reflection, I shared: "If we want to utilize an approach where we compare biopolymers and small molecules to elucidate differences between human populations, then a robust method would be to compare the full set of molecules that mediate DNA expression and are mediated by DNA expression. This means conducting a comparative analysis of not only the genome, as has been done in previous attempts to study differences among races. We must comprehensively profile the transcriptome, proteome, and metabolome. Of the 99.9 percent similarity among genomes of varying races, how much similarity and difference exists in genome expression and why?"

My thinking was drawn from a previous semester's graduate biochemistry course in which I studied and presented research findings on initiation complex assembly. The research suggested that euchromatic regions of DNA were coding regions, based on the researchers' observation of initiation complex assembly throughout those regions. I noted one major limitation: The researchers did not demonstrate gene expression. Why stop at the assembly of the complex? Similarly, for comparative analysis of genomes to determine racial difference, it seemed necessary to look beyond the code toward global expression patterns and their environmental influences. After I shared this input in class, my classmates and professor in the course made valuable contributions through the lenses of their disciplines, completing the discussion. Seemingly, they would not have considered suggesting a more comprehensive strategy for investigating racial difference. Similarly, I could not have begun to unpack, as my peers did, the implications that lie within concluding that biological differences existed or failed to exist among races.

COURTESY OF ASHLEY WARFIELD-OYIRIFI

Ashley Warfield-Oyirifi does lab work at the University of Illinois, Urbana–Champaign, where she is studying how dietary compounds influence the expression, activation and signaling of molecules that regulate cancer metastasis.

For the first time, primary literature in biochemistry mattered to me beyond the methods and molecular findings. Beyond the potential for clinical applications. The literature spoke to my lived experience, my existence. My identity and all our identities as humans. It was interesting. It was challenging. It was engaging to consider the societal implications of molecules. But it was not long before the celebration of how biochemistry and molecular biology could be used to chime in on questions about culture and society turned to lamentation. "Why have I not been prompted or challenged to understand lived experiences through biochemistry before?" I wondered.

Redefining diversity

Why do U.S. approaches to education imbue us with artificial notions of a dichotomy between laboratory science and lived experiences? I began spending late nights and long days pondering this question. This false dichotomy is perplexing, because the array of biomedical, psychosocial and sociopolitical dimensions that mediate (or are mediated by) life and physical sciences is immense and can serve as rich educational material. I call it pedagogical capital. This capital often remains untapped in conventional university-level instruction of the hard sciences. As a result, many students with capacities and goals to be adept scientists accede to an illusion of choice between studies and careers that are socially engaging and those that are scientifically rigorous. As pbs.org reported in the February 2016 story "African-Americans overrepresented among low-paying college majors," the common practice of teaching science, technology, engineering and mathematics, or STEM, subjects without regard for social implications ultimately snowballs to the displacement of students of color from sciences and often into lower paid service-oriented careers.

How do we undo this? A true and systematic commitment to diversity in biochemistry and molecular biology means recognizing the inseparable relationship between molecular interactions and lived experiences. To accomplish meaningful diversity in biochemistry, we will need to redefine diversity and understand it as a variation in the types and applications of content offered to students rather than varying shades of students in lecture halls. We must extend the reach of course content beyond applications of the scientific moment, such as the current preoccupation with precision medicine, rather than relying on admissions offices' special-interest recruitment strategies. It is up

to university educators to train diverse students to contemplate diverse (yet robust and sustainable) solutions to a diverse and limitless set of biochemistry and molecular biology questions.

Steps to take

Here are four steps to attract, serve and retain heterogeneous populations of students through your instruction.

1. Become a learner. Seek out scholarly reading on societal implications of molecules.

Literature from the history and philosophy of science and medicine is a stimulating place to start looking for methodically gathered and recorded information about scientific knowledge production. You can gain great insight for courses by understanding the intellectual and social history that led to the modes of scientific investigation we practice. You'll find suggested reading at the end of this essay.

Strategies: When reading, do not make scientist status or scientism a condition for deep engagement. Zoom out and think about how to integrate information into a problem set or favorite course lecture rather than looking for sophisticated explanations or appreciation for technical details.

2. Recenter instruction to include inquiry and application alongside concepts and theories.

A groundbreaking text for my thinking was political anthropologist Faye Harrison's "Outsider Within: Reworking Anthropology in the Global Age." This book and its approaches serve as a model for reconstructing disciplines to extend the reach of inquiries, methods and findings. In chapter 2, "Unburying theory, repositioning practice," Harrison examines how her discipline celebrates theoretical knowledge at the expense of acknowledging how practice can inform theory, create knowledge and advance the discipline.

A similar unbalanced commitment to concepts and theories exists in biochemistry education and calls us to reposition praxis as a central value. To introduce variation in biochemistry content, we must stop using lectures solely to present biochemical equations, concepts and theories. This approach tends to be misaligned with best practices suggested by scholars of instructional design and educational psychology, which evidences contextual, connected, active learning as highly effective. A 2014 article in the Proceedings of the National Academy of Sciences, "Active learning increases student performance in science, engineering, and mathematics," calls for the use of active learning to increase STEM undergraduate degree completion. Interrogating social applications of biochemistry provides invaluable content for the type of synthesis, analysis and evaluation that defines active learning. In a 2014 article in the International Journal of Science Education, Derek Hodson points out the risk of conflating learning science with learning to address socio-scientific issues. This distinction helps to emphasize that we want to integrate social inquiries of molecules into current material rather than make substitutions.

Strategies: Revamp a syllabus to include one social situation for every 3 to 5 lecture topics. Ask yourself, "Can a student extrapolate why this rigorous course might be important to a grandparent, general citizen or legislator?" Read about adult-learning theories and audit a course in science education to retrain yourself as a multimodal, thought-provoking educator.

3. Share what you've learned. Regularly discuss how molecular events have societal implications.

Scientific spaces at universities can serve as a vacuum, separating academic content from lived realities. Classroom practices must eliminate this dialysis effect that filters students from their societal status each time they enter a biochemistry class. Commit space in a syllabus for students to choose how they apply and explore class content. Some may choose medical applications and others socioeconomic issues. Be an advocate and model for accurately exploring the biochemistry of anything. Be careful. This advocacy may force you to rethink your own research questions and the interests they serve.

Strategies: Assign students to evaluate the biochemistry of current events. Or, in the interest of time and scale, prepare a five-minute weekly segment discussing information you've read from step 1 (above) and how it intersects with molecular concepts.

4. Be patient and careful and anticipate the benefits

Recentering thinking and teaching easily could become a life's work. It is a slow and imperfect journey. Patience is key to the cycles of adjusting course strategies, responding to feedback, and adapting to social moments and cohorts of students. This kind of teaching requires extra time and lacks documentability (for tenure promotion), but immense rewards come at no expense to student learning or course rigor. Look for the following benefits and adjust until you notice them.

Rewards: Students develop as thinkers and problem-solvers rather than learners who know discrete biochemical concepts with no guaranteed ability to apply them. Professors develop their instructional practices, develop a relevant and responsible pedagogy, and challenge many types of learners. There is great potential for a lifelong sense of professional fulfillment from coupling biochemistry instruction with civic engagement to increase learners' critical abilities. Further satisfaction is likely from seeing the outcomes of these new thinkers' work and the impact of recruiting

Reading list

Thomas Kuhn, "The Structure of Scientific Revolutions," University of Chicago Press (1962).

"Kuhn challenged the then prevailing view of progress in 'normal science'. Normal scientific progress was viewed as 'development-by-accumulation' of accepted facts and theories. Kuhn argued for an episodic model in which periods of such conceptual continuity in normal science were interrupted by periods of revolutionary science. The discovery of 'anomalies' during revolutions in science leads to new paradigms."

— en.wikipedia.org/wiki/The_Structure_of_Scientific_Revolutions

P. Freire, "Pedagogy of the Oppressed," Herder and Herder Press (1970).

"Freire outlines a theory of oppression and the source of liberation. In Freire's view, the key to liberation is the awakening of critical awareness and the thinking process in the individual."

— bookrags.com

Alondra Nelson, "The Social Life of DNA: Race, Reparations, and Reconciliation after the Genome," Beacon Press (2016).

"We know DNA is a master key that unlocks medical and forensic secrets, but its genealogical life is both revelatory and endlessly fascinating … Nelson incisively shows that DNA is a portal to the past that yields insight for the present and future, shining a light on social traumas and historical injustices that still resonate today."

— beacon.org/The-Social-Life-of-DNA-P1140.aspx

Anthony Ryan Hatch, "Blood Sugar: Racial Pharmacology and Food Justice in Black America," University of Minnesota Press (2016).

"How contemporary biomedicine has shaped race and racism as America's health disparities increase … Hatch argues that the advent of metabolic syndrome … (repackages) race within biomedical and genomic research."

— upress.umn.edu/book-division/books/blood-sugar

Author's note:

Kuhn and Freire are universal texts. The other two suggestions are geared toward interests at the intersections of medicine, race, food and science. However, whatever your research interests, there are texts explaining how your discipline may play out in society or how it evolved into its current form. These texts can inform and inspire teaching strategies, course material and students' thinking.

Share your story

Have you worked to diversify classroom content and find social meaning in basic science? If so, we want to share your story. Please send us examples of ways that you situate biochemistry and molecular biology in a social context. Send an email to asbmbtoday@asbmb.org.

and retaining students with varying backgrounds, interests and goals.

Let's reimagine a biochemistry that attracts and retains the best students of all backgrounds, without a systematic exclusion of those interested in panning beyond the protein.

My approach

Although I have not personally reconciled the disjunction between biochemistry and life science instruction, I have found satisfaction in situated science (adapted from Donna Haraway's term "situated knowledges") — investigations of molecular events coupled with the experiences and culture where these events occur or are promoted. I am completing my Ph.D. studies in an applied field, nutrition, where I am studying how dietary compounds influence the expression, activation and signaling of molecules that regulate cancer metastasis. From my findings, I am prepared to coordinate a community-based curriculum that will determine if awareness of the biochemistry behind eating can influence chemoprotective dietary habits in cancer survivors. Together, these studies can speak to health disparity in cancer mortality by highlighting options other than sometimes inaccessible clinic-based preventative care. I appreciate the combined social relevance and scientific rigor of this nutrition-based project.

However, I envision a day when students of biochemistry are not driven to declare an alternative course of study to connect their biochemical investigation to its societal value. I believe that with a commitment to diversifying content rather than only students, that day will come.

Ashley Warfield–Oyirifi (warfild2@illinois.edu) is a Ph.D. student at the University of Illinois, Urbana-Champaign. Having navigated the cultures of life and physical science, blackness and wellness, she is passionate about conducting scientific investigations that are situated in a larger societal context.

From back-porch evolution to learning slang at the bench

Shantá D. Hinton is an associate professor of biology at the College of William and Mary in Williamsburg, Virginia. Here she describes an early conversation with her grandfather about snakes and frogs that inspired her interest in science, explains how she turns her failures into motivation, and shares the values that have served her well as a mentee and now a mentor.

Tell us about your current career position.

After a year-long sabbatical, I recently returned to the biology department at the College of William and Mary, a primarily undergraduate research university that offers students the best of both worlds. It blends the one-on-one faculty contact and mentoring associated with a small school with the faculty expertise and research opportunities typical of research-intensive institutions. It also offers me the best of both worlds: to be a scholar at the bench while engaging novices in research experiences that often produce educated scientists. My research investigates the role of a particular protein we initially thought was just a "dead" enzyme as a regulator in signal transduction cascades (cellular communication).

What key experiences and decisions helped you reach this position?

This is a complicated question for me. My matriculation as a student at a primarily majority institution, or PMI, the University at North Carolina at Chapel Hill, and a historically black college or university, or HBCU, Howard University, as well as serving as faculty at both an HBCU and a PMI, provided opportunities to develop strengths that allowed me to reach my current position. If pressed to point out a key decision and experience that allowed me to obtain tenure at the College of William and Mary, it would be choosing my postdoctoral position at Cold Spring Harbor Laboratory. This experience challenged me and shaped my career in the best way. I trained as a cell and developmental biologist as a doctoral student; I was thrust into a hardcore biochemical lab as a postdoctoral fellow. And the most important thing happened to me during a lab meeting. My PI said, "This is my standard for a journal publication, nothing below this. Each of you should aim for this or higher to publish from this lab." I smiled inside because for the first time expectations for me (beyond my family) at a PMI were the same as for any other gender, nationality, ethnicity, etc. No excuses. It was time to complete the task and soar.

COURTESY OF SHANTÁ D. HINTON

Shantá D. Hinton, an associate professor at the College of William and Mary, says her postdoctoral position in a "hardcore biochemical lab" at Cold Spring Harbor Laboratory challenged her and shaped her career.

How did you first become interested in science?

My first interest in science came through my late maternal grandfather, Jesse Hinton Sr. Sitting on the steps or working in the garden with my cousin and me when we were children, he explained the concept of evolution of frogs and snakes. In particular, I was fascinated with the concept that snakes had legs but supposedly lost them through evolution. Because I am afraid of snakes and would not touch them (except helping a late dear friend who was a herpetologist), time or books would have to prove grandpa's story. Of course, I was absolutely delighted by the 2015 article in Science, "A four-legged snake from the Early Cretaceous of Gondwana." Grandpa, who completed the 10th grade, had great wisdom; his story was confirmed, and it brought back

memories of my introduction to the boundless wonders of science.

Were there times when you failed at something you felt was critical to your path? If so, how did you regroup and get back on track?

One critical failure happened in the social sciences. I failed my very first oral exam in my 10th-grade history course. That class still ranks as the most terrifying, engaging and invigorating experience in all my academic matriculation. For the first five minutes each day, the teacher was a drill sergeant, orally quizzing students on previously taught material, with only 15 seconds to understand and address the question. The timer buzzed, and I heard, "Hinton, you're out. Your grade is a 50." No one likes to be embarrassed. So I spent hours learning the material and creating questions that I might be asked to ensure the buzz was never associated with my name again. All my fellow students did the same, creating such an enjoyable class that we ran from the cafeteria to attend it. We competed for the best time in answering a question. After my initial failure, I learned to read and study, to synthesize information to formulate new questions and/or hypotheses — which is so critical as a scientist. I also learned that failing is a necessary part of the journey to success. Now, whenever I experience failure, the next day I start executing an action plan to develop the failure into a success. When this is not possible, I release the failure and move forward. In essence, I use my failures as a platform to set and achieve higher goals. I am sure this is a relief to those who endured the venting about my early failures, including my family, best friend and mentors. In addition, I have a rule never to take a failure as a personal assault, even when it may be.

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This is challenging, but it is my rule, so I have to work through it. Lastly, my family taught me at a young age that the best way to defeat failure or an enemy is to be successful, which means you have to move forward and progress. I am the sole person responsible for my actions.

What advice would you give to young persons from underrepresented backgrounds who want to pursue a career in science similar to yours?

Believe in yourself beyond your knowledge and skills; envision yourself beyond your present status. There will be moments where you are the only one who believes in you. Pursue science because of a genuine interest, while being very careful of the appearance that it is a benefit or an advantage for someone like you in the sciences. Align yourself with mentors who will tell you the truth, even if it may alter (hopefully, only for a brief moment) the relationship. Learn your weaknesses; do not be afraid to share with your mentors, and ask their help to change these weaknesses into strengths. Understand that paying it forward doesn't mean you are obligated to carry everything on your back or alone. Also, don't be afraid to evolve. Lastly, stay focused on your goals while being flexible, constantly reminding yourself why you like science, and enjoy the scientific process.

What are your hobbies?

I am an avid CrossFitter, which helps with stress. In addition, I love to attend comedy shows and plays, especially on Broadway. Laughter and music always heal my soul and help me cope with a failure.

What was the last book you read?

"Hidden Figures" by Margot Lee Shetterly. Coincidentally, I stopped reading "Something Must Be Done About Prince Edward County: A Family, a Virginia Town, a Civil Rights Battle" by Kristin Green to read "Hidden Figures" for an event at my institution. Therefore, I appreciated when "Hidden Figures" referred to events in Prince Edward County.

Do you have any heroes, heroines, mentors or role models? If so, describe how they influenced you.

My parents (Larry D. Petway and Mamie L. Hinton) and maternal grandparents (the late Jesse Hinton Sr. and the late Mamie R. Hinton). As a first-generation college student, it was important for me to have love and structure. These heroes provided more than that; they made important sacrifices and preached the value of an education. They made a conscious decision (along with my aunts and uncles, who decided not to attend college) to invest in me becoming the first in the family to graduate from college. Although they didn't under-

stand the process, they worked hard as a team and spoke it into existence. I am grateful that they all lived to see me obtain a Ph.D. My research program is based on the love, structure, honesty and directness that my heroes provided for me; this model has served me well as a mentor.

What is it that keeps you working hard every day?

My curiosity, always learning and choosing the correct discipline; I like pursuing edgy projects. I am fortunate to investigate a field of enzymes (protein tyrosine phosphatases) that will celebrate its 30th anniversary this year. More importantly, I am absolutely thrilled to investigate a unique catalytically inactive member (MK-STYX) of this field whose prototype's name alludes to the river Styx in Greek mythology, the river of the dead. I loved reading Greek mythology as a teenager and still watch movies pertaining to Greek mythology. It is an honor to introduce undergraduates and master's students to the joys of research and co-author manuscripts with them within in a field that is in its infancy. On my worst day, knowing that I can walk into my lab full of vibrant, intelligent, creative and eager students who may be playing music (while being productive) or introducing me to new slang such as "rekt" (wrecked or destroyed) while keeping score of their rekt assailants on the white board, will make me smile. The joy that keeps me going is that they develop into these amazing young scientists, the majority of whom enter doctoral programs. They are the ones who are cited as first authors on the papers in the field; that is an amazing legacy for us. Lastly, I am still working alongside them. I haven't had to sacrifice my love of the bench, at least not yet. This has truly enriched my students' lives and my life.

About the Research Spotlight

The American Society for Biochemistry and Molecular Biology's Research Spotlight highlights distinguished biomolecular and biomedical scientists from diverse backgrounds as a way to inspire up-and-coming scientists to pursue careers in the molecular life sciences. Eligible candidates include Ph.D. students, postdoctoral fellows, and new or established faculty and researchers. To nominate a colleague for this feature, contact education@asbmb.org.

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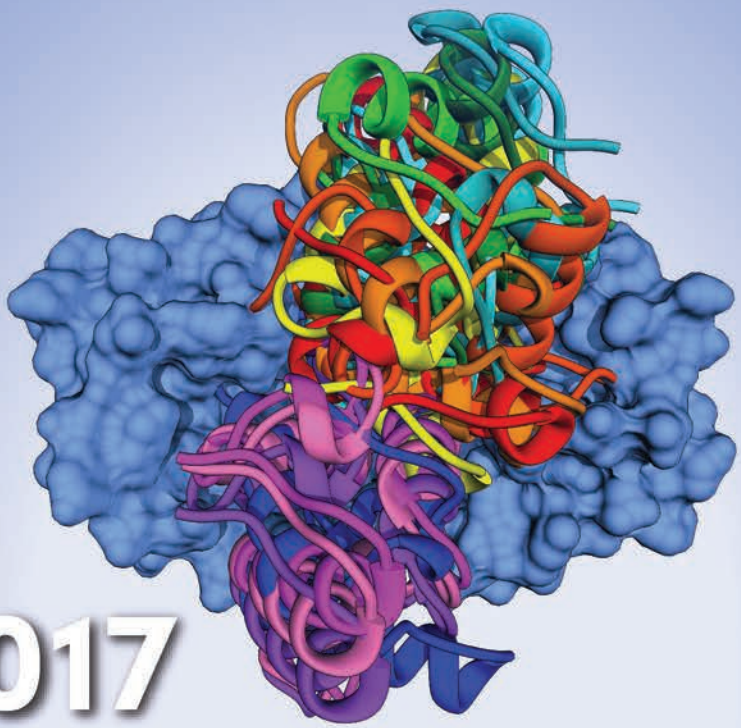

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