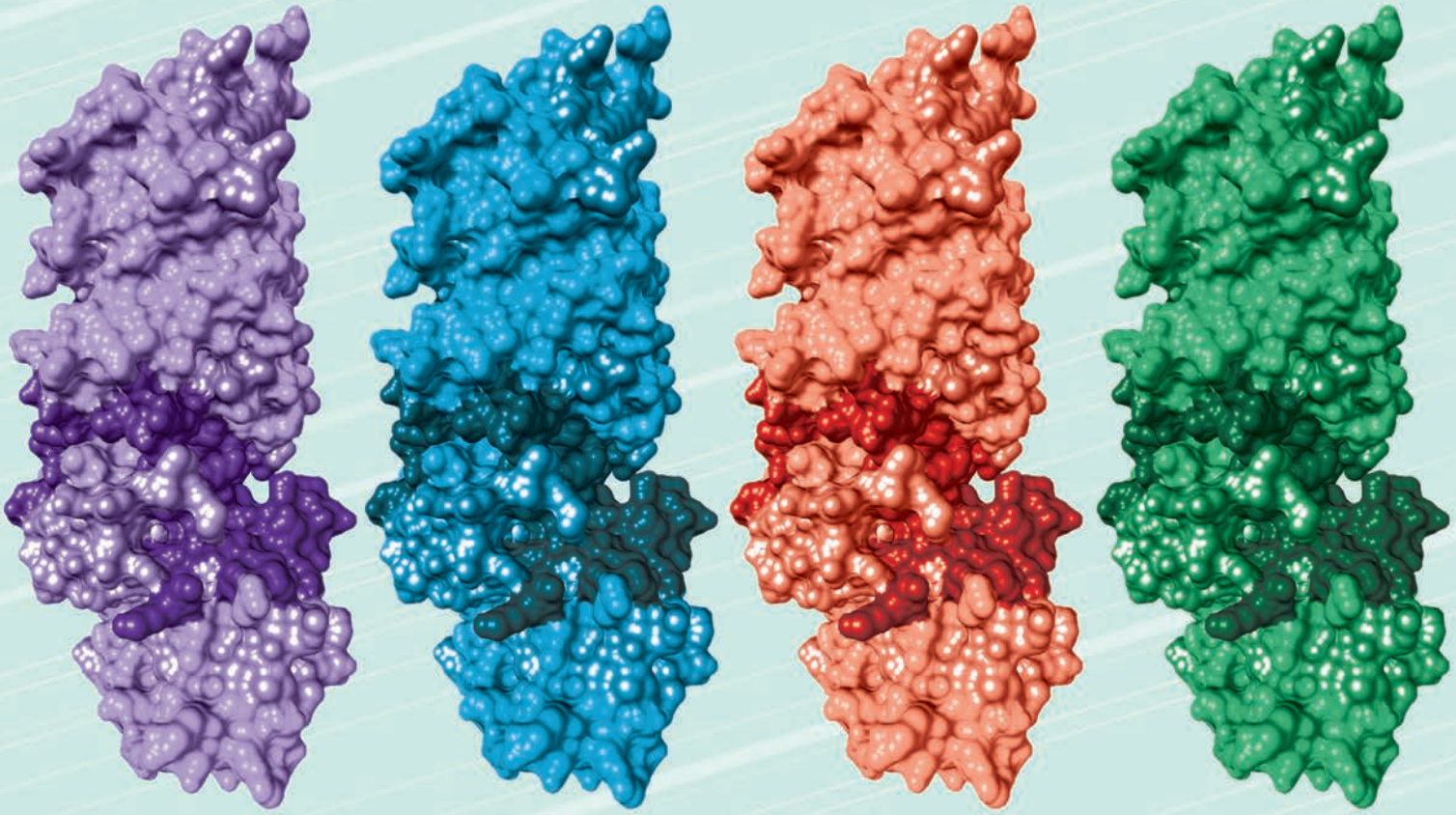
ASBMB today

Vol. 12 No. 9 October 2013



'CLOSE TO A MIRACLE'

Researchers are debating the origins of proteins

American Society for Biochemistry and Molecular Biology

OPEN LETTERS

An open letter to our readers who have something to say but need a place (and maybe even permission) to say it

Dear Reader,

This is your magazine. Seriously, it is. You support it when you renew your ASBMB dues, share its contents with your friends and colleagues, crack it open on the train and even when you use it as a coaster for your coffee mug. It's yours.

Over the past two years, we've worked hard to get more of *you* in these pages. We've asked for your science-inspired poems (thanks for humoring me), your unique perspectives (keep 'em coming) and, most recently, your inspiring stories of failure and triumph (the "Derailed but Undeterred" series). Your contributions have transformed this magazine into one with greater depth, unique storytelling and diversity of ideas.

For our next essay series, to be published in 2014, we want your letters. Now, yes, we always welcome your letters to the editor, but this time we're looking for open letters — ones addressed to someone or something (keep reading if "something" sounds odd) but intended for public dissemination.

Perhaps you, like our in-house science writer, Rajendrani Mukhopadhyay, once had a faculty member say just the right thing when you were having a nervous breakdown during your Ph.D. qualifying exams, and you want to thank that person publicly. Perhaps there's a technique or an instrument that's been the bane of your existence, and you need to vent your frustrations and tell it exactly what you think of it. You might even have sent a letter to someone years ago that now deserves wider distribution.

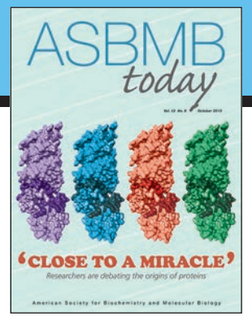
To have your open letter considered for publication, do the following:

- Send us your letter in a Word document or in the body of your email. Letters with fewer than 1,000 words are preferred, but longer letters won't be rejected outright.
- Include a brief author biography of 100 words or fewer.
- Send your letter to asbmbtoday@asbmb.org by Dec. 31, 2013.

I look forward to reading your epistolary masterpiece!

Sincerely,
Angela Hopp
Editor, ASBMB Today

contents



OCTOBER 2013

On the cover: ASBMB Today senior science writer Rajendrani Mukhopadhyay writes about what we know about the origins of proteins. 12

MANY THANKS TO TIMOTHY COLLIER AND RON BOSE AT THE WASHINGTON UNIVERSITY SCHOOL OF MEDICINE IN ST. LOUIS FOR THE COVER IMAGE.

DERAILED *but* UNDETERRED

F. Peter Guengerich of Vanderbilt University, an associate editor for the Journal of Biological Chemistry, writes about how working on the family farm made him a disciplined scientist. 10

John Exton, an associate editor for the Journal of Biological Chemistry, talks about his book about the lab of Nobel laureates Carl and Gerty Cori. 14

IMAGE COURTESY OF MOUNT SINAI HOSPITAL

Tony Pawson (1952-2013) is remembered in this Retrospective by John M. Kyriakis. 6

Regina Stevens–Truss provides a status update for the HOPES seed-grants program, which is intended to enhance STEM K–12 education through partnerships and hands-on projects. 36

ASBMB today

A monthly publication of
The American Society for
Biochemistry and Molecular Biology

www.asbmb.org/asbmbtoday

president's message

Listing unsolved problems

BY JEREMY BERG

When the great mathematical scientist George Dantzig was a first-year graduate student at the University of California, Berkeley, in the 1940s, he missed a lecture one day and went late to copy the homework problems that the professor had put up on the board at the end of class. He thought the two problems that day were harder than previous ones, but he pushed on and within a few weeks turned in his solutions. Six weeks later, the professor showed up at Dantzig's apartment, wanting him to read the introduction of a paper he had written so that he could get the manuscript describing Dantzig's solution to one of the problems submitted for publication. Dantzig was confused. It turned out that the lecture that Dantzig had missed had been on important unsolved problems in statistics. After completing his coursework, he went to talk to the professor about a dissertation topic. The professor indicated that the two solutions to the previously unsolved problems were more than adequate. Dantzig polished his solutions a bit and got his degree (1).

Having such lists written down can be interesting as a tool for assessing progress over the years. How much progress has there been on the questions from the previous edition? Are there entirely new questions that could not even have been articulated earlier?

As I noted last month (2), my coauthors and I are in the process of revising our textbook, "Biochemistry." In addition to taking stock of fields that have made tremendous progress since the previous edition, I also try to enumerate some of the most interesting open questions in biochemistry, at least for myself and sometimes for inclusion in the book. These questions can be fundamental or applied, narrow or broad. Having such lists written down can be interesting as a tool for assessing progress over the years. How much progress has there been on the questions from the previous edition? Are there entirely new questions that could not even have been articulated earlier? Let me list three of the questions that have been intriguing me at this point.

The first is one of the great questions in all of human history: **What is the origin of life?** Over time, attempts to address this question through studies of the abiotic synthesis of amino acids and nucleic-acid precursors, enzyme-free replication of nucleic acids, and the spontaneous formation and reproduction of membrane-bound, cell-like structures have revealed insights and provided constraints limiting possible origins, but many questions remain. Of course, a wide range of evidence indicates that all known life shares a common ancestor, and this sometimes is interpreted to mean that life originated only once. However, it is possible that the origination of structures with many of the properties of living things, while undoubtedly a rare event, could have occurred more than once, but that life from other origins left no known traces and could not compete with our branch once it was established. In any case, further studies of the origin of life certainly will yield new insights into chemistry and biochemistry and — who knows — may lead to publications of which we are all likely to remember both the results and where we were when we first heard about them.

The second question involves the relevance of the differences between the dilute and relatively simple buffer solutions that biochemists are fond of studying and more accurate representations of the crowded and partially organized environments inside cells. **Under what circumstances does extrapolating from results from simple solutions yield significantly incorrect conclusions about the biochemistry inside cells?** For some enzyme systems, particularly those with unstable or highly diffusible intermediates, substrate channeling, where the products of one active site are channeled directly into another active site without being released into solution, has been demonstrated. However, demonstration of such channeling can be quite challenging, and it has not been investigated for most systems. For many signal-transduction systems, complexes of proteins are assembled through specific yet transient and relatively loose interactions. These complexes both store information about signals and function in signal amplification and other types of modulation. Simple biochemical models that assume rapid diffusion and mixing almost certainly are wrong in most cases, but the circumstances under which the deviations between these models and reality are significant remain to be explored fully, and more sophisticated models need to be developed and tested.

My third question is this: **What is the molecular basis of memory?** Studies from neuroscience have revealed that the storage of memory is intimately connected to the number and strengths of synapses (connections) between neurons. A number of key molecules have been identified, including the neurotransmitter serotonin, the second messenger cyclic AMP (cAMP), cAMP-dependent protein kinase and the transcription factor CREB (cAMP response element binding protein). Nonetheless, a clear articulation of how memories are stored and recalled remains elusive. A very recent paper (3) has implicated another molecule, in this case, a histone-binding protein, to the age-related loss of memory acuity. Are memories stored in the form of specific chromatin structures that, in turn, control synaptic strengths? It may be that our understanding of the molecular basis of memory will continue to evolve, but new discoveries may result in more dramatic insights. Continued progress may result in intellectually satisfying understanding but also may generate new translational opportunities. As I continue to age, I am sure that if simple treatments were available that would restore my memory to the effortless recall of my youth I would be near the front of the line.

Relatively early in my tenure as director of the National Institute of General Medical Sciences, I organized an effort for the NIGMS staff to develop a set of top-10 lists of important unsolved problems. You may be comforted to know that this concept was met with a substantial amount of resistance, as staff members were concerned that these "government bureaucrat"-generated lists were going to be used in a heavy-handed manner to drive the agenda for NIGMS-supported science, an affront to the strong appreciation of the value of investigator-initiated approaches that so permeates the institute. Nonetheless, I think we found it to be a stimulating exercise that promoted understanding of the perspectives of different individuals and groups within the institute. In that same spirit, I would propose that interested members of the American Society for Biochemistry and Molecular Biology and others contribute their ideas. Please send your question along with a few sentences about why you think it is interesting or important to jberg@pitt.edu or post it as a comment to this column. With a robust response, the results may be useful in helping the society move forward and in making our case regarding the importance of biochemistry and molecular biology to the public and to Congress.

Jeremy Berg (jberg@pitt.edu) is the associate senior vice-chancellor for science strategy and planning in the health sciences and a professor in the computational and systems biology department at the University of Pittsburgh.

REFERENCES

1. http://www.snopes.com/college/homework/unsolvable.asp
2. http://www.asbmb.org/asbmbtoday/asbmbtoday_article.aspx?id=48597
3. Pavlopoulos, E. et al. *Sci. Transl. Med.* **200**, 200ra115 (2013).

Have you taken the challenge?

BY SHAILA KOTADIA

With sequestration resulting in across-the-board budget cuts, scientists are facing difficult times. To reverse this reckless action and for the U.S. to continue to be a leader in scientific progress, Congress needs to know the importance of government funding for basic research. Thus, the American Society for Biochemistry and Molecular Biology issued the 100 Meetings Challenge once again this year.

Last summer, Benjamin Corb, ASBMB's director of public affairs, challenged the society's members to meet locally with members of Congress. This year, we face a new challenge, as limited biomedical funding is resulting in job losses and lab shutdowns across the country. Members were urged to speak with their senators and representatives to lay out the hardships facing scientists and the dire consequences of funding cuts. The ASBMB public affairs office then set up meetings, provided a training webinar, supplied leave-behind packets and prep materials, and gave advice to participants. By the time you read this, we will have accomplished our goal of 100 meetings.

The response from Congress was overwhelmingly positive. Almost all of the lawmakers and staffers, regardless of political affiliation, were very supportive of funding for the National Institutes of Health and the National Science Foundation. Many urged the ASBMB participants to have their colleagues also voice their concerns and tell their stories. Only time will tell if Congress can work harmoniously to reverse sequestration. In the meantime, here is what members had to say about their district visits:

Dan Raben, a professor at Johns Hopkins University, was our first volunteer to visit both of his senators and his district representative. After meeting with the office of U.S. Sen. Barbara Mikulski, D-Md., Raben told us, "It is always comforting to know there are knowledgeable people in Congress who understand our concerns and are working as hard as we are to address the issues we feel are important to the biomedical research enterprise in this country."

A staff member for U.S. Sen. Al Franken, D-Minn., arranged a meeting at the Minnesota State University Moorhead campus with professor Mark Wallert to save Wallert the long drive to one of Franken's district offices. The visit proved fruitful. Wallert said the staffer promised she "would make every effort to have Sen. Franken visit my research laboratory to talk with me and my students this coming academic year."

Malini Raghavan, a professor at the University of Michigan, met with U.S. Rep. John Dingell Jr., D-Mich. Raghavan said that "Rep. Dingell's office had several suggestions to increase the local visibility of our research, including organizing open houses to explain our work to the public and communicating the impacts of our work via media channels."

Some ASBMB members attended meetings together, which was quite helpful for scientists new to the process. Hardik Patel, a researcher at The Feinstein Institute for Medical Research, met with staffers in the office of U.S. Sen. Kirsten Gillibrand, D-N.Y., with Kristy Lamb, a postdoc at Weill Cornell Medical College who previously participated in an ASBMB Hill Day.

"Kristy was magnificent and very enthusiastic. I learned a lot from her," Hardik said. "Thank you very much for this wonderful opportunity. I thoroughly enjoyed my participation and feel very good about it."

Jean Cook, an associate professor at the University of North Carolina at Chapel Hill School of Medicine, was creative during her visit with the staff of U.S. Sen. Kay Hagan, D-N.C. "I brought a photo of my lab along with the ASBMB packet, and we discussed how the NIH money goes not just toward the experiments but primarily toward the salaries and stipends of trainees," she said.

With the second annual challenge completed and our goal of 100 meetings met, the ASBMB public affairs office plans to make this an ongoing tradition. However, we need to keep our voices strong throughout the year. Stay tuned to see how you can participate in our next mission. Collectively, we can make a difference!

Shaila Kotadia (skotadia@asbmb.org) is an ASBMB science policy fellow.

'Still solving big problems'

HOOD

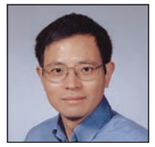
The editor of the MIT Technology Review, Jason Pontin, in late August highlighted American Society for Biochemistry and Molecular Biology member Leroy Hood in his list of top innovators over the age of 70. "We meet extraordinary older innovators all the time, who after a lifetime of creativity are still solving big problems, generating wealth or expanding our conception of what it means to be human," Pontin wrote. Hood, who is 74, is president and co-founder of the Institute for Systems Biology in Seattle. Hood developed the automated DNA sequencer, which made possible the mapping of the human genome and revolutionized the field of genomics.

Barbour wins achievement award for research, teaching

BARBOUR

Suzanne Barbour has won the Virginia Commonwealth University School of Medicine's WISDM Professional Achievement Award for her teaching, university service and research. VCU officials noted that Barbour, a member of the ASBMB Education and Professional Development Committee, is a dedicated mentor and proponent for minority access to research careers. "Her mentoring goes well beyond undergraduate students to include high-school students through postdoctoral scholars," said Ann Nichols–Casebolt, VCU's associate vice president for research development. She continued: "She has worked with them in her lab, taken them to research conferences, and provided them opportunities to learn the roles and responsibilities of a scientist."

Chen named endowed chair at Penn State



CHEN

Gong Chen at Pennsylvania State University was appointed the Verne M. Willaman chair in July in recognition of his research and teaching. A neuroscientist studying brain development and repair, Chen and his group have developed an approach to regenerate mouse neurons after injury or Alzheimer's disease and are exploring whether the approach can be used in humans who've suffered stroke, brain injuries or neurodegenerative diseases. Chen's team also is using induced pluripotent stem cells, harvested from human skin cells and then matured into brain cells, to better understand neurodegenerative disorders. Chen previously received the Ohse Award for Excellent Basic Research from Yale University and a National Research Service Award from the National Institutes of Health.

A pat on the back for postdocs

To observe National Postdoc Appreciation Week, ASBMB staffers headed over to the Johns Hopkins School of Medicine on Sept. 20. Ben Corb, ASBMB's public affairs director, and Shaila Kotadia, an ASBMB science policy fellow, delivered pizza and gave thanks.

IN MEMORIAM: Darrell Neilsen Ward (1924 – 2013)

WARD

Darrell Neilsen Ward, who led the biochemistry department at the now-University of Texas MD Anderson Cancer Center in Houston for two decades, died in June at the age of 89. Originally from Utah and known to love a good practical joke, Ward is said to have fibbed about his date of birth to join the Marine Corps and serve in World War II at the age of 17. He took advantage of the GI Bill and attended Utah State University for his undergraduate work and then went on to earn his master's degree and Ph.D. at Stanford University. He moved his growing family in 1952 to do a postdoctoral stint at Cornell University and then in 1956 joined MD Anderson. It was Ward's lab that discovered that the luteinizing hormone is a heterodimer rather than a homodimer, and for that work he won the Endocrine Society's Ayerst Award for Distinguished Service. He was a longtime member of the editorial board of the Journal of Biological Chemistry.

Retrospective

Tony Pawson (1952 – 2013)

BY JOHN M. KYRIAKIS

On Aug. 7, the field of signal transduction and, indeed, our entire scientific community lost one of its giants, Tony Pawson. Pawson made seminal contributions to our understanding of how receptor tyrosine kinases implement and propagate specific signals throughout the cell. The best known of these contributions was the discovery of the Src homology-2 (SH2) domain and the insight that this domain binds phosphotyrosine, thereby enabling the formation of modular multiprotein signaling complexes.

Anthony James Pawson was born in Maidstone, England, on Oct. 18, 1952. His father was an accomplished athlete (a 1952 soccer Olympian and champion cricket player). His mother, a high-school biology teacher, sparked her son's interest in science.

Tony Pawson received his early education at Winchester College, an elite English public school. From there he moved on to Clare College at Cambridge University, graduating in 1973. He completed his Ph.D. in 1976 in the laboratory of Alan Smith at the Imperial Cancer Research Fund. There he studied how the proteins of the Rous sarcoma virus mediate oncogenesis and promote retroviral replication.

Pawson continued to work on transforming retroviruses during his postdoctoral training in Steven Martin's laboratory at the University of California, Berkeley. Prompted by the discovery that the RSV transforming protein v-Src was a tyrosine kinase, Pawson discovered that the transforming protein of the Fujinami avian sarcoma virus, v-Fps, was also a tyrosine kinase.

In 1981, Pawson became an assistant professor at the University of British Columbia in Vancouver. He continued his studies of v-Fps. He and his colleagues discovered that a noncatalytic region of v-Fps was subject to noncatalytic insertions and that this noncatalytic region in v-Fps was structurally similar to a noncatalytic portion of v-Src. He dubbed this region Src homology-2 (SH2 – with SH1 being the catalytic domain). A third conserved region, the SH3 domain, was discovered later. SH2 and SH3 domains then were found to exist in a vast number of signaling proteins. Of note,

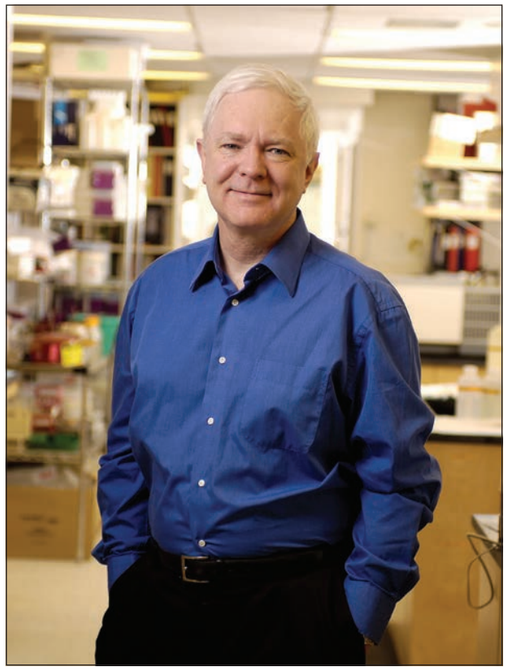


IMAGE COURTESY OF MOUNT SINAI HOSPITAL

several proteins, including the Crk oncogene, appeared to consist solely of SH2 and SH3 domains.

While the importance of tyrosine phosphorylation was evident from cell biological findings, the discovery of the SH2 domain was pivotal in defining how phosphotyrosine signals. Again, Pawson was at the center of these findings. In a particularly important advance, he and others showed that isolated SH2 domains bind phosphotyrosine, thereby permitting the recruitment of SH2-containing proteins to autophosphorylated tyrosine kinases — including receptor tyrosine kinases — and other phosphotyrosine-containing proteins. A major example of this sort of signaling was discovered in 1992 in Pawson's laboratory. Thus, the SH2-containing scaffold protein Shc bound to phosphotyrosines on the EGF receptor. This leads, in turn, to tyrosine phosphorylation of Shc. The phosphotyrosines on Shc then recruit another SH2 adapter protein, Grb2, the SH3 domains of which enable formation of a stable complex with the Ras guanine nucleotide exchanger Sos. This process of modular protein assembly brings Sos to the plasma membrane, where Ras resides, and promotes Ras GDP/GTP exchange and activation. Activated GTP-Ras then recruits several protein kinase signaling pathways, including the ERK MAP kinases.

In 1985, Pawson moved to the Samuel Lunenfeld Research Institute of Mount Sinai Hospital in Toronto (now the Lunenfeld–Tanenbaum Research Institute), rising to serve as director from 2000 to 2005. His influence on Canadian science during this time cannot be overestimated. In addition to achieving the pivotal discoveries noted above, he recruited numerous outstanding scientists to the institute, promoted the incorporation of new technologies into signaling research (notably proteomics) and founded biotechnology companies. He was also the recipient of several Canadian science awards — including, in 2006, the Companion of Honor.

Pawson was also the recipient of numerous international awards, including the Gardiner Award, the Wolf Prize and the Kyoto Prize. He was on the short list to win the Nobel Prize.

Important advances continued to emerge from the Pawson laboratory. Indeed, in July of this year, the laboratory described a detailed analysis of the diversity of Shc signaling at different time points after EGF receptor engagement. The group used mass spectrometry and other emerging technologies to show that Shc forms a dynamic series of transient tyrosine phosphorylation and protein-interaction events to control the pleiotropic cellular responses to EGF.

With the sudden and untimely passing of such a great scientist, one is left wondering what might have been — what important discoveries might have been made and which young scientists might have emerged from his laboratory, trained and encouraged to go on to greatness themselves. Given that the transition of discoveries in biomedical science from bench to bedside takes many years, this loss becomes still more unfortunate.

In taking the long view, it is important to remember that Pawson's seminal discoveries arose from decades of research that began with studies of a virus that affects chickens and culminated with important breakthroughs directly relevant to human disease. Pawson himself made this insightful remark at the time he received the Kyoto Prize: "Governments increasingly want to see immediate returns on the research that they support. But it is worth viewing basic science as a long-term investment that will yield completely unexpected dividends for humanity in the future. I believe that this progress underscores the importance of giving free rein to human inventiveness." We are saddened by the loss of such a figure but inspired by the legacy of outstanding inventiveness exemplified by Tony Pawson.

John M. Kyriakis (jkyriakis@asbmb.org) is an associate editor for the Journal of Biological Chemsitry.

ASBMB TODAY LOOKS BACK

We have had the privilege of publishing over the years dozens of Retrospective articles about the great men and women who have contributed to our current understanding of biochemistry and molecular biology. This summer we launched a special collection of those remembrances and biographies on our website. Visit **www.asbmb.org/asbmbtoday** and click on "Collections" to see ones you might have missed or could use in the classroom.

Two more Tabor young investigator award winners

BY JOSEPH P. TIANO

Turning the light on cytochrome P450

Lionel Cheruzel, an assistant professor at San Jose State University, won a Journal of Biological Chemistry/Herbert Tabor Young Investigator Award for his work on the light-driven hybrid cytochrome P450 BM3 biocatalyst.

Cheruzel received the award at the 18th International Conference on Cytochrome P450: Biochemistry, Biophysics and Structure in Seattle from JBC Associate Editor F. Peter Guengerich of Vanderbilt University.

Cheruzel's research interests are developing hybrid P450 enzymes and photocatalytic chemistry. The cytochrome P450 superfamily is a large and diverse group of enzymes that catalyze the oxidation of organic substances. They are found in all organisms, from bacteria to humans, and Cheruzel works with the bacterial cytochrome P450 BM3. His laboratory is focused on creating hybrid cytochrome P450 BM3 that catalyzes oxidation reactions using visible light as its energy source by combining the photochemical properties of photosensitizers with the oxidation powers of cytochrome P450s.

CHERUZEL

Cheruzel grew up in the south of France before moving to the U.S. in 1999 to obtain his Ph.D. from the University of Louisville in Kentucky. He then spent three years doing a postdoc at the California Institute of Technology before joining San José State University.

X-linked synaptophysin marks the spot

Sarah Gordon, a postdoctoral researcher at the University of Edinburgh, won a Journal of Biological Chemistry/Herbert Tabor Young Investigator Award for her work investigating the effect of mutations identified in individuals with X-linked intellectual disability on the function of the protein synaptophysin.

Gordon was named the winner of the award at the 5th Conference on Advances in Molecular Mechanisms Underlying Neurological Disorders in Bath, U.K., where JBC Associate Editor F. Anne Stephenson was in attendance.

GORDON

Gordon is from Australia, where she obtained her bachelor's and Ph.D. degrees from the University of Newcastle. She moved to the University of Edinburgh to work in the laboratory of Michael Cousin and investigate the functional and pathological roles of synaptophysin. Synaptophysin is a synaptic vesicle glycoprotein expressed in all neurons in the brain and spinal cord; however, very little is known about its function. It is implicated in X-linked intellectual disability.

"We are only just now beginning to understand the importance of synaptophysin in maintaining synaptic health," she said. "In the future, we hope to further characterize the mechanisms underlying the presynaptic functions of synaptophysin and further delineate how this impacts on neurological disease."

Joseph P. Tiano (tiano233@hotmail.com) is a postdoctoral fellow at the National Institute of Diabetes and Digestive and Kidney Diseases in Bethesda, Md.

NIH funds new program to decode exRNA communication signals

BY DONNA KRIDELBAUGH

The National Institutes of Health awarded $17 million for its new Extracellular RNA Communication Program aimed at decoding exRNA signals as a form of cell-to-cell communication. This new program will focus on understanding the basic biology of exRNAs and developing techniques to use exRNAs as potential biomarkers and clinical therapies.

Recent studies have confirmed that small RNAs can be transported to other cells, potentially affecting gene expression and downstream cellular processes. The presence of exRNAs also has been associated with diseases in humans, including life-threatening cancers, neurological disorders, and heart and kidney diseases. However, the specific transport mechanisms and functions of exRNAs remain a mystery.

"We have a tremendous opportunity to explore a recently discovered, novel way that cells communicate," stated NIH Director Francis S. Collins in a press release. "Expanding our understanding of this emerging scientific field could help us determine the role extracellular RNA plays in health and disease, and unlocking its mysteries may provide our nation's scientists with new tools to better diagnose and treat a wide range of diseases."

To date, the NIH Common Fund has funded 24 projects within four primary focus areas:

1. biogenesis, distribution, uptake and function;
2. biomarker development;
3. clinical therapy development and
4. data management and resource repository.

A call for funding in a fifth focus area has been reissued this fall to develop a human exRNA reference profile from existing healthy blood and body fluid sample collections.

Two American Society for Biochemistry and Molecular Biology members are among the awardees who have received program funding. Anil Sood of the MD Anderson Cancer Center will lead a project titled "Novel Extracellular RNA-Based Combinatorial RNA Inhibition Therapy." The project will focus on blocking the export and uptake of exRNAs associated with ovarian cancer and other tumor-derived exRNAs.

Mark Gerstein of Yale University and co-investigators will spearhead the data management and analysis effort. The team will develop an exRNA atlas that will map exRNA communications within the human body. Program data and associated data-analysis tools will be made available to the public through the NIH program website, in addition to data deposition in the NCBI's dbGaP database.

Learn more about program details and funding opportunities at the NIH ExRNA Communication Program website: http://commonfund.nih.gov/exrna/.

Donna Kridelbaugh (donna.kridelbaugh@gmail.com) is a freelance science writer and editor, specializing in career-development topics. She is founder of the Science Mentor blog project, which is focused on providing a step-by-step guide to self-mentoring for scientists. Learn more about her blog at about.me/science_mentor or follow her on Twitter at www.twitter.com/science_mentor.

JUST A KID FROM THE FARM

BY F. PETER GUENGERICH

I'm not sure I really qualify to contribute here. I had good parents, a happy childhood and no real setbacks. However, the world I live in today is very different from the one I grew up in. I did not even know people lived like I do now, flying around to talk at meetings, etc.

My father came to the United States from Bavaria as a boy, with his family, in 1913. My grandfather, a common laborer in Germany who had to borrow money from relatives for the trip, found work as a hired hand for farmers. My father had to start school over, because he knew no English, and did not even attend high school. My father and my grandparents worked hard and were able to rent land and start farming themselves. Eventually my father, at the age of 50, began to buy a farm of his own.

I would not describe my family as poor, although my parents were very frugal and strived to fulfill the adage that farmers "live poor and die rich." Dad had dairy cattle, which had to be milked twice a day, and we had no hired help. I remember him working all the time, and there were no vacations or even weekends off.

When I was 10, Dad told me one night that he thought I was old enough to drive a tractor. He gave me an operating manual, told me to learn the gearshift pattern and said that he would show me how the next day. At the age of 12, I also could drive a truck. By then I was raising cattle of my own.

Every morning and evening was devoted to taking care of cows; Saturdays were all field or barn work; and summer meant baling hay, cultivating corn, combining wheat, and so on. In central Illinois, it was cold in the winter and hot in the summer.

The public schools I went to were pretty decent, in retrospect. I found I could excel in class, and my parents probably were surprised and pleased. I probably could have done better had I applied myself; I was really uncertain about how good I was. To be honest, I found many of the things we did — welding, plowing, raising cattle — more interesting than the majority of the high-school courses. However, I was really excited about chemistry, in particular, and many of the aspects of math.

I began to realize that my father's farm was not going to be big enough to be self-supporting in the future, with economic pressures, so I needed to think about borrowing a lot of money to expand or doing something else. I thought about being a veterinarian but never followed through (with the lousy surgical skills I found I had later in life, that was probably good for the animals). Taking the advice of one of my high-school teachers, I enrolled in the food technology program at the University of Illinois. I liked the chemistry courses and was making excellent grades overall, but after a year I decided that I would be bored to death if I remained in food science. I considered nutritional science, which seemed like a better idea at the time. During the summer after my sophomore year, I met professor Harry Broquist and got into biochemistry, working in his lab as a National Science Foundation fellow for two summers. Once I found how exciting biochemistry was, I never looked back. My relationship with Broquist was to last for the next 42 years, until his death.

I graduated from Illinois with high honors, got a Ph.D. in biochemistry (with Broquist) at Vanderbilt University, did a postdoc with Jud Coon at the University of Michigan and was an assistant professor

at Vanderbilt at 26. I was surprised that the faculty had been impressed enough with me as a grad student to give me a job. At the ripe old age of 34, I was a full professor in an excellent biochemistry department. Over the years, I have traveled all over the world, published a lot of papers, and trained an army of students and postdocs. I get to do fun things and am even paid for it. But I never forgot where I came from.

Due to my limited interest in English courses and the like as a young man, it took me a long time to learn to write the way a biochemist really should. Coon really emphasized writing, and I thank him for that. I have to admit that I learned a lot of what I know from reading and from the "feel" of what sounds good, but I did go on to become an associate editor at the Journal of Biological Chemistry (and now criticize others).

Did I succeed in spite of my background? No. I'd rather think that any success I've had was because of it. Following old habits, I still arrive in the lab early (it beats dealing with cows at that hour), and I work on weekends. I am mechanically inclined and fix equipment myself when I can — just like farmers do. I watch our money and try to use it wisely. When I started my independent career, I resolved that if I did not succeed it would not be due to lack of effort. I do not believe anyone has ever questioned my work ethic or my penchant for organization. These are things I learned on the farm.

As a postscript, today my sister and I own the farm, and I actively manage it. I still have an affinity with the farmers, and I think many people could learn something from them — even professors.

F. Peter Guengerich (f.guengerich@vanderbilt.edu) received a Ph.D. at Vanderbilt University and is the Tadashi Inagami professor of biochemistry there. He is an associate editor for the Journal of Biological Chemistry and frequent contributor. In 2005, he received the American Society for Biochemistry and Molecular Biology's William Rose Award.

Dear Reader,

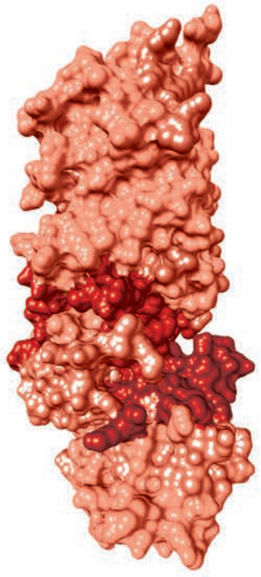
We are committed to sharing your ideas and stories. Please consider submitting to our next series, "Open Letters." ***See the first page in this issue for details.***

Best,
Angela Hopp, Editor, ASBMB Today

‘CLOSE TO A MIRACLE’

Researchers are debating the origins of proteins

BY RAJENDRANI MUKHOPADHYAY



Proteins traverse the width and breadth of cells to carry signals and cargo from one end to another, package and replicate DNA, build scaffolds to give cells their shapes, break down and take up nutrients, and so much more. But rarely do we stop to ask: How did these diverse and sophisticated molecular machines come to be?

Despite proteins’ profound impacts on life, their origin is not well understood. What caused a string of amino acids to start doing something? Or are strings of amino acids inherently programmed to do things? These are questions with which researchers in the protein-origin field have been grappling.

Researchers have a better grasp of the processes of selection and evolution once a function appears in a peptide. “Once you have identified an enzyme that has some weak, promiscuous activity for your target reaction, it’s fairly clear that, if you have mutations at random, you can select and improve this activity by several orders of magnitude,” says Dan Tawfik at the Weizmann Institute in Israel. “What we lack is a hypothesis for the earlier stages, where you don’t have this spectrum of enzymatic activities, active sites and folds from which selection can identify starting points. Evolution has this catch-22: Nothing evolves unless it already exists.”

WHERE’S THE STARTING POINT?

For more than a decade, researchers have been probing the protein-origin question using molecular biology and computer models. The group led by Michael Hecht of Princeton University has made libraries of proteins that are not derived from existing proteins that have undergone millennia of Darwinian selection. Hecht and colleagues made one particular library that contained more than a million polypeptide chains composed of hydrophobic and hydrophilic residues. They demonstrated that, after being expressed in Escherichia coli, the simple polypeptides were capable of folding (1).

With these folded sequences, Hecht and colleagues next tested if these entities were capable of performing any biochemical function, such as binding small molecules and cofactors and catalyzing reactions. “They don’t do them well, but they do them well above background noise,” says Hecht.

After that, Hecht’s group turned to E. coli strains deleted for genes that provide essential functions for survival. The investigators transformed these strains with their peptide library and found that a couple of their polypeptides were able to rescue the E. coli and let them grow on minimal medium (2). “Our proteins — made from scratch and never (having) been through evolution — can provide a life-sustaining function,” Hecht says.

In silico experiments complement data from bench-based experiments. Jeffrey Skolnick and Mu Gao at the Georgia Institute of Technology designed homopolypeptides and collapsed them using a structure-prediction algorithm (3). They then selected sequences at random that were proteinlike when matched to folds found in the Protein Data Bank. They found that each cavity in the artificial structures had a match in real proteins. Plus, there weren’t that many cavities. The cavities had the inherent capacity to bind small molecules and other ligands. “You show in a system, which was simply proteinlike but there is no selection for function, that you got a lot of properties — the binding sites, the geometries, the protein–protein interfaces. This would suggest the system fundamentally has the capacity to engage in function. Maybe it’s crummy function, but it’s still function,” says Skolnick. “This is telling you the systems are primed to do biochemistry.”

‘IF YOU DON’T HAVE A DRIVER FOR FUNCTIONALITY, YOU WILL NOT GET COMPLEXITY’

But Jack Szostak at Harvard University and Andrei Lupas at the Max–Planck Institute for Developmental Biology in Germany say these experiments don’t go far back enough in time. Both think that function had to come well before polypeptide chains became long enough to fold. “Functionality must come before complexity, because something must drive the emergence of complexity,” Lupas says. “If you don’t have a driver for functionality, you will not get complexity” in the form of structure.

Getting function in the first place is tough going. Szostak did an experiment with Anthony Keefe in 2001 (4). They tested 6 trillion peptides, each with 80 randomly selected amino acids, for ATP binding. “We were able to select out small, single-domain proteins that did bind ATP. But they were rare, on the order of one in 10^{11} sequences,” says Szostak. “Getting function from randomness is hard.” For selection to start happening to peptides, there has to be that spark of function. How that spark appears remains the big, elusive question in the field of protein origin.

Lupas says that evolution of peptides and proteins cannot be considered in isolation. He says it’s conceivable that RNA, considered to be the first biologically active molecule in the primordial soup, co-opted short abiotic peptides. These abiotic peptides, perhaps no more than five amino acids in length, were recruited to carry out some processes that ribozymes are unable to do, such as redox reactions with free radicals. Furthermore, ribozymes are not very thermostable and are easily hydrolyzed. Lupas says it’s possible that ribozymes partnered with abiotic peptides that were able to stabilize them.

As ribozymes picked up these abiotic peptides, the pool of these useful short peptides started to dwindle. “There wouldn’t be enough, so there will be a competitive situation, which would reward those ribozymes that could string up amino acids by themselves,” says Lupas. “If your ribozyme-based organism develops the ability to ligate amino acids, it will have an advantage over others because it doesn’t have to scavenge for the peptides.” This would lead to selection of peptides that have desirable functions. Once those functions were in place, the peptide could grow larger and more complex and begin to adopt folds and cavities.

Lupas thinks that function had to precede structure, because producing a complex structure is an incredibly hard job. “After 3.5 billion years of evolution, nature still has a substantial folding problem,” he states. He points out that, under normal circumstances, about one-third of a modern cell’s resources is devoted to protein quality control and turnover. “We’re not talking about a few proteases here and there. We’re talking about substantial resources of the cell just for this routine maintenance,” says Lupas. “You wouldn’t have to commit this amount of resources if protein folding was not problematic.” While Szostak agrees the hypothesis is elegant, he says there isn’t much experimental evidence to bear it out.

Szostak says that the origin of protein function also brings up the question of how many amino acids were around for making the first proteins. “There is pretty good evidence that at least some of the standard 20 amino acids came in late” in evolution, says Szostak. “Some of the simple, easy-to-make ones, like glycine and aspartate, were probably there right from the beginning.” The reduced number of amino acids plays into the folding issue, because there may be constraints in folding peptides made from a smaller number of amino acids.

Overall, what the field of protein evolution needs are some plausible, solid hypotheses to explain how random sequences of amino acids turned into the sophisticated entities that we recognize today as proteins. Until that happens, the phenomenon of the rise of proteins will remain, as Tawfik says, “something like close to a miracle.”

PODCAST

Visit www.jbc.org to listen to ASBMB Today science writer Rajendrani Mukhopadhyay’s interview with Charles W. Carter Jr. of the University of North Carolina at Chapel Hill, whose recent “Paper of the Week” in The Journal of Biological Chemistry discusses primitive peptides and challenges the RNA world hypothesis.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer and blogger for ASBMB. Follow her on Twitter at www.twitter.com/rajmukhop.

REFERENCES

1. Kamtekar, S. et al. *Science* **262**, 1680 – 1685 (1993).
2. Fisher, M.A. et al. *PLoS ONE* **6**, e15364 (2011).
3. Skolnick, J. and Gao, M. *Proc. Natl. Acad. Sci.* USA **110**, 9344 – 9349 (2013).
4. Keefe, A.D and Szostak, J.W. *Nature* **410**, 715 – 718 (2001).

Q&A with John Exton

BY RAJENDRANI MUKHOPADHYAY

John Exton of Vanderbilt University long has been fascinated by a laboratory run by a husband–wife team. This husband–wife team happens to be Carl and Gerty Cori, both Nobel laureates who received the prize in physiology or medicine in 1947 for their work on glycogen metabolism. Their laboratory, which was active from the 1930s through the 1960s at Washington University in St. Louis, spawned six more Nobel laureates and a host of famous biochemists. Earlier this year, Exton, an associate editor of the Journal of Biological Chemistry, turned his fascination with the Coris into a book called "Crucible of Science" published by Oxford University Press and available through Amazon.com and Barnes & Noble. This interview has been edited for length and clarity.

What was the impetus to write this book?

When I was a postdoc and a young faculty member here at Vanderbilt, my research was very close to the research that the Coris did. I was very familiar with their scientific findings. That was No. 1. No. 2, more importantly, was that my two principal mentors here at Vanderbilt were Charles Park and Earl Sutherland. Both were students of the Coris. They were influenced by the Coris, and their influence, in turn, translated to me. The third thing was that this was a fabulous laboratory. Both the Coris got the Nobel Prize, and six people who worked there also got the Nobel Prize. It's a very unique laboratory that had never been written up. It was astonishing to me that there never had been any book about this fabled laboratory that had influenced American biochemistry so strongly.

(The Coris) put biochemistry in a new light. Prior to that, people just worked on amino acids and vitamins. (The Coris) really got into metabolism and enzymes. They weren't the only ones to do it, but they pushed biochemistry into a new era. It was a new age for biochemistry. That was one of their great contributions.

As I read the book, it was like reading a "Who's Who" of biochemistry.

Obviously the Nobel laureates are very impressive, but many of the major players in biochemistry worked there as well. It was a cavalcade of fine biochemists who went through that lab.

How did you decide you were going to tackle this book?

Well, I had to get information about the Coris, obviously, so it was a lot of work there. Luckily, many of the people who worked in the lab, including the Coris, did have very good autobiographies, so that was a great help. Without those autobiographies, I probably never would have been able to do it. That was a big factor.

So you had a big stack of reading?

Interesting reading! If it was boring, I never would have done it. These people were great scientists, but they had fabulous, interesting biographies.

Did you spend much time talking to people?

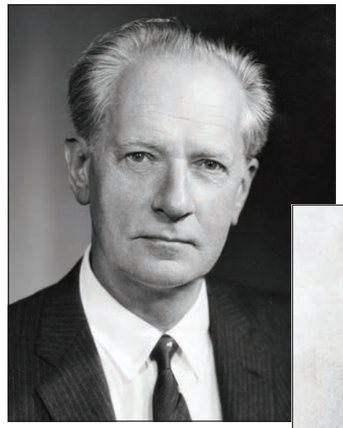
Unfortunately, a lot of them are dead. Two of them died quite recently — Christian de Duve and Bill Daughaday. But their scientific progeny were still alive, and I could still talk to them.

How did you decide what tone to strike with the book?

It's a scientific history, so I couldn't ignore the science. But I didn't want to overload it with science because the general public would throw up their hands in horror. It had to be a combination of science and personal interest elements, which I found very interesting.

Of all the scientists in the book, who resonated with you most?

I would say the Coris. They were just outstanding people. They were brilliant. They were knowledgeable. They had tremendous command of different languages. They had interesting lives before they came to America (from Europe). How they first arrived in America under pretty awful circumstances and then moved on and created this incredible laboratory — I just couldn't be other than impressed by them. Their creation was unique — a crucible of science.



Carl and Gerty Cori received the Nobel Prize in physiology or medicine in 1947 for their work on glycogen metabolism. Their laboratory spawned six more Nobel laureates and many famous biochemists.

What do you mean by unique?

They came from Europe and had lived through World War I. They went through medical school together. They decided, when they got through that, (Europe) was a dangerous place and there was a lot of anti-Semitism. They sensed that there was another war coming. They came to America for that reason. Then they rose from this second-rate cancer institute in Buffalo to create this incredible laboratory. They both got the Nobel Prize. Gerty was the first American woman to get a Nobel Prize. That is quite an achievement. They created a laboratory from which six other Nobel laureates emerged. That's definitely unique. There is no other laboratory in the United States like that.

How did you come up with the title of the book?

It came out of my head. I can't remember how that came to me. I thought it was a brilliant title. It came as an act of God or something. I can't tell you exactly where it came from and why it came. But it came. Of course, when it happened, I knew instantly it was right.

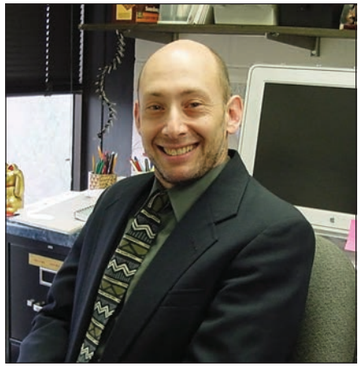
Continued on page 18

Meet Jeffrey Pessin

A new associate editor for the Journal of Biological Chemistry

BY RAJENDRANI MUKHOPADHYAY

Jeffrey Pessin, director of the Diabetes Research Center at Albert Einstein College of Medicine, joined the ranks of the associate editors at the Journal of Biological Chemistry in November 2012. Pessin has won awards for his work on the molecular underpinnings of diabetes and in 2011 was elected to be a fellow of the American Association for the Advancement of Science. The interview has been edited for length and clarity.



Would you briefly explain what your research group is studying and how you entered the field?

We are examining the signaling pathways and integrative physiology that are responsible for diet-induced adipose tissue inflammation and development of fatty-liver disease. I got into this area because Michael Czech (now at the University of Massachusetts) gave a seminar when I was a graduate student (at the University of Illinois). I was very impressed by the seminar. So I applied to his lab, and he accepted me. He was interested in insulin regulation and glucose metabolism. That, to me, was just a fascinating topic. The science and the experience of discovery were unbelievable. It was a tremendous environment. Dr. Czech's laboratory was the first to identify the complex subunit structure of the insulin receptor and to identify the nature of the facilitative glucose transporter proteins. When I opened my own lab, I wanted to do work along the same lines, because I was so excited by the data and the findings. One thing just evolved into the next and the next, and now I've been doing this for 30 years! We're still finding new and exciting data by examining the mechanism controlling glucose and lipid metabolism that underlies the fundamental basis for insulin resistance and Type 2 diabetes.

Is your research mostly basic science?

There has been a shift these days. When I first started, our research efforts were entirely basic, using tissue culture or biochemically reconstituted systems in vitro. We still do some basic, hardcore biochemical research, but primarily our interests are in using animal models to study integrative physiology and the mechanisms responsible for altered pathophysiologic states. Science has dramatically changed over the years. For example, only a few years ago, if you needed to express a protein or identify a gene, you had to clone it yourself. Now you simply order it. Moreover, making genetically engineered mice was a very expensive, time-consuming and labor-intensive process. Although still expensive now, many genetic mouse models are available, and more are becoming available at a rapid pace. Even for those not yet (readily) available, there are a variety of sources that will make the mice for you. I like to consider our efforts preclinical, as we use a lot of knockout and transgenic mice.

How did you choose science as a career?

I knew I wanted to be a scientist when I was in college. Before then, I wanted to be a professional basketball player. But I wasn't tall enough, so I didn't quite make it as a college player. So I thought, "I'd better learn some things!" When I went to college (at City University of New York), I started out as a chemist, because my adviser told me that to be a good biochemist I needed to be a good chemist first. I did my undergraduate and master's degrees in chemistry. Then I decided to apply to biochemistry departments because I wanted to learn about metabolic pathways and enzymes. That's what I started doing as a graduate student. Toward the end of my graduate career, Mike Czech came to the university to give a talk. I was so inspired that I said, "That's the guy I want to work for!"

Do you still play basketball?

No, I'm too old. I stopped when I was in my mid-40s because of my knees. I injured my knees too much. At the University of Iowa (Editor's note: Pessin was a member of the faculty there between 1983 and 2003), I played in the prime-time league. I played with B.J. Armstrong and Brad Lohaus. So I've played with some NBA players. It was tough playing against those guys, because they were bigger, stronger and faster, but I was able to hold my own. It was actually a lot of fun. Now I play tennis. It's a lot easier on the body!

What does it mean to you, on a personal level, to be an associate editor for JBC? What was your reaction when you were asked to be an associate editor?

I was honored but concerned over the amount of effort that this would take. After talking to (Editor-in-Chief Martha Fedor), I decided it was an important aspect of the peer-review process and that I should give it a try. I made my career publishing in the JBC. If you ever look at my CV, you'll see that for the first 25 years it's mostly JBC.

What do you do outside of the lab? Hobbies?

I am an amateur cabinetmaker and make various types of furniture. I started it when I was in graduate school. My wife and I, we both grew up in New York. It was a pretty difficult place to live in the 1960s and 1970s. There was a lot of crime with drug violence. Once, there was a gun fight right in front of my house. I grew up in a rough neighborhood. We both decided we wanted to get out of there, so when I graduated college we decided I was going to graduate school (outside of New York). We came from poor families. I picked the school that gave me the biggest stipend, which was the University of Illinois. We moved there. We were out of place. We both grew up in Brooklyn, and here we were in the middle of the Midwest, where we knew nothing about anything. There were two people with whom we had our orientation picnic, Pam Anderson and Peter Torgenson. We hit it off with them, and they took us under their wing to show us what it was like to live outside of New York!

Peter did a lot of woodworking, and he showed me how to handle wood, how to join pieces together using just chisels to cut mortise and tenon joints. Then I bought a couple of books. Peter and I would

Continued on page 18

Continued from page 17

talk about woodworking, and we would do projects together. I've made three-quarters of our bedroom furniture. I've made nightstands, dressers, headboards and lots of picture frames. I just built my sister a set of cabinets for her kitchen. It takes time, and I do it slowly just for fun.

What do you think is the most exciting thing about science these days?

The rate of discovery now is incredible compared to before, and we're only still touching the tip of the iceberg. It's a very exciting time, but it's also much more difficult. There's a lot more information you have to sift through. But as we're learning more, it's becoming more comprehensible, because things are beginning to make sense now. That's why we are in the best time to develop therapeutics.

In the old days, it was hit-and-miss. Almost all drugs before the last 10 years came from random screenings. But we're actually at the point now where we can make integrated predictions about how a drug will work and how to select for those with higher therapeutic potential. We are also beginning to develop personalized medicine. There are a couple of examples. Plavix is a drug like that. (Editor's note: Plavix, also called clopidogrel, is an anti-blood clotting agent.) There are certain people who have an enzyme difference that prevents the metabolism of Plavix into its active form, and these patients should be treated with other antiplatelet therapies.

The sad part is that the funding is the worst it has ever been. I've never seen funding so difficult … in my whole (scientific) history since 1975. We've gone through very difficult times in the past, but nothing like this. We are at the point where we can make tremendous breakthroughs, but, at the same time, we're being held back because of a lack of funding.

For scientists in training, do you have any words of wisdom or a favorite motto?

Don't try to predict where science will take you. It is much better just to enjoy the journey.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer and blogger for ASBMB. Follow her on Twitter at www.twitter.com/rajmukhop.

Continued from page 15

Who do you hope will read this book?

Historians of science. I want biochemists to read it. They would understand the biochemistry. Some people have suggested that graduate students read it.

What do you hope people will get from reading this book?

There is a vast history of science that people just don't know about. It's a terrible waste. One thing I hope people will get from this book is how to do science. That's the most powerful thing that the Coris did — they had a very rigorous approach to science. For example, don't go into a theory with preconceived notions. Let the facts find themselves. Don't ignore the literature, because when you read the literature, you know what's already been done, and you don't want to repeat it! They were great exponents of the scientific method.

Your sense of humor comes through in the book. You obviously had fun.

Oh, my approach to this whole thing was I didn't care if I made a penny or not. I just loved doing it.

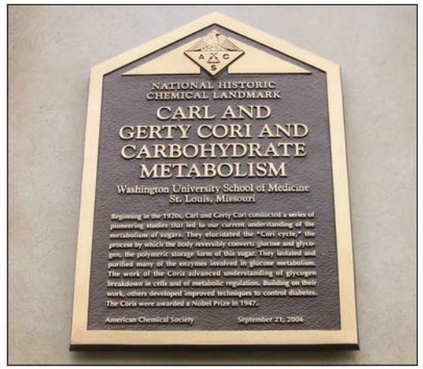


PHOTO PROVIDED BY PHILIP SKROSKA, ARCHIVIST AT THE BERNARD BECKER MEDICAL LIBRARY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE.

The Coris worked in South Building, which is now designated as a National Historic Chemical Landmark by the American Chemical Society.

How to become a good lab manager

BY ELIZABETH SANDQUIST

Do you ever feel you were unprepared for a career as the head of a research lab?

You chose the research profession because you were fascinated with the world around you and wanted to discover on a molecular level the ways in which life exists. Additionally, you wanted the freedom to choose your own field of research and study what interests you most.

You long to be at the heart of the lab — directing experiments, analyzing data and writing papers — but you find yourself caught up in other tasks — ordering reagents, dealing with a troubled graduate student, attending yet another committee meeting, anything but bench research.

You have found that being the head of the lab is more than just making big discoveries; it is about managing a small business. Lab-management skills, while used every day by scientists, are not directly taught to young scientists. Rather, they are learned secondhand. While much is to be learned from this follow-by-example approach, it has its limits. We have all heard horror stories of principal investigators with poor leadership and organization skills, but how can we keep from becoming a character in one of these stories?

Lab management can and should be learned in a more directed manner

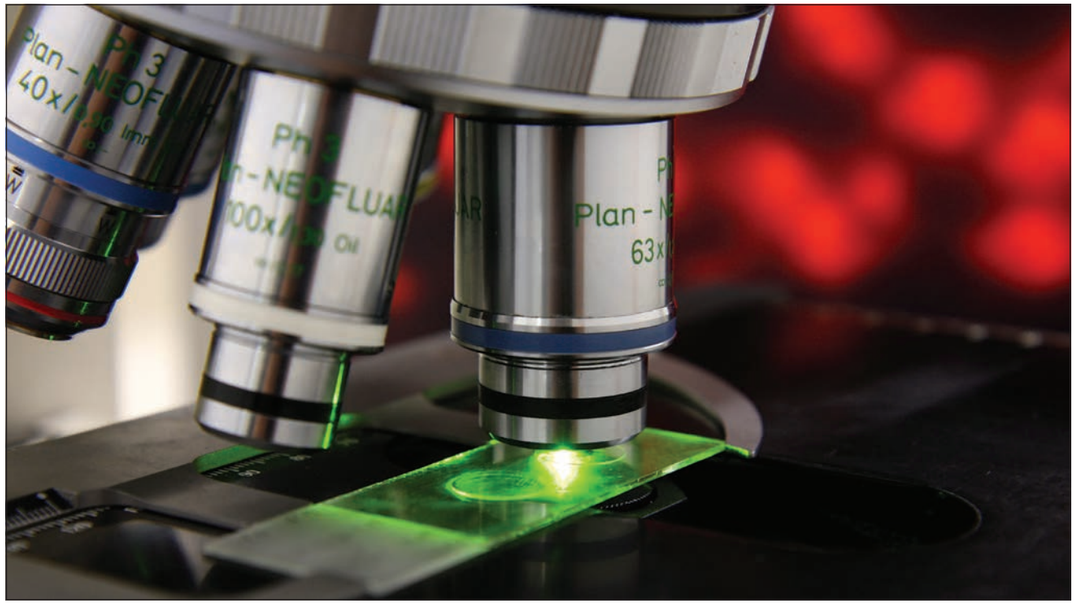
"Laboratory managers are often promoted from the ranks of the technical staff," says Rodney Forsman, the immediate past president of the Clinical Laboratory Management Association and an assistant professor emeritus at the Mayo Clinic College of Medicine in Rochester, Minn. "If an individual has the capacity to learn the science of laboratory medicine, they can learn the necessary management skills, given the desire and aptitude to do so."

Management skills are important for science careers of all types. Whether you work at the bench or away, the ability to organize your work and supervise those under you is critical.

Management can be divided into four main categories:

1. Planning allows a lab manager to know where the lab is going.

2. Organizing is also an important job for a lab manager as he or she determines who does which project and technique, manages the timelines and budgets for multiple projects, and keeps current with research in the fields.



3. Leadership is extremely important for a lab manager, as it often sets the environment and pace of the lab. Good leadership can inspire lab members toward productivity and creativity and help members work together.

4. Controlling a lab involves the evaluation of lab members' and projects' progress and the ability to correct problems as they arise.

Planning: considering the big picture

With all the responsibilities that lab management entails, it is easy to make sure the T's get crossed but to lose sight of the bigger goal.

"Self-awareness is vital in time management! It is so easy to believe that you are being productive when you are merely being busy," says Kathy Barker, author of "At the Helm: A Laboratory Navigator," a book that instructs new investigators in lab management. "Being able to stand back and truly assess your effectiveness is hard, but it is the only way to make every day count."

A common suggestion from the experts interviewed was to have a five-year strategy. In a study by McKinsey & Company, all successful, thriving labs utilized three- to five-year plans.

While lab members need technical skills to complete individual experiments, it is the lab manager's job to ensure that all experiments are aimed toward a common goal. The ability to see the bigger picture allows lab members to evaluate a project's progress and determine future projects, manuscripts and grants. A five-year plan allows you to gauge the progress of your research and keep it goal-oriented.

Once you know where you want your research to be, you can plan experiments much more efficiently. This becomes especially important when a lab is managing multiple grants of varying lengths. Having a long-term plan also is helpful for tenure-track faculty so they can stay on schedule and achieve the requirements needed for tenure in the appropriate time.

"Perhaps scientists don't create five-year plans because they don't think they need to: They are overwhelmed with detail and trust that, as they take care of the day-to-day details, the path will emerge. It usually doesn't. It just becomes more obscured with endless tasks," Barker says.

Similarly, a mission statement can guide a lab and keep it on track. "A mission statement helps to remind the PI of what her priorities are," Barker says. "It is hard to keep your eyes on the prize with all the personnel, funding and administrative decisions that have to be made daily. Reminding yourself that your mission is, say, children's health or the mentoring of young scientists helps you to recognize what tasks will help you fulfill your plans and so be more productive."

Write a mission statement that will help you and your lab members remember, when things get tough, why you are in science and why your project is important.

Also, scientists love to ask questions, but sometimes that can lead researchers down rabbit holes. A mission statement can guide you in experiment planning so that time is not wasted pursuing trivial or tangential research.

Organization: more than a clean desk

Organization takes a number of forms in lab management. Time, people and your physical lab space must be organized and orderly for research to run smoothly. There never will be enough time in the day to complete all the tasks you hope to accomplish, so it is important to know when to say no.

While an open relationship with lab members is encouraged, sometimes you need to close your office door. "With

Top 10 lab-management tips

1. You can learn management skills.

2. Have a five-year plan for your lab.

3. Set clear standards and expectations.

4. Optimize your management style for each lab member.

5. Listen to your lab members.

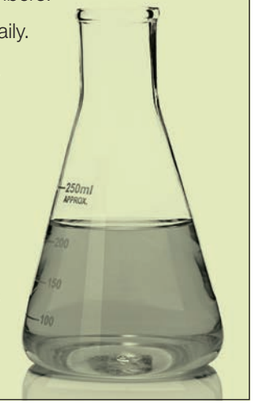
6. Walk around the lab daily.

7. Learn when to say no.

8. Be prepared when small amounts of free time become available.

9. Get to know the people at your institution who can help you.

10. Celebrate successes with your lab.



time and experience, you should develop the ability to better know what requests will help you in your research and career and which ones will impede you," Barker says. "You get better at looking into the future to see that you might get no immediate benefit to agreeing to be on a certain committee but that in six months you might gain a chance at more graduate students or a better relationship with an administrator."

Lab meetings are a great way to help keep a group of people organized and focused on their goals. Meetings with the whole group allow lab members and the PI to remain informed of events within the lab. They also can be a good forum for brainstorming and troubleshooting.

The McKinsey & Company study of successful labs also found that top labs have regular lab meetings, both formal and informal. One-on-one meetings also are important for both the lab member and the PI, as experiments and issues can be discussed in greater detail.

However, lab meetings can become an inefficient use of time if they are not organized. Having a meeting agenda can keep conversations on track and avoid the need for multiple meetings about a single issue. Records of lab meetings also can be used to measure research progress.

Leading by design

Many of the scientists and managers interviewed noted that not all successful leaders are the same. The first step toward reaching your leadership potential is to recognize your leadership style. Multiple resources exist online that allow you to recognize and analyze the way you lead. Then you can focus on the strengths and weaknesses of that leadership style and work to improve it.

Additionally, you can compare the type of leader you actually are to the kind you would like to be. "It is advantageous to identify a successful mentor who can not only be a model for your behavior but a sounding board for issues you may not have dealt with previously," Forsman says. "The mentor should have experience beyond the laboratory, especially in dealing with organizational protocol and key individuals outside the laboratory."

Jon Lorsch, formerly a professor of biophysics at the Johns Hopkins University School of Medicine and now director of the National Institute of General Medical Sciences, suggests that you optimize your management style for each lab member. "You cannot motivate or help everyone in the same way," he says. "For example, some people respond well to a lot of attention. Other people like to have more time to think about data or their next experiment between discussions with their PI. You need to be able to modulate your style to optimize it for each person in your lab."

Resources for lab managers

Take a look at the following list of resources for more information and tips on managing a successful, thriving lab.

- Clinical Laboratory Management Association. Body of Knowledge for Medical Laboratory Management. www.clma.org (2010).
- Howard Hughes Medical Institute and the Burroughs Wellcome Fund. Making the Right Moves: A Practical Guide to Scientific Management for Postdocs and New Faculty. http://www.hhmi.org/resources/lab-management/moves.html (2006).
- University of Houston Bauer College of Business Executive Education programs: http://bauer.uh.edu/executive-education/.
- Barker, K. "At the Helm: Leading Your Laboratory" (2nd ed.). Cold Spring Harbor Press (2010).
- Beards, M. "The secret of high productivity in the research lab." McKinsey & Company (2009).
- Mendeley, a free reference manager and PDF organizer: www.mendeley.com.
- LabGuru, Web-based research and laboratory management software: www.labguru.com.
- I Opt Leadership Report: http://www.iopt.com/leadership-report.php.

Richard DeFrank, an associate professor of management at the University of Houston C.T. Bauer College of Business, emphasizes the importance of lab members knowing you are involved and available. One way to achieve this is to walk around. Every day, make an effort to walk around the lab and visit with each lab member. These conversations do not have to be in depth; rather, this method allows you to stay up to date on daily activities and shows that you are open and interested in your lab members' work.

On a related note, many people emphasized that lab managers should walk the talk. In other words, do what you say. This action builds trust and respect from colleagues and fellow scientists. If you desire students to be in the lab from 8 to 5, they are far more likely to do so if you are also there from 8 to 5. Lorsch gives an example: "I give a practice talk for my group for every new lecture I make and ask them for (and take) their feedback. That way, when I make them give practice talks and get feedback, they know I am not asking them to do something that I don't do."

Most of the experts emphasized the importance of listening. A good leader not only directs lab members and tells them what to do, but he or she also listens to his or her employees.

"Make sure you are not the person doing most of the talking at lab meeting," Lorsch says. "If you are, there is a problem." Instead, he suggests that you empower senior members of the staff to teach and mentor junior members.

Taking time to listen is also important because a lot can be gained from your lab members. One way to do this is to organize brainstorming sessions. "This gets creativity flowing, empowers people to think about new research directions for themselves and the rest of the group, and often generates good ideas," Lorsch says. Not only does this make lab members feel appreciated, but it also provides them with a learning experience. Most importantly, it gives you a different perspective on your research than you would have if you worked in isolation.

Lastly, know when to relax and have fun. Taking time to celebrate as a lab is great for morale and can act as an incentive to reach lab goals. Science is full of disappointments, and perseverance is essential for survival. Taking time to relax and enjoy your accomplishments will give lab members and you the energy to continue. "Have a sense of humor," Lorsch says. "This is probably the most important advice I can give."

Controlling: making sure your employees succeed

Managing a lab means that there are times when things go wrong and you are expected to fix it.

"Managers often lament that 'all problems come in on two feet,' which highlights the importance of honing your people skills," says Forsman.

One of the best ways to prevent issues with employees is to be clear about standards and expectations from the start. Every lab member comes from a different background. Most of the issues rise from a lack of communication about expectations. Without clear expectations, you cannot expect lab members to do something just how you like it. It is equally important for lab standards to be maintained, or they will not be followed.

DeFrank and Lorsch both suggest motivating lab members through rewards rather than fear. "When people are doing well, make sure you tell them so," Lorsch says. "When things are going slowly, make sure you give encouragement along with advice." People are more likely to be productive and create high-quality work when they are happy and working toward a goal rather than fearing punishment. As Barker puts it, "share interests, not issues." These rewards do not need to be significant or monetary; what matters is that they are sincere.

Lastly, try to give lab members a sense of control over their work. Many grad students want to have labs of their own one day, and experiment planning is a skill they need to learn now. Additionally, a sense of pride and ownership can go a long way to motivate employees while freeing you to spend time on other issues.

If you don't have your own lab yet, begin learning about lab management now. While you may not run a whole lab, your boss will give you smaller tasks to manage. The ability to manage a little will bring opportunities to lead larger future projects.

Many of the techniques for managing a lab also can be used on a personal level for career development. "Because the graduate school-postdoc-assistant-professor-etc. pathway is so apparently scripted, it may appear that the path ahead is solid and paved and doesn't need so much personal input," Barker notes. "The system and the busyness can lull one into complacency, but the job has grown so much bigger than the training prepares the PI for."

The key to returning to the work you love, science, is to manage your lab well through planning, organization, leading and controlling. It may take some work, but the payoff will be rewarding to you and your lab members. Remember: If you can learn science, you can learn lab management.

Elizabeth Sandquist (elizabeth.overmoe@med.und.edu) is a graduate student at the University of North Dakota pursuing a Ph.D. in biochemistry and molecular biology. Follow her on Twitter at www.twitter.com/ilovebraaains.

Online Extra

Managing a lab is a lot like running a small business. To learn how business skills can help your lab succeed, check out the article "The business of running a lab" at http://bit.ly/HLNN9y.

How to write a killer cover letter for a postdoctoral application

BY BILL SULLIVAN

Many graduate students applying for their first postdoctoral positions underestimate the importance of the cover letter. While it may be true that your awesomeness is beautifully outlined on your curriculum vitae, your cover letter often will dictate whether the busy principal investigator puts your application at the top of the heaping pile or into triage.

First impressions are everything for some people, so leave nothing to chance. If you provide only your CV, you aren't being very personable, and you lose a precious opportunity to highlight some things that make you stand out. On the other hand, a cover letter is also an opportunity to shoot yourself in the foot, so here are a few do's and don'ts.

Consider this the first demonstration to your future PI that you are resourceful and thoughtful – if you fail to do your homework, it does not build confidence that you will be diligent with your project.

Start off right. Address your potential future PI properly, as "Dr. (insert surname here)." If you begin your letter with "Dear Sir/Madam" or "To Whom It May Concern," your application could be dismissed as generic and untailored for the position. A letter that appears to come off an assembly line is likely to ride directly into the trash bin. If you do not invest the time to learn about the PI and his or her research, then the PI is not likely to invest the time to read your application.

After the salutation, the first statement should be a formality that states why you are writing to the PI. It is important to respect how hectic a day in the life of a PI can be, so get right to the point – something like, "I am applying for the postdoctoral position available in your laboratory that was recently advertised (where)."

The second sentence should specify your current position, place of work and mentor. If you are not immediately available for hire, it is useful to mention when you will be able to start. End the first paragraph with just one or two concise sentences that hint at why you are the ideal candidate for the position — you will expand on these points next.

In the second paragraph, elaborate on why you should be considered for the postdoc — not just any postdoc, mind you, but this particular postdoc in this particular lab. Yes, it is infinitely easier to use the same cover letter for the dozens of postdoctoral positions for which you are applying, but that is not going to cut it. These uniform letters are easy to detect and usually dismissed as lazy and insincere. If you fail to convince the PI that you are taking the postdoc search seriously, then the PI is not likely to take you seriously. It is essential that you customize your letter, emphasizing how your background is aligned to the PI's studies and the specifics called for in the advertisement. Consider this the first demonstration to your future PI that you are resourceful and thoughtful — if you fail to do your homework, it does not build confidence that you will be diligent with your project. Equally important to convincing the PI that you have the right stuff is conveying your excitement for learning something special that is studied by his or her lab. Strive to balance what you would give to the lab and what you would gain from it.

In paragraph three, it is time to brag about a few key achievements, such as your most important paper or two, a grant or fellowship, or other notable honors (an award-winning presentation at a conference, for example). You also can briefly mention that you have

Continued on page 26

Breaking through the tunnel vision

Toward a unified model for the role of sphingolipids in apoptosis

BY LEAH J. SISKIND AND LEVI J. BEVERLY

It's complicated and context dependent! A truer statement has never been spoken, especially when it comes to the wild world of sphingolipid metabolism and the regulation of cell-stress responses by sphingolipids.

In the past, many laboratories focused on only one (or perhaps a small handful) of the thousands of known sphingolipids and declared that their sphingolipids of interest were the all-powerful modulators of whichever stress responses they were studying that day.

However, just when we think we have triangulated the identity or role of a lipid species involved in a particular cell-stress response, the lipid itself teaches us a valuable lesson about just how slippery it really is. Even small manipulations of a single sphingolipid entity can alter metabolites dramatically or flux through the entire metabolic pathway, making it difficult (if not impossible) to attribute the phenotype to the originally targeted sphingolipid.

Furthermore, the field is just now beginning to understand that sphingolipid metabolism is so important to cells that when the expression of one enzyme isoform is altered the system will compensate by altering the expression of other isoforms to maintain homeostasis. Likewise, sphingolipid enzymes have been shown to heterodimerize, which appears to be important for their activity. This was recently reinforced in publications from Lina Obeid's laboratory at Stony Brook University and Tony Futerman's laboratory at the Weizmann Institute of Science (1, 2). It's complicated!

When it comes to the regulation of apoptosis by sphingolipids, we have fallen victim to this type of narrow-minded tunnel vision, which has led us to overemphasize single roles for single lipid species. For example, the dogma in the field has been for years that a simple balance between pro-apoptotic sphingoplipids such as ceramide and anti-apoptotic sphingolipids such as sphingosine-1-phosphate could dictate cellular life-versus-death decisions. However, recent data from the laboratories of Jerry Chipuk at The Mount Sinai Hospital, Douglas Green at St. Jude Children's Research Hospital and Holger Wesche at Amgen have called on the field to reevaluate the dogma that S1P's sole function is purely pro-survival and that decreasing its levels is sufficient to induce cell death (3, 4). It's (perhaps) context dependent!

It long has been known that there is interplay between the BCL2-like proteins and sphingolipids in the regulation of apoptosis. The first examples of this were in the early 1990s, when it was shown that overexpression of BCL2 or BCLxL blocks ceramide-induced apoptosis (5, 6). Molecular mechanisms for interactions between the BCL2-like proteins and sphingolipids have been proposed by many groups. For example, Marco Colombini's laboratory at the University of Maryland College Park showed in model systems that ceramide channel formation is inhibited by BCLxL via binding ceramide in its hydrophobic pocket (7). In addition, both the Colombini laboratory at the University of Maryland and Richard Kolesnick's laboratory at Memorial Sloan-Kettering Cancer Center showed synergism between ceramide and BAX in permeabilization of mitochondria during apoptosis (8, 9).

Recent data by our laboratories at the University of Louisville shed additional light on cross-talk between these two families. We show that pro-apoptotic BAK regulates ceramide generation during apoptosis via activation of a ceramide synthase (10). Importantly, activated BAK is a more potent activator of CerS (11). Further, we show that the anti-apoptotic BCL2 proteins directly interfere with BAK activation of CerS by binding and inhibiting BAK (11). This intricate system of cross-talk is complicated further by the fact that the six different anti-apoptotic BCL2-like proteins preferentially interact with BAK, suggesting that expression levels and availability of both the pro- and anti-apoptotic BCL2-like proteins need to be taken into account when considering how this system regulates ceramide metabolism. Data from the laboratories of Chipuk and Green also suggest that metabolites of ceramide are required for the full potential of BAX and BAK to induce apoptosis after certain stimuli (3).

The combination of these data, as well as myriad not discussed herein, makes it clear that we no longer can live in an isolated laboratory where we care about only our favorite protein or lipid species of interest. In addition, we must not be quick to pass judgment on whether newly published data or findings fit perfectly within the prevailing dogma, but rather we need to view the field as a whole and let the data guide us to new dogmas.

The only way we will be able to achieve this lofty goal is to change the way we think about our field, the people in our field and the goals of the field. The idea of a unified model for the role of sphingolipids in regulating apoptosis may be just a pipedream of the narrow-minded scientist who is interested in viewing the world through tunnel vision. Perhaps it is more likely that each apoptotic stimuli or each cell type will throw us a few curve balls that go against the model. This does not mean that the research is right or wrong, but it could be just as correct as the current model. In either case, we need to remember that it's complicated and context dependent!


Leah J. Siskind (leah.siskind@louisville.edu) is an associate professor at the University of Louisville Medical Center's pharmacology and toxicology department. Levi J. Beverly (Levi.beverly@louisville.edu) is an assistant professor in the medicine department and the pharmacology and toxicology department. Both are members of the James Graham Brown Cancer Center.

REFERENCES

1. Mullen, T.D. et al. *J. Lipid Res.* **52**, 68 – 77 (2011).
2. Laviad, E.L. et al. *J. Biol. Chem.* **287**, 21025 – 21033 (2012).
3. Chipuk, J.E. et al. Cell. **148**, 988 – 1000 (2012).
4. Rex, K. et al. *PLoS One* **8**, e68328 (2013).
5. Fang, W. et al. *J. Immunol.* **155**, 66 – 75 (1995).
6. Martin, S.J. et al. *Cell. Death Dis.* **2**, 253 – 257 (1995).
7. Perera, M.N. et al. *Biochem. J.* **445**, 81 – 91 (2012).
8. Ganesan, V. et al. *Apoptosis* **15**, 553 – 562 (2010).
9. Lee, H. et al. *PLoS One* **6**, e19783 (2011).
10. Siskind, L.J. et al. *J. Biol. Chem.* **285**, 11818 – 11826 (2010).
11. Beverly, L.J. *et al. Biochem. J.* **452**, 111-119 (2013).

Continued from page 24

experience training more junior people if that is the case. But don't give a laundry list of every minor award — that is why you submit a CV. The cover letter is the trailer, and your CV is the movie.

End your cover letter with the same professionalism you used at the opening. Thank the PI for his or her time and consideration. Be sure to provide your contact information and state that you look forward to hearing from him or her. Everything discussed above should fit onto a single page — 1 ½ pages at most.

There are a number of important don'ts that apply to cover letters. Things that might seem trivial to you actually can be turnoffs. Use plain email stationary free of distracting backgrounds or pictures. Choose a font that is not too big, not too small, not in color, definitely not comic sans and NOT IN CAPS. A plain, boring font like 12-point Arial or Helvetica is easy on the sore eyes of a PI struggling to read the 87th postdoc application. At midnight. After struggling with an online manuscript submission. I can hear the chorus of nonconformists arguing that unconventional fonts and graphics make their applications stand out. Of course it does, but I contend that it is a gamble to present yourself in this manner. If you have the goods, you don't need the glam.

Some applicants waste valuable sentences describing how they "deeply admire" the "esteemed" laboratory or how they always dreamed about working with the PI. When the cover letter is heavy on flattery, the applicant usually is light on talent or productivity. If your cover letter contains significant blocks of text copied straight from the advertisement, you may be construed as someone with poor language skills or unable to paraphrase. It should go without saying that spelling and grammatical mistakes are inexcusable and often taken as a sign of laziness and carelessness — two of the worst attributes a scientist could possess. Finally, avoid slang and attempts at humor, and do not end your sentences with an exclamation point!

I hope these tips help you land that perfect postdoctoral position.

Bill Sullivan (wjsulliv@iu.edu) is an associate professor at the Indiana University School of Medicine. Follow him at www.twitter.com/wjsullivan.

jbc THE JOURNAL OF BIOLOGICAL CHEMISTRY

mRNA: in the right place at the right time

BY NATALIE OSAYANDE

In a minireview in The Journal of Biological Chemistry, Carolina Eliscovich, Adina Buxbaum, Zachary Katz and Robert Singer at the Albert Einstein College of Medicine of Yeshiva University explain the importance of localizing elements of mRNA sequences and how advanced biochemical and cell-imaging techniques are being used to better understand mRNA movement.

Localizing elements in mRNA sequences are important for cell-fate determination, directed cell movement and tissue functionality. They also play key roles in embryonic patterning and somatic cell differentiation. mRNA localization also can restrict protein production, amplify protein concentration and direct protein integration into macromolecular complexes.

RNA-binding proteins are multifunctional regulators responsible for processing, localizing and controlling translation of mRNA targets. RNA-binding proteins recognize specific cis-acting mRNA localization elements, or as the authors call them, "zipcodes." These zipcodes, just a few nucleotides in length, can be contained in simple elements or in secondary structures or stem loops. While many localizing elements have been characterized in multiple models, neither a specific sequence pattern nor structural pattern has been closed in on to date.

However, the authors emphasize that technological advances, such as cross-linking and immunoprecipitation, or CLIP, have identified localizing elements and isolated RNA-protein complexes under physiological conditions. Fusion of a localizing element to a reporter RNA helps visualize localization patterns within a cell. These techniques are good but limited, as they cannot elucidate binding specificity and affinity. This is overcome by using live imaging methodologies, including high-resolution and live microscopy.

High-resolution fluorescence in situ hybridization, or FISH, has shown that as many as 70 percent of analyzed mRNAs in the Drosophila embryo, for instance, demonstrate subcellular localization. Using live microscopy, single mRNA molecules have been studied, showing that mRNA localization occurs through directional transport along cytoskeletal elements, random diffusion and local trapping of mRNAs, vertorial export from the nucleus and trapping, or local protection from degradation. Live imaging has been used to study movement within the nucleus where mRNA move by diffusion; the cytoplasm, where diffusion is faster because the environment is less restrictive; and neurons, where active transport localizes mRNA into dendrites.

By combining different methodologies, researchers are getting a clearer picture of how mRNA localizes and how that localization is related to gene expression, which one day may lead to customized treatments for diseases.

Natalie Osayande (natalie.osayande@spartans.ut.edu) is an undergraduate at the University of Tampa studying biochemistry.

Thematic review series: redox-active protein modifications and signaling

BY AKSHAT SHARMA

Signal transduction is complex. As electrons fly between players in a signaling pathway, protein conformations change, which renders them amenable to interactions with other proteins. And eventually an extracellular message reaches the nucleus, and gene expression takes place. Or not.

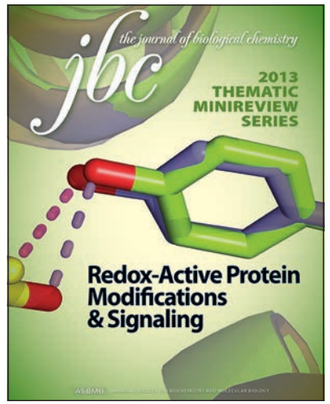
In view of the large-scale phenotypic changes that signal transduction can bring about, it is easy to forget that the script of some of these changes is written in the most basic and ancient of chemical reactions: that of oxidation and reduction. In that sense, the Journal of Biological Chemistry's recent series of thematic minireviews, organized by Associate Editor Ruma Banerjee at the University of Michigan Medical School, is a return to basics: a reminder that the cell accomplishes tasks of great complexity by keeping things simple.

First up in the series is an examination of the biological chemistry of peroxynitrite. A reactive nitrogen species, peroxynitrite is formed by the union of superoxide and nitric oxide radicals. It is implicated in a variety of biological contexts, such as the oxidation of thiol groups found on cysteine residues as well as direct one-electron oxidations, such as those of cytochrome c2+. The cellular pathology seen in neurodegenerative and inflammatory disease conditions is attributed largely to peroxynitrite-mediated nitration and oxidation of vascular wall components and vital signaling molecules. On the other hand, the use of intraphagosomal peroxynitrite by macrophages to eliminate phagocytized moieties is an effective way a cellular toxicant also may be channeled to do good. Author Rafael Radi rightly has christened peroxynitrite a "stealth" oxidant: The species is formed under fortuitous circumstances but exerts potent and far-reaching effects.

The next piece in the series celebrates the versatility of post-translational modifications of cysteine residues via the process of S-nitrosylation. The transfer of a nitroso group onto reduced cysteine residues exemplifies S-nitrosylation and yields S-nitrosocysteine, a species that is both an intermediary and a regulator of NO-induced signaling pathways. Given the sheer diversity of organ systems and physiological conditions that are affected by NO-mediated signaling, Harry Ischiropolous and his co-authors wisely ask if there is a selective mechanism that dictates the S-nitrosylation of different proteins. If so, what is this mechanism? Is it a mechanism influenced by certain structural cues found on the proteins involved, or could the other amino acids in the milieu be facilitators of S-nitrosylation over other post-translational cysteine modifications? The proteomic approach this minireview takes provides a big-picture view of not just S-nitrosylation but also the influences that post-translational modifications may exert on each other.

The theme of post-translational cysteine modifications and redox regulation of signal transduction continues in the third minireview in the series, where Mauro Conte and Kate Carrol take up the cause of cysteine sulfenylation and sulfinylation. The ephemeral nature of the sulfenyl group makes it a sensitive, rapidly responding redox switch that modulates the activity of protein tyrosine kinases and phosphatases and ubiquitinylating and SUMO-ylating enzymes as well as transcription factors. That sulfenylation effectively stage manages cell signaling propagated by the epidermal growth factor family of ligands is revealing of its importance in maintaining homeostasis. Sulfinylation, on the other hand, appears to have a more specific role in the regulation of the antioxidant peroxiredoxin enzymes.

A primary reason cysteine is special among the amino acids lies in its ability to form disulfide bridges via the oxidation of its sulfhydryl group. As important as disulfide bridges are to maintaining the structural integrity of a protein, they can, as authors Claudia Cremers and Ursula Jakob at the University of Michigan show in the next minireview, act as molecular switches reconciling the structural changes in proteins with the transduction of signals and/or gene expression. An excellent example of this is the zinc centers in proteins containing zinc-binding motifs. Once thought to be purely structural features, zinc centers are now revealing themselves to be regulatory hubs wherein oxidation of the cysteine thiols that coordinate the ion leads to zinc release and the formation of disulfide bridges. This brings about conformational changes in the protein which may, for example, enhance or detract from DNA binding and thus gene expression. Furthermore, reduction by thioredoxins and glutaredoxins lends the element of reversibility to disulfide bridge formation, enabling them to function as true switches.



Apart from disulfide bridges, thioredoxins and glutaredoxins also oversee the regulation of S-glutathionylation – the focus of the next minireview by Kenneth Tew and his co-authors at the Medical University of South Carolina. S-glutathionylation occurs in response to reactive oxygen and nitrogen species and so is an additional layer of control over the signaling processes that the latter may influence. For example, the S-glutathionylation of Fas under oxidative conditions enhances apoptosis. S-glutathionylation is a relatively uncommon cysteinyl modification, which places it in a unique echelon of disease biomarkers. And, indeed, changes in patterns of S-glutathionylation of proteins are correlated with incidence of inflammatory, neurodegenerative and cardiovascular diseases and cancer. As more putative S-glutathionylation candidates are unearthed, the mechanism is poised to be an important diagnostic marker in the pathogenesis of major diseases that plague this day and age.

Lest it be thought that redox signaling is important only in disease states, the next minireview, by Alessandra Stangherlin and Akhilesh Reddy at the University of Cambridge, makes a strong case for the involvement of redox signals in the regulation of circadian oscillations. Based on the studies cited in the minireview, it seems increasingly likely that the control of peroxiredoxin timekeeping may well rest within the redox state of ambient thiols. That circadian rhythms and the generation of ROS cross-regulate demonstrates that circadian and redox cycles are strongly linked.

Finally, the last piece in the minireview series, "The Redox Proteome," by Young-Mi Go and Dean Jones at Emory University, is a summative treatment of the themes of redox biology addressed in the series. Moreover, the article is a harbinger of the future of the field of redox biochemistry. While considerable attention has been paid to the redox activities of particular proteins, a systems-biology approach to uncovering what makes different sulfur switches tick will serve to reveal more not only about disease pathogenesis but about basic physiology itself.

Akshat Sharma (asharma28@wisc.edu) received his M.S. in microbiology from North Dakota State University and is a Ph.D. student in the department of medical microbiology and immunology at the University of Wisconsin, Madison. Read his blog at http://fasterkilltcell.wordpress.com/.

THE JOURNAL OF LIPID RESEARCH

New antibody-based test for detecting tuberculosis infection

BY MARY L. CHANG

In an article in the October issue of the Journal of Lipid Research, researchers in Singapore report the development of a new antibody-based method for detecting Mycobacterium tuberculosis, the causative agent of tuberculosis infection. Mycolic acid, whose long fatty acids are the main component of M. tuberculosis' bacterial cell wall, is found in infected patients' sputum and appears to be the perfect target for such an assay.

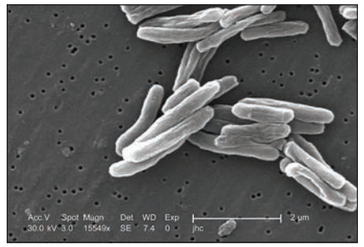
According to the Centers for Disease Control and Prevention, one-third of the world's population is infected with M. tuberculosis. The World Health Organization reports that more than 95 percent of deaths caused by tuberculosis worldwide occur in low- and middle-income countries. Treatment for TB is most effective when the infection is diagnosed quickly, but developing countries are likely to lack the resources that allow for such quick diagnosis.

Current TB diagnosis methods using blood cultures, mucosal sputum smears, polymerase chain reaction and chest X-rays in such settings are not ideal because of the poor sensitivity and high expense of the tests, the length of time it takes to receive results, and the lack of infrastructure in which to conduct the tests. While assays to detect protein and glycolipid antigens of the bacterium exist, none represents a true improvement over standard diagnostics, and too few studies have been done to confirm their usefulness.

In the study reported in the JLR, Conrad E. Chan of the National University of Singapore and colleagues there and at DSO National Laboratories in Singapore first screened a phage display library to isolate four specific antibodies for mycolic acid. Then they optimized a rapid lipid-extraction protocol to use these antibodies in detecting mycolic acid in mycobacterial culture. Sensitivity of each antibody to detect mycolic acid was tested against serially diluted concentrations of M. tuberculosis-derived mycolic acid as well as against synthetic mycolic acid subclasses. To free mycolic acid's covalent bond with a bacterium's inner cell membrane, alkaline hydrolysis proved to be a quicker method than treatment with hexane, which required overnight incubation. The most sensitive of the four isolated antibodies detected 4.5 nanograms of mycolic acid or methoxy mycolic acid by ELISA, a result similar to other currently used, antibody-based diagnostic assays.

The researchers used high-resolution tandem mass spectrometry to analyze the alkaline hydrolysis products to confirm that the isolated antibodies were indeed detecting mycolic acid accurately. While MS analysis is powerful and practical in clinical use, it is not likely feasible for use in a point-of-care test in developing countries. While Chan et al. admit that their assay is less sensitive than using MS, they note that it is able to detect dead bacterial fragments, whereas conventional assays require that live, intact bacteria be present for positive results. The researchers conclude that further testing on clinical sputum samples will help validate the clinical utility of these isolated antibodies for use in assays.

Overall, Chan and colleagues have proved it is possible to extract lipids efficiently and quickly and detect them in a rapid-format assay if needed and without expensive equipment and extensive training. This gives hope that future assays can be developed to diagnose deadly infections like TB more quickly, even in resource-poor settings.



CREDIT: RAY BUTLER AND JANICE CARR OF WIKIMEDIA COMMONS.JPG
Centers for Disease Control and Prevention

Mary L. Chang (mchang@asbmb.org) is publications manager for the Journal of Lipid Research and Molecular & Cellular Proteomics.

MCP MOLECULAR & CELLULAR PROTEOMICS

Mitochondrial DNA, mating and mussels

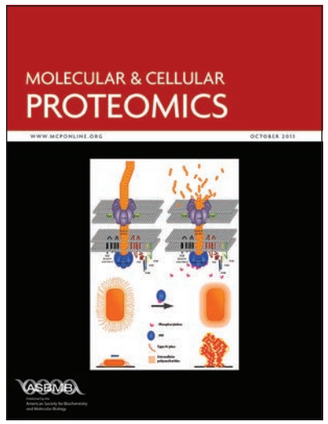
BY RAJENDRANI MUKHOPADHYAY

In humans and most other animals, offspring get all their mitochondrial DNA from their mothers. But in mussels and other related bivalves, fathers also give their offspring their mitochondrial DNA. In a recent paper in the journal Molecular & Cellular Proteomics, researchers propose a new model to explain this mechanism of mitochondrial DNA inheritance, which is called doubly uniparental inheritance, or DUI. The model also puts forward a possible explanation for sex determination in mussels, the mechanisms of which are not known.

IMAGE CREDIT: WILSON44691 OF WIKIMEDIA COMMONS.JPG
Mussels and barnacles in the intertidal near Newquay, Cornwall, England.

"We thought that study of DUI might lead to deeper understanding of the function and evolution of mitochondrial DNA in general, with implications in a variety of areas," says David Skibinski at Swansea University in the U.K. "This could include areas of benefit to humans, for example, in understanding genetic conditions caused by mitochondrial DNA or assisted reproduction. In evolution, this could include understanding of evolutionary forces and even the endosymbiotic theory of mitochondrial origin."

Mussels are an intriguing case study for DUI. "DUI is present in about 40 bivalve species and could have an origin as old as 400 million years ago. It is a mystery why it exists in some species but not others," says Skibinski.



Besides learning more about mitochondrial DNA evolution and function, Skibinski explains that DUI in mussels also plays into sex determination in the animals. "At fertilization, embryos destined to be male must also pass mitochondria into an aggregate in the gonadal tissue and then into their own sperm. Precisely how this is all achieved is not known at the moment," he says.

Skibinski and colleagues decided to look into the proteomic differences between eggs destined to become males (showing the sperm mitochondria aggregation phenomenon) and eggs destined to become females (not showing the mitochondrial aggregation phenomenon). The small proteomic differences they found confirmed a hypothesis they had about DUI: A maternal effect is involved. Mussel dads may be generous in passing along their mitochondrial genomes, but moms still have the final say.

The maternal effect seems to involve proteasome proteins. In fertilized eggs that go on to become male, the proteasome may inactivate the cellular machinery that normally results in mitochondrial dispersal. The sperm mitochondria presumably remain as an aggregate ready for passage into the sperm of the next generation. In fertilized eggs that go on to become female, the proteasome may be less active, and the sperm mitochondria presumably are dispersed among the cells of the embryo.

Thus, the proteasome in the eggs from the females seems to determine whether the resulting offspring are male or female. This is now an area the investigators are looking into in more detail.

Rajendrani Mukhopadhyay (rmukhopadhyay@asbmb.org) is the senior science writer and blogger for ASBMB. Follow her on Twitter at www.twitter.com/rajmukhop.

ONLINE EXTRA

Join Geoff Hunt, ASBMB's public outreach coordinator, and Rajendrani Mukhopadhyay, ASBMB's science writer, for an ASBMB Journal Club about this MCP paper. They will speak with David Skibinski and some of his coauthors to understand how studying mitochondrial inheritance in mussels informs our understanding of mitochondrial DNA evolution in general. Please periodically check ASBMB's Facebook, Twitter or Google+ sites to get the day and time announcement for this exciting conversation.

New editorial board members

THE JOURNAL OF LIPID RESEARCH

Hooman Allayee
University of Southern California, Keck School of Medicine

Ramiro Jover Atienza
University of Valencia, Faculty of Medicine

Maurizio Averna
University of Palermo

Erhard Bieberich
Georgia Regents University

Alan R. Brash
Vanderbilt University Medical Center

Jerold Chun
The Scripps Research Institute

Jonathan Cohen
University of Texas Southwestern Medical Center at Dallas

Lauren A. Cowart
Medical University of South Carolina

Russell Debose-Boyd
University of Texas Southwestern Medical Center at Dallas

Maria Febbraio
University of Alberta

Rana K. Gupta
University of Texas Southwestern Medical Center at Dallas

Anatol Kontush
INSERM UMRS 939

MacRae F. Linton
Vanderbilt University Medical Center

Pingsheng Liu
Institute of Biophysics, Chinese Academy of Sciences

Mohamad Navab
University of California, Los Angeles

Valerie O'Donnell
University of Cardiff

Flavio Nervi Oddone
Pontificia Universidad Catolica de Chile

Takao Shimizu
University of Tokyo

Mary G. Sorci-Thomas
Wake Forest School of Medicine

Dmitri Sviridov
Baker IDI Heart and Diabetes Institute

MCP MOLECULAR & CELLULAR PROTEOMICS

Savithramma Dinesh-Kumar
University of California, Davis

Benjamin Garcia
University of Pennsylvania School of Medicine

Stephen Haggarty
The Broad Institute

Yasushi Ishihama
Kyoto University

Niclas Karlsson
University of Gothenburg

Boris Macek
University of Tübingen

Manuel Mayr
King's College London

Shabaz Mohammed
University of Oxford

Pulling back the curtain on biotech careers

Bio-Link website shows students that the scientific enterprise has the room — and the need — for workers of all sorts

BY ANGELA HOPP

For students with interests in science and technology but with limited knowledge of related professions, figuring out what steps to take toward those careers can be intimidating and deflating. This is especially true for students who could become the first in their families to go to college and for students who want to attend college but can't afford the rising cost of four-year degrees.

To simplify the search for information about biotech careers, the organization Bio-Link, based at City College of San Francisco, established the online resource Biotech-Careers.org. The site provides a breakdown of which academic credentials typically are required for certain positions, how much those positions usually pay, what day-to-day life is like for workers with those jobs, how to network and find internships, and how to land permanent positions.

Sandra Porter, a microbiologist and former community college professor, is one of four co-principal investigators on the National Science Foundation grant supporting many of Bio-Link's efforts, including the careers website. Porter says that, while many organizations and agencies, including the National Institutes of Health, have developed career sites dedicated to science, technology, engineering and math, collectively known as STEM, most of those sites focus on paths requiring advanced degrees.

"For biology career sites, the job descriptions were limited to careers in medicine, health science and academic research," Porter says. "Although these sites do provide information, the emphasis placed on higher-level jobs and advanced degrees might do more harm than good and keep minority students out of scientific fields by reinforcing their concerns about careers in science, technology, engineering or math."

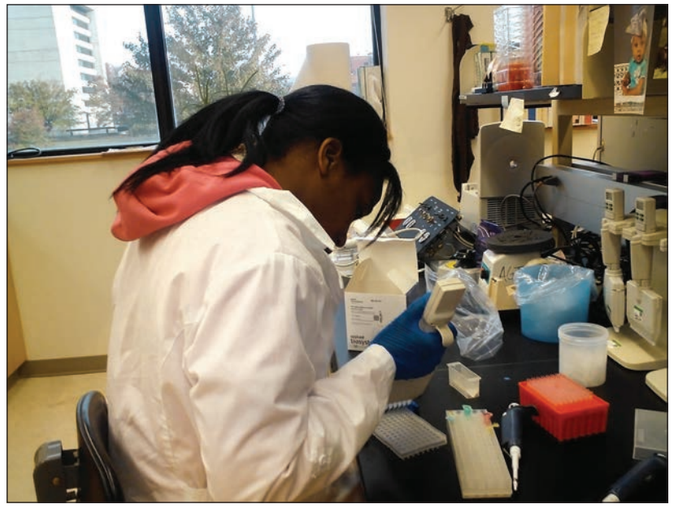


IMAGE CREDIT: BIO-LINK

After double-majoring in chemistry and biology at Virginia State University, Cagney Coomer decided to pursue an associate's degree and certificate in biotechnology at the Bluegrass Community and Technical College in Kentucky. Her work at the University of Kentucky Advanced Genetic Technologies Center is featured on Biotech-Careers.org.

Elaine Johnson, Bio-Link's executive director and principal investigator, notes that large numbers of high school students, in particular minorities, "who might use these jobs as a path to better opportunity, are either uninterested in STEM careers or see multiple reasons to stay away." She explains: "When asked why they find these careers unappealing, students cite concerns about high education costs, insufficient preparation, difficult course work and a lack of information about STEM careers."

Bio-Link is in a good position to help allay some of those concerns. Established in 1998, it is an NSF-funded National Advanced Technology Education Center of Excellence. Bio-Link collaborates with

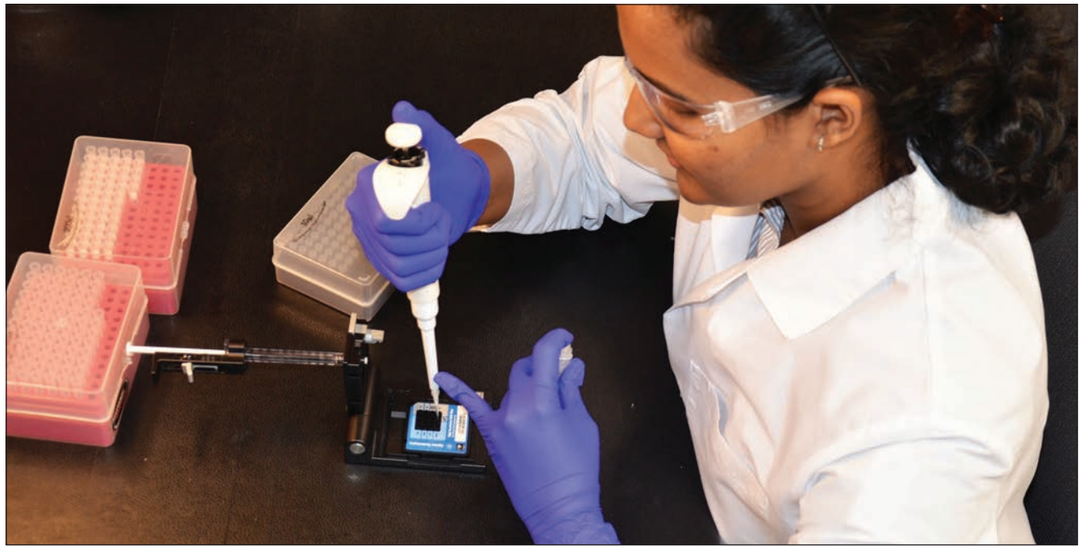


IMAGE CREDIT: BIO-LINK

After earning a bachelor's in biochemistry and a master's in bioinformatics in India, Suchitra Ramani went on to pursue an advanced certificate in biotechnology at Austin Community College. Her work as a research associate at Bioo Scientific Corp. in Austin is featured on the website.

U.S. community colleges to improve programs preparing students for careers in the life sciences. Almost 200 companies, agencies and universities today employ grads from programs with Bio-Link
ties.

Another co-PI at Bio-Link, Linnea Fletcher, director of the Austin Community College biotech program and a former NSF program officer, emphasizes that biotechnology "has become a mature industry with more jobs that do not require a Ph.D. or other advanced degree." She points to the affordability of one-year certificates and two-year degrees offered by community colleges.

"Students may consider STEM programs more attractive if they know it's possible to finish a community college degree in two years and enter the workforce," Fletcher says. "An added advantage is that most community colleges work with local industry advisory boards to ensure that the skills they teach are aligned with the skills needed by local companies."

Lisa Seidman, also a co-PI and a faculty member at Madison (Wis.) College, says that Bio-Link promotes teaching practices that help students come to understand scientific concepts and apply them when on the job. She says that learning subjects in context, such as mathematics, increases confidence and prepares students to perform laboratory calculations in workplace settings.

Indeed, Biotech-Careers.org has several videos showing students getting practical experience through internships while attending school. "Student concerns about the difficulty of science courses and their lack of confidence in their high-school preparation could be mitigated through biotech programs' greater emphasis on hands-on skills and working in the lab," Fletcher says.

Bart Gledhill, a longtime co-PI at Bio-Link and former veterinarian and researcher at the Lawrence Livermore National Laboratory, points out that the careers website doesn't focus solely on workers with community college credentials. The testimonials from undergraduates, graduate students and adult students pursuing second careers prove there are positions out there for professionals of all sorts.

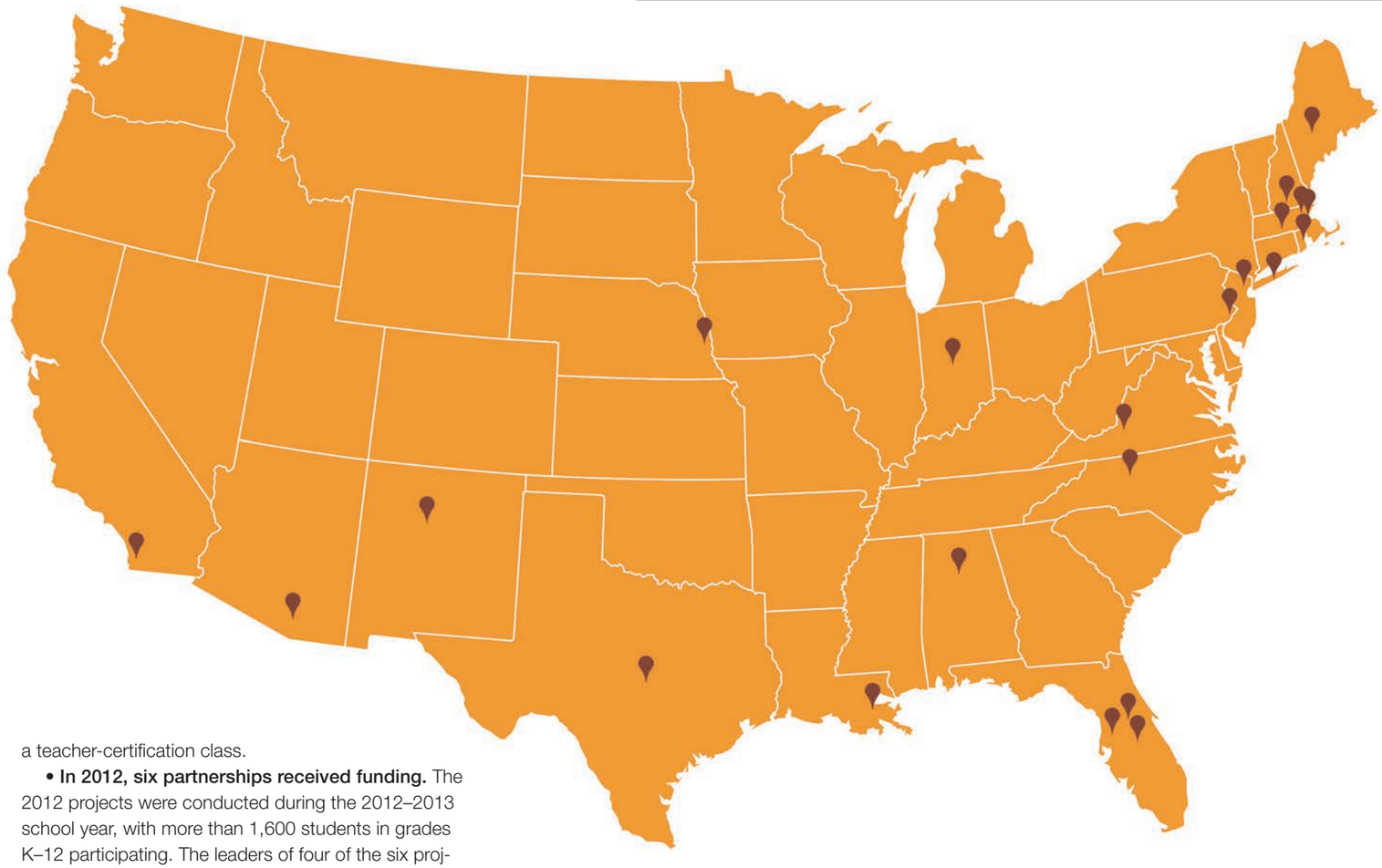
Most importantly, Gledhill says, the stories, photo diaries and videos show students "people like themselves — of varied ethnicities, histories and backgrounds — working in life science jobs."

Angela Hopp (ahopp@asbmb.org) is editor of ASBMB Today. Follow her at www.twitter.com/angelahopp.

HOPES seed-grants program to enhance STEM K–12 education: impact and what's next

BY REGINA STEVENS-TRUSS

The HOPES initiative has resulted in 27 partnerships in 22 cities across the U.S. and has affected the education of more than 3,600 fourth- through 12th-graders. Pins indicate the 22 cities where HOPES partnerships and projects have been initiated.



- ALBUQUERQUE, N.M.
- BIRMINGHAM, ALA.
- CAMBRIDGE, MASS.
- ELON, N.C.
- FARMINGTON, MAINE
- INDIANAPOLIS, IND.
- KISSIMMEE, FLA.
- LEXINGTON, MASS.
- MANCHESTER, N.H.
- MONTCLAIR, N.J.
- NEW ORLEANS, LA.
- OMAHA, NEB.
- ORLANDO, FLA.
- PHILADELPHIA, PA.
- PROVIDENCE, R.I.
- SAINT LEO, FLA.
- SALEM, VA.
- SAN DIEGO, CALIF.
- SAN MARCOS, TEXAS
- TUCSON, ARIZ.
- WEST SAYVILLE, N.Y.
- WORCESTER, MASS.

In 2009, when we envisioned the Hands-on Opportunities to Promote Engagement in Science program, we didn't anticipate the sweeping impact the program would have across the nation. But as the map to the right indicates, this project has the potential to permeate hundreds of schools and impact the science education of thousands of students.

The program

Part I: a three-hour workshop during the American Society for Biochemistry and Molecular Biology annual meeting intended to aid K–12 and college educators' partnerships

Part II: a competitive grant opportunity, funded in part by the National Science Foundation, intended to foster new partnerships that develop after the ASBMB annual meeting

Part III: the performance of the funded project during the school year

See the October 2011 issue of ASBMB Today (1) for a full description of the HOPES program.

Follow-up of the funded projects

In the first two years of the HOPES program, 16 funded projects have been conducted.

• **In 2011, 10 partnerships received funding.** The 10 projects were conducted during the 2011–2012 school year, with more than 2,000 students primarily in grades 4 through 12 engaging in hands-on science projects. We asked project leaders for some demographic information on the students impacted by each project. Five of the 10 project organizers reported that more than 25 percent of the students involved were from ethnic groups that traditionally are underrepresented in the sciences or were from low socioeconomic households. Nine of the projects were conducted with students in grades 9 through 12, three with students in grades 5 through 8, one with students in grade 4, one with a community college class and one with a teacher-certification class.

• **In 2012, six partnerships received funding.** The 2012 projects were conducted during the 2012–2013 school year, with more than 1,600 students in grades K–12 participating. The leaders of four of the six projects reported that more than 50 percent of the students involved were from underrepresented groups. Four projects involved students from low socioeconomic households. Two projects were conducted with 10th- through 12th-graders, one with seventh-graders, two with fifth- and sixth-graders, and one with kindergarteners through fifth-graders. See the September 2012 issue of ASBMB Today (2) for samples of project outcomes.

• **In 2013, 11 new partnerships received funding.** These projects will be conducted during the 2013–2014 school year. (See list of project descriptions on Page 38.)

What's next?

The HOPES program may be a model that could be used to decrease the educational gap between children in the U.S. Although the program does not target projects in schools with underrepresented students, the majority of the projects funded so far appear to affect a high percentage of students from public K–12 schools, which tend to be populated by students from ethnic groups classically

underrepresented in the sciences and by students from low-income households.

With the U.S. population becoming increasingly ethnically diverse and projected to have a nonwhite majority by 2050 (3), it is paramount to find ways to ensure that the next generation of primary- and secondary-school students is well educated. A well-educated public is important for national security reasons, and a public educated in science, technology, engineering and math will ensure our economic advantage in the world.

We hope to continue to conduct the HOPES workshop during the annual meeting. We also plan to continue to inform educators in cities not hosting the ASBMB annual meeting about the HOPES project; just this past August, the program was highlighted in Seattle at the ASBMB's biannual Student-Centered Education in the Molecular Life Sciences special symposium. We are working on securing funds to continue the mini-grant program that supports the educational partnerships that have impacted student education successfully.

Regina Stevens-Truss (Regina.Stevens-Truss@kzoo.edu) is an associate professor of chemistry at Kalamazoo College and a member of the ASBMB Minority Affairs and Educational and Professional Development Committees.

REFERENCES

1. http://www.asbmb.org/asbmbtoday/asbmbtoday_article.aspx?id=14596
2. http://www.asbmb.org/asbmbtoday/asbmbtoday_article.aspx?id=17893
3. http://www.cnn.com/2008/US/08/13/census.minorities/

2013 Hopes Grant Recipients

1. Engineering biology: outreach and opportunities for K – 12 students: a collaboration between Natalie Kuldell at the Massachusetts Institute of Technology and Rebekah Ravgiala at Tyngsborough High School in Tyngsborough, Mass.

2. Fostering science interest among 6th-grade students using engaging, inquiry-based activities at Western Alamance Middle School: a collaboration between Jennifer Uno at Elon University and Susan Dixon at Western Alamance Middle School, both in Elon, N.C.

3. Curiosity: a secrecy of over a century, from polypoid giant cells to cancer stem cells: a collaboration between Yinsheng Wan of Providence College and Scott Macbeth at Classical High School, both in Providence, R.I.

4. Fostering undergraduate biology student engagement in local high-school biology classrooms: a collaboration between Ann Williams at the University of Tampa, Audrey Shor of Saint Leo University in St. Leo, Fla., and Denise Dennison at Wharton High School in Tampa, Fla.

5. Adventures in macromolecular structure and chemistry: a collaboration between Craig Mello at the University of Massachusetts at Worcester and Javier Anduaga at BASIS Mesa in Arizona.

6. Introduction to gel electrophoresis and DNA analysis: a collaboration between James Hazzard at the University of Arizona and Stephen Wollerman, Leslie Shultz–Crist and Richard Reyes at San Miguel High School in Tucson, Ariz.

7. Promoting in-depth human health exploration through guided individual projects utilizing genomic sequencing technologies: a collaboration between Maarten Chrispeels and Danjuma Quarless, both at the University of California, San Diego, and Matthew Leader at High Tech High School in San Marcos, Texas.

8. CSI biology — engaging high school students in hands-on molecular biology and biochemistry using forensics: a collaboration between Nancy Eddy Hopkins at Tulane University and David Swift at Riverdale High School in Jefferson, La.

9. Understanding the production of carbon dioxide and its potential effects on climate change: a collaboration between Steven Miller at Indiana University and Norman Leonard at Pike High School in Indianapolis

10. Epidemiological investigation of commonly acquired infections at animal shelters as a method to teach high-school students microbiology and veterinary medicine: a collaboration between Dan Purcell at the University of New Mexico and David Osmond at The ASK Academy in Rio Rancho, N.M.

11. Genes, mutations and diseases — understanding the origins of genetic disorders through experimental learning: a collaboration between Edwin Li at Saint Joseph's University in Philadelphia and Matthew Jurkiewicz at Bishop McDevitt High School in Harrisburg, Pa.

open channels

LETTER TO THE EDITOR

I recently read the American Society for Biochemistry and Molecular Biology-sponsored Nondefense Discretionary Science Survey after hearing about it from news outlets, and I wanted to congratulate the ASBMB for doing its part to bring this issue to light. Even as an M.D.-Ph.D. student who can fall back on a clinical career, the precipitous fall of research support has been disheartening to the extreme. Bleak messages are showing up in news outlets pretty regularly now, and it's disappointing to know that our society appears unwilling to back our careers.

Most graduate students, in my experience, got into the field of biomedical research out of a desire to help humanity. All we are asking for is the opportunity to do work that ultimately will lessen human suffering, but the general impression from the public is that this work is not a priority. As the survey points out, the government already is making a sizable investment to train us, but trained personnel are of no use to the common good if we cannot be paid to do the work that we're trained for. I fear that we are going to lose the next generation of scientists as a result of this climate. I cannot, in good conscience, recommend a research career to the undergraduates who approach me without warning them of the bleak outlook and urging them to consider other opportunities first. I work at a major research university, and I find that the very people I would call role models — tenured and university distinguished professors — struggle to stay afloat. How am I to have any faith in the future of our profession when even the strongest among us are brought to the brink of failure?

– CODY WESTON, PENNSYLVANIA STATE UNIVERSITY COLLEGE OF MEDICINE

ON THE WILD TYPES BLOG

Poop, prunes and proteomics: one of these is not discussed in this blog post

While much research of late has been focused on understanding what makes up a microbiome in various parts of our bodies and how it affects health and disease, there is less of a focus on how we respond to these communities of bacteria. But to study that, researchers first need to know which proteins in the huge mix of proteins are actually ours. Teasing out the host proteins has been a technical challenge.

In a paper just out in the journal Molecular & Cellular Proteomics, researchers tackled this issue by developing a method that can pick out the proteome of the host gut and see how it changes to shape the gut environment and nurture its teeming community of microbes.

"While it is important to enumerate all the microbes that inhabit our bodies, it may be even more important to measure the ways in which we, as hosts, have evolved ways to shape the microbes' environment, and how changes in that environment can, in turn, shape our own health," says senior author Josh Elias of Stanford University.

Read more about this work at www.wildtypes.wordpress.com.

BIOCHEMISTRY TWEETS

@Rommunism: My Biochemistry book says that polynucleotides in their entirety are "excessively awkward". Polynucleotides and I have that in common.

@dr_leigh: CV needs to self-promote some more. i suck at self-promotion.

@katiesci: I used to think writing a journal article would be like writing a term paper. #itsnot

@A01337z: Nightmares have a name. And that name is Biochemistry #Medicine

@haylstormz: Officially a biochemistry major. Goodbye life.

@NicoleCraneWVU: Aced my biochemistry exam, but I can't figure out how to get out of the Ag Science building. Common sense is lacking.

2014

ASBMB ANNUAL MEETING

April 26–30, 2014 • San Diego, CA

Abstract Submission Deadline: November 8, 2013

ASBMB Topic Categories: #2000 - 2465

Travel Award Application Deadline: November 19, 2013

ASBMB
American Society for Biochemistry and Molecular Biology

www.asbmb.org/meeting2014