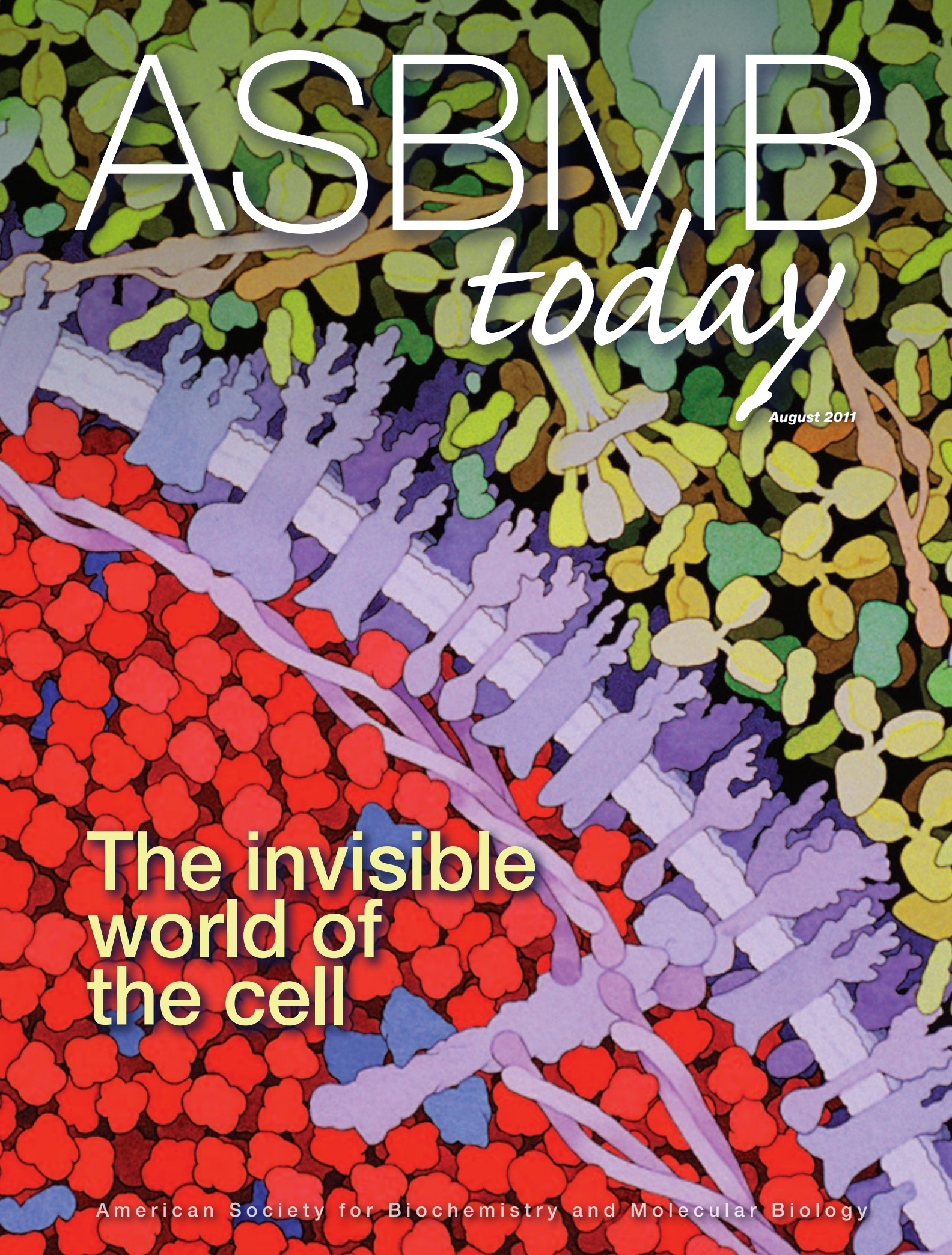

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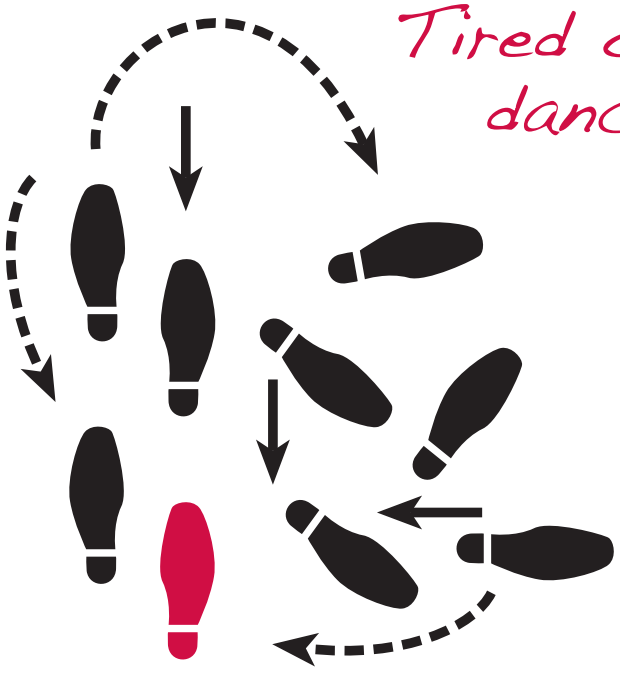

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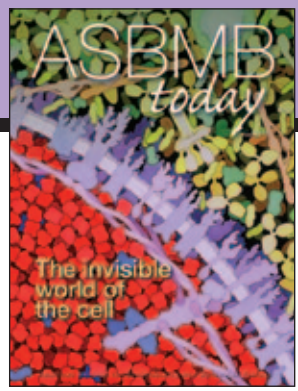

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On the Cover:
David Goodsell's drawings showcase scientific knowledge and art. Here, he depicts the cross-section of a red blood cell. 22

IMAGE COURTESY OF GOODSELL.

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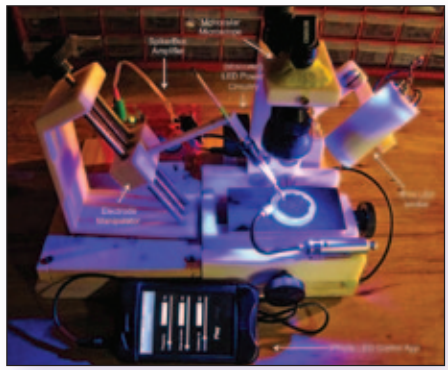

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president's message

The best in bench-to-bedside research: honoring Cindy Parseghian

BY SUZANNE PFEFFER

Imagine a scenario in which a group of scientists with a common goal agree to meet every year at a lovely location to share their results and to discuss the most important next steps needed to move that science forward. The group would work under the presumption that all results, reagents and information would be shared openly and all members would collaborate wherever possible to help the group achieve its shared goal. The meetings would end with a panel discussion to help identify the most important next steps to be taken over the subsequent 12 months. Members would support each other during manuscript and grant reviews and cooperate wherever possible to move the science forward. Sound unusual? If only all research could be carried out this way.

Cindy Parseghian, president of the Ara Parseghian Medical Research Foundation, established precisely this type of framework to bring together researchers seeking a cure (or beneficial treatments) for Niemann-Pick Type C disease. Niemann-Pick Type C is a genetic disorder in which homozygous carriers of mutations in NPC1 or NPC2 proteins accumulate excess cholesterol and glycosphingolipids in their lysosomes. The disease causes progressive neurological deterioration leading to death, usually during childhood. Sadly, Cindy lost three of her four children to NPC disease. In 1994, together with her husband, Michael, and well-known, former Notre Dame football coach (and father-in-law) Ara Parseghian, Cindy created a foundation to support NPC research and bring together clinicians and researchers to try to find a cure. In 1997, with support from the APMRF, the gene for NPC1 was identified (1); in 2000, the gene responsible for NPC2 disease also was identified (2). Cindy has devoted countless hours over many years to fundraising for NPC research; the APMRF recently helped create the Center for Rare and Neglected Diseases at the University of Notre Dame to carry forward NPC disease research. This summer, Notre Dame's dean of sciences, Gregory Crawford, and his wife, Renate, rode their bicycles more than 2,000 miles to raise funds and awareness for NPC disease (3).

The APMRF continues to sponsor annual conferences to bring lab findings more quickly to the clinic. Topics presented range from the molecular roles of NPC1 and NPC2 proteins to the initial results of pilot trials of potential drug therapies in affected children. Some scientists report results from high-throughput drug screens designed to identify compounds that clear cholesterol from the lysosomes of cultured mutant cells; others report on studies of genetically modified mice generated to determine which parts of the cerebellum are most sensitive to loss of NPC function or which drugs may benefit mouse or cat models of the disease. Parents of children with NPC disease also attend these meetings and remind the scientists that time is not on their side. The stories told by parents leave every researcher wishing he or she could do more.

What is unique about these meetings is the gathering of basic researchers

Suzanne Pfeffer and Cindy Parseghian, president of the Ara Parseghian Medical Research Foundation.

together with clinicians and families as well as the requirement that all discussions be carried out completely openly. The expertise of everyone present is brought to bear on how best to do more for children with NPC disease. Could this model be applied to other diseases or important scientific questions? Because NPC disease affects only about one in 100,000 individuals, there is not a large number of patients or researchers working in this area. This is a serious disadvantage when planning clinical trials, but it can be a significant advantage in terms of facilitating interactions among key researchers and encouraging open dialogue.

Mutations in NPC1 protein are responsible for 95 percent of disease cases. This protein spans the membrane 13 times and has three large lumenal domains, each containing numerous disulfide bonds. More than 250 different mutations have been described, located in every region of this large glycoprotein. American Society for Biochemistry and Molecular Biology members Daniel Ory (Washington University) and William Balch (the Scripps Research Institute) have shown that NPC mutant proteins are poorly exported from the endoplasmic reticulum after synthesis due to slow folding (4). Similar mutations have been found in the cystic fibrosis anion transporter (CFTR); thus, the same compounds that may help drive misfolded CFTR to the cell surface or increase CFTR expression might also be of value to NPC patients. Indeed, in cell culture models, ASBMB member Frederick Maxfield (Weill Cornell Medical College) and collaborators have found that histone deacetylase inhibitors may increase levels of functional NPC protein in lysosomes (5). Other therapeutic strategies currently being used involve cholesterol chelation by cyclodextrin or glycosphingolipid synthesis inhibition by miglustat (N-butyl-deoxynojirimycin or Zavesca).

These days, there is a lot of interest in translating lab discoveries into patient therapies. Yet there are few examples that I am aware of that demand and reward the kind of close, successful collaboration achieved by APMRF scientists and clinicians. The National Institutes of Health's Clinical and Translational Science Award consortium was established in 2008 with the goal of reducing the time it takes for laboratory discoveries to become treatments for patients and to engage communities in clinical research efforts. With a budget of $500 million per year and 60 medical school members, the CTSA program also seeks to address the critical need to train the next generation of clinical and translational researchers.

CTSA directors, take note: Cindy Parseghian knows how to foster the most productive interactions between NPC researchers. Her approach should serve as a guide to stimulate collaborative science to tackle any disease. Researchers take note: When we share a common goal, the entire community wins. When we share our results, we can only benefit from the feedback obtained. Cures will be found fastest if we work together. The paths to the cures will be straightest if we draw them together. Cindy Parseghian, we salute you.

ASBMB President Suzanne Pfeffer (pfeffer@stanford.edu) is a biochemistry professor at the Stanford University School of Medicine.

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Bringing it all back home

Spend some time with your member of Congress this summer.

BY GEOFFREY HUNT

Stuck in the lab this summer? Don't lament a missed exotic vacation; instead, take the opportunity to embark on an equally exciting local adventure by getting to know your member of Congress. Legislators will depart Washington, D.C., to spend the recess between Aug. 6 and Sept. 6 back in their home districts interacting with constituents. From hosting town-hall meetings to shaking hands at local grocery stores, congressional representatives use this month to listen to the concerns and opinions of voters. While these discussions often focus on local topics like the economy and gas prices, they also represent great opportunities for scientists to put research in the spotlight.

One of the best ways to increase the visibility of your own research is to invite your representative to visit your laboratory. American Society for Biochemistry and Molecular Biology member Mark Wallert fondly recalls hosting Sen. Amy Klobuchar, D-Minn., at his lab at Minnesota State University Moorhead in 2009. "It was a great opportunity to promote the research we do and let our students share their excitement for science with the senator," he said. Wallert added that the experience provided "a rare opportunity to express my appreciation for the senator's work for Minnesota and to encourage her to support enhanced funding for higher education in general and biomedical research in particular."

Universities and research institutes often are important economic centers of districts, so lawmakers have vested interests in the performance and innovation outputs of researchers. Furthermore, giving legislators firsthand demonstrations of the experiments being performed at lab benches not only shows how funding for scientific research is being put to use but also creates indelible memories of the kind of cutting-edge work being done in their districts.

Politicians love using personal anecdotes to bolster their positions when debating legislation. More than pictures or words on a page, the hands-on experience offered by lab tours gives them compelling evidence they can use to convince others of the importance of supporting the scientific community.

Last month, Sen. Mark Kirk, R-Ill., met with researchers and patient advocates during a tour of Northwestern University. While there, Kirk vowed to promote legislation that would strengthen support for stem-cell research, recalling the few treatment options his father had while suffering from pulmonary fibrosis and pointing to "the limitless potential of stem-cell research" as a means to treat disease and alleviate the kind of suffering his father experienced.

Lab visits also allow for the development of mutually beneficial personal relationships with lawmakers and their staffers. Wallert said he was impressed that Klobuchar "was kind enough to extend an open invitation to schedule time to meet with her in Washington, D.C."

Meanwhile, ASBMB Public Affairs Advisory Committee member Janet Shaw, a professor at the University of Utah, has maintained a close relationship with the office of Rep. Jim Matheson, D-Utah, meeting regularly with the congressman and his staffers both at her institution and in Washington during ASBMB's annual Hill Day.

In addition to allowing time for talking about scientific issues and breakthroughs, the August recess offers constituents a chance to weigh in on the potential impact of proposed cuts to research.

Be sure to contact the ASBMB public affairs staff at publicaffairs@asbmb.org for assistance if you are interested in engaging your member of Congress, whether it is by writing to him or her in support of scientific research, inviting him or her to tour your lab, or visiting his or her office in Washington. It's critical to have your voice heard!

Geoffrey Hunt (ghunt@asbmb.org) is the ASBMB science policy fellow.

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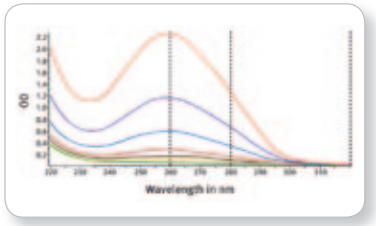

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Aguanno garners mentorship award

Ann Aguanno, an associate professor of biology at Marymount Manhattan College, is a 2011 recipient of a Council on Undergraduate Research Biology Mentorship Award. The awards recognize biologists who demonstrate superior mentorship of undergraduate students in research.

Aguanno is director of the American Society for Biochemistry and Molecular Biology Undergraduate Affiliate Network northeast region. She has an active research program that is investigating the role of a member of the cyclin-dependent kinase family in the development of mammalian tissue systems. She also has an active undergraduate program, guiding the research of students majoring in biology. The program has enjoyed much success as of late, receiving multiple grants and honors.

Berg honored with public service award

American Society for Biochemistry and Molecular Biology President-elect **Jeremy M. Berg** is the recipient of a 2011 Public Service Award from the American Chemical Society. The annual award recognizes outstanding contributions to public service or to the development of public policy that benefits the chemical sciences.

Berg is associate vice chancellor for health policy and planning at the University of Pittsburgh and is a professor in the University of Pittsburgh School of Medicine's department of computational and systems biology. Research in his lab is centered on molecular recognition by proteins in biological systems with the goal of understanding these processes on the structural, thermodynamic and kinetic levels. Through this analysis, he hopes to attain a more complete understanding of the mechanism of these systems.

Wessler receives FASEB Excellence in Science Award

Susan R. Wessler, who holds a University of California president's chair and is a distinguished professor of genetics in the department of botany and plant sciences at the University of California, Riverside, has been named the recipient of the Federation of American Societies for Experimental Biology 2012 Excellence in Science Award.

The award recognizes women whose outstanding career achievements in biological science have contributed significantly to furthering our understanding of a particular discipline. Wessler is recognized internationally for her work in plant genome structure and stability.

Wessler's research looks at transposable elements in plants with a focus on the characterization of active transposable elements and determination of how they contribute to genome evolution and adaptation. To address these questions, Wessler uses a combination of genetic, biochemical and genomic approaches.

Six ASBMB members win Protein Society awards

Six American Society for Biochemistry and Molecular Biology members recently received awards from the Protein Society.

D. WAYNE BOLEN, of the University of Texas Medical Branch, was honored with the Christian B. Anfinsen Award for resolving the long-standing question of how urea denatures proteins and how compatible osmolytes force folding.

JOHANNES BUCHNER, a professor in the department of chemistry at Technische Universität München, was given the Hans Neurath Award for his numerous contributions to protein science, specifically in the context of protein folding and molecular chaperones.

MICHAEL SUMMERS, a Howard Hughes Medical Institute investigator and professor of chemistry and biochemistry at the University of Maryland Baltimore County, was given the Carl Brändén Award. Summers received the award for his contributions to advancing understanding of retrovirus structure, assembly and function, primarily using NMR spectroscopy.

BRENDA SCHULMAN, a Howard Hughes Medical Institute investigator and co-director of the molecular oncology program at St. Jude Children's Research Hospital, and **WEI YANG**, of the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health, were jointly awarded the Dorothy Crowfoot Hodgkin Award. Schulman was honored for her contributions to the understanding of the ubiquitin and ubiquitin-like systems

WAGNER

BROWN

through structural, biophysical and biochemical insights. Yang was recognized for studies that led her to propose a model of two-metal ion catalysis for a large class of nucleic acid enzymes.

GERHARD WAGNER, the Elkan Rogers Blout professor of biological chemistry and molecular pharmacology at Harvard Medical School, received the Stein and Moore Award for his contributions to protein science and for shaping the field of protein NMR.

IN MEMORIAM

James Brown

James Robert Brown was born in Port Angeles, Wash., on August 17, 1930, and died in Austin, Texas on May 7, 2011, at the age of 80.

Brown entered the University of Washington in 1949, but his studies were interrupted by service in the U.S. Army during the Korean War. He completed his bachelor's degree in chemistry in 1956 and obtained a doctorate in biochemistry from the University of Washington Medical School in 1963, working with Hans Neurath on the fundamental protein characterization of pro-carboxypeptidase.

Brown was awarded a NATO postdoctoral fellowship to work at the Medical Research Council Laboratory for Molecular Biology in Cambridge, England (1963 – 1965), where he participated in sequencing chymotrypsin and elastase with Brian Hartley and Frederick Sanger. Together with Hartley, Brown developed the method of diagonal electrophoresis to locate disulfide bridges in proteins. He obtained a second NATO fellowship (1965 – 1966) to work in the biophysics department at the Weizmann Institute of Science in Rehovoth, Israel, before joining the University of Texas at Austin, where he worked as a faculty member and then as a research scientist with the Clayton Foundation Biochemical Institute until his retirement in 1992. While in Austin, Brown determined the primary structure of both human and bovine serum albumin.

A modest and reserved individual with an ironic sense of humor, Brown loved his family, science, music and the natural world and supported a number of humanitarian and progressive causes throughout his life.

Postage stamps honor two ASBMB members

The U.S. Postal Service recently issued Forever stamps honoring four American scientists. Former American Society for Biochemistry and Molecular Biology President Severo Ochoa and ASBMB member Melvin Calvin were among the featured scientists. The two other stamps recognized botanist Asa Gray and physicist Maria Goeppert Mayer.

According to a press release from the USPS, "With these stamps, the third in the American Scientists series, the Postal Service honors four Americans who, while dedicating their lives to understanding the fundamental process of nature, made extraordinary contributions to the advancement of science."

Calvin was the first scientist to trace in detail the process of photosynthesis, and he conducted pioneering research on using plants as an alternative energy source. He won the Nobel Prize in chemistry in 1961.

Ochoa was the first scientist to synthesize ribonucleic acid, and he competed in the race to decipher the genetic code. Ochoa won the Nobel Prize for physiology or medicine in 1959 and was the president of ASBMB in 1958.

PHOTOS: U.S. POSTAL SERVICE ©2010.

Doctoral candidate Erin Greiner, 27, received her award at the Gordon Research Conference: CAG Triplet Repeat Disorders, which was held June 5–10 in Italy and attended by Journal of Biological Chemistry Associate Editor Joel Gottesfeld. PHOTO: JEFF CANTLE.

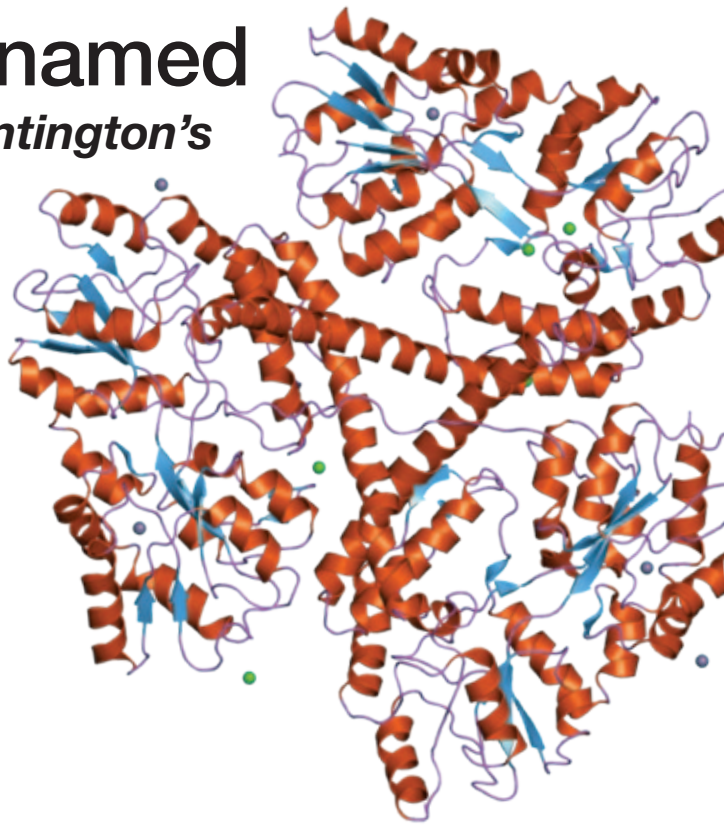
Inaugural winners named

UCLA student takes aim at Huntington's

Erin Greiner, a doctoral candidate in the department of chemistry and biochemistry at the University of California, Los Angeles, was named the first recipient of the Herbert Tabor/Journal of Biological Chemistry Young Investigator Award.

Greiner's research focuses on the function and mechanism of the huntingtin protein, the causal protein in Huntington's disease. She uses spatiotemporal-proteomic and systems-biology approaches to profile full-length Htt-interacting proteins from HD and wild-type mice to uncover novel protein networks and potential therapeutic targets in the mammalian brain.

Greiner, a Grand Rapids, Mich., native, is co-mentored by Joseph A. Loo of UCLA's department of chemistry and biochemistry and X. William Yang of its department of psychiatry and biobehavioral sciences. Greiner completed her undergraduate work at The College of Wooster in Ohio.



UMass student is pursuing anti-hepatitis C therapies

Keith Romano was named an award series winner for his promising work with hepatitis C virus at the University of Massachusetts Medical School.

Raised in Sturbridge, Mass., Romano followed in the footsteps of his parents, who both worked in science and medicine. He completed his undergraduate degree at Colby College in Waterville, Maine, and now is pursuing an M.D./Ph.D. at UMass. For the past five years, he has worked with Celia Schiffer in the department of biochemistry and molecular pharmacology.

HERBERT TABOR YOUNG INVESTIGATOR AWARD

Romano's research aims to overcome HCV protease inhibitor resistance. He has determined high-resolution crystal structures of the NS3/4A protease in complex with viral substrates and drugs synthesized by his team's medicinal chemist, Akbar Ali. This work has led to a better understanding the molecular basis of drug resistance against four leading HCV protease inhibitors — telaprevir, danoprevir, vaniprevir and MK-5172.

"I hope that these findings facilitate the more rational evaluation of novel drug candidates," Romano says, "and provide a direct path for designing more efficacious and tolerable anti-HCV therapies."

M.D./Ph.D. candidate Keith Romano received his award at the 25th annual symposium of the Protein Society, which was held July 23-27 in Boston and attended by JBC Associate Editor Norma Allewell. PHOTO COURTESY OF BRENDAN HILBERT.

Postdoc is recognized for her work with cytochrome P450

Sarah Barry received her award at the 17th International Symposia on Cytochrome P450, which was held June 26-30 in Manchester, U.K., and attended by JBC Associate Editor F. Peter Guengerich.
PHOTO COURTESY OF BRIAN FLEMING.

Sarah Barry, a postdoctoral researcher at the University of Warwick in the U.K., received the award for her investigations into cytochrome P450 enzymes.

A native of Dublin, Barry earned her bachelor and doctoral degrees in chemistry at University College Dublin, where she studied the development of small molecule enzyme mimics with Peter Rutledge. Barry is currently sponsored by the Biotechnology and Biological Sciences Research Council, and she is working under the direction of professor Greg Challis while investigating the biosynthesis of the phytotoxin thaxtomin A, a key virulence factor produced by the plant pathogenic bacterium Streptomyces scabies.

HERBERT TABOR YOUNG INVESTIGATOR AWARD

With collaborators from Cornell University and the University of Manchester, Barry has been pursuing the function and mechanisms of the cytochrome P450 enzymes that are involved in the biosynthesis of the phytotoxin. Thus far, she says, they have found that one P450 enzyme "is capable of direct nitration, which is an unprecedented activity for a cytochrome P450." Barry emphasizes: "This research is highly interdisciplinary, encompassing organic, inorganic analytical and biological chemistry as well as molecular genetics."

The toxic professor syndrome

BY YUSUF A. HANNUN AND DANIEL M. RABEN

Academic biomedical research is experiencing many existential problems as relative funding dries up. This already is resulting in serious consequences for the very fabric of American biomedical investigation, its attractiveness as a career, and its long-term viability. Established investigators are disillusioned and overwhelmed, beginning investigators are disheartened, and students are turning away from pursuing academic careers in biomedical investigation.

It is intriguing that this critical issue has not become a subject of intense national debate. One would assume that the National Institutes of Health, the National Science Foundation, the Association of American Medical Colleges and other key academic societies already would have approached this issue at a strategic level. Moreover, it seems that academic societies are stuck in the primary mode of soliciting increased funding for the NIH and the NSF from Congress, rejoicing when this happens and despairing when it does not.

It should be noted that while attempting to increase government-sponsored funding is a highly laudable goal, it nevertheless is a distinct issue from assuring that a sustainable size of the workforce can be supported by existing (and projected) funding.

Since the NIH is devoted to enhancing human health and is focused on funding research that advances our understanding of human health and disease, and since the NIH has emerged as the key funding source for biomedical investigation, it seems appropriate that they take a lead in tackling this issue. So how can we attract the NIH's attention and get it to deal with this crippling problem?

Below, we propose to capture this issue and spur its serious study by formulating a new syndrome: the toxic professor syndrome. Preliminary analysis of the pathogenesis of this syndrome utilizing simple biochemical theory suggests key nodes for intervention and for developing sustainable policy.

Symptoms

The toxic professor syndrome afflicts all levels of academic rank in biomedical research. It displays a wide range of severity, from isolated anxiety over funding to fulminant disillusion and resignation from careers in biomedical research. All subjects spend increasing time chasing funding and less time advancing research, teaching and mentoring. As this imbalance is aggravated, a toxic mood permeates the entire enterprise, with increasingly sour, antagonistic and at times offensive behavior. Moreover, this toxicity spreads to trainees who increasingly shun academic careers to avoid this toxic fate.

Etiology

The etiology, pathogenesis and treatment of this syndrome are not well studied but appear primarily to trace to a mismatch between the number of independent investigators and the funds available for sustaining a healthy steady state. The latter remains dominated by NIH extramural funding, especially R01 funding.

To be sure, the NIH and NSF are not the sole causes of the toxic professor syndrome. When NIH funds increased many years ago, there was a clear expansion at many universities. More faculty members were hired, leading to an increase in the number of grant applications. Additionally, universities required investigators to obtain increasing portions of their salaries from their direct funds. In effect, and unwittingly, the NIH has emerged as the key supporter of biomedical research as well as faculty salaries. As such, academic medicine and its administrative leaders have become increasingly dependent on the NIH for basic operation. The price has been a highly leveraged financial system, leading to stress and contributing to what is effectively unfunded or underfunded faculty.

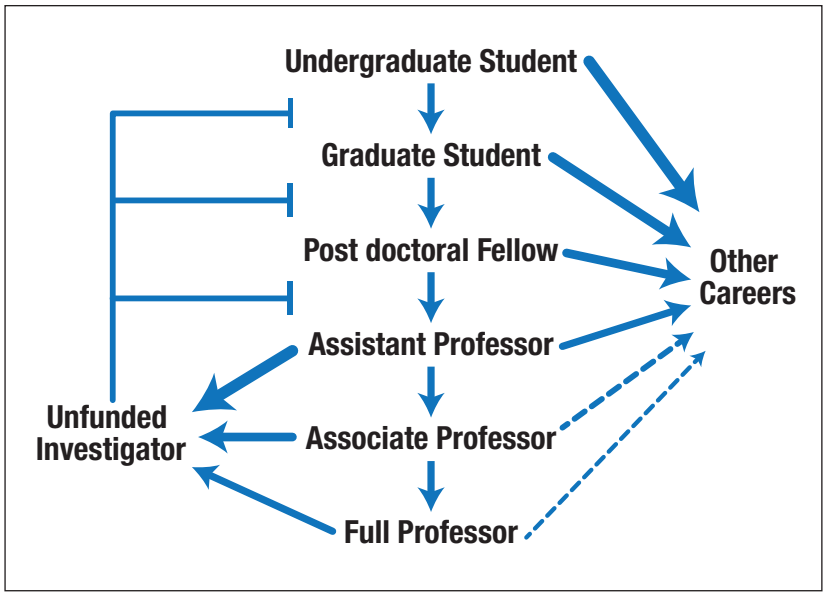
Pathogenesis

The pathogenesis of this disorder can be understood by analogy to simple metabolic pathways with a rate-limiting initial step, subsequent reactions that advance precursors/products on a metabolic pathway, and simple feedback mechanisms (Fig. 1). As flux through the pathway slows at key junctures, there is an accumulation of toxic intermediates and byproducts, primarily the unfunded investigators. This profoundly influences the operation of the system. Not only are those faculty members unable to conduct the research to which they have already committed lifetimes of study and preparation, but they become financial burdens on their departments and colleges. The professors send negative feedback signals to earlier steps in the pathway, alerting junior faculty, postdoctoral fellows, graduate students and even undergraduate students to the overflow in the system, thus discouraging students from pursuing training and careers in academic research.

Treatment

So what is the cure? The solution will entail devising a rational approach for the growth and sustainability of biomedical research as we move into the 21st century. We cannot offer specific solutions, but we do suggest some areas of study and further investigation.

One approach will require action by the NIH, preferably in conjunction with academic societies and college administrators (e.g., AAMC). From an experimental point of view, these toxic academic pathways are amenable to modeling approaches and economic analyses. For example, one could predict a reasonable steady-state number of investigators who can be supported by the system (the NIH, universities and other funding sources) and the natural turnover of those investigators, allowing the determination of a healthy rate of influx into the system. The NIH can help control the influx by awarding a predetermined number of R01s to beginning and early career investigators. The current policy of inflating this number simply backfires; it increases the flow through the assistant professor level and creates a bottleneck that spills into the unfunded investigator pathway (Fig. 1).



The pathway to professorships. The pathway leading from undergraduate trainee to academic professor is indicated. The influence of other, non-professorship, careers and feedback inhibition from unfunded professors also is indicated.

Academic institutions, individually or collectively (e.g., through AAMC), also could help. Lessening the salary burden on individual proposals would enhance the ability of an investigator to conduct research with a reduced number of awards. Analysis should also extend to defining the necessary size of the workforce and supplemental components as well as approaches that incentivize academic institutions to participate in defining sustainability.

There are additional examples of efforts to alleviate, if not cure, this syndrome. The American Society for Biochemistry and Molecular Biology Public Affairs Advisory Committee has outlined a series of recommendations for providing a healthier environment. These essentially involve refocusing NIH priorities toward individual-investigator, RO1-driven research.

The syndrome often affects some tissues (disciplines) more than others. As interest in basic research declines in favor of translational or big science research, some tissues suffer from a lack of support. Additionally, investigators often find their research takes them into areas where their fields historically have been unappreciated. In our field, lipid researchers have found that as they venture into areas where the importance of lipid research has not been recognized finding expert review on study sections becomes difficult. The ASBMB Lipid Research Division is working with NIH administrators more fully to understand this aspect and provide researchers with a cadre of eligible, mid- to senior-level investigators who are willing to sit on various study sections.

The above solutions depend on organizational interventions. Clearly, members of the community must help alleviate this syndrome through active participation and prodding of action at all levels (within departments and academic centers, through representative societies, and by voicing studied opinions in national forums).

In conclusion, by presenting the current crisis in biomedical research as a syndrome approaching epidemic proportion, it is hoped that it becomes the subject of serious study and analysis. Collective and individual efforts are required. This should, in turn, stimulate innovative and exciting insights — and eventually cures — for this pervasive syndrome.

Yusuf A. Hannun (hannun@musc.edu) is the Ralph F. Hirschmann professor and chairman of biochemistry and molecular biology at the Medical University of South Carolina as well as chairman of the ASBMB Lipid Research Advocacy Committee. Daniel M. Raben (draben@jhmi.edu) is a professor in the department of biological chemistry at the Johns Hopkins University School of Medicine and director of the ASBMB Lipid Research Division.

Angel investment from the masses

A new type of funding agency taps everyday donors to fund pilot science projects.

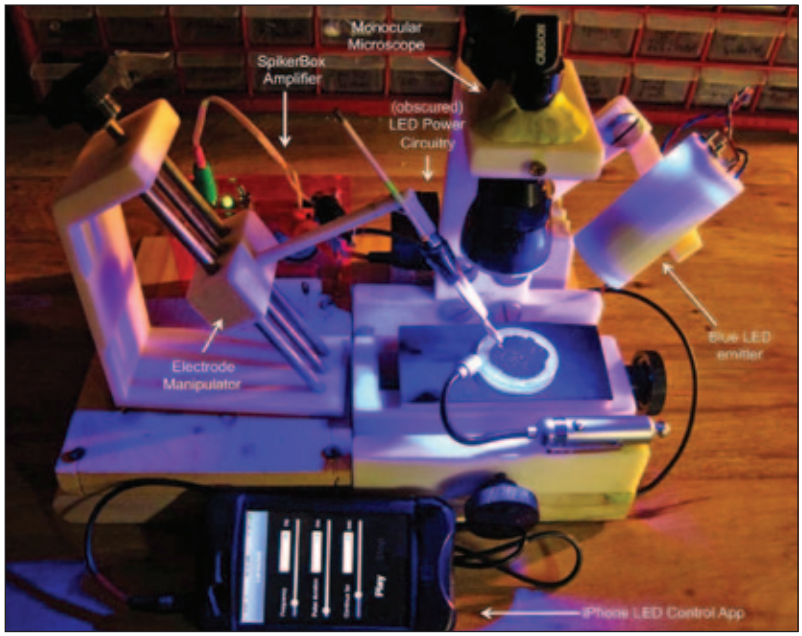
BY JIANFEI (JEFFREY) ZHAO

During the snowy winter of 2008, David Vitrant, then a graduate student at the University of Pittsburgh, felt the chilling effects not only of the dead cold but also of the funding shortage facing young researchers. "There was very little government or foundation money available to our generation," recalled Vitrant. Frustrated by the lack of funding, Vitrant took matters into his own hands. Inspired by the success of microfinance for small businesses and the rural poor in developing countries, he worked together with his college friend Mark Friedgan to create FundScience, a new funding scheme geared toward young scientists, to raise money and distribute small grants.

Vitrant is not alone. David Fries, a marine engineer at the University of South Florida and a co-founder of SciFlies, another science microfinancing organization launched in 2009 but currently under reorganization, laments that there is very limited funding for researchers to start pilot projects to explore new ideas. To address the paucity of traditional grants, a small but growing number of nonprofit organizations solicit small contributions from everyday donors to fund academic research projects that typically require grants in the range of a few thousand to tens of thousands of dollars. Once proof of concept is established using such seed grants, the applicant can follow the traditional route to apply for larger grants. A more commercially minded type of microfinancing for science also exists. Unlike SciFlies and FundScience, the Open Source Science Project will "retain partial ownership of any for-profit company that grows out of a funded research project," according to its co-founder, Priyan Weerappuli.

Having laid the groundwork by generating media attention and surveying potential donors, all three organizations are now accepting grant proposals. To ensure scientific rigor, all proposals are subject to peer review, either by invited reviewers from university faculty members (FundScience and OSSP) or coordinated by the American Association for the Advancement of Science (SciFlies). Each organization has a different requirement for the eligibility of applicants. Only a student, after obtaining the approval of his or her institution and principal investigator, can apply for a FundScience or OSSP grant, while SciFlies only accepts applications from PIs. Unlike traditional grant applications, the ultimate judge is each donor, not the reviewers. To attract potential investors who may not have a science background, the applicants need to write an exciting proposal abstract aimed at the general public, according to the FundScience website.

Bridging the gap between researchers and the public is another goal that all three organizations embrace. Vitrant said that scientists work "in a vacuum striving for scientific knowledge." To engage the donors in the funded projects, FundScience uses social media, such as blogs, YouTube videos and Facebook. Grantees are required to post regular reports to the websites, informing and educating the public.



A prototype machine to demonstrate optogenetics, funded by FundScience and developed by Backyard Brains with senior engineering design students from the University of Michigan. Reprinted with permission from www.backyardbrains.com.

Though the idea of direct public funding for science is gaining traction, the organizations are at early stages of development. They have a limited choice of projects for funding on their websites. The OSSP only accepts proposals involved in water quality and water resource utilization, and FundScience focuses on hypotheses related to the pathogenesis or modeling of diseases. The organizations want to narrow their focus during the proof-of-concept trial and expand their funding scopes later. One of the biggest challenges the microfinancing organizations face is battling the misconception that research can lead to a quick cure. "A considerable number of potential investors … appear to believe (to varying degrees) that the scientific research process is a linear process leading us from ignorance to enlightenment," says Weerappuli.

In spite of the hurdles, the founders are passionate about their organizations. As Fries puts it, "I'm sometimes more fascinated by SciFlies than by my own research." Vitrant works fulltime for FundScience. And progress is being made. $512.20 provided by FundScience, an amount that is too tiny to attract the attention of regular funding sources, was all the money needed to allow five undergraduate students at the University of Michigan to make a prototype tool they used for a project in optogenetics. Another grantee is ready to publish results partially funded by FundScience. It is still a long way from addressing the funding shortage for early-stage science projects; however, "the progress has been heartwarming," Vitrant said.

The traditional funding of basic science has largely relied on the patronage of wealthy individuals and, through national funding agencies, taxpayers. Now, with the support of microfinancing, scientists can be less frustrated by funding and more focused on science when they test new projects.

Jianfei (Jeffrey) Zhao (zhao_jianfei@yahoo.com) is a postdoctoral fellow at the National Cancer Institute.

For more information:

- FundScience: fundscience.org
- SciFlies: sciflies.org
- Open Source Science Project: theopensourcescienceproject.com

onlinegraduationsurvey

The American Society for Biochemistry and Molecular Biology annual online graduation survey has been sent to the departments and programs we have on file as offering degrees at undergraduate and/or graduate levels in biochemistry, molecular biology, the biochemistry track in chemistry, or biotechnology. WE NEED YOUR HELP. If your department or program offers such a degree and your chairperson/department head/coordinator has not yet completed the survey, please encourage him or her to do so, or if your program has not received the survey, please contact us at education@asbmb.org.

This survey is used to follow trends in demographics, to identify programs that are especially successful in graduating minorities, and to compare minority progress within our discipline with that in other scientific disciplines.

We have compiled a list of programs that offer degrees in biochemistry, molecular biology, chemistry and biotechnology on the ASBMB website at http://bit.ly/ASBMBGradSurvey. This list allows prospective students to identify potential programs and for graduate programs to identify recruiting contacts and to provide direct links to their websites.

Thank you,

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Anne-Claude Gingras: probing phosphatase complexes

Using the power of proteomics, Gingras is providing new insights into phosphatase activity, regulation and interaction.

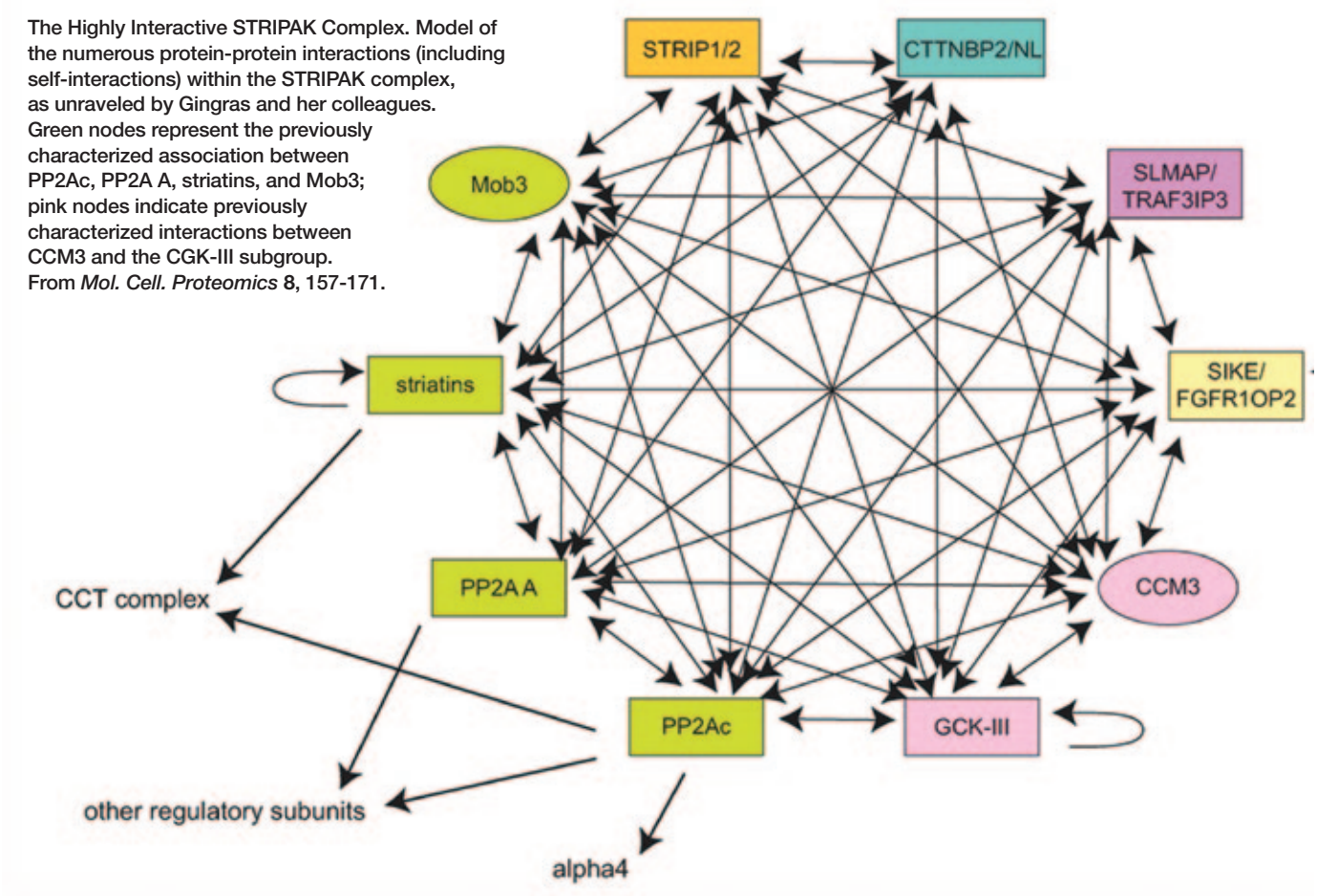
BY NICK ZAGORSKI

There are two sides to every story, two halves that make a whole. In signal transduction, the cascade of protein activity that converts extracellular signals into an intracellular response, the complementary parts of the tale are the protein kinases and phosphatases — the complementary enzymes that drive signal transduction by adding and removing phosphate groups on target proteins.

As a graduate student in the mid 1990s, Anne-Claude Gingras was struck by the contrast between knowledge of these two enzymes. "We knew so much more about the kinase side of the story than about the phosphatases," she says. "That didn't seem right, so I wanted to investigate phosphatases further."

Now a senior investigator at the Samuel Lunenfeld Research Institute at Mount Sinai Hospital in Toronto as well as an associate professor in the department of molecular genetics at the University of Toronto, Gingras has done just that — and more.

Not yet 40 years old, Gingras rapidly is establishing herself as an international leader in understanding how phosphatases are



The Highly Interactive STRIPAK Complex. Model of the numerous protein-protein interactions (including self-interactions) within the STRIPAK complex, as unraveled by Gingras and her colleagues. Green nodes represent the previously characterized association between PP2Ac, PP2A A, striatins, and Mob3; pink nodes indicate previously characterized interactions between CCM3 and the CGK-III subgroup. From *Mol. Cell. Proteomics* 8, 157-171.

regulated and how they recognize their substrates. She's also become an innovator in the proteomics field, having developed experimental and computational tools that can better characterize dynamic protein-protein interactions.

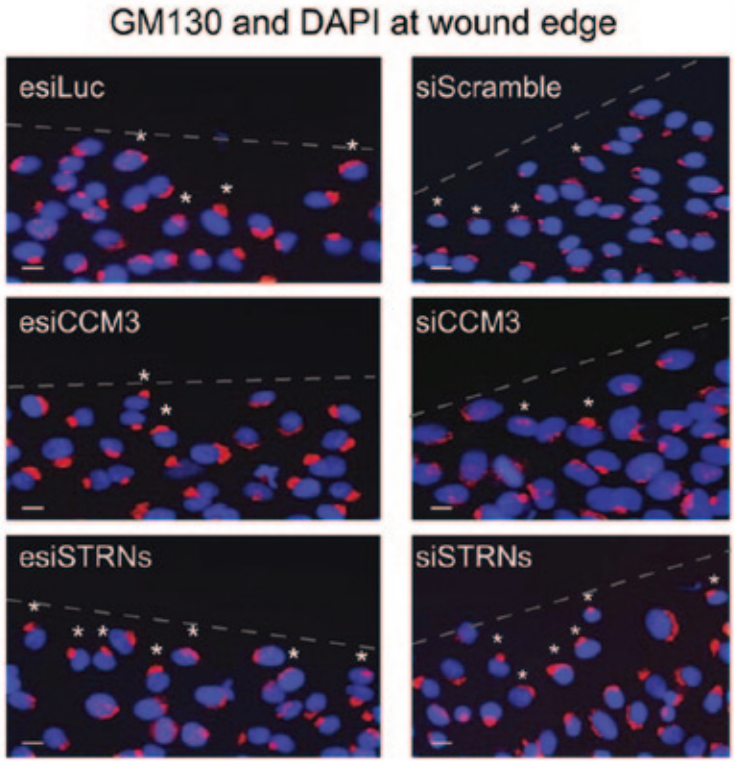
It's quite a trajectory for someone who just 17 years ago was a bright but self-professed naïve graduate student who could barely speak or write English. But it's a path that anyone who has worked with Gingras will say is well deserved.

Cookbooks and circuitry

The first monumental step in this research journey occurred in 1994, when Gingras set foot at McGill University to begin graduate school. Though only a little more than 150 miles from her hometown on the outskirts of Québec city, the vibrant multicultural metropolis of Montreal seemed like another country to the young Québécois.

"I had never really left home before," she says, "but I knew I had to broaden my horizons, and learn English, if I could fully realize my potential. I thought that going to school in Montreal would be a great compromise. I could do research in English at McGill yet order food in French and therefore not die of starvation in my first year."

And while the first few months were challenging, her talents shone through fairly quickly. For while Gingras may not have been worldly, she did possess a great deal of scientific know-how.



STRIPAK and the Golgi. Another of Gingras' recent discoveries with STRIPAK is its role in Golgi orientataion. Here, cells depleted of STRIPAK component CCM3 by esiRNA (left) or chemical siRNA (right) show reduced numbers of Golgi properly positioned (white asterisks) in response to a wound (shown by dashed line). esiLuc and siScramble are negative controls. From *J. Biol. Chem.* 286, 25065-25075.

For starters, her parents, both nurses, had fostered Gingras' creative and intellectual spirit since early childhood. "My father spent his spare time working on electronics, and I used to love helping him install transistors on circuit boards," she recalls. "He also had a fascination with chemistry and aerospace — my grandmother told me some pretty entertaining stories relating to his improper storage of rocket fuel — and hoped that one of the kids would become an astronaut or a chemist. I ended up the closest."

Gingras' mother, meanwhile, helped her develop her creative side and her lab hands by teaching her crafts and cooking. "She also bought me this super cool book of experiments called 'Le Petit Débrouillard' ('The Small Resourceful One'). I did every experiment in the book, some more than once."

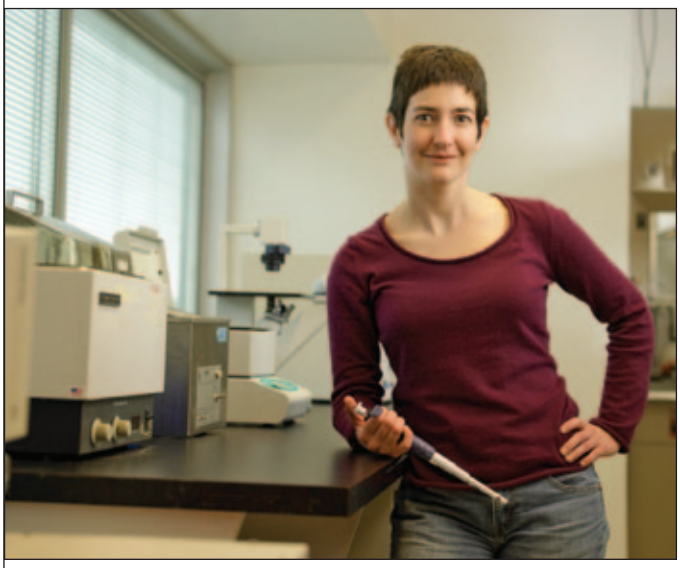
After high school, Gingras stayed close to home and attended Laval University, where she studied biochemistry. The program at Laval focused heavily on laboratory and experimental work, and, by the time she graduated, Gingras had already developed significant hands-on experience.

"However, what really convinced me to go to graduate school was my summer project working for a just-starting young professor, André Darveau. As a new appointee, Darveau had a small team and taught me several important techniques himself while giving me a lot of independence. I really caught the research bug!"

Darveau also helped Gingras select some potential graduate advisors to meet with at McGill, which eventually led to her accepting a position with Nahum Sonenberg, whose group studied the mechanisms that control protein translation.

A productive start

Right as Gingras joined the lab, another graduate student, Arnim Pause, had just cloned two insulin-regulated small proteins that bind to eukaryotic translation initiation factor 4E, the protein that binds the cap on the end of messenger RNA



Rising science star Anne-Claude Gingras uses proteomics and other approaches to understand phosphatase biology and cell signaling networks.

and brings the RNA to ribosomes. These two peptides, 4E-BP1 and 4E-BP2, were found to inhibit cap-dependent translation when they bound.

"The topic was fresh and exciting, and I was able to work on a project that became a nexus for all of the lab's interests," she says. "I could contribute to projects ranging from structural biology to virology to mouse development."

The work cemented an interest in how protein phosphorylation regulates protein activity and also set off a graduate training career of which even the most demanding taskmaster would be proud. The various projects she collaborated on at McGill resulted in nearly 50 scientific publications, a number that continues to grow to this day.

Gingras is quick to point out she owes a good deal of that remarkable number to arriving at Sonenberg's lab at an extremely opportune time and that most of the work was collaborative.

In addition, she spent a little longer than average in her graduate lab as she waited for her partner, Brian Raught (now a researcher at the Ontario Cancer Institute), so they could move on together. "That worked out really well," she notes. "I had enough data to graduate, but I knew once I started my postdoc the pressure to get positive findings would start again. But in this intermediate period, I had this window where I could try these fun, fishing-type projects, and I took full advantage of that opportunity."

One of Gingras' favorite studies during her McGill time was a project that combined old-school gel electrophoresis with mass spectrometry to identify 4E-BP1 phosphorylation sites regulated by the mTOR signaling pathway, which then led to identifying the in vivo hierarchy of 4E-BP1 phosphorylation. That publication played a big part in stimulating a desire to do postdoctoral training in proteomics.

Fortuitously, one of the best proteome researchers, Ruedi Aebersold at the Institute for Systems Biology in Seattle, was a long-time collaborator of Sonenberg.

"Ruedi had just published his first ICAT paper, which documented the use of stable isotopes to quantify proteins," she says. "I had already collaborated extensively with Ruedi's group, particularly Steve Gygi, who is now at Harvard, to identify phosphorylation sites on various translation factors, and I thought that was the place to go to learn how to perform quantitative proteomics and phosphoproteomics."

La grande débrouillarde

In 2005, after her three-year stint in Aebersold's lab, Gingras found herself a wanted woman. Research institutes from across the globe were offering jobs to the rising star. In the end, she decided to come back close to home and joined the Samuel Lunenfeld Research Institute in Toronto.

"Having spent a little time in Canada," she says jokingly, "I knew that Toronto was a superb environment for signaling biology. But during the interview process, what also became apparent was the collaborative spirit that ran through the Toronto community."

"Researchers here work together whenever it makes sense, which provides an extremely stimulating research environment both for faculty and trainees. And given the type and scope of research that I wanted to perform, robust collaborations were essential."

Gingras believes this human element cannot be understated. Even more than her many published papers, Gingras values the many great scientists she has had a chance to work with over the years and the opportunities those interactions opened up.

"The research world is smaller than you think," she says, "and the people you meet along the way will probably come back into your life at some point. So, for young scientists out there, when someone requests some cells or protein from you, be as nice as possible, because you never know what may happen in the future."

As for the present, Gingras' group combines interaction proteomics, phosphoproteomics, functional screens and other approaches to identify and characterize protein phosphatase complexes, several of which she initially identified through discovery proteomics. One such phosphatase complex of interest, which Gingras first discovered while working under Aebersold, is PP4cs, which is linked to DNA damage repair and also is associated with resistance to the potent cancer drug cisplatin.

Another current project, and the subject of two recent

Journal of Biological Chemistry articles, is a large protein complex termed striatin interacting phosphatase and kinase, or STRIPAK. This complex contains both a phosphatase and a kinase bridged by a protein called CCM3 (so named because when mutated, it causes blood vessel defects in the brain called cerebral cavernous malformations). Her group has found that STRIPAK is involved in polarizing Golgi in cells, and they are now further characterizing structure and function.

In the near future, however, Gingras hopes to take a broader approach and try to model signaling networks quantitatively, and she has begun doing some studies in yeast. "On the phosphatase front, we still need to carry out detailed biochemical analyses to understand how they are regulated and how they recognize their targets," she notes. "But at the same time, we need to look at the network level if we want to figure out all the implications of crosstalk and feedback loops."

What's the score?

"Proteomics has tremendously advanced, even in the few years since I arrived at Lunenfeld," Gingras says, "and it has been very exciting to watch this progress. But new possibilities also bring up new challenges, things like ensuring that data quality is kept high and that the data can be shared in an appropriate format with the whole scientific community."

Gingras believes specialized journals like Molecular and Cellular Proteomics, of which she is an editorial board member, have been pioneers in this respect, but more general journals still need to improve their mechanisms to ensure data quality and data sharing. "Funding agencies should also step up and help facilitate funding of projects that address these issues, such as maintaining data repositories."

Of the many challenges that fall under the umbrella of figuring out what to do with all the data, Gingras has most keenly been intrigued with data scoring.

"It is a major issue in the field," she says. "Proteomics can identify all sorts of protein-protein interactions, but how can we be sure they are genuine? I hate to imagine a proteomics study producing a novel interaction, but later on a poor graduate loses weeks or months of work unsuccessfully doing biochemical follow-ups because the interaction was spurious."

To rescue frustrated students across the world, Gingras teamed up with colleague Alexey Nesvizhskii at the University of Michigan to develop an innovative computer program called SAINT (for Significance Analysis of Interactome); this groundbreaking probability-based program analyzes several metrics to quantify protein interactions in a data set as true or false.

The seeds for SAINT go back more than eight years, starting with some informal discussions and idea exchanges between Gingras and Nesvizhskii when they were both postdocs with Aebersold. "Back then, though, we didn't have the technology to realize our ideas, but a couple of years ago we reconnected and thought, you know, this could work now."

Gingras believes tools like SAINT will have tremendous impact on how researchers analyze, score and report their protein-protein interactions. With Mike Tyers at the University of Edinburgh in Scotland, Gingras has been working on a complementary program called ProHits that lets scientists store, search and analyze mass-spectrometry data. She now is working on interfacing ProHits and SAINTS to create a thorough software tool.

Since that first day in Sonenberg's lab, Gingras' life certainly has been a whirlwind of activity, but 17 years, more than 80 papers, and several novel discoveries later, she still is ready for more.

"The power of modern mass spectrometers for quantification is only beginning to be tapped into by systems biologists," she says. "In interaction proteomics, for example, most large-scale studies involve static interaction maps, which reveal nothing about protein complex assembly, the stoichiometry of the subunits or the dynamics of the interactions. Over the next few years, we will see all these quantitative measures implemented into large projects both in systems biology and clinical proteomics. It's going to be fun."

"Soon, I will no longer be considered a young researcher," she adds, "but in this field I can stay young at heart for a very long time."

Nick Zagorski (nicozags@gmail.com) is a freelance science writer.

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Why pursue a Ph.D. in the biosciences?

Part 1: Dealing with economic misconceptions and aligning expectations with career realities.

BY MICHAEL J. BRADLEY

Several criticisms have recently been leveled at biomedical doctorate programs in the U.S. (and elsewhere) (1–4). Many of these negative comments stem from the notion that typical doctoral programs are structured to train academic researchers, yet the biomedical academic research job climate has not looked promising since the National Institutes of Health budget doubling (3,5). The time to degree in doctorate programs has gotten longer on average during the past few decades, and larger proportions of graduates spend increasing periods of time working as postdoctoral researchers (1–4). As the number of postdoctoral fellows working at U.S. academic research institutions has skyrocketed during the past couple of decades, competition for faculty positions has intensified (1–6). Postdoctoral researchers often feel that applying for academic positions is like a long, drawn-out crapshoot, regardless of publication record (6). So why pursue a doctorate in the biosciences?

This article examines the economic reasons for obtaining a bioscience doctorate. While doctoral programs are not for everyone, the criticisms cited above mostly argue that the time to degree, low wages during training, and poor employment prospects after graduation call into question the choice of pursuing a science doctorate. However, with the exception of challenges in the academic job market, these issues largely are misrepresented compared with recent employment surveys of science degree holders (7,8). Misaligned expectations and bad advice can make for a depressing graduate school experience and subsequent job search. Conversely, developing a clear sense of what it takes to get the degree and forming realistic career expectations lie at the heart of making sure that pursuing a bioscience doctorate is not a waste of time (2).

Training

There are many mitigating factors that make the actual research training period (graduate school and potentially postdoctoral work) worthwhile. At most institutions in the U.S., graduate students in the biomedical sciences are not charged tuition and are paid a living wage-level stipend. It's not a lot of money, considering that peers with bachelor's and master's degrees working in a variety of fields earn, on average, 50 to 100 percent more money (9). But there is added value that will stay with each student for the rest of his or her professional life (see below).

In addition, graduate students and postdoctoral fellows usually can take advantage of other benefits during training. Most bioscience doctoral programs have excellent healthcare plans at little or no cost to the student. The often-flexible schedules of laboratory research allow for participation in workshops and other nonlaboratory experiences in which students can pick up additional skills including mentoring, negotiating and teaching. Most importantly, graduate students and postdocs in the molecular and cellular biosciences have the opportunity to work on truly fascinating projects.

Careers

Getting a doctoral degree provides a shot at landing a top research job in industry, academia or government. This could lead to a career marked by important discoveries that benefit society and stimulate the economy, new cures for diseases, and new knowledge that lays a foundation for future advances. Certainly such jobs are never guaranteed for a graduate, and landing them likely involves additional postdoctoral training after graduate school. However, is it really a crapshoot for a newly minted doctoral graduate in the biosciences to have a fulfilling and financially rewarding career? Not so, according to a 2010 National Science Foundation report titled "Science and engineering indicators" (7). For example, the report states that doctoral degree holders in science and engineering enjoy lower unemployment rates (typically 1 to 2 percent) and greater gender equality in compensation relative to other science degree holders.

Income

It's true that the initial investment in time spent earning a doctoral degree combined with lower wages, lower savings for buying a house and investing, and lower retirement contributions during the training period could put a graduate student at a financial disadvantage. For many biochemistry and molecular biology students, these issues are outweighed by the satisfaction they get from doing laboratory research. However,

the average long-term payoff for the initial time investment also makes a degree worthwhile in purely economic terms. According to a 2002 U.S. Census Bureau report (10), only those with professional degrees make more in average projected lifetime earnings than those holding doctoral degrees. A doctoral degree also increases the likelihood of getting and keeping jobs in science and engineering (7). These jobs collectively have a much larger median salary ($70,600 per year in 2007) than that earned by the total U.S. workforce ($31,400 per year in 2007).

> “Postdoctoral researchers often feel that applying for academic positions is like a long, drawn-out crapshoot, regardless of publication record.”

The median income of doctoral degree holders in science and engineering is consistently above both that of master's and bachelor's degree holders (7). While median incomes peak and flatten between $60,000 and $75,000 per year at 10 to15 years post degree for the bachelor's and master's degrees, doctoral degree holders' median income continues to climb, and peaks above $90,000 per year at 25 years post degree.

A recent report (8) by the U.S. Bureau of Labor Statistics also noted that direct involvement in research and development, for which many employers require a Ph.D., resulted in a higher wage distribution among scientists. For example, in 2008 the median income among biochemists and biophysicists working in R&D was $85,870 per year.

Growing doctoral demand

The percentage of doctoral degree holders in science and engineering who are nearing retirement is higher than that of other degrees. This will contribute to stronger job growth for doctoral-level candidates in the near future (7).

The BLS report (8) projects a 21 percent growth in employment of biological scientists (37 percent for biochemists/biophysicists) between 2008 and 2018. The growth rate is expected to be driven by new opportunities in biotechnology, including the development of new drugs, medical treatments and diagnostics, efforts to increase crop yields, and biomaterial and biofuel developments. This employment growth forecast also is characterized as “much faster than the average for all occupations.”

However it is important to keep in mind that during the past five-plus years, the biotechnology and pharmaceutical industries have been restructuring, refocusing priorities, and even shrinking their workforce or subcontracting core business-critical R&D components, sometimes abroad (11). Nevertheless, as economic conditions improve, the bioscience industry is expected to grow in the coming years, which will yield new biotechnologies, fuel the economy and create new, high-quality jobs (8).

Career choices

Simply getting a doctorate in bioscience is no guarantee of gainful lucrative employment. This especially is true for people pursuing a tenure-track bioscience job in academia (1 – 6). However, there are many career choices in industry, government and nonprofit organizations for doctoral degree holders in biochemistry, biophysics, and molecular and cellular biology. A doctoral degree in the biosciences has value in work settings outside of research and development, including management, marketing, consulting, regulatory and government advising, science writing and patent law.

No matter the career, employers value candidates with doctoral degrees for their independence, drive, initiative, creativity, perseverance, work ethic and problem solving capabilities.

Michael J. Bradley (michael.bradley@yale.edu) is a postdoctoral fellow in the department of molecular biophysics and biochemistry at Yale University.

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The Singapore ArtScience Museum: a modern marvel of science, technology and art

New museum bridges art and science.

BY LILLIAN KUO

Traditionally, art museums and science museums segregate into mutually exclusive entities, with a separate building for each. Such a distinction may be convenient, but it overlooks the intimate relationships between the two endeavors. Art can influence science, and similarly, developments in science and technology have catalyzed artistic innovation. The estrangement between science and art has, however, been reconciled at the ArtScience Museum at the Marina Bay Sands in Singapore. This new museum bridges the gap between the disciplines to focus on the great accomplishments and advances that were inspired collectively by science and art. The museum provides a magnificent display of art and science across multiple cultures and centuries.

Singapore's ArtScience Museum is shaped like a blossoming lotus or open palm. PHOTO: WILLIAM CHO

The ArtScience Museum itself is an architectural masterpiece. The breathtaking structure designed by Israeli-born architect Moshe Safdie not only is an artistic inspiration, but it also promotes environmental sustainability. Safdie's architecture exemplifies the museum's goal to unite art and science by providing an aesthetically pleasing structure that utilizes cutting-edge construction and design technologies. In his design, Safdie conducted his "search for rational geometry" by modeling 10 fingers into what could be interpreted either as an open palm or a lotus blossom. The structure of the museum often is referred to as the welcoming hand of Singapore. The fingers radiate out from the center of the building, increasing in size and height to generate four floors of gallery space. The tips of the fingers contain skylights to allow for natural exhibition lighting.

The structure of the museum also is functionally significant. The open palm of the lotus design channels rainwater 35 meters down toward a central atrium and into a waterfall that collects in a small reflection pool. The rainwater subsequently is recycled back into use for the building's plumbing system. As a further testament to the technological innovation of the design, the ArtScience Museum represents the first building in Singapore to be constructed from glass fiber-reinforced polymer — a material that is lightweight and extremely strong and versatile.

Once they have taken in the stunning exterior of the museum, visitors enter the building beneath a marquee that reads, "ArtScience: A Journey through Creativity." As an introduction to this journey, the first gallery, "Curiosity," asks visitors to question their surroundings. Spectators start by stepping onto a floating staircase that ascends into the gallery. Along the sides of the staircase are banners posing questions about art and science, such as "Are the artistic and scientific processes so different? What possibilities arise from the merging of the two?" The hope is to get visitors to reflect on the original nature of art and science and see how these two seemingly separate disciplines in fact have affected

our world synergistically in many positive ways. As an example of the productive relationships between art and science, "Curiosity" displays the creative and scientific engineering thought processes of Safdie and colleagues in building the museum. On exhibit are his original sketches and design models as well as descriptions of the engineering research utilized during construction.

The second step in the journey is "Inspiration," a gallery focused on six pivotal works of art and science innovation. These works were selected to illustrate how art and science working in concert have affected humanity, sociology and technology across various cultures and centuries. The inventions on display include a replica of Leonardo's Flying Machine, an airborne paper Kongming lantern, a high-tech robotic fish, an architectural design model of the ArtScience Museum, a molecular model of buckminsterfullerene, and an ancient Chinese scroll. Interactive screens allow visitors to learn more about these objects and inventions. Visitors are encouraged to create their own art- and science-inspired projects, which they can then share as postcards that are produced at interactive kiosks.

The "Van Gogh Alive" exhibit gives a multisensory exposure to the artist's work.

The last step in the journey takes visitors to the tallest finger of the museum and into the "Expression" gallery. This gallery consists of a dynamic multimedia theater featuring a video presentation highlighting various accomplishments in art and science throughout history. Visitors learn about the artistic and creative processes that culminated in the development of scientific and technological innovations in architecture, flight, nanotechnology, robotics and navigation.

In addition to the permanent collection, the ArtScience Museum currently features several temporary exhibitions, including "Dali: Mind of a Genius" (through Oct. 30, 2011) and "Van Gogh Alive" (through Nov. 6, 2011). The Dali exhibit consists of more than 250 works of art encompassing a wide range of media, including paintings, sculptures, collages, photographs, gold and glassworks. Dali's art provides a view into the complex cognitive science behind his artistic creations. In contrast, the Van Gogh exhibit illustrates the interplay between the arts and science by providing visitors with a multisensory journey through the works of Vincent Van Gogh. Unlike conventional wall art displays, more than 3,000 Van Gogh images are projected across immense screens on the walls, ceiling and even the gallery floor. This visual experience is further amplified with a musical score to accompany the art. This pairing of Van Gogh's art with the latest audio-visual technologies culminates in a dynamic experience that embodies the philosophies of the museum.

The ArtScience Museum harmonizes the worlds of science and art in a spectacular collection of artwork and scientific innovation. As visitors walk through the permanent and temporary exhibits, they will appreciate how the unity of these two disciplines has affected various stages in the history of mankind. From early influences on ancient Chinese invention to Safdie's pioneering design of the museum itself, it is clear that art and science are symbiotically aligned.

Whether visitors seek to enjoy the exhibitions casually or intend to learn the specific scientific and engineering details of modern architecture, they will be in awe upon entering the ArtScience Museum. This unique space not only provides visitors with an educational adventure but also motivates and empowers them to find and nurture their own creativity and innovation in art and science. The manifestation of scientific and artistic curiosity, inspiration and expression in one museum certainly is a modern marvel worth visiting.

Lillian Kuo (kuols@mail.nih.gov) is a postdoctoral fellow at the National Cancer Institute.

David Goodsell: The master of mol art

Spectacular drawings by David Goodsell showcase scientific knowledge and creativity.

BY SERGEI SHIKOV

Visualization of cells and macromolecules is indispensible for understanding their function. Whether we are looking at the cellular compartments or trying to understand a certain biological process at the molecular level, the power of a visual image is enormous. Direct visual methods such as light and electron microscopy reveal a coarse view of the cellular structure. X-ray crystallography and NMR allow us to get atomic details of the individual molecules. Biochemistry and biophysical methods provide quantitative information about isolated systems. Despite having all these tools and information, we still miss a complete view of a cell on the nanometer scale (1).

David Goodsell of The Scripps Research Institute, an artist by nature and scientist by training, bridges that knowledge gap and takes us into the invisible world of a cell. In his drawings, he beautifully combines scientific information from many different methods with his artistic vision.

Nature and nurture

Goodsell started painting early in his childhood, taught by his grandfather, who was an accomplished artist. In college, Goodsell majored in both chemistry and biology but not in art. His graduate school years (with Richard Dickerson at the University of California, Los Angeles) coincided with the increased use of computers in structural biology. While writing molecular graphics programs to visualize crystal struc-

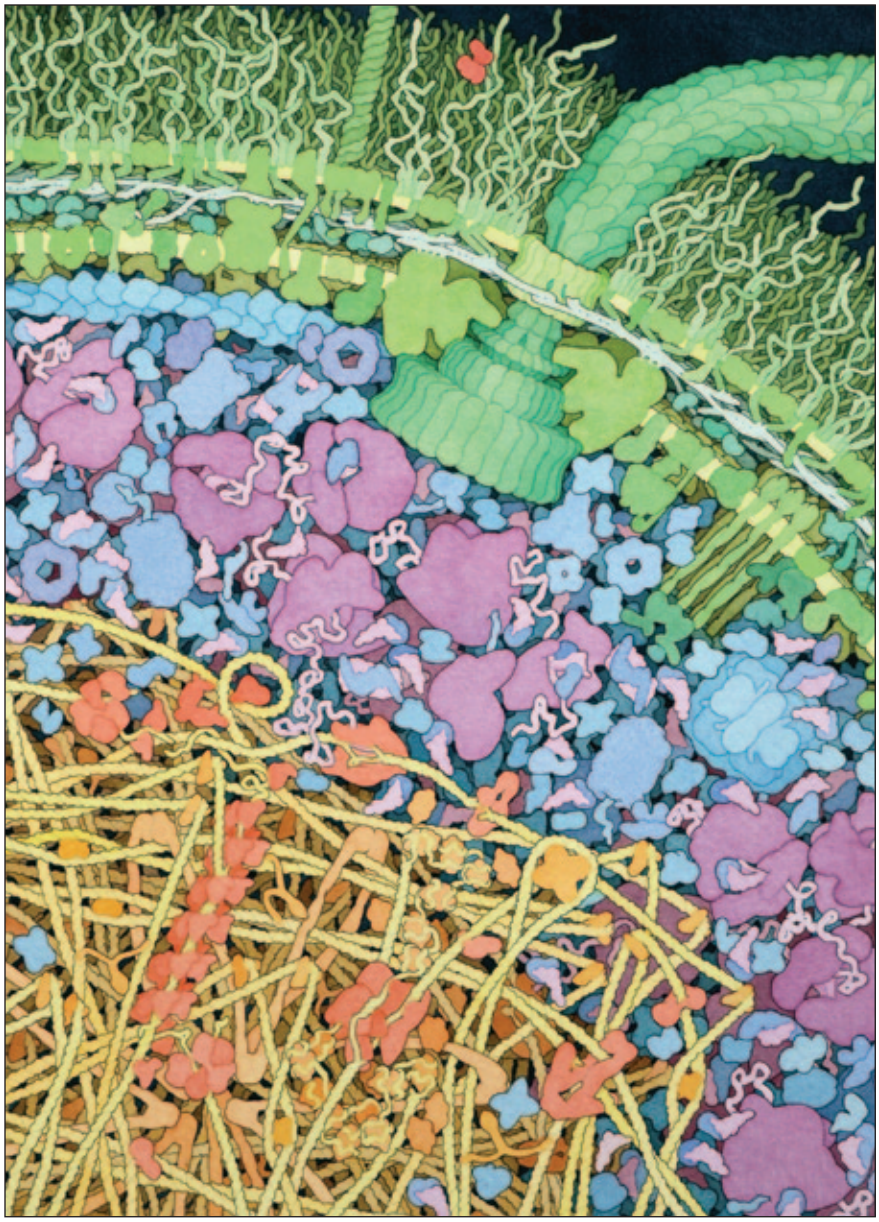

Fig. 1. Cross section of an Escherichia coli. A large flagellar motor (in green) crosses the cell wall, turning the flagellum. The cytoplasmic area is colored blue and purple. The large magenta molecules are ribosomes, and the L-shaped pink molecules are tRNA. The nucleoid region is shown in yellow and orange. COURTESY OF D.S. GOODSELL.

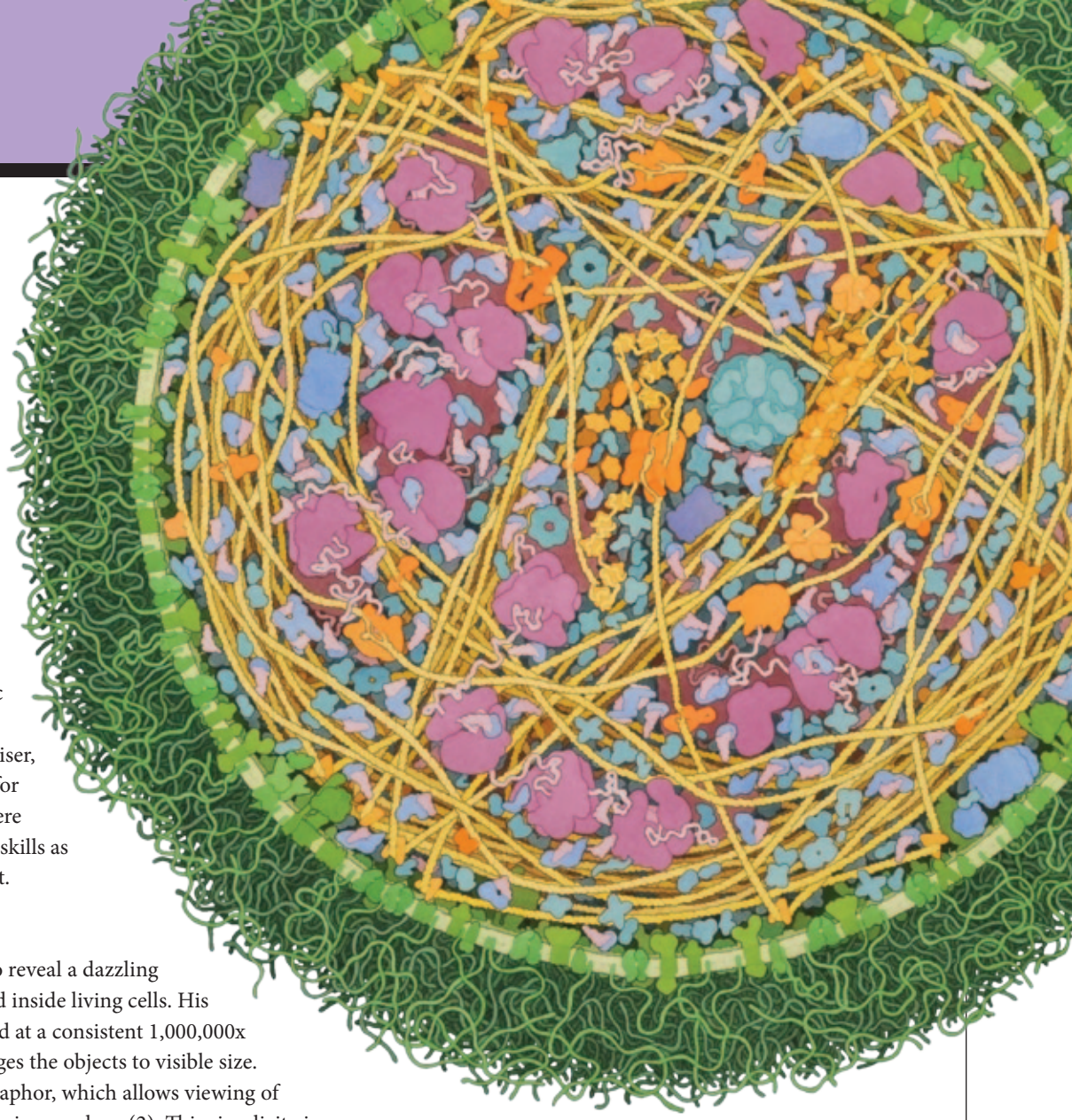

Fig. 2. Mycoplasma mycoides. DNA is shown in orange, cytoplasmic proteins in blue and pink, ribosomes are purple, and lipoglycan layer is green.
COURTESY OF D.S. GOODSELL.

tures, Goodsell became increasingly interested in scientific illustration. His professional interest in molecules gradually intertwined with the artistic desire to paint them. He credits his postdoctoral adviser, Arthur Olson (at Scripps), for creating an atmosphere where Goodsell could develop his skills as both a scientist and an artist.

Artistic style

Goodsell uses watercolor to reveal a dazzling view of the molecular world inside living cells. His drawings usually are printed at a consistent 1,000,000x magnification, which enlarges the objects to visible size. He uses a cross section metaphor, which allows viewing of many molecules in the same image plane (2). This simplicity is somewhat reminiscent of the post-impressionist style of Henri Rousseau. Goodsell draws molecules with flat colors and outlines to emphasize their relative sizes. These artistic choices simplify the view of a bustling intracellular world.

E. coli (Fig. 1) is one of Goodsell's favorite subjects. Knowing a stunning amount of information about this bacterium allows the artist "to show everything that is needed to make a living object." Goodsell likes to use simple color schemes to highlight the function and location of the molecules. Whether he draws a bacterium or a human cell, it is easy to identify compartments by looking at the colors. DNA and nuclear proteins are drawn yellow and orange, ribosomes are shown in magenta, cytoplasmic proteins are shown in blue, and the membranes are colored green. The overall size and shape of the macromolecules are based on atomic coordinates. The relative amount of molecules is derived from biochemical data, and their locations are from electron micrographs.

To appreciate the amount of effort spent on a drawing, one has only to zoom into a recent painting of a Mycoplasma mycoides (Fig. 2). A close look at the elaborate lipoglycan layer alone surely will leave you amazed.

Paintings can tell great stories. Goodsell often uses his illustrations to describe a biological process vividly. His painting of the neuromuscular synapse, for example, shows the molecular action of the entire synaptic cycle (Fig. 3). An expert in vesicular trafficking, structural biologist Frederick Hughson of Princeton University concludes, "David's work is amazing!"

Science outreach

If you visit the Protein Data Bank website (www.rcsb.org), you will not miss the "Molecule of the Month" column posted on the home page. Every month for more than a decade, David Goodsell has been contributing an illustration and a concise description of a featured biological macromolecule, such as clathrin (Fig. 4). Most of the structural images are created using a computer program that Goodsell developed as a postdoctoral fellow. With more than 60,000 structures currently deposited in the PDB, Goodsell has plenty of work to do.

Usually, figures appearing in original scientific publications must strictly represent the data, and thus very little image manipulation is allowed. However, artistic freedom is essential for a comprehensible and memorable illustration used for educational purposes (3), and several of Goodsell's images can be found in classic textbooks, such as "Molecular Biology of the Cell." In addition, Goodsell himself has written and illustrated a number of books, including "The Machinery of Life," "Our Molecular Nature: The Body's Motors, Machines and Messages" and "Bionanotechnology: Lessons from Nature."

Illustrations by Goodsell are making a great impact on science education. Microbiologist David Rudner at Harvard Medical School uses Goodsell's images in his molecular biology of bacteria course and finds them "incredibly instructive – both mnemonic and predictive… They stimulate general discussion and foster hypotheses." Alice Ting, a professor at MIT, also uses Goodsell pictures for teaching and in her seminars to illustrate how crowded and complex the interior of the cell is. "Other illustrations don't convey this nearly as well as the Goodsell drawings," she notes.

Goodsell recently has c-ontributed a series of articles to the journal Biochemistry and Molecular Biology Education. In each paper, he describes in great detail the scientific background behind the illustrations in the second edition of "The Machinery of Life." BAMBED editors Judith and Donald Voet agree that Goodsell's work provides "enormous aid to the teaching and learning of biochemistry and molecular biology" (4).

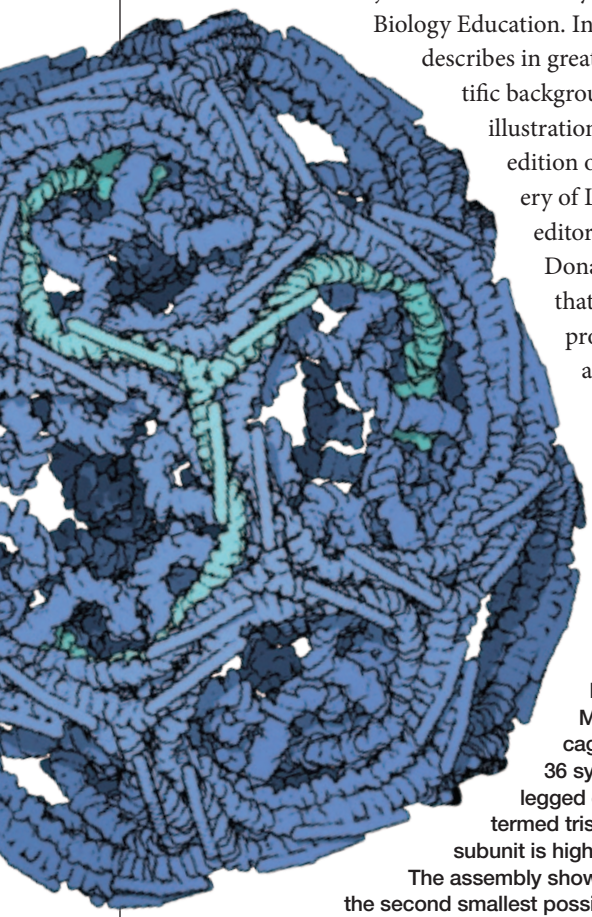

Fig. 4. Clathrin (April 2007 Molecule of the Month). A clathrin cage composed of 36 symmetrical three-legged components termed triskelions (single subunit is highlighted in green). The assembly shown here represents the second smallest possible cage structure. COURTESY OF D.S. GOODSELL.

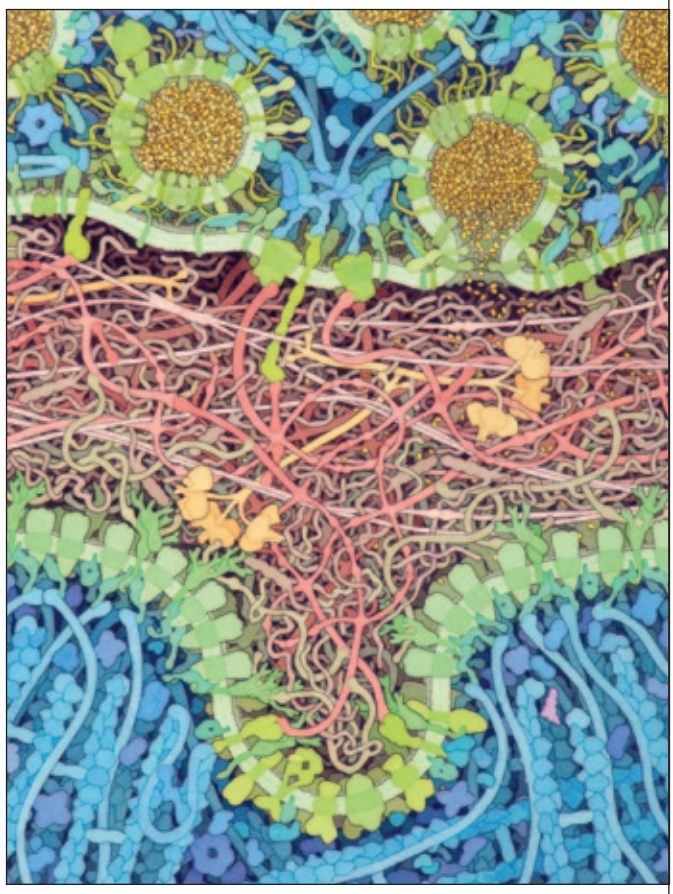

Fig. 3. Neuromuscular synapse. The acetylcholine-laden vesicles are carrying and releasing the neurotransmitter into the synaptic cleft. A few of the acetylcholine molecules bind to receptors on the muscle cell. The cleft itself is packed with many elongated proteins including laminin, collagen, perlecan and flower like acetylcholinesterase molecules serving to render inactive the neurotransmitter. COURTESY OF D.S. GOODSELL.

As Goodsell says, his artwork is meant to give any reader "a pictorial overview of the molecules that orchestrate the process of life." For the scientist, he hopes that his work "will continue to provide a touchstone for intuition" (5).

Sergei Shikov (sergei1976@gmail.com) is a freelance science writer in Boston, Mass.

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10 tips for green meeting travel

Ways to save time and money and lower your environmental footprint when traveling.

BY JLYNN J. FRAZIER

An increasingly important trend in the travel industry is the concept of going green, being more eco-friendly and implementing sustainable practices and standards. Whether you travel for work or leisure, the tips below are easy, can save you time and money, and will reduce your environmental footprint.

1. **Unplug before you leave.** When you are packing your bags, don't forget to close down the house. Some ideas include turning off and unplugging electronics, turning down the thermostat and turning off the water. If you are gone for an extended time, you also should put a hold on your daily newspaper delivery.

2. **Check in electronically.** Save time, money and paper by checking in for your flight online before you leave. Most airlines allow you to check in up to 24 hours before your flight. This saves time at the airport, and, if you are checking bags, you often get a reduced baggage fee when you prepay during your online check in. If you have a smartphone or other mobile device, you can store your boarding pass electronically and avoid printing a paper version.

3. **Pack a travel mug or water bottle.** Coffee is a must have for meetings. Consider bringing a reusable coffee mug or water bottle on your next trip. Not only will you be reducing the amount of trash produced, but coffee stays warmer longer in your insulated mug, and you often can receive a discount on your coffee by supplying your reusable container.

4. **Share a ride.** If the meeting you attend offers a shuttle service, consider signing up to share a ride rather than renting a car. If you are taking a taxi to the meeting, consider sharing rides with new colleagues you met who are going to the airport.

5. **Just say "no" to daily cleaning service.** Many hotels now have signs or cards that you can place on your door or pillow to indicate that you do not need new linens or towels. Most of us probably do not change our bed linens at home every day, so why do it at a hotel?

6. **Explore on foot.** At many large meetings, complimentary shuttles run throughout the day to bring participants from hotels to the meeting convention centers or hotels. Although it's tempting to hop on the shuttle, lace up your shoes and walk to the meeting. Meetings often start early and end late, but nothing is more refreshing than taking a short break at lunch or in the evening to explore the city on foot. It also is the best way to browse the various menus to pick a restaurant or find a coffee shop for the morning.

7. **Bring a digital camera.** Want to bring home a souvenir from the meeting? All you need is a digital camera and a few rechargeable batteries and you are ready to collect images to share with friends and family. An email with photos or an e-postcard is a fun way to stay in touch with family and friends while on travel.

8. **Recycle your name badge.** Before you leave the meeting, return your name badge to the meeting organizers. The paper can be recycled, and badge holders that are in good condition can be repurposed for future meetings.

9. **Go paperless.** Paperless meetings are controversial, because, for many, having a printed meeting program to read is a valuable resource. Beyond the program, meetings usually are flush with handouts, brochures and product information. The best way to reduce paper use is to pick up less paper. When you visit booths or literature tables at your next meeting, ask if they can provide information on a portable drive or give you a business card with a Web address at which information can be found. If you have a smartphone, snap a photo of the QR code so you can look at more information later.

10. **Provide feedback.** The American Society for Biochemistry and Molecular Biology sends out electronic surveys after each of our meetings to evaluate and improve the meeting experience for our current and future members. If there are changes that you would like to see, mention your observations and green ideas in a meeting survey.

Jlynn J. Frazier (jfrazier@asbmb.org) is the ASBMB conference manager.

Ninety percent of the job is half communication

It's time to reinvent the liberal arts curriculum to more effectively integrate it with STEM and other majors.

BY PETER J. KENNELLY

With apologies to Yogi Berra

Many of you reading this may be too far removed from the glory days of the 1950s Yankee dynasty anchored by Mickey Mantle, Elston Howard, Whitey Ford, Moose Skowron and the incomparable Yogi Berra to recognize the source of my somewhat dysfunctional title. While Yogi's accomplishments as a ballplayer, coach and manager led to his induction into the Baseball Hall of Fame, among the general public he was, and is, more often remembered for his unique ability to turn a phrase. "Ninety percent of this game is half mental" is one of the most iconic of Yogi's impressive collection of malapropisms. It also is a fitting example of the power of (in)effective communication, a power so great that it can overshadow or even supplant the impression others have of a person's accomplishments and skills within his or her discipline. Hence, Berra will live on in our society's collective consciousness in large measure because of his talent for summarizing universal truths in eccentrically memorable forms.

Communication skills: in demand, yet on the decline

Once upon a time, every job ad in Science, Nature and other major science, technology, engineering and mathematics trade publications concluded with a line describing the specific computer software with which a successful applicant was to be familiar. Strong discipline-specific skills and experience, while highly desired, weren't necessarily sufficient to trump a lack of computer skills. Today, in want ads, proficiency with computers largely has been supplanted by written and verbal communication skills. While this evolution in part reflects a rise in computer proficiency and continuing improvements in both hardware and software, it also reflects a decline in a fundamental skill that can trace its ancestry to one of the original three R's. Ironically, this comes at a time when virtually anyone with Internet access can play the role of commentator, news reporter or movie producer on a global stage.

The reasons for this decline in the basic ability to say what one means in an era characterized by global communication are many. Sound bites, Twitter, cable TV, crowded classrooms and latchkey parenting all have contributed. As a consequence, employers cite lack of communication skills as the No. 1 problem with employees and one of the top five reasons why an interview fails to produce a job offer for a candidate. Yet many college students continue to map out plans of study that assiduously avoid any elective courses rumored to involve essays, reports or any other form of substantive writing. One of our first priorities in addressing this issue must be to change student attitudes. We must somehow dispel the myth that grammar, syntax, spelling and vocabulary are concepts peculiar to the ivory tower of academics, concepts that will melt away once students traverse the looking glass into the real — and more reasonable — world.

A fundamental element of both science and business

As teachers, we need to do a better job of illustrating that record keeping and information dissemination are integral to the scientific process. I like to tell my students that if something is not recorded, for all practical purposes, it did not occur. We must emphasize the role of proper communication between co-workers in maintaining a safe working environment. Most importantly, we need to bring our students face to face with the real world. Contact a local biotech or pharma firm and ask whether it would be willing to host a fieldtrip or to come to campus and have employees speak to students about the expectations for scientists working under the requirements of Good Laboratory Practices, vertebrate animal protocols, U.S. Food and Drug Administration regulations and so on. Then students will encounter in clear and dramatic form the careful, constant and rigorous record keeping requirements typical of the working world.

Finally, how we instruct and assess students can influence their behavior. One of the greatest deficits I have

noticed among aspiring biochemists and molecular biologists is their limited vocabularies. I often wonder if some of the more bizarre answers that appear on my quizzes and test papers reflect a desperate attempt to find some dimly recalled "right" word. Despite large course loads and class sizes, we can make an impact if we consistently give assignments and tests that require, if not a full-blown essay, the synthesis of a list, phrase or couple of sentences without multiple choice cues. In grading these answers, it is equally important that we apply standards that recognize and reward those students able to synthesize clear and cogent answers that display depth of vocabulary. Too often, we simply give credit if the student writes down a particular word without any consideration of context. If simply mentioning the right word is sufficient regardless of the appropriateness or accuracy of the remainder of their answer, students adapt by putting down as many words as possible rather than choosing the most appropriate one. If they can receive full points because we can see what they were trying to say, what incentive do students have to improve?

Reinvigorating the liberal arts curriculum

"Communication skills" is a deceptively simple phrase encompassing a veritable hydra-headed array of activities: oral and written, personal and electronic, technical and popular, listening and speaking. Providing students with opportunities to amass a serviceable set of communication skills lies beyond the capacity of an individual STEM department. It requires a coordinated effort by the entire educational system. Ironically, the original goal of the North American higher education system was to produce Renaissance men, and eventually women, who — while well versed in a specific subject area — possessed a common foundation in logic, deductive and inductive reasoning, history, communication and quantization. The liberal arts curriculum was meant to provide a means to equip students from all majors to engage in lifelong learning.

What went wrong?

- a slow erosion in the emphasis placed on the liberal education curriculum in the face of the explosion in our knowledge of STEM areas
- the substitution of getting a job instead of learning as the primary goal of higher education
- the depersonalization of higher education with a concomitant increase in school enrollment and class sizes

The time has come to reinvent the liberal arts curriculum in a form that more effectively integrates it with STEM and other majors. Instead of the current emphasis on covering individual topics (e.g., selecting one course each from psychology, literature, philosophy, economics, world history and political science), the emphasis should shift to continued development of important skills: oral communication, written communication, mining information from classic and electronic archives, ethics, critical reasoning skills, teamwork and societal responsibilities. This is not to say that history, philosophy and sociology cannot serve as vehicles for developing these skills but that the manner in which students are taught and evaluated should be given priority over the number of subjects or chapters covered. The selection of skills as the organizing force will drive the creation of new courses in which various separate subjects become integrated around some larger theme. A globalization theme, for example, would meld elements of economics, history, philosophy and geography.

The time has come for the liberal curriculum to emerge from its exile as a hodgepodge of electives to a full partner in developing students whose depth of discipline-specific knowledge is complemented by an adaptable set of intellectual skills.

Peter J. Kennelly (pjkennel@vt.edu) is a professor and head of the department of biochemistry at Virginia Polytechnic Institute and State University. He also is chairman of the ASBMB Education and Professional Development Committee. A report from the Education and Professional Development Committee.

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Recent developments in the generation and application of lipid probes

Innovations in lipid synthesis capitalize on bioorthogonal reactions and click chemistry to elucidate biological activities.

BY MICHAEL D. BEST

The hydrophobic nature of membranes and membrane-interacting proteins presents difficult challenges in understanding the structure and organization of these systems. Here, Michael Best outlines the recent advances in the development of functionalized lipid probes that have provided valuable tools in revealing the complexity of membranes and membrane proteins.

The toolbox for functionalized lipid probes has expanded considerably over the past several years due to concurrent advances in the synthesis and application of lipid analogs. These innovations have opened up exciting new avenues for using functionalized lipids to probe biological processes that are lipid dependent.

Synthetic methods

Synthetic methods for generating complex lipids have come to maturation over the past several years, efforts that have facilitated numerous advances in lipid biology, including the identification of novel roles for phosphatidylinositol polyphosphates, glycophosphatidylinositol anchors, lipid A and glycosphingolipids. The discrete derivatization of lipid structures at varying positions within these molecules provides functionalized lipid probes that can aid in characterizing the biological roles of natural lipids. Indeed, many derivatization strategies have been shown to be effective for introducing beneficial functionality while maintaining biological activity even with relatively simple lipids, such as diacylglycerol (1) and phosphatidic acid (2).

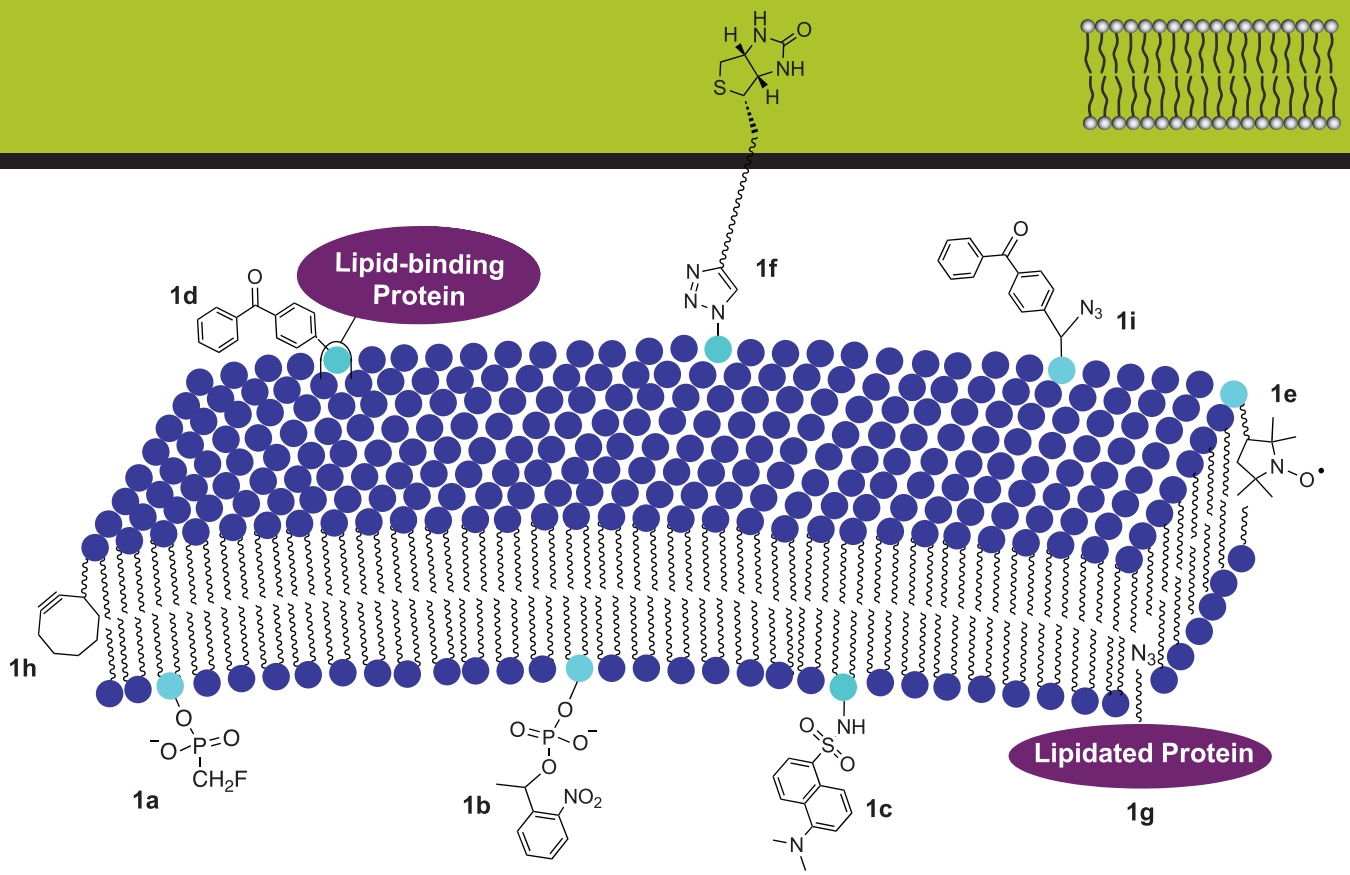
Lipid probe strategies

In the application of lipid probes to biological studies, a number of synthetic modifications have proved fruitful (figure). These have recently been reviewed (3) and are briefly summarized below. Metabolically stabilized analogs (1a) are useful for avoiding undesirable reactions of molecules that might otherwise succumb to endogenous enzymatic modification that could interfere with investigations into biological function. Caged functional groups (1b) can allow lipid analogs to become activated in response to an external stimulus, such as photo-activation. Such activation allows investigators to probe the spatial and temporal regulation of lipid-mediated biological processes.

Probes bearing reporter tags introduced within the structure also have proved popular. Fluorescent dyes (1c) allow for optical imaging of lipids in vivo, permitting the identification of subcellular localization. Photoaffinity tags (1d) can be used to crosslink lipids to proximal proteins, which enables the study of interactions between lipids and proteins that do not otherwise involve covalent bonds. In addition, spin labels (1e) can be introduced to analyze the chemical environment around lipids, conveniently allowing investigators to determine, for instance, the depth of penetration of a lipid component into the membrane bilayer. Finally, biotinylated probes (1f) are effective for affinity purification or surface immobilization.

Bioorthogonal labeling

Recently, dramatic advances in probe-based biological studies have resulted from bioorthogonal labeling and most notably the use of click chemistry, which involves reactions of azides with alkynes to yield triazole products (4, 5). Bioorthogonal reactions employ paired molecules that are designed to react only with one another, avoiding the threat of unwanted reactions that is posed by functional groups that are common within the cellular milieu. The selective derivatization of a target biomolecule within the extremely complex settings of cell extracts, live cells or living organisms, thus, allows for the study of specific biomolecules in contexts that are chemically complex.



Examples of functionalized lipid probes used for characterizing biological properties.

Furthermore, bioorthogonal reactions generally employ small functional handles, such as the prototypical azide and alkyne of click chemistry, which limit structural perturbations that could interfere with natural biomolecular functionality.

In combination with lipid-probe strategies, bioorthogonal labeling has enabled recent forays into lipid biology. For example, the proteomic analysis of covalent protein lipidation has been achieved through the incorporation of azide- or alkyne-derivatized acyl chains onto proteins (1g) followed by selective purification and identification (6). In addition, live-cell fluorescence-imaging studies using analogs of phosphatidic acid (7) and phosphatidylcholine (8) have been performed through derivatization of alkyne-tagged lipid analogs (1h) via click chemistry.

Another type of study that has been facilitated by bioorthogonal chemistry is that of activity-based protein profiling, which employs small molecule probes for the collective characterization of proteins based on function (9). These probes generally bear a latent handle that can be derivatized after protein labeling, often through click chemistry, to selectively characterize only those proteins that interact with the probe (1i). Such studies recently have been advanced using phospholipid analogs to identify and characterize lipid-modifying enzymes (10) and protein-lipid binding interactions (11).

Michael D. Best (mdbest@utk.edu) is an assistant professor of bioorganic chemistry at the University of Tennessee-Knoxville.

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International, collaborative science courses

South and North American scientists team up to offer training in biochemistry and cell and molecular biology.

BY ADRIANA BASSINI, L.C. CAMERON, ENRIQUE M. DE LA CRUZ, SUZANA ESTEVES, RAFAEL LUZES, JOHN A. MERCER, JOSE R. SOTELO AND MARGARET TITUS

Introduction

Undergraduate students in South America have limited opportunities to interact with researchers from outside of their institutions and countries. In addition, academic and private-sector research scientists in South America historically have had limited opportunities to present and discuss their work in an international setting, thereby diminishing the broader impact of their work and training. Although investment in scientific infrastructure has grown in some Latin American countries, it is increasingly apparent that a platform for discussion and communication of scientific activities is needed within South and Central America as well as with partners from the greater international scientific community.

In 1993, three Brazilian researchers joined eight Uruguayan researchers to host a course about the molecular basis of muscle contraction in Montevideo, Uruguay, for 28 undergraduate and graduate students (1). The course had several purposes. First and foremost, the pedagogical mission was to advance undergraduate teaching and research by providing hands-on research experience in biochemistry, cell biology and molecular biology complemented by lectures from established investigators from throughout South America. In addition, the course focused on strengthening discussion and collaboration among South American scientists with common interests who otherwise would have had limited opportunities for interaction. This first course was sponsored by the International Union of Biochemistry and Molecular Biology as well as Brazilian and Uruguayan funding agencies.

The student and faculty evaluations of the 1993 course reflected its value to South American students. Indeed, the course proved to be the sole opportunity for many students to have a rigorous introduction to the curriculum topics. Research and training collaboration among scientists from neighboring South American countries was an important by-product of the course for its participants. The success of the course indicated that expansion to include participants from nations beyond South America was a worthy goal.

An early focus of the International Institute for Collaborative Cell Biology and Biochemistry was to facilitate discussion and collaboration among the small community working on non-muscle myosin V motors at that time. In 2000, the International Symposium on Myosin V was held in Paraty, Brazil. As a result of the scientific connections and personal friendships forged at the meeting, Ernesto Carafoli proposed the formation of the International Cell Research Organization course on molecular motors, which was held in Rio de Janeiro, Brazil, in 2001. The course was organized such that experts from broad disciplines in cell and molecular biology presented in three educational forums: 1) general lectures in their respective fields geared toward a general audience with a broad science background, 2) specific lectures relating to their own research and 3) research laboratory practicals using state-of-the-art methodologies and analyses to investigate the behavior of biological systems. This three-tier format has been utilized by subsequent courses.

Present course format

IICCBB courses have been held in the U.S., Mexico, Brazil and Uruguay. They typically have about 100 attendees and span two weeks: two one-week lecture series and lab practicals with a research symposium during the intervening weekend in which faculty present seminars on their current research activities. The faculty members are diverse, spanning disciplines from neuroscience to proteomics. Students present their work in posters and short research talks during the symposium as well as in presentations of the results from lab practicals, which cover protein biochemistry, computational modeling of biological processes, analysis of cellular function, generating and analyzing gene expression/protein profiling data, and investigating phylogenetic relationships between protein family members. The lab practicals are limited to 30 to 40 students, since the goal is to have hands-on research experience in small groups.

Students participating in the 2010 Pan-American Advanced Institutes program on the function and regulation of the cytoskeleton, hosted in Rio De Janeiro, Brazil. This and another PASI were initiatives of the IICCBB group.

Selection of students

A fundamental goal of the course is to make students aware of the interdisciplinary nature and diversity of researchers in biochemistry and cell biology. Screening of student applicants is competitive, with emphasis on potential for bioscience research. The variation in scientific backgrounds of the students is taken into account, and the incoming class is selected to represent a broad distribution of backgrounds that include cell biology, biochemistry, genetics, biophysics and bioengineering. In addition, the student body represents a broad spectrum of nationalities and affiliations. Achieving these objectives requires active and far-reaching recruitment efforts, a task that includes students and faculty previously involved in the courses as well as advertising with widespread visibility.

The 2010 participants stated in evaluations that the course had a positive impact on their career development: It increased student motivation for pursuit of a scientific career and, in some cases, also encouraged them to seek training abroad. Numerous collaborations, student internships and faculty sabbaticals have resulted from relationships formed during the courses. Nonscientific activities, such as faculty-versus-student beach soccer matches and late-night churrascos, contribute to the development of long-lasting friendships.

Funding

Due to the international nature of the IICCBB courses and necessary travel for many participants, the expenses associated with organizing the courses are considerable. Numerous funding agencies have generously supported the IICCBB's efforts throughout the years, though the support is frequently inadequate to defray all expenses associated with the course. Student travel and accommodations are priorities. Participating faculty members often pay for travel and other course-related expenses from their personal funds.

Future

The IICCBB has succeeded in organizing over 20 courses and symposia with more than 1,500 students from more than 28 countries and over 100 faculty members from more than 15 countries. We are working to secure funding to offer regularly scheduled annual IICCBB courses in countries throughout the Americas. The long-term mission is to expand and merge these efforts with others to foster scientific networks that are truly global and contribute to the development of scientific capacity in nations currently lacking these connections. Student feedback regarding career-development impact, in addition to the research collaborations and publications that have emerged from contacts established at IICCB-organized events, indicates that the courses are successful on several levels and that we are on track to accomplish this mission.

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For more information:

For more information about IICBB-sponsored events, visit http://www.iiccbb.org.

THE JOURNAL OF LIPID RESEARCH

A new role for cytochrome P450 3A4

BY MARY L. CHANG

Cytochrome P450 3A4 is an incredibly important enzyme in the human body. It's the protein that breaks down common drugs like the fever reducer and painkiller acetaminophen and the antibiotic erythromycin. Cholesterol also is broken down by the CYP3A family of enzymes and is believed to be mostly metabolized into 4β-hydroxycholesterol. In a commentary appearing in the August issue of the Journal of Lipid Research, Ulf Diczfalusy and Ingemar Björkhem discuss some new data suggesting another function for the enzyme based on end products discovered by Akira Honda and colleagues: the 25-hydroxyation of cholesterol.

Many studies have been conducted using 25-hydroxycholesterol, which is a potent regulator of lipid metabolism. However, the origins of this oxysterol have not been entirely elucidated. Honda et al.'s straightforward investigations in their article, "Cholesterol 25-hydroxylation activity of CYP3A," suggest that the presence of 25-hydroxycholesterol in human circulation may be the result of CYP3A4 activity. When the authors inhibited the enzyme, 25-hydroxycholesterol levels fell. Conversely, when they increased the amount of the enzyme present in vitro, observed cholesterol levels increased. Thus, their data strongly support the idea that CYP3A is one of the enzymes responsible for catalyzing the 25-hydroxylation of cholesterol.

Mary L. Chang (mchang@asbmb.org) is managing editor of the Journal of Lipid Research.

THE JOURNAL OF BIOLOGICAL CHEMISTRY

The JBC unveils thematic minireview series

BY ANGELA HOPP

The Journal of Biological Chemistry recently published two more thematic minireview series. The following is a snapshot of their contents. For more information about the JBC's thematic minireview series, visit www.jbc.org/site/thematics.

The biochemistry of epigenetics

Shepherded by JBC Associate Editor Joel Gottesfeld of The Scripps Research Institute, the first thematic series contains five minireviews about the mechanisms responsible for epigenetic regulation of gene expression (primarily, the methylation of specific nucleotide bases and post-translational modifications of histone proteins) and the role of small noncoding RNAs in said mechanisms.

In the first review, authors Zhao-xia Chen and Arthur D. Riggs report recent findings about mechanisms of methylation and the maintenance and reversibility of this chemical modification of DNA in mammals. The review addresses links between DNA methyltransferases and chromatin-associated proteins and post-synthetic modifications during cell division and provides evidence for the role of base excision repair in germ cells and early embryos as a mechanism for controlling genomewide demethylation.

A review by Sayyed K. Zaidi, Daniel W. Young, Martin Montecino, Andre J. van Wijnen, Janet L. Stein, Jane B. Lian and Gary S. Stein takes on the question of how DNA methylation states and chromatin structure are coordinated with phases of the cell cycle. The authors also address the role played by small noncoding RNA molecules in the maintenance of epigenetic marks from generation to generation.

In "Combinatorial readout of dual histone modifications by paired chromatin-associated modules," Zhanxin Wang and Dinshaw J. Patel write about the mechanisms by which the cellular machinery reads the epigenetic code so that programs of gene regulation and development are properly orchestrated.

Duane D. Winkler and Karolin Luger review the structural dynamics and biophysical transitions of nucleosome reorganization. Members of the histone chaperone family are implicated in multiple roles linked to epigenetic gene regulation. The two-subunit complex known as FACT, which stands for "facilitates chromatin transcription," is discussed as a histone chaperone of interest, and the authors explore models for FACT function and how FACT allows RNA polymerase to pass through nucleosome-bound DNA.

Visit this thematic series online at www.jbc.org/site/thematics/epigenetics.

Computational systems biology

The second thematic minireview series was organized by Arcady Mushegian and JBC Associate Editor Joan W. Conaway, both of Stowers Institute for Medical Research, who conceived of the collection during a 2009 special symposium on systems biology held by the American Society for Biochemistry and Molecular Biology.

The meeting sought to explore how systems-level analyses can both generate and test hypotheses about the molecular features of living systems, the series organizers said, and the minireview collection is intended to feature the promise that such systems approaches hold.

In the first minireview, authors Yan Zhang and Vadim N. Gladyshev focus on approaches to identify new mechanistic and evolutionary pathways that involve metalloenzymes. The genomic representation of enzymes whose activity is trace-element dependent can provide new insights into the exploitation of trace elements by organisms over the course of evolution.

The new science of metabolomics is the focus of a minireview contributed by Guo-Fang Zhang, Sushabhan Sadhukhan, Gregory Tochtrop and Henri Brunengraber. The authors consider the need for bioinformatic strategies to make meaning of amassing data, and they assess the promise of developing biomarkers to follow the complex physiological consequences of the flux of innumerable metabolites within the cell.

In the next review, Oliver Fiehn, Dinesh K. Barupal and Tobias Kind cover how such resources as GenBank and the Protein Data Bank can be used to reveal novel pathways and enzymatic activities that underlie metabolomic activity.

In "Building protein-protein interaction networks with proteomic and informatics tools," Mihaela Sardiu and Michael Washburn survey evolving methodologies for systematically identifying protein-protein interactions as a dimension of functional proteomics. The recent development of protein-interaction networks based on quantitative proteomics data sets is an important step in allowing researchers to consider diverse and subtle levels of protein-protein mechanisms of cellular control.

In the fifth minireview, Hon Nian Chua and Frederick P. Roth present computational methods for mining science literature and data to elucidate the mechanisms of both intended and unintended drug effects. The authors seek to understand the consequences of genetic and chemical perturbations as revealed in genome-wide analyses published from a variety of sources. The investigators illustrate that by evaluating data in a systematic way, research findings from a diversity of experimental settings and models can be marshaled to identify new drugs and drug targets.

The final component, authored by James A. Evans and Andrey Rzhetsky, highlights new strategies for mining the literature "not only to learn what has been reported but also to gain information about how a research area has developed and the history and/or biases that shape the way researchers think about a problem," the organizers write.

Read this thematic series online at www.jbc.org/site/thematics/computational2.

Angela Hopp (ahopp@asbmb.org) is managing editor for special projects at ASBMB.

What do you want to do after school?
The path to a career in genetic counseling.

BY CATHERINE GRISWOLD

The beginnings

"What do you want to do after school?" is a question faced by many students as they progress from high school to college and beyond. Answering this question was not easy for me. Growing up, I toyed with the idea of becoming a doctor, a teacher and a scientific researcher. It was as if I was on a pendulum swinging from one possibility to the next. However, as I began my search for the perfect major and career, one thing remained clear to me: I liked science.

Once I came to that realization, things started falling into place. After careful consideration, I decided to major in neuroscience. As I became more involved with the courses in my major, I became more convinced that this was a wise decision. Neuroscience not only allowed me to study the biological sciences in depth but also offered exposure to the psychological sciences. This diversity appealed to me.

However, even after deciding on a major, the question of what I wanted to do after school still lingered. I had a course of study that I loved, but I still needed to find a career I would be enthusiastic about after I graduated. I began considering my options, utilizing all available resources. One day, as I was reading a textbook, I discovered genetic counseling. The book's brief description intrigued me and left me wanting to know more. I learned that genetic counseling combines medical genetics and counseling to help people understand the genetic components of disease. Genetic counselors provide risk assessment, education and support for individuals at risk for inherited conditions. The job sounded interesting, but I still had questions.

I began seeking more information from professors and career counselors at my school, who were very supportive and assisted me in whatever way they could. Eventually, I connected with a fantastic resource: the National Society of Genetic Counselors (www.nsgc.org). Its website enabled me to find local genetic counselors, learn more about how to enter the field and discover available graduate programs.

Armed with knowledge about the profession, I grew more excited about this career possibility. However, a twinge of uncertainty still remained. I wanted to make certain this was the correct profession for me. One other field remained that I wanted to explore before I committed to a career in genetic counseling: laboratory research.

So I contacted a genetics professor at my university and committed to a year-long thesis project using yeast to perform a genomic survey. Although I enjoyed certain aspects of research, I discovered that I preferred working with people and that the laboratory environment did not mesh well with my personality. However, as I continued educating myself about genetic counseling, I learned that genetic counselors do have opportunities to participate in various research projects, which was comforting in case I ever wanted to have a research focus.

Making the goal a realization

Now that I was feeling more confident about my career path as a genetic counselor, I had the task of attaining that goal. I knew graduate school would be a requirement, so I researched the programs available. When I began the process of selecting a graduate program, there were approximately 25 genetic counseling programs nationwide, and each admitted, on average, five to 10 students a year. Despite the competitive nature of the programs, I was determined to reach my goal.

Most genetic counseling programs strongly encourage students to gain experience working with a practicing genetic counselor prior to the application process, so I shadowed a local genetic counselor. I was fortunate to observe her daily clinic responsibilities, including her interactions with patients, and I used these observations to further my understanding of genetic counseling. This was an invaluable experience.

Also, to strengthen my application, I gained advocacy experience. I learned that past applicants had volunteered with crisis hotlines, pregnancy centers and domestic violence shelters. As a result, I committed to a volunteer position at a local women's clinic. This allowed me to assist with basic administrative tasks in a medical setting and offered exposure to different medical terms and clinical scenarios.

Once I confirmed that I had fulfilled all the requirements, I submitted my applications and waited. At last, several graduate programs informed me that

I had been selected to continue on to the interview stage. Though this news thrilled me, I knew that the process was far from over. I had to face the next hurdle in my journey to becoming a genetic counselor: the interview.

I spent the next few months preparing for and participating in multiple graduate program interviews. The process let me gain a more detailed picture of each program I was considering by visiting and conversing with faculty and current students. I also was able to evaluate each program's geographic location, which was an important part of considering my options, because I would need to relocate.

Once the interviews were completed, another period of waiting began. This waiting period, however, was different from the last one. This time I was waiting for a specific day to come: match day. I learned that match day was the day when final acceptance decisions were disclosed to each applicant. On that day I would learn if I was accepted, waitlisted or rejected from the programs to which I had applied. The suspense surrounding the date was high, and I tried to keep myself busy by focusing on coursework and clearing my schedule for match day. I wanted be available to receive the news from each program as it came in.

When match day finally arrived, I learned that I had either been accepted or waitlisted at several programs. Everything began to fall into place. I completed my undergraduate degree, and, with the wheels now in motion, I began making preparations to relocate for graduate school.

The final steps to the beginning of a career

Transition from undergraduate to graduate school was not simple, and there were moments when the course load felt overwhelming, but the presence of a strong support group consisting of family, friends, classmates and faculty helped to make the transition easier. However, the initial question still remained: What would I do once I finished school?

Genetic counseling as a profession is quite diverse, offering multiple subspecialties. Some of the more commonly associated areas include prenatal, pediatric and cancer counseling. However, genetic counselors work in many other capacities, such as research and policy development. Based on my experiences in graduate school and my own career requirements, I was able to narrow down my options. In the end, I decided to apply for a job in a prenatal clinic.

Being new to genetic counseling, this seemed like a good fit on multiple levels: It would afford me the opportunity to see a variety of clinical scenarios while working in an environment that was complementary to my personality. It would also allow me to participate in various educational opportunities by attending conferences and teaching.

I still can recall sitting in my apartment the day I received the phone call offering me the position. It felt great to know that, after all the hard work of preparing for this day, it had finally come. I accepted the position with the understanding that I would still need to take and pass the genetic counseling certification examination.

Looking back on the experience, I can appreciate how each step was necessary in my development into a competent genetic counselor. I now work with families, assisting them in comprehending and coping with potential genetic diagnoses. It is rewarding to be able to support the families during challenging times in their lives. After all the time spent on the proverbial pendulum, I am happy to be able to say that I am working in the field of my choice and have begun the first job of the rest of my career.

Catherine Griswold (CMGriswold@carilionclinic.org) obtained her undergraduate degree from Drew University and completed her graduate degree at the University of Maryland, Baltimore. She now is a certified genetic counselor at Carilion Clinic in Roanoke, Va.

Giving minority investigators a hand

NIDDK network provides mentorship and advice.

BY MARION B. SEWER

Navigating the demands of an academic position can be stressful and overwhelming, and a lot of new assistant professors may find successfully balancing the many responsibilities of academia to be an isolating, daunting task. Moreover, studies have shown that scientists from populations that are underrepresented in the sciences are less likely to seek advice or support from senior colleagues. Minority faculty also are more likely to be recruited to serve on institutional and society committees, adding to their duties.

To provide minority faculty with mentorship and advice on areas such as grantsmanship, laboratory management and balancing the demands of career and family, the National Institute of Diabetes and Digestive and Kidney Diseases created the Network of Minority Research Investigators almost a decade ago. NMRI's mission is to support biomedical research investigators and technical personnel from traditionally under-served communities. The network facilitates the participation of members of underrepresented racial and ethnic minority groups in the conduct of biomedical research in the fields supported by NIDDK, such as diabetes research, endocrinology and nutrition. NMRI also provides a platform for the exchange of ideas between network members and the NIDDK.

Of the 27 institutes and centers at the National Institutes of Health, NIDDK is the only one that has a formal program to foster the development of minority junior faculty. Since its inception, the network has had more than 120 members from 109 colleges, universities and institutions across the country. Currently, NMRI boasts approximately 90 members. The network was the brainchild of Lawrence Agodoa, who is the director of the Office of Minority Health Research Coordination at NIDDK. Agodoa has been instrumental in ensuring the sustained success of NMRI. Not only is he an NIDDK representative, but his research background and clinical training provide a unique and accessible perspective to which NMRI members can relate.

A popular NMRI initiative is its mentoring program, which matches members at different stages in their careers. The goal of the program is to foster the development of junior faculty by providing a formal platform to provide expertise, support and advice. Typically, mentors and mentees have similar research interests, career goals or shared life experiences.

NMRI holds a meeting every spring at which members come together to network, share research findings, get information on new initiatives from funding agencies, gain insight on the promotion and tenure process, and share anecdotes and exchange strategies used for thriving in academia.

Arguably, one of the highlights of the annual conference is the mock study sections. Prior to the meeting, members have the opportunity to submit previously reviewed research proposals for discussion and critique at the meeting. At the conference, attendees form groups and discuss the strengths and weaknesses of each proposal. The responses from questionnaires completed after the meeting routinely show that members find the mock study section a valuable tool that enhances grant-writing skills and provides tangible tips for communicating more effectively and developing a logical research plan.

Past meetings also have included discussions on new initiatives being implemented at the institute, presentations on research in health disparities, strategies for developing a national reputation and effective ways of managing laboratory personnel.

Marion B. Sewer (msewer@ucsd.edu) is an associate professor in the Skaggs School of Pharmacy and Pharmaceutical Sciences at the University of California, San Diego.

A report from the Minority Affairs Comittee.

For more information

For more information about the Network of Minority Research Investigators or to apply for membership, contact Winnie Martinez (martinezw@mail.nih.gov) at the Office of Minority Health Research.

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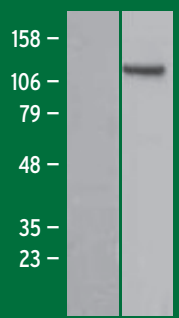

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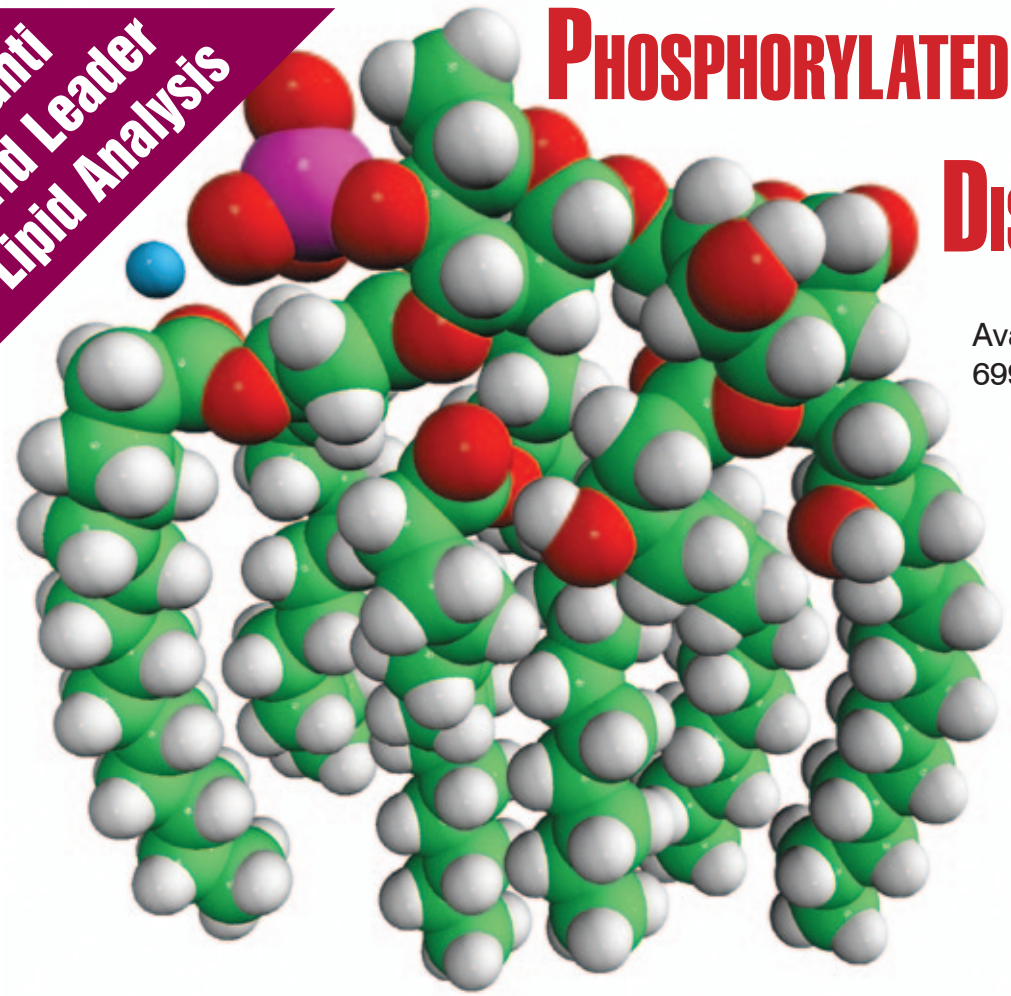

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