Richard Lifton Takes Exome Sequencing beyond Mendelian Genetics

Rick Lifton was moving house. After 23 years in New Haven at Yale, Lifton was packing up in July for Manhattan, where on September 1 he would become the 11th president of the Rockefeller University. The job comes with an on-campus residence, a spectacular free-standing house overlooking New York’s East River that is also used to host official entertainments and gatherings. “I haven’t counted the bedrooms yet. I think it’s five,” Lifton reported.

Lifton will have firmer ideas about his new house and new job by the time he arrives in San Francisco on December 3 to give the keynote address for ASCB 2016. It won’t be Lifton’s first time at ASCB, he said. He gave a Keynote, continued on p.18

Bruce Alberts Wins Lasker-Koshland Achievement Award

Bruce Alberts, a pioneer in the study of DNA replication, a former ASCB President, and a living legend in cell biology, has been awarded the Lasker-Koshland Special Achievement Award in Medical Science. The Lasker-Koshland is a lifetime achievement award for scientific research and for scientific leadership. Alberts qualifies on a multitude of fronts. He has been a professor of biochemistry for 41 years at the University of California, San Francisco (UCSF), the editor-in-chief of Science (2008–2013), the president of the National Academy of Sciences (1993–2005), and the lead author of the ubiquitous textbook Molecular Biology of the Cell, first published in 1983 and now in its sixth edition. He was a residually appointed U.S. Science Envoy from 2009 to 2011, representing the U.S. State Department worldwide on scientific issues.
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President’s Column

On Research Funding and the Power of Youth

by Tony Hyman, Arshad Desai, and Peter Walter

“A person who has not made his great contribution to science before the age of thirty will never do so.” While this quip of Albert Einstein’s certainly does not generally apply to cell biologists, it is well recognized that innovation in science and technology tends to be driven by youth. We only have to look at pioneers of Silicon Valley, physics at the turn of the 20th century, or the average age at which Nobel prize winners perform their ground-breaking work (Figure 1) to remind ourselves that any society that wishes to push true innovation needs to fund their research based on promise, and it needs to promote their paths to early independence.

Despite this fact, in the system of the National Institutes of Health (NIH) that funds the vast majority of research in cell biology in the United States, the age at which young investigators launch their independent research careers has been increasing over the past several decades. In the early 1980s, more than 20% of NIH RO1 research–grant recipients were under 36 years of age. As of 2014, less than 2% were under 36 (Figure 2). The failure to fund the most outstanding young scientists and support innovative experimentation at an early career stage has diminished the creativity and innovation of the American research enterprise.

The obstacles confronting young investigators are complex and have been a persistent part of the research enterprise for decades. For example, the lengths of graduate and postdoc training have grown over the past three decades such that young scientists are often in their early to mid 30s before transitioning to a faculty position. Furthermore, the length of time between appointment to a faculty position and securing an NIH RO1 grant has also grown: In 1980, it took less than one year on average, whereas in 2013 the average was five years.

These delays mean that the average early-stage investigator is close to 40 years old before receiving his or her first NIH RO1, the standard indicator of career independence. Other factors affecting independence include, but are not limited to, the difficulty of obtaining preliminary data, the structure of peer review, and the rise of team-based approaches.6 These delays to full career independence have many adverse consequences. Importantly, the next generation of researchers are strongly discouraged by the present system that requires grant-seeking rather than scientific experimentation. The long wait to become an independent researcher has also led many talented young scientists to leave the research workforce for a variety of career and family reasons and has discouraged many others from entering in the first place.

Past and Current Methods of Funding Young Investigators

The advancing age at which a young investigator gains independence has been obvious to the NIH for several decades, motivating it to try several methods to promote and encourage scientific independence for early-stage investigators, defined as those within 10 years of their terminal degree, as well as for new
investigators, anyone who has never received a major NIH grant.

The NIH introduced the First Independent Research Support and Transition (R29) award in 1986. This grant was intended for young faculty members within five years of leaving their postdoctoral work, but the level of support of the grant was very modest relative to an R01. An evaluation of the program revealed that R29 awardees were less successful at applying for subsequent R01s than young faculty members who applied directly for R01s. The sense was that the restrictions imposed by the program hindered these young scientists in their most critical developmental years. For these reasons, the R29 was discontinued in 1998.

The Pathway to Independence (K99/R00) awards were introduced in 2006. The K99 phase of the award supports scientists in the last two years of a postdoc, and successfully transitioning to the R00 phase supports the first three years of an independent position. Nearly 90% of K99 awardees move into faculty positions and into the R00 phase of the program. Furthermore, nearly half of K99/R00 recipients go on to receive an R01. The NIH made over 400 K99 awards and nearly 570 R00 awards in 2015. The size of K99 awards varies by institute, while R00 awards have a maximum yearly support of $249,000.

The NIH Director’s Early Independence (DP5) awards were introduced in 2011. These awards are directed to scientists who move directly from graduate school to a faculty position, with a maximum level of support of $250,000 in each of five years. These awards have not been around long enough to determine how successful DP5 awardees are at receiving a subsequent R01. Furthermore, the program is quite small, providing no more than 20 awards per year, so this program will likely not have a significant effect on the average age at which young investigators achieve independence.

The NIH Director’s New Innovator (DP2) awards were introduced in 2007 for early-stage investigators, providing five years of support for a maximum of $300,000 per year. The primary requirement is that the investigator be “unusually creative” in his or her proposal, and no preliminary data or itemized budget is necessary. The NIH originally awarded fewer than 10 DP2 awards per year until the program expanded in 2012 to allow 40 to 60 awards each year. Due to the small size and youth of this program, no data are presently available concerning how DP2 awardees fare when applying for R01s.

Prior to 2007, success rates for new investigators’ R01 submissions were significantly lower than those of established investigators. In 2007, the NIH enacted a policy to equalize the success rates of new and established investigators. This policy essentially boosts the scores of new investigators so that this group is funded at a rate similar to that of established investigators. The results of this policy are mixed. The success rates for early-stage and non-early-stage new investigators has improved. The success rate for non-early-stage new investigators is very close to that of established investigators, while the success rate for early-stage investigators lags behind these other groups.

The scientific community itself should determine how best to solve the complex and persistent problems confronting young investigators.

Figure 1. An age distribution for scientific genius. The ages at which individuals produced Nobel-prize winning insights over the 20th century. Figure modified with permission from Jones, Reedy, and Weinberg (reference 1).
Despite these efforts from the NIH, the graying of the biomedical professoriate has not abated, suggesting that a stronger effort will be required to solve this serious problem. In fact, members of the U.S. Congress have begun debating legislative methods to find ways to fund more young scientists. The broad-stroke legislative mechanisms currently being suggested do not seem promising. The scientific community itself should determine how best to solve the complex and persistent problems confronting young investigators. Current policies are damaging U.S. science, with long-term consequences for American innovation. Other countries are investing in the future of their scientific workforce, and we need to do the same.

**An ERC-like Mechanism to Fund Young Researchers in the United States**

Recently, some ideas on funding young researchers have come out of Europe, with the establishment of the European Research Council. The ERC was launched in 2007 as the first pan-European science-funding agency, and it funds investigators of all ages from all European Union–member countries and additional affiliate nations. Funding is provided in three major scientific domains: Physical Sciences and Engineering, Life Sciences, and Social Sciences and Humanities.4

Within each domain, the ERC provides three types of grants based on an investigator’s experience: ERC Starting Grants for those 2–7 years post PhD, ERC Consolidator Grants for those 7–12 years post PhD, and ERC Advanced Grants for established investigators (Figure 3).

In 2014, nearly 24% of ERC funding was set aside for ERC Starting Grants and another 32% was set aside for ERC Consolidator Grants. Thus, nearly 56% of all ERC funding was devoted to investigators within 12 years of receiving their terminal degree in 2014; the average age of these Starting Grant awardees is about 35 years.

Similar to competitive U.S. grants, all ERC grants are peer-reviewed and funding is awarded based on merit scores. Importantly, all grant applicants in a specific category—Starting, Consolidator, or Advanced—compete only against applicants from the same category. The crucial point is that young faculty members competing for ERC money do not have to compete with established investigators who have considerable track records, preliminary data, and likely a sizable lab. Rather, researchers in each career stage compete with each other. This allows funding decisions to be better steered toward the needs of the different stages. Starting grants can be funded mainly based on promise with little need for preliminary data, while Advanced grants are funded based both on the investigator’s track record and on the grant itself. A just-completed retrospective evaluation of completed ERC grants finds a remarkably positive outcome, with almost three-fourths of the grants being judged to have produced either a scientific breakthrough or some major advance.

![Figure 2. Percentage of NIH R01 investigators age 36 and younger (in blue) and age 66 and older (in red) in fiscal years 1980 to 2010. Reproduced from Rockey (reference 5).](image)
The closest American comparison to an ERC Starting Grant is the NIH Director’s New Innovator (DP2) award, which funds innovative research by scientists who are within 10 years of their PhD or equivalent degree. Individual DP2 and ERC Starting Grants are roughly the same size (ERC: €300,000, or ~$340,000; NIH: $300,000 per year) and duration (five years). However, the overall sizes of the programs are dramatically different. In 2013, the NIH provided 51 DP2 awards, whereas the ERC awarded 300 Starting and 312 Consolidator awards.

Establishment of an ERC-like system in the United States could be used to focus on funding for young scientists. To construct this system, the NIH should work with the community to determine the proper size of this program with regard to how many young scientists should be funded by this mechanism. The NIH might expand the size of the DP2 program to roughly 500 awards per year. Expanding the program consistently over a 5-year period until it is similar in scope to the European system would allow the research enterprise to recalibrate its funding strategies accordingly. As young scientists compete for and win these new funds, the ability of young scientists to conduct innovative research and launch independent labs would be greatly improved. An ERC-like system in the United States that greatly expands the DP2 program would address the underlying problem in the research enterprise of underfunding young investigators and would also promote innovation and risk-taking in experiments.

Comparing the Grant Review Process on Opposite Sides of the Atlantic

The evaluation of grants from young investigators requires a fine-tuned review system that can evaluate promise and integrate it effectively in the ranking of the applicants. We, together with many others, have been involved in assessing ERC applications to the LS3 (Cell & Developmental Biology) panel of the ERC for the past 6 years. One of us is also currently serving on a NIH study section and another has served on many past occasions. This experience has allowed us to compare review methodologies and to identify features of the ERC review process that are worth considering for implementation in NIH study sections.

The NIH study section has been compared to early-years American Idol, where a Simon Cowell-esque reviewer’s snarky comment guarantees the demise of a promising application. This reputation is unfair—study section members by and large work extremely hard to deliver a fair evaluation and study section meetings are respectful and well run (although there is on rare occasion behavior that merits the American Idol comparison). However, there are systemic issues with the evaluation process that leave study section members in the dark as to what they have collectively decided.

The ERC panel meetings, held in Brussels, employ an evaluation process that promotes a group effort to assess and rank all applications. For the Starter and Consolidator stage applications, in whose evaluation we have been involved, the review process has two steps—application review (Step 1) followed later in the year by an in-person interview (Step 2) of the applicants. ERC Starting Grants can be funded mainly based on promise.
applicants who pass the threshold at Step 1.

For the Step 1 meeting, each application is pre-reviewed by four panel members who provide preliminary scores and brief written evaluations about the proposal and the applicant. The subject areas covered are broad (e.g., stem cell biology, plant development, genetics, and biochemical reconstitutions of cellular processes have all been discussed in our ERC panel) and panel members are expected to review applications as generalists, which in our experience focuses the evaluation process on the bigger picture view of the proposal and of the applicant’s caliber. At the meeting, all applications are discussed; for each application the lead reviewer presents the application together with her or his evaluation of the proposal and the applicant, followed by brief comments from the other three reviewers before a discussion involving the panel as a whole. At the end of each discussion an informal preliminary score is obtained by counting hands in favor of an overall A, B, or C grade.

The critical part of the ERC panel meeting happens when the preliminary scores for all applications are tallied and a ranked list is generated. The panel then re-visits the entire set of applications and spends significant effort to adjust the ranking after having listened to the discussion of all applications. This is the most important part of the meeting when the critical “gray zone” applications are considered relative to each other and the decision on who to invite for an interview (in the Step 1 evaluation) or who to recommend for funding (in the Step 2 evaluation after the in-person interview) is made. In our panel, for the particularly difficult set of applications around the border (which is clearly defined at the start of the meeting), a paper vote is taken to finalize the ranking. Other panels likely use different mechanisms as each panel is given considerable leeway with respect to precisely how they want to address the ranking challenge. But importantly, by this mechanism the panel ends up working together as a group to develop a fair and robust process to “draw the line,” which leaves panel members with the satisfaction that they have done their job as a group of peer reviewers.

For the applicants that do not succeed, the reviewing panel members provide a brief panel report highlighting the key reasons behind the panel’s decision, which helps applicants reframe applications for future consideration.

By contrast, as is likely familiar to many ASCB members, in an NIH study section half the applications are triaged, providing those applicants with only the written reviews, which are often divergent. For the reviewed applications, each of the three assigned reviewers first states her or his score followed by a brief presentation of the application by Reviewer 1. Reviewers 2 and 3 provide additional input, and the panel members are then invited to discuss the application. However, it is rare for non-experts to participate given the targeting of review assignments to experts and the need to complete application reviews in a short time period. At the end of the open discussion, the three reviewers re-state their scores, generating a score range. All panel members then privately enter a number into an online scoring sheet that is typically within the range; on occasion, a panel member chooses to score outside the range (he or she has to declare this intention to the panel). All scores count equally to determine the average final score. As has been noted before and will not be belabored here, forceful reviewers influence which end of the scoring range ends up being favored by non-expert panel members.

After the private score is entered by each reviewer, that specific application is never mentioned again in the study section. Unlike with ERC panels, the study section never gets the opportunity to consider all of the applications that they have been asked to review, which in our view underutilizes the collective strength of the panel members. Thus, at the end of the day study section members are in the dark about exactly what they decided for many of the gray zone applications. Effectively, they provide a somewhat random ranking in the middle range to a program officer yet percentile
calculations based on the averaged scores cloak this uncertainty with an illusion of objectivity and numerical precision.

In our view, the key challenge of addressing relative ranking after all proposals have been discussed is a critical and important missing element in the NIH review process. We appreciate that conflicts of interest pose a challenge here—in the ERC panels this issue is addressed by an honor code of panel members staying silent when applications they may be in conflict with are being discussed (and, to be fair, the declared conflicts in both ERC and NIH panels rarely represent true conflicts of interest but rather reflect institutional affiliations or one-off multi-lab collaborations). In our experience, this honor code approach has worked remarkably well because reviewers approach their duties as professionals. This approach opens up the panel to work together as a group and provide a ranked list to the funding agency that follows the recommendation of the panel based on their collective expertise, as opposed to scores with minor fractional decimal variation that end up dictating the fate of many applications—and with it, the fate of many young careers.

While the ERC is only a decade old, its impact on science in Europe is becoming amply evident.⁹ Key to the ERC’s success is its establishment of a three-tiered application system that promotes young scientists and a fair and robust review process that demands significant commitment from the panel members but also provides them with the power of conducting peer review where the panel works as a group to draw the line. In our view, the NIH needs to consider experimenting with similar young scientist–targeted programs and evaluation systems where the reviewers are tasked with collectively ranking the applications under consideration, instead of perpetuating the statistical uncertainty created by the secret vote and the inability to revisit applications after their individual discussion.

Note
We thank Bruce Alberts, Lisa Dennison, and Chris Pickett for valuable input.

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MBoC Special Issue

FORCES on and within CELLS

More information at ascb.org/mboc-forces
Submissions requested by January 15, 2017, at www.mbcpapers.org
For younger scientists who chiefly know Alberts as the first name on their textbook, his CV is an eye opener. At last count, he holds 18 honorary doctorates, is an honorary member or fellow in 12 foreign science academies, is a commander in the Order of the British Empire, and won the U.S. National Medal of Science in 2014. For his DNA replication work, he won the Canada Gairdner International Award in 1995.

Current ASCB President Peter Walter with Keith Yamamoto, a former editor-in-chief of the ASCB journal Molecular Biology of the Cell, hailed Alberts’ commitment to lab science, education, and science policy.1 “With his fertile scientific intellect and stellar research contributions, his deep commitment to essential science education, and a remarkable clarity of vision for policies and practices that would advance or improve both research and education, Bruce juggled a daunting blend of research, education, and administrative responsibilities for over two decades,” they said.

Indeed Alberts has been a tireless advocate for reforming science education at every level from K–12 and beyond. “If you look at the way we teach middle school students about cells, it’s horrifying to a scientist,” Alberts explains in a wonderful animated/live action video created by the Lasker Foundation to illustrate his Lasker-Koshland page.2

Alberts was the moving force behind the founding of the Science and Health Education Partnership between UCSF and the San Francisco Unified School District in 1987. Known as SEP, for 30 years the program has been sending UCSF grad student and postdoc volunteers into city schools where they present exciting science demonstrations while showing kids what living scientists look like and what they do. In turn, SEP has brought talented San Francisco high schoolers into UCSF labs as interns.

As an ASCB member, Alberts was a strong advocate for the Society to become an active force in the science education revolution, supporting the founding of a new ASCB journal devoted to using scientific methods to dissect science education, now called CBE—Life Sciences Education (LSE). Alberts still serves on the LSE Editorial Board, where he was a charter member in 2001. In 2008, the ASCB created the Bruce Alberts Award for Excellence in Science Education in his honor.3 Besides his 2008 term as President of ASCB, which he first joined in 1991, Alberts has served on virtually every ASCB committee from Local Arrangements to Council to the E.B. Wilson Medal selection committee. ▪

—John Fleischman

Reference and Footnotes


ASCB Member Benefit: One-on-One CV Review

Need some help with a cover letter, CV, resume, statement of teaching philosophy, or other document for the next step in your career? Members of the ASCB are willing to help. Just fill out a short form (www.ascb.org/cvreview), and we’ll put you in touch with a reviewer. Then the two of you can decide which digital collaboration tool to use (email, Google Docs, Skype, Wikispaces, etc.). You must be a current ASCB member to take advantage of this service. ▪

—Thea Clarke
One-Day Course Offered to Help Basic Scientists Transition to Industry

Interested in making a transition to biotech or pharma, or know someone who is? Then you’ll be delighted to hear that ASCB is again partnering with the Keck Graduate Institute to offer a one-day mini-course designed to help basic scientists become more competitive for jobs in industry. The short course, Managing Science in the Biotech Industry, will be held in San Francisco right near Moscone Center on Friday, December 2, 2016—the day before the ASCB Annual Meeting.

The course will introduce students and postdocs to bioscience commercialization processes through case study analysis and group problem-solving exercises. There will also be a number of interactive sessions on how to combine your scientific, business, and social skills to make you competitive for a professional career.

Registration is capped at 100 graduate students and postdocs on a first-come, first-served basis. The cost is $125, which includes tuition, curriculum material, and a networking lunch with representatives from local biotech companies. Register at www.ascb.org/biotech-mini-course.

—Thea Clarke

Mentoring in Active Learning and Teaching (MALT) 2017 Fellowships

To support the increasing need for undergraduate biology instructors prepared to offer authentic research experiences as part of a student-centered classroom, the ASCB is sponsoring a small number of fellowships of up to $2,000 to allow current and future undergraduate biology instructors to travel to, observe, and work with faculty who are experienced in using course-based undergraduate research experiences in their classes.

These participants will work with their mentors to develop their current or prospective research work into a multi-session, classroom-based undergraduate research experience, to consider best teaching practices for the implementation of this experience, and to put their new skills into practice in their own classroom.

The fellows will pursue methods of teaching that align with Vision and Change principles. Learn more at http://visionandchange.org.

Recipients will be awarded up to $1,500 for an in situ observation trip and laboratory supplies, depending on their justification and proposed budget, and an additional $500 following completion of mentor and program assessment. This program also provides a $500 mentor stipend. After applying the new skills, MALT Fellows will report findings to the scientific community.

Applications for MALT Fellowships will be due on January 15 and July 15, 2017. To apply, please visit the MALT website at www.ascb.org/mentoring-in-active-learning-and-teaching-malt.

—Mike Wolyniak, Hamden-Sydney College

Join an ASCB Committee

Interested in joining one of ASCB’s committees? More information about each committee is available on the ASCB website (click on “Communities/Committees”). Email your CV and a short statement of interest now to Thea Clarke (tclarke@ascb.org) to be considered for 2017.
Want to Work for a Bioscience Company? PhDs Explore Industry Options

On the first morning of the July 11–16 Bioscience Management Summer Course cosponsored by ASCB and the Keck Graduate Institute (KGI), KGI president Sheldon Schuster stopped by to make a few remarks. Welcoming the 50 students from the United States and other parts of the world who attended the program at the KGI campus in Claremont, CA, Schuster joked, “Students become so enthusiastic that they sometimes think they can go out and start a business.”

Although they were fast learners, none of the students announced immediate plans to launch start-ups. But they did express abundant enthusiasm for both the new knowledge they acquired and the new network of friendships they made during the biotech course.

Midway through the program, on July 14, the New York Times coincidently published a highly relevant article entitled “So Many Research Scientists, So Few Openings as Professors.”

As the article noted “Now, as a new crop of graduate students receives PhDs in science, researchers worry over the future of some of these dedicated people; they’re trained to be academics and are often led to believe that anything else is an admission of failure.”

But, as president Schuster had already counseled the students attending the program, which ASCB cosponsored for the third year, “Don’t let anyone tell you that working for industry means giving up science. Nothing could be further from the truth!”

That point was further underscored by Steve Casper, dean of the KGI School of Applied Sciences, who ran a session on Commercializing Science that set the stage for the rest of the course. Casper noted that although only 8% of available industry positions are in research, plenty of other positions need filling, in product development, project management, marketing and sales, business development, regulatory affairs, quality assurance, and other areas. In a world where only 8% of PhDs will get tenure at a university, preparing for a business career clearly makes sense for many scientists.

That was the case for postdoc Nyasha Chambwe of the Institute for Systems Biology in Seattle, WA, who was drawn to the ASCB-KGI program because “I’ve always had an interest in business, and the business of science, but I’ve never had any training.” She learned a lot, she says, including the important fact that just discovering a new medicine isn’t enough. To make treatments available, an effective marketing strategy is necessary.

Bioentrepreneurship Basics

Although the program offered a lot, Casper managed expectations. He informed the students that the one-week course would “not substitute for extensive management training,” such as students would receive in an MBA or Postdoctoral Professional Masters degree program. But, he said, it would introduce them to “the language and concepts of bioscience business,” using lectures on bioentrepreneurship, in-depth cases studies of problems typically facing bioscience businesses, and workshop-type breakout groups of small teams working on practical problems, such as whether to invest in a start-up.

Despite its brevity, the program gave third-year graduate student Ahsan Choudary of the University of Texas (UT) Health Science Center in Antonio, TX, “an opportunity to collaborate with people from across the country and learn some great skills” that will directly impact his work in a consulting firm he co-founded, Commercialization Catalysts. The firm collaborates with UT’s Office of Technology Commercialization and has prioritized 20 technologies that the company believes are ready to go to market. “What I really liked about the course was the fact that we have learned hands-
Enrique Daza, a PhD candidate at the University of Illinois Urbana-Champaign, and Courtney Young, a PhD candidate at the University of California, Los Angeles, show off their 3D printer project medical devices.

on techniques that we can take back home with us” in the areas of market sizing, intellectual property, regulatory affairs, and other topics taught during the five days. “All of that is going to prove very helpful,” Choudary says.

Besides interactive academic sessions, students also worked in teams on a project using “Printbot” 3D printers. Under the guidance of Anna Hickerson, they used the printers to make medical implants for five diseases: infant tracheobronchomalacia, hip arthroplasty, genioplasty, shoulder osteoarthritis, and hyperscoliosis. Ten teams of five students each worked separately on assigned medical implants. They researched the relevant disease, its current treatment and market, and other matters necessary to make a decision about commercializing the implant. On the final day, they made presentations to panels of judges and recommended whether to invest in the 3D printable product. Two winning presentations were selected, with each winning team member receiving a large chocolate bar and cheers from fellow students. Every team received feedback.

Learning academic theory in the morning followed by the group 3D project in the afternoon when theory could be concretely applied was a training format that postdoc Alexandra Noel of Louisiana State University in Baton Rouge praises. Noel was drawn to the program's interdisciplinary aspects as a way to gain a perspective on career possibilities that would merge her research degree with knowledge about “real world companies creating products or drugs that could really help patients.” She adds that the program “is definitely worth pursuing.”

Real-World Knowledge

Two high-profile keynote speakers and two networking lunches with business professionals contributed to the students’ real-world knowledge of the bioscience industry. Speaker Art Riggs told the story about his work with colleagues in Genentech that led to the first successful expression of a human gene in bacteria and producing the hormone somatostatin. He described the collaborative process that led to the company’s success after near failure and responded to very active student questioning. Executive coach and consultant Judy Heyboer, formerly the senior vice president of human resources at Genentech, provided pragmatic and frank guidance on how to succeed in business careers. She shared the research finding that the key to successful teams is “nice people” and discussed the importance of good mentors.

“The fact that the program presents a little bit of a lot of different things is the key for me,” says Vanessa Cox, a biochemistry PhD candidate at Georgia Institute of Technology. Having a consulting-type project to work on, together with case studies, as well as marketing and other classes, has been helpful, she says, providing not only academic knowledge but also personal insights regarding her preferences. “It’s confirmed where I’ll probably want to go”—into industry R&D as the foundation for a diverse career—Cox says.

Likewise for Stanford University first-year biochemistry postdoc Darshan Trivedi, who wanted to know how science actually is commercialized, “This was a perfect venue” to be introduced to the key business concepts. “Now we know the jargon,” he said, and can basically understand what is happening when business acquisitions or other industry events are reported. Trivedi noted that scientists often feel they will be looked down upon if they join industry, but “that’s where a lot of things are going now…”

—David Clarke, Science Writer

[S]cientists often feel they will be looked down upon if they join industry, but “that’s where a lot of things are going now….”

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The Rockefeller University/HHMI

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Tobias Walther
Harvard/HHMI

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Yamini Mootha
Massachusetts General Hospital

Quality Control
Anne Bertolotti
MRC Laboratory of Molecular Biology, Cambridge, UK
Laurie Glimcher
Weill Cornell Medical College
Ramanujan “Manu” Hegde
MRC Laboratory of Molecular Biology, Cambridge, UK

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Cellular Communities
- Bonnie Bassler
  Princeton University/HHMI
- Juergen Knoblich
  Institute of Molecular Biotechnology (IMBA), Vienna, Austria
- Dianne K. Newman
  California Institute of Technology/HHMI

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- Denise Montell
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- Aviv Regev
  MIT and Broad Institute of MIT and Harvard/HHMI

Nuclear Organization
- Susan Gasser
  Friedrich Miescher Institute for Biomedical Research and University of Basel, Switzerland
- Rob Singer
  Albert Einstein College of Medicine and Janelia Research Campus/HHMI

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Deadlines
- October 13 Final Abstract Submission (poster consideration only)
- November 10 Hotel Reservations
- November 17 Meeting Registration Cancellation (to be eligible for a refund)
- November 17 Room-Share Request
- November 22 Hotel Cancellation via onPeak, ASCB’s Official Housing Partner

Minisymposia Topics
- Actin Dynamics
- Autophagy/ESCRT
- Cell Biology of the Nucleus
- Cell Cycle, Cell Division, and Cell Death
- Cell Mechanics
- Genome Replication and Gene Regulation
- Intermediate Filaments
- Membrane Organization, Dynamics, Traffic, and Regulation (except Autophagy/ESCRT)
- Microtubule Dynamics
- Multicellular Interactions, Tissues, and Development
- Organelles and Spatial Organization of the Cell
- Post Transcriptional Gene Regulation
- Prokaryotic Cell Biology
- Signaling and Differentiation
- Synthetic and Systems Biology
- Evidence-Based Education: Evaluation of Cell Biology Innovations
Imaging the Cell in the 21st Century: Challenges and Opportunities in Fluorescence Microscopy

Organizers: Hari Shroff, NIBIB/NIH and Justin Taraska, NHLBI/NIH

Sunday, December 4
4:15 pm-6:50 pm

Learn the answers to key questions about imaging: What sets the spatial resolution in a super-resolution experiment? How can one image in thick samples with a quality comparable to that in single thin cells? What are the prospects for better and brighter probes? Which imaging technology is right for a biological problem? How can different methods be correlated to provide information from multiple modes of imaging in the same sample?

Cryo-EM: What It Can Do Now and How You Could Get Started

Organizer: Grant Jensen, California Institute of Technology/HHMI

Monday, December 5
4:15 pm-6:50 pm

This workshop will begin with explanations of the fundamental challenges in biological EM; the key principles of cryo-preservation, electron imaging, and detector technologies; and the three basic modalities of cryo-EM (electron crystallography, single particle analysis, and tomography). It will then provide updates on what each modality can do now, who should be thinking about trying cryo-EM, and National Institutes of Health plans to establish regional cryo-EM centers.

Leveraging CRISPR for Precision Biology

Organizers: Jacob Corn, University of California, Berkeley, and Martin Kampmann, University of California, San Francisco

Tuesday, December 6
4:15 pm-6:50 pm

This in-depth workshop will cover the use of CRISPR-based approaches for genome-wide genetic screens, including loss-of-function screens (CRISPR nuclease, CRISPRi) and gain-of-function screens (CRISPRa). It will also cover basic and advanced genome editing using CRISPR-based tools and topics such as guide RNA design, evaluation of off-targets, ways to improve efficiency, and working in cells and organisms.

Visit ascb.org/2016meeting/workshops for more information
Special Interest Subgroups

Plan to arrive early to attend Special Interest Subgroup Sessions!

This is where ASCB members totally drive the scientific agenda; the focus of Saturday is on a wide range of topics self-organized by groups of interested scientists. These are among the most popular scientific sessions at the ASCB meeting, which is why we are now offering two separate sessions on Saturday, starting at 8:30 am!

Saturday Morning Subgroups
8:30 am – 12:30 pm

Subgroup A: Small GTPase Regulation of Membrane Traffic in Health and Disease
Organizers: Suzanne Pfeffer, Stanford University; and Yuxiao Wang, University of California, San Francisco

Subgroup B: Neuronal Cell Biology: Cytoskeleton and Trafficking
Organizers: Stephanie Gupton, University of North Carolina, Chapel Hill; and Laura Anne Lowery, Boston College

Subgroup C: Actomyosin Contractility: From Reconstituted Networks to Morphogenesis
Organizers: Ronen Zaidel-Bar, Mechanobiology Institute Singapore; Margaret Gardel, University of Chicago; and James Sellers, NIH/NHLBI

Subgroup D: Emerging Model Systems
Organizers: Bob Goldstein, University of North Carolina at Chapel Hill; and Nicole King, University of California, Berkeley/HHMI

Subgroup E: Crosstalk between Autophagy and Secretion
Organizers: Hesso Farhan, University of Oslo, Norway; and Mondira Kundu, St Jude Children’s Research Hospital, Memphis

Subgroup F: Bottom-Up Cell Biology
Organizers: Daniel Fletcher, University of California, Berkeley; and Matthew Good, University of Pennsylvania

Subgroup G: Evolutionary Cell Biology
Organizer: Holly Goodson, Notre Dame University

Subgroup H: Science with Undergraduates: Authentic Experiences from the Laboratory to the Classroom (and in Between)
Organizers: Derek A. Applewhite, Reed College; Sabrice Guerrier, Millsaps College; Omar A. Quintero, University of Richmond; and Joshua C. Sandquist, Grinnell College

Subgroup I: “CRISPR-Trac”: Live Cell Dynamics of Chromosomes and Transcripts Interrogated by Cas9-sgRNA Labels
Organizers: Thoru Pederson, University of Massachusetts Medical School; and Robert H. Singer, Albert Einstein College of Medicine; Howard Hughes Medical Institute, Janelia Campus

Subgroup J: Patterning the Cytoskeleton: PTMs, MAPs and ABPs
Organizers: Kristen Verhey, University of Michigan Medical School; and Antonina Roll-Mecak, NINDS/NIH

Saturday Afternoon Subgroups
1:30 pm – 5:30 pm

Subgroup K: Accelerating Science and Publication in Biology (ASAPbio)
Organizers: Prachee Avasthi, University of Kansas Medical Center; and Jessica Polka, Accelerating Science and Publication in Biology (ASAPbio)

Subgroup L: Using the Human Protein Atlas - Tips and Tricks
Organizer: Tove Alm, KTH Royal Institute of Technology

Subgroup M: Emerging Roles of ROS-Related Redox Signaling in Cell Biology
Organizers: Daniel M. Suter, Purdue University; Christian Gonzalez-Billault, Universidad de Chile; and Jonathan R. Terman, University of Texas Southwestern Medical Center

Subgroup N: The Cell Biology of Stem Cells
Organizers: Diane Barber, University of California, San Francisco; Rick Horwitz, Allen Institute for Cell Science, Seattle; Michael Graham Espey, NCI/NIH

Subgroup O: 4th Biannual Frontiers of Cytokinesis
Organizers: Amy Maddox, University of North Carolina, Chapel Hill; Doug Robinson, Johns Hopkins University; Dimitrios Vaylonis, Lehigh University; Julie Canman, Columbia University; Ulrike Eggert, King’s College London; and Jian-Qui Wu, Ohio State University

Subgroup P: Building the Cell 2016
Organizer: Susanne Rafelski, Allen Institute for Cell Science, Seattle

Subgroup Q: Translational Cell Therapy for Cancer
Organizer: Lisa Butterfield, University of Pittsburgh; and Daniel J. Powell, University of Pennsylvania; and Society for Immunotherapy of Cancer

Subgroup R: Mechanisms and Consequences of Cell Size Regulation
Organizers: Fred Chang, University of California, San Francisco; and Orna Cohen-Fix, NIDDK/NIH

Subgroup S: Nanotechnology Approaches for Interrogating Cell Signaling
Organizers: Young-wook Jun, University of California, San Francisco; Bianxiao Cui, Stanford University; and Shawn Douglas, University of California, San Francisco

Subgroup T: Cilia, Signaling, and Human Disease
Organizers: Peter K. Jackson, Stanford University School of Medicine; and Jeremy Reiter, University of California, San Francisco

Wednesday Subgroup
8:30 am – 11:05 am

Subgroup U: Understanding T Cell Activation, Developing Tools for Cancer Immunotherapy
Organizer: Xiaolei Su, University of California, San Francisco
keynote talk at ASCB in 1998. At that time, Lifton was noted for his genetic studies of hypertension, identifying rare mutations that drive either extraordinarily high or low blood pressure and tracing all to mutated genes that severely misregulate renal salt absorption. “But it’s been a long time,” said Lifton, “and a fair amount has changed since then.” That is an understatement.

Focused Forensic Genetics
Exome sequencing is what changed everything. Lifton was one of the pioneers of a new kind of forensic genetics that combines emerging genomic sequencing technologies with a different sampling approach focused exclusively on the exons. These are the roughly 180,000 protein-coding genes, which make up 1% of the human genome but are thought to harbor the vast majority of the mutations with large effects in human disease. With exome sequencing, the Lifton lab has pried open the hitherto hidden genetic underpinnings of a startling range of human conditions from tumors that produce endocrine hormones to idiopathic pulmonary fibrosis to congenital heart disease.

Following the initial sequencing of the human genome in 2001, it was clear that re-sequencing the genome by massively parallel sequencing was possible but extremely expensive. Given that the vast majority of mutations with large phenotypic effects that had been mapped in an unbiased fashion and then identified had proved to be attributable to effects on protein-coding regions and flanking intron–exon boundaries, selectively sequencing the 1% of the genome comprising coding sequence seemed an attractive approach for Mendelian discovery. Although Lifton had developed methods for physically purifying mRNAs by hybridization to cloned DNA as a graduate student in the 1970s, the idea of doing the analogous simultaneous selection of DNA of all exons of the human genome nonetheless seemed audacious, said Lifton, who before his new Rockefeller post, was Chair of Genetics at Yale Medical School and a Howard Hughes Medical Institute investigator. The idea of exome sequencing was in the zeitgeist of the time, and a number of academic labs and companies worked on the idea.

Lifton is careful to point out that others, especially Jay Shendure at the University of Washington, also developed robust methods for exome capture. Lifton and colleagues developed an analogous capture approach working with scientists at Nimblegen, iteratively testing and modifying protocols to come up with a robust protocol for production and data analysis. Lifton notes with some pride that their initial variant-calling algorithm was put together by Murim Choi, a postdoc in the lab who used “good intuition about sources of experimental variation, off-the-shelf mapping algorithms, and coding expertise derived from Perl for Dummies.” They eventually were satisfied that they could identify homozygous and heterozygous sequence variants with high sensitivity and specificity.

Proof of Principle
As an initial “test drive” of the technology, in 2009 they pulled off the hat trick in genetic medicine—the first definitive diagnosis of a human genetic disorder by genomic or exomic sequencing. The chance came with a patient referred to Lifton to establish a molecular diagnosis of Bartter syndrome, a rare congenital defect that affects how the kidneys reabsorb sodium. Features of the clinical diagnosis didn’t quite fit, suggesting the diagnosis might not be Bartter syndrome. The Lifton lab sequenced and analyzed the patient’s exome, identifying a novel homozygous mutation in a gene highly conserved across the evolutionary spectrum from Drosophila to humans and strongly linked to absorption of chloride in the colon. This suggested that the disease was not in the kidney but in the colon. Lifton referred the conclusion back to the treating physicians who confirmed his diagnosis of congenital chloride malabsorption with tests of chloride levels in the colon. The diagnosis also had therapeutic
implications because there was an existing therapy for the condition. Five other patients with suspected Bartter syndrome were also shown to have colonic malabsorption instead.

Surely when the physician's report came back, there was a celebration in the Lifton lab? “It was clearly a wonderful validation of our approach,” Lifton allowed, but he remembered the far larger questions that came to him immediately. “Sure, it was, ‘Wow. This really works.’ But to me, this was just a proof of principle. The more interesting question over the last seven years arises from the observation that we know what happens in humans when about 3,000 of our 20,000 genes are mutated. But now that we have sequences of many branches of the phylogenetic tree, we know that all the vertebrates are basically dealing with the same gene set. Sure, there are some rapidly evolving gene sets, such as genes of the immune system, but the vast majority of human genes have been kept around for at least the last 500 million years, undoubtedly because of impaired reproductive fitness if they are lost. This strongly suggests that there are going to be strong phenotypes that result from mutations in many, many additional genes. And if that’s true, why haven’t we previously recognized these phenotypes as simple Mendelian traits?”

The Search for Lost Phenotypes

Lifton continued, “So we started thinking about classes of mutations that would have large phenotypic effect but would not show typical patterns of Mendelian segregation in families. For example, heterozygous mutations that drastically impair reproductive fitness will nearly always be de novo mutations and appear only sporadically in the population. These could not previously be sought. Similarly, mutations that only impart phenotypic effect following specific environmental exposures or via interaction with one or more additional genetic loci may recur in families but not show typical patterns of Mendelian transmission. Diseases caused by somatic mutations, including but not limited to cancer, were still other possibilities. Through the last seven years, we’ve tested each of these paradigms and have discovered new genes and biology underlying a wide range of diseases for which genetic contributions were suspected but not established.”

Lifton said that two good examples of the contribution of de novo mutation are autism and congenital heart disease, which unexpectedly have both proved to be frequently caused by de novo mutations that cause the loss of function of genes involved in chromatin remodeling. An additional surprise for both diseases has been that a very large number of genes in this pathway—likely more than 100—can be mutated to give similar phenotypes. Most interestingly, he notes, in many cases de novo loss of function mutations in the same genes in this pathway are found in patients with congenital heart disease and autism.

There are real clinical implications here, he believes. “We’ve known for a long time that children with congenital heart defects, after their hearts are surgically corrected, frequently go on to have adverse neurological outcomes. We haven’t known if that was attributable to anoxia before surgery, a poor outcome from surgery, or the underlying biology. These findings clearly indicate that in many cases it’s the underlying biology that’s driving the outcome.”

An example of a disease featuring gene–environment interaction from recent work is pulmonary fibrosis, in which his group, collaborating with Christine Garcia’s lab at the University of Texas Southwestern Medical Center, discovered mutations in the genes PARN and RTEL1 that cause disease in conjunction with inhaled environmental exposures. “You may be fine if you’re never exposed to an environmental co-factor,” Lifton explained. Susceptibility to certain infections could be another example. “You may be fine with a mutation in the interferon response pathway unless exposed to a Neisseria that causes meningitis,” in which case your ability to fight it off is drastically impaired.”

All of this, Lifton believes, points to a clear path forward to answer the truly big question revealed by exome sequencing: “What is the consequence of a mutation in every gene in the human genome?”

Getting there, said Lifton, is not going to be easy. “What remains to be done in human genetics? The answer is practically everything.”

—John Fleischman
ANNUAL Meeting

Learn it, Film it, Nail it—Shoot Your Own 60-Second Elevator Speech Video at ASCB 2016

You’ve been dreading it. Everyone says that you need an Elevator Speech, right? Your advisor, your lab mates, they all say that you need a very short, very simple speech that explains what you do in the lab and why it’s important. Yet the idea of cramming the last few years of your research life and all your elegant data into a minute gives you a headache. Take a deep breath. And take advantage of an opportunity to learn the art and science of delivering a knock-out Elevator Speech in San Francisco this December. At ASCB 2016, you can learn the basics, practice with peers, film yourself on your smart phone, and enter the On-Site, All-Video, Mostly-Selfies, 60-Second Elevator Speech Contest run by the ASCB’s Public Information and Public Policy Committees. The contest winner gets a snazzy prize, but win or lose you’ll break the ice on the essential business of taking your science to the world.

The premise is simple: The elevator door closes and you’ve got a trapped audience—a U.S. Senator, your dean, or Drake. Go for it! Sell your science in 60 seconds. The first step in San Francisco is the Public Policy Committee’s Advocacy Toolbox Workshop on Monday, December 5, 10:00 am. There you’ll learn (and practice) the essentials of elevator talking.

Then to enter the Elevator Speech Contest, take a video of yourself and upload it to YouTube or Vimeo. Then go to www.ascb.org/elevatorspeech and fill out the form with the link to your uploaded video. Don’t have the means to record your video in San Francisco? Come to the ASCB Booth in the ASCB Learning Center on Tuesday, December 6, 10:00 am–10:45 am. A camera awaits you. All entries must be in by Tuesday at 11:00 am. The winner and runners-up will be shown at PIC’s 2016 Celldance Video and Elevator Speech Awards Tuesday at 12:00 in the Career Center Theater inside the ASCB Learning Center.

—John Fleischman

ASCB Poster Competition Judges Needed

The ASCB Minorities Affairs and Education Committees are looking for judges for the ASCB Poster Competition that will be held during the 2016 ASCB Annual Meeting in San Francisco, on Saturday, December 3, 2016, from 3:30 pm–5:30 pm. There will be 80–100 posters to judge, but no more than two or three per judge.

If you are interested in judging, please sign up at https://my.ascb.org/initiatives/#/apply/75.

If you have any questions, please contact Thea Clarke at tclarke@ascb.org.
Coming Attractions—Celldance Studios Announce New Microscopic Blockbuster Productions

Celldance Studios, aka ASCB’s Public Information Committee (PIC), has unveiled its list of three Celldance 2016 “Tell Your Own Cell Story” productions that will premiere at ASCB 2016 in San Francisco this December (www.ascb.org/celldance2016). The three short (three- to four-minute) videos will feature eye-popping live cell imaging framed in accessible narratives that will dazzle both biologists and the public. The three ASCB member labs chosen are are those of Daniela Cimini, Virginia Polytechnic Institute and State University; Matthieu Piel, Institut Curie; and Roberto Weigert, National Cancer Institute, NIH.

Each of the three labs will receive a $1,000 unrestricted production grant from ASCB plus full postproduction services including final editing, a legal musical score, credits, titles, and promotion, all at ASCB expense. Each video-making lab has an assigned PIC member/producer to act as a go-between and advisor for the video-makers. In this role, Claire Walczak will work with the Cimini lab, Heidi Hehnly-Chang with the Piel group, and Elisa Konieczko with the Weigert lab.

Here is what the three video-making labs are planning:

- Many people remember diagrams of cell division from their high school biology class, according to Cimini, but her video will update that stale, static memory using the latest 21st century live cell imaging to reveal the dynamic, colorful, and essential process of mitosis.
- The Weigert video will take viewers into the cell with subcellular intravital microscopy, a technology that allows them to tackle the audacious challenge of making visible what’s going on at the cellular level in living multicellular animals. The Weigert lab has succeeded in filming the critical cellular process of membrane trafficking in live mice and rats, revealing the strange beauty behind this nuts and bolts process of cellular life.
- The Piel group has a heroic tale to tell. Through advanced microscopic imaging technology, they will follow the epic journey of a dendritic cell through twisting mazes and tight quarters to the lymph nodes, where it dies, releasing a critical signal alerting the body’s immune system to danger. Piel likens the dendritic cell’s task to the Ancient Greek warrior who ran from the battlefield at Marathon to Athens where he gasped the news of victory and collapsed dead. It will be an epic story on a microscopic scale, Piel promises.

This is the third year of Celldance Studio’s “Tell Your Own Cell Story” videos where ASCB member labs are given resources and backup support to bring their big discoveries to the little screen in more than living color. The 2014 and 2015 Celldance videos can be seen at www.ascb.org/past-celldance-winners.

—John Fleischman
The ASCB is grateful to its Corporate Members for 2016

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- International Center for Genetic Engineering and Biotechnology (ICGEB)
- Travel Awards
- Nuaire
- Collateral Listing on Mobile App

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The ASCB thanks the following organizations for supporting the 2016 ASCB Annual Meeting*

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The ASCB thanks the following organizations for supporting the 2016 Doorstep Meeting on the Cell Biology of Cancer

- Calico Life Sciences LLC
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Since you’re a member of the ASCB, GEICO could help you save on car insurance, too. In fact, when you get a quote, be sure to mention you’re a member ASCB and you could get a special discount.

Simply go to geico.com/sci/ascb, call 1-800-368-2734 or contact your local GEICO agent for a fast, no-obligation insurance quote.

Did You Know…?

The ASCB Annual Meeting Is Only One of the Many Benefits of ASCB Membership

Did you know that as an ASCB member you can save up to 58% (savings vary by member type) on your Annual Meeting registration? However, the Annual Meeting is by no means the only benefit ASCB offers its members.

Another member benefit is the ASCB Member Directory, which you can use all year long to expand your network. Use the Supplementary Information search tool in the ASCB Member Directory to find potential collaborators who share your interests or to search for a member by institution name or location. Just go to www.ascb.org, click on “Membership” and then on “Membership Directory,” and log in using your ASCB username and password.

It is important to update your profile to include information on your major research interests, experimental approach, model system, teaching activity, and funding resources so potential colleagues can find you. To update your profile go to www.ascb.org. Click on “MyASCB” and log in. Click on “My Account” and then click “Personal information,” “Update your ORCID,” or “Interests” to enter information about yourself.

Check out all the benefits of your ASCB membership at www.ascb.org/member-benefits.
Ask scientists about their career pathway and they will undoubtedly share a story about one of their mentors. Many will describe the ways in which they were inspired, supported, or encouraged by a mentor. Others will describe being pushed to achieve more than they thought possible. And yet others will describe how they succeeded despite their mentors (often referred to as tormentors).

Unfortunately, there are also a multitude of stories from trainees who left along the way, not because they lacked interest, motivation, or ability but because they did not feel supported, encouraged, or understood by one or more mentors. Often these trainees acknowledge the roles and responsibilities they played (or should have played) in making the relationship work, but they note, often longingly, that they wish their mentor(s) had tried to understand them, to make them feel as if they belonged in science, and to help them better navigate the training environment. And this becomes even more important and impactful when the talented mentee is a member of a group already underrepresented in science.

National Efforts to Improve Mentoring Relationships

The newly established National Research Mentoring Network (NRMN; www.nrmnet.net) is partnering with individuals, institutions, and organizations around the country to improve the access of diverse mentees and mentors to resources that can help enhance the quality of those mentoring relationships. NRMN operates on the hypothesis that granting all researchers access to evidence-based mentorship, professional development, and networking opportunities and resources will increase the success and persistence of those scientists from groups that are currently underrepresented in the biomedical sciences workforce.

The NRMN, part of the National Institutes of Health’s Diversity Program Consortium, is designed to address the problem of underrepresentation of scientists from key populations across the biomedical sciences.

The program’s overarching goal is to contribute significantly to national efforts to increase the size, quality, diversity, and research productivity of the biomedical workforce. NRMN programs are designed to 1) increase access to mentoring across career stages; 2) to improve mentoring relationships, broadly defined, through training; 3) to increase access to research resources and career development, and 4) to promote the value of mentoring across the nation.

Now starting its third year, NRMN is up and running and reaching thousands of mentors and mentees across the country and would welcome your participation. We all face challenges in our mentoring relationships and typically have little guidance on the best ways to resolve them. Listed below are some amazing resources from NRMN’s wide range of free mentorship and professional development programming. For further information about each, visit www.nrmnet.net and select a topic from the drop-down menu under “Programs.”

- The NRMNet guided virtual mentorship platform, which pairs mentors and mentees from around the nation, centers around weekly discussion topics that emphasize diversity, inclusivity, and culture.
“I went from ‘I’m not good enough,’ to ‘OK, I have to set my sights lower; I’m probably not going to be a researcher… maybe an assistant to a researcher.’ But then I discovered somebody who saw that I had more potential, who taught me how to be a scientist.”

—J. Marcela Hernandez, The Ohio State University

Visit www.nrmnet.net to hear Hernandez’s full story.

We all face challenges in our mentoring relationships and typically have little guidance on the best ways to resolve them.

online platform, built in partnership with MentorNet, links each mentee to another person who has successfully navigated or is currently navigating a similar career path. Using regularly delivered discussion prompts, the program guides mentor–mentee pairs in critical conversations designed to enhance the success of diverse scholars and scientists. Each mentoring relationship is programmed to last four months and is supported by short training videos throughout. After the fourth month the mentee can continue with the same mentor or switch mentors. These virtual pairs meet synchronously or asynchronously on the Web or on the phone. The system is very flexible.

Intensive grant writing coaching groups that address both grant proposal writing basics (for those with limited experience with proposal submission) and advanced proposal tactics (for those with substantial experience working on a proposal submission or resubmission) are offered regularly. Such coaching is critical because most first grant submissions are not funded and many writers, especially those from underrepresented groups, do not resubmit! Rejection is normal and resubmission after revising a proposal with the help of a coach is a key to being funded.

The opportunity to be a grantsmanship coach or scientific/methodology advisor and provide guidance to mentees within a grantwriting coaching group is available. Complete descriptions of these roles, eligibility, and expectations and links to the online applications can be found at https://nrmnet.net. Selected coaches engage in training and real-time advising and coaching.

Evidence-based training workshops to maximize the effectiveness of mentoring relationships as a mentor or a mentee are available. NRMN offers research mentor training curricula and workshops for mentors working with trainees across disciplines and career stages in the following formats: in-person, self-paced online, and synchronous online. NRMN also offers training, curricula, and resources for mentees to help them more successfully navigate their mentoring relationships.

Training on facilitating and implementing a mentorship training program at one’s home institution is available. New workshops are coming in 2017.

Mentor certifications are offered to formally recognize research mentors who have demonstrated certain key skills and experience with respect to mentorship. Mentors can be recognized as an NRMN Mentor, NRMN Certified Mentor, or NRMN Master Mentor depending on the depth of their qualifications and can add this acknowledgement to their own CVs.
The MyNRMN mentorship networking platform, a powerful social networking platform for students and researchers, connects users with one another for anything from general questions about research and professional development as a scientist to scheduling more formal mentorship appointments one-on-one or as a group. Simply go to the https://nrmnet.net site and sign up.

If you are interested in participating in NRMN’s programming, visit https://nrmnet.net.nih-notice and create a profile to get started.

Expanding National Capacity

Among the goals of NRMN are to serve as a national hub to enhance mentor and mentee training efforts, to disseminate best practices in training and empower others to implement them, and to study the impact of training at a national level. A particular area of focus has been to improve the ability of mentors and mentees to be more culturally aware and responsive, meaning they are better able to examine and recognize their own bias, cultural ignorance, or uncertainty about addressing cultural diversity and to learn from mentees from whom they may differ.

To build national capacity for mentor and mentee training, NRMN has embarked on offering train-the-trainer workshops using an evidence-based approach.1 More than 200 individuals have been trained to implement mentor or mentee training at their institutions. Longitudinal tracking via an annual survey of training implemented by these individuals is underway using a centralized evaluation system, supported in part by NRMN. Moreover, NRMN has recruited and trained a cadre of Master Facilitators who provide mentor, mentee, and facilitator training for diverse populations across career stages in science, technology, engineering, mathematics, and medicine. The cadre includes 35 faculty and staff representing 16 institutions across 11 states from various disciplines in the basic and health sciences. Visit the NRMN website or contact mtc@nrmnet.net to learn more about how you can get involved, to find out which NRMN Master Facilitators are near you, and to link to future reports and publications describing the impact of these initiatives.

Welcome to NRMN!  
—Christine Pfund, University of Wisconsin-Madison, and MariaElena Zavala, California State University-Northridge

Reference


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Are you publishing a book? If so, let ASCB know! Send the title, publisher, ISBN information, and a thumbnail (300 dpi) of the cover. We’ll include it in the ASCB Newsletter. This publicity is available only to ASCB members. Please send submissions to Thea Clarke at tclarke@ascb.org.
PROFESSIONAL DEVELOPMENT

NRMN grantwriting programs are designed to help researchers currently planning or working on a grant proposal develop professional skills to:

• Master grant proposal basics
• Prepare grant submissions
• Accelerate success in obtaining grant funding

VIRTUAL MENTORING

The NRMN Virtual Mentoring Program is a four-month experience with regular, guided interactions between mentors and mentees at a distance. The virtual mentoring experience will help mentors and mentees:

• Develop meaningful mentoring relationships beyond their own institutions
• Work closely and regularly with another person who is navigating a career path in science
• Navigate conversations critical to the success of diverse scholars

RESEARCH RESOURCES

• Find funding opportunities and fellowships
• Learn modern research methods from leading experts through online lectures
• Participate in live online discussion panels
• Discover opportunities for participation in upcoming scientific meetings and events.
• Tap into exciting research in collaboration with diverse scientists from across the U.S.
• Establish a network of professional support

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Professional Development Core
University of Minnesota
Christine Pfund, PhD
Mentor Training Core
University of Wisconsin-Madison
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Participation is FREE!

Register with NRMN today to benefit from the full list of programs!
With the election approaching, we are on the cusp of new leadership, new agendas, and new ideas, so now is a good time to assess how biomedical research has fared under the Obama administration. Here’s a look at some of President Obama’s actions that promoted and advanced biomedical research over the past eight years.

Obama was first sworn into office on January 20, 2009, and a month later he enacted the largest annual increase in research and development funding in our nation’s history with the American Recovery and Reinvestment Act of February 2009 (ARRA). The National Institutes of Health (NIH) received $8.2 billion in extramural funding from the ARRA to help stimulate the economy by accelerating discoveries in biomedical research. Many cell biologists benefited from this infusion of funds, including researchers studying regenerative medicine and airway epithelial cells, among many areas. ASCB even benefited from a $2.5 million NIH ARRA grant that helped bring to fruition The Cell: An Image Library, a comprehensive public collection of cell images designed to assist the scientific community.

Right on the heels of the ARRA stimulus package, Obama invited scientists and research advocates to a White House ceremony where he signed his first executive order, which overturned President George W. Bush’s rule that limited research on embryonic stem cell lines. Obama’s executive order directed the NIH to develop guidelines and regulations to govern federally funded human embryonic stem cell research. The ASCB was on the forefront of efforts during Bush’s administration to overturn his executive order. It was an essential issue for many ASCB members who were stymied in their research by the limited number of available cell lines as well as by the necessity of working with existing cell lines that were compromised. Obama’s action freed the hands of many scientists—especially cell biologists—to conduct embryonic stem cell research in a responsible, ethical, and productive manner.

Obama has clearly expressed his administration’s commitment to scientific research. For example, in a speech on April 29, 2013, commemorating the 150th anniversary of the National Academy of Sciences, he told the assembled scientists, “…for 150 years, you’ve strived to answer big questions, solve tough problems, not for yourselves but for the benefit of the nation. And that legacy has endured from the Academy’s founding days. And when you look at our history, you’ve stepped up at times of enormous need and, in some cases, great peril.” He reiterated that point in the speech by saying “in all the sciences, we’ve got to make...
sure that we are supporting the idea that they’re not subject to politics, that they’re not skewed by an agenda, that, as I said before, we make sure that we go where the evidence leads us. And that’s why we’ve got to keep investing in these sciences.”

Obama put forth three ambitious biomedical initiatives in the course of his administration. In 2013, he introduced the BRAIN Initiative to uncover new ways to treat, prevent, and cure brain disorders such as Alzheimer’s disease, Parkinson’s disease, schizophrenia, autism, epilepsy, and traumatic brain injury. The initiative has garnered $1.5 billion in public and private funds and has more than 100 academic papers tied to it.

The president went on to launch the Precision Medicine Initiative in January 2015. The initiative provides more than $200 million toward advances in research, technology, and policies aimed at enabling a new era of medicine in which researchers, providers, and patients work together to develop individualized care.

On January 12, 2016, at his final State of the Union address, Obama continued his commitment to biomedical research with his introduction of a third ambitious undertaking, the Cancer Moonshot Initiative. He announced that he was putting Vice President Joe Biden, who lost his son Beau to cancer in 2015, at the helm of this ambitious effort to once and for all end cancer. This $1 billion initiative encourages public and private efforts to double the rate of progress in cancer prevention, diagnosis, treatment, and care in a quest to make a decade’s worth of advances in five years. This endeavor caps off the final year of a presidency that has consistently recognized the capabilities of our scientists, including basic researchers.

Obama has faced pressure and pushback from a polarized Congress but has maintained his administration’s commitment to science and innovation. We do not know what November’s election will bring to the scientific community, but it’s fair to say that the administration’s endeavors over the past eight years have helped advance biomedical research.

—Tommy Mattocks, Public Policy Coordinator

Footnote

1The Cell: An Image Library is now managed by the National Center for Microscopy and Imaging Research under perpetual license from ASCB and is part of The Cell Image Library.

Congressional Biomedical Research Caucus

The Congressional Biomedical Research Caucus held a briefing featuring Allan Basbaum of the University of California, San Francisco. His talk, “Pain Research: On the Verge of a Breakthrough,” can be viewed at www.coalitionforlifesciences.org.
Third Annual MBoC Special Issue on Quantitative Cell Biology

Coming in November 2016.

www.molbiolcell.org

Issue Co-Editors: Diane Lidke, Jennifer Lippincott-Schwartz, Alex Mogilner, and Valerie Weaver

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Reflections on Making the Leap

At ASCB, and especially at COMPASS, we frequently visit the topic of nonacademic careers. Many of us have discussed the growing imbalance in academia, with greater numbers of PhD students being prepared for a niche job market—the tenure-track professorship—that is not growing at a commensurate pace. Today, only 1 in 10 graduates will end up in a tenure-track position, meaning nonacademic careers have become the majority choice for PhDs in the biomedical fields. Fortunately, academic institutions are increasingly adjusting to this reality by incorporating nonacademic options into their career planning efforts for PhDs.

Even with collegial and institutional support, the decision to leave academia is ultimately a very personal one. At its root, it is a process of deep self-reflection, self-realization—and no small amount of fear and self-doubt. Though the process is different for everyone, it’s inevitably difficult terrain to navigate, fraught with professional and emotional peril.

Few PhDs are mentally prepared to leave academia. Why would we be? Implicit in the modern doctoral career path are the dual assumptions that true success happens only in a very narrow window—the “professor or bust” mentality—and that this success is readily achievable for anyone with talent and a strong work ethic. So what do you do if, somewhere along the winding path to graduation, one or both of these implicit assumptions no longer rings true to you? How do you prepare for a career outside of academia? And how do you break the news to the people who’ve been guiding you toward an academic future?

Here are some of my thoughts, born of recent experience and reflection.

Make an Informed Decision

Explore your interests. When you realize that you no longer want to pursue research, a glaring question enters your mind: What am I going to do next? You’ve probably spent years preparing for a life of research, without giving much thought to the alternatives that are out there. So the first thing to do is to fully explore your career options. There are many resources available to help you with this (for example, the Individual Development Plan). I would add: network! It’s a cliché, but networking really can be invaluable when looking for a new career. Anytime you meet someone whose job title intrigues you, exchange contact information and ask to speak with the person about his or her career. Informational interviews will help you learn what a job is really like and illuminate a viable path to getting there. Even when you don’t meet in person, reach out on LinkedIn. People are usually more than willing to offer free advice. After all, there’s a good chance that they were once in the same position as you!

Also, take advantage of volunteer work. It will allow you to judge whether you’ll enjoy the job, gain some experience, and develop connections that can potentially lead to employment opportunities in the future.

Recognize your expansive skillset. The natural inclination to associate doctoral training with technical expertise makes it easy to overlook the broad range of skills you’ve developed over your graduate career. Many of your skills that have little to do with experimental prowess are highly sought after in nonacademic jobs. Spent a lot of time writing manuscripts and presenting at conferences? Communication skills are extremely valuable in the medical writing, science journalism, and science policy fields. Worked productively in a team setting? Nearly every corporate environment, from pharmaceutical companies to consulting firms, will reward you. Try to flesh out your skills and strengths to gauge whether you’ll flourish in the careers that you find most attractive.

Dedicate time away from the bench for proactive career development. Figuring out where you want to go and how you’ll get there means spending some time away from the bench. To make measurable progress, dedicate time exclusively to professional development...
every week. It's very easy to get sucked into the research vortex, as there's always another experiment waiting to be done. But spend all of your time running assays, and you may start to feel as though you're spinning your wheels.

Let your advisor in on your thinking early and often. Breaking the news to your mentor that you’re considering leaving academia can be awkward and intimidating. There are certainly horror stories about some who do not take the news well. In my own interactions, I’ve found that mentors generally have your best interest at heart but often haven’t been exposed to all of the career choices that are out there. Broaching the topic of alternative careers is somewhat akin to speaking from the outside of an echo chamber. Moreover, they may not appreciate the current job plight for PhDs. Keep in mind that the career prospects of the last generation of scientists were quite different from what scientists face today.

But in any case, your advisor can't help you if you keep your internal dilemma to yourself. Let your mentor know about your desire to pursue a nonacademic position as soon as it takes serious hold in your mind. Maintaining an open line of communication, however uncomfortable it may be, is better than a silent struggle that provides no opportunity for help and guidance.

Then, When It’s Time…

Be able to explain how your new career benefits science. Anytime you're looking to switch careers, it's essential to be confident that the new job fits your goals and values. For dyed-in-the-wool scientists, a large part of this means believing that your career contributes to science. This can be difficult if those around you consider nonacademic positions to be unimportant. A job that doesn't explicitly advance knowledge in a specialized field may not seem scientifically valuable to someone who has built his or her career doing just that.

It's therefore worthwhile to have a convincing explanation as to how your job will contribute to the scientific enterprise, writ large. Explaining the job's value to your mentor and colleagues will help you build confidence that you're making the right choice. If you really know this job is the one for you, it should be easy to give a convincing rationale. Likewise, if you find it difficult to explain, this is a red flag to pause and reflect further. Remember that you’ll never persuade everyone, so the most important thing is to feel secure in your own decision.


Many of your skills that have little to do with experimental prowess are highly sought after in nonacademic jobs.
Develop a firm transition plan that leaves your research in order. Research is a continuous process, and at any given point we’re generally juggling multiple projects at several different stages of completion. So there will rarely be an ideal time to leave a lab, and your departure will certainly have an impact on the lab’s progress. You can ease the transition by letting your advisor and labmates know as early as possible if you intend to leave. This will give everybody time to logically apportion your projects and develop a strategy for completing the work you started.

Anecdotally, it’s actually quite common for manuscripts to be published months—and in some cases, years—after one of the authors has left for a new position. So an unfinished paper is not in and of itself a reason to stay should a new opportunity arise.

Be prepared for abrupt change. Nonacademic jobs typically operate on a very different timeline from academia. There’s generally no such thing as giving an employer your one-semester’s notice, except in the confines of a university. So while you may spend months or years searching for a job, when an offer comes you may need to transition out of academia quickly. If you’re serious about changing careers, be prepared for a potentially rapid up-ending of your professional trajectory if an offer presents itself.

Don’t let fear of the unknown hold you back. It is entirely natural to be nervous about entering a new job. This is especially true for those in academia. It’s not uncommon to spend five years or more at the bench earning a PhD, and then another three to five years (or longer!) as a postdoc. After such a prolonged period research becomes second nature, and “cutting the research cord” can be scary. But if you’ve really thought long and hard about your new career path, these reservations are largely instinctive and will pass with time. Don’t allow fear to metastasize into paralysis: If the decision to leave is right for you, swallow the fear and go for it!

Finally, and Most Importantly…

Don’t let anyone dissuade you from believing that your passion has value. The professional value of what you’re passionate about will be determined by those who are willing to pay you to do what you love. But the personal value of your career is, and always should be, determined by you and you alone. Your academic mentors can help you develop and mold your passion, and provide you with the resources to achieve it. But at the end of the day, only you are capable of defining it.

—Travis J. Bernardo

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MINORITIES Affairs

Broadening Participation in the Life Sciences

The strength and malleability of the life sciences community going forward will depend on our ability to build a life sciences workforce that is representative of the great diversity of people and backgrounds in our society. We envision a diverse workforce that is ready to collaborate and innovate to solve today’s challenging problems as well as those lying ahead. As we consider the impacts of these potential solutions, it is important not to lose touch with the different sectors of society these innovations should benefit. A large body of evidence from both academia and the private sector demonstrates that high-performing teams are diverse in their makeup—they embrace gender, ethnic, and racial diversity. Yet an important question remains: How do we achieve this diversity?

The answer to this question continues to be of vital importance to the U.S. scientific enterprise. Much effort has been put into understanding the challenges associated with recruiting, retaining, and mentoring individuals from diverse backgrounds in the context of our life sciences workforce. This is evidenced by the fact that the National Institutes of Health (NIH) and the National Science Foundation (NSF) have dedicated funding and grant mechanisms that aim to foster the design of programs that will catalyze such diversification. An important element of these new efforts is the potential to harness data collected from these studies in the way of assessments and measurable outcomes. Research efforts that analyze these data will help us better understand how to build and sustain a diverse life sciences workforce in an effective and thoughtful way. For these reasons, it is with great enthusiasm that we received the September 1, 2016, issue of CBE—Life Sciences Education (LSE), an issue focused on Broadening Participation in the Life Sciences (www.lifescied.org/content/15/3.toc).

This issue presents snapshots of our progress in building a diverse life sciences workforce at different levels of academia. This issue highlights various strategies for constructing inclusive programs at different levels of scientist training. This issue also highlights effective pedagogical interventions that target mentors and faculty, not just students or trainees, as a means to foster long-term changes in our scientific communities.

As Co-Chairs of the ASCB Minorities Affairs Committee (MAC) it is our mission to find ways to help the ASCB foster the building of a diverse life sciences workforce. But just as the larger life sciences community will benefit from the success of these efforts, we all share a common responsibility and ability to contribute! We encourage you to examine the articles in this special issue of LSE and look for ways in which your local scientific communities can contribute to these efforts. Thank you for continuing to help us to meet this challenge of diversifying our scientific community!

—Franklin Carrero-Martínez, National Science Foundation (MAC Co-Chair), and Verónica A. Segarra, High Point University (MAC Co-Chair)
2016 MAC Summer Workshops Foster the Career Development of Life Scientists at Different Stages in Their Training

The Minorities Affairs Committee (MAC) is a standing committee of the ASCB whose goals include fostering the professional development of scientists from underrepresented groups. One of the ways in which the MAC accomplishes this goal is by organizing and hosting summer workshops for ASCB members who are pursuing and/or aspiring to academic careers at research-intensive or teaching institutions. This year’s summer workshops were held at the Rizzo Conference Center at the University of North Carolina (UNC), Chapel Hill.

Third Annual FRED Program Mentoring Workshop
One of these workshops, a three-day Career Development Workshop for Junior Faculty and Mentors, was the kick-off event for the third year of the MAC’s Faculty Research and Education Development (FRED) Mentoring Program (www.ascb.org/fred-home). The FRED program is a structured mentorship workshop designed to promote grant funding success among junior faculty at institutions with a strong commitment to recruiting students from backgrounds underrepresented in cell biology. As part of this year-long program, each early-career scientist is paired with a senior faculty research mentor who has a strong track record of grant funding.

The goal of the FRED program is for the mentee to prepare a strong research or educational grant proposal for submission to a funding agency like the National Science Foundation (NSF) or National Institutes of Health (NIH). Members of the MAC catalyze communication and interactions between mentees and their mentors. Unstructured time during the workshop allows mentees to meet their individual needs for feedback from mentors and MAC members. The 2016 cohort of mentors and mentees included scholars from a variety of institutions and with diverse research interests. More information about the FRED cohorts and their experiences in the program can be found on our website.

Members of the 2016 Cohort of FRED Mentors and Mentees are:
- Mentee: Nathan Bowen, Clark Atlanta University
  Mentor: Anita Corbett, Emory University School of Medicine
- Mentee: Deepa Bedi, Tuskegee University
  Mentor: Rajeev Samant, University of Alabama at Birmingham
- Mentee: Martha Grimes, University of New Mexico
  Mentor: Renato Aguilera, University of Texas at El Paso
- Mentee: Dana-Lynn Koomoa-Lange, University of Hawaii at Hilo
  Mentor: Jian-Ying Wang, Baltimore VA Medical Center
- Mentee: Ileng Kumaran, Cold Spring Harbor Laboratory and Farmingdale State College
  Mentor: Lalita Shevde-Samant, University of Alabama at Birmingham
- Mentee: Rodrigo Maillard, Georgetown University
  Mentor: Susan Taylor, University of California, San Diego
- Mentee: Pablo Vivas-Mejia, University of Puerto Rico
  Mentor: Nita Maihle, Georgia Cancer Center

MAC 11th Annual Junior Faculty and Postdoctoral Fellows Career Development Workshop
Partially overlapping with the FRED workshop is the second summer workshop organized by the MAC—the Annual Junior Faculty and Postdoctoral Fellows Career Development Workshop (www.ascb.org/macjrfacultyworkshop). Now in its 11th year,
This workshop explores a variety of topics essential to a successful academic career, including mentorship, lab management, getting published, and securing tenure. Sessions on grant opportunities from the NIH and NSF are also part of the three-day program.

Workshop participants from this year’s cohort valued the opportunity to learn new skills and information and cited the opportunities for networking as one of the most valuable elements of the program. The highlight of this year’s program was that it drew panelists and speakers from local research-intensive and teaching-intensive institutions, tapping into the area’s resources, expertise, and underrepresented minority scientists. Local institutions represented included Duke University, UNC Chapel Hill, North Carolina State University, and High Point University. Panelists and speakers included high-profile scientists like HHMI investigator Erich D. Jarvis, recipient of the 2015 E.E. Just Lecture Award from ASCB.

The MAC is looking forward to next year’s workshop series and has already started to evaluate which workshop elements worked best and would be most useful for incorporation into future programming.

**MAC Visiting Professors Program**

The MAC was pleased to sponsor four scientists to begin and/or sustain collaborative professional development experiences with a more established and accomplished biologist and ASCB member over the course of at least one year. The Visiting Professors Program offers research support for professors at minority-serving institutions to work in the laboratories of ASCB members at research-intensive institutions for 8–10 weeks during the summer. Visiting professors are provided with a stipend, funds for research expenses, and travel expenses, and each host scientist receives funds to give a seminar at the visiting professor’s institution. The MAC Visiting Professors Program is supported by an Innovative Programs to Enhance Research Training grant from the National Institute of General Medical Sciences/NIH. The four visiting professors collaborating with host scientists in 2016 are:

- **Visiting Professor: Chastity Bradford, Tuskegee University**
  Host Scientist: Abdelkarim Sabri, Temple University
- **Visiting Professor: Jamaine Davis, Meharry Medical College**
  Host Scientist: Ian Wilson, The Scripps Research Institute
- **Visiting Professor: Lissette Delgado-Cruzata, John Jay College/City University of New York**
  Host Scientist: Regina Santella, Columbia University
- **Visiting Professor: Ishara Mills-Henry, Framingham State University**
  Host Scientist: Melissa Kosinski-Collins, Brandeis University

—Verónica Segarra (MAC Co-Chair), High Point University
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**Young, Gifted, and First-Generation Minority Science Students Motivated by “Prosocial” Values**

There are as many motives for taking introductory science courses as there are undergraduates, but if you look closely at groups of freshman science students such as those from underrepresented minority (URM) backgrounds, you can see striking motivational differences. That’s a major finding in a new study of freshmen by California State University, Long Beach, psychology researcher Matthew C. Jackson and collaborators. The researchers found that URM first-generation college students with “prosocial values,” e.g., a strong belief that science could help members of their communities, were more likely to identify as being scientists over time.

**Cell News—Taking Better Aim with CRISPR**

CRISPR/Cas9 has become the Swiss Army knife of cell biology, giving researchers the ability to slice and dice genomes with effortless precision. Except that is not always the case. To gauge what affects the accuracy and effectiveness of CRISPR/Cas9, ASCB member Thoru Pederson and colleagues at the University of Massachusetts Medical School, Worcester, took a closer look at its dual components, the non-specific endonuclease Cas9, which cleaves DNA strands, and the synthetic guide RNA (gRNA) of ~20 nucleotides that is the targeting device.

**Cell News—Solving the Hook that Connects Cargo to Motors**

Inside cells, cargo is carried inside tiny bubbles and pulled along tracks by molecular motors. But like a boxcar on a train track, something has to connect the cargo container to the locomotive engine for the cargo to move. ASCB members Courtney Schroeder and Ron Vale at the University of California, San Francisco, solved the structure of the Hook domain of Hook3, a Golgi/endosome cargo adaptor that interacts with dynein.

**Cell News—Cytoskeleton Regulator Affects Nucleus Shape in Migrating and Invading Cells**

Metastasis is a worst-case scenario in cancer, and certain cellular processes make cancer cells more likely to metastasize. In migrating cells, the protein fascin regulates F-actin, a structural component that helps cells keep their shape and move. Fascin expression is correlated with increased metastatic potential in cancer. Asier Jayo and colleagues in ASCB member Maddy Parson’s lab at King’s College London published a new study that identifies a new binding partner for fascin in a range of cell types, the nuclear envelope protein nesprin-2.

**Cell News—a New Class of UPR Inhibitors**

When unfolded or misfolded proteins accumulate in the cell’s endoplasmic reticulum (ER) an unfolded protein response (UPR) is triggered to mitigate the damage. The UPR has been implicated in a number of neurodegenerative diseases including Alzheimer’s, Parkinson’s, and Huntington’s. Ways to control the UPR have long been a research goal. Now a new class of UPR inhibitors, Ceapins, has been discovered by ASCB members Ciara Gallagher and Peter Walter at the University of California, San Francisco.

Upcoming Early Career Meetings

**ARKLATEX Interdisciplinary Cell Conference**

Shreveport, LA
November 5, 2016

ASCB is pleased to provide Early Career Meeting Grants to graduate students and postdocs to organize one-day meetings. Such meetings usually involve two or more institutions (within the United States or international), and topics can range from basic science to career development as long as there is clear relevance to the broadly defined field of cell biology.

The next deadline to apply for funds is **January 16, 2017**. Applicants must be or become members of the ASCB. For more information visit www.ascb.org and click on “Meetings.”
Use the Career Resource Wizard to sort by career stage (undergrad, grad school, postdoc, faculty) and topics of interest.

ASCB Career Development Resources:

**Mentoring**

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Confocal micrograph showing nerve cells growing along fibers (purple) made from a specially modified silk that is similar to that made by spiders and silkworms. Schwann cells, whose nuclei are shown in blue, attach to the fibers and support the growth of the nerve cells. This system is being looked at as a possible treatment for damaged nerves and, in the long term, spinal cord damage. This image (www.cellimagelibrary.org/images/38921) was prepared by John Priestley and is licensed under a Creative Commons Attribution, Non-Commercial, No Derivatives License.

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The Cell Image Library (www.cellimagelibrary.org) is a freely accessible, easy-to-search, public repository of reviewed and annotated images, videos, and animations of cells. Portions of the Cell Image Library were developed by ASCB under a Grand Opportunities grant from the National Institute of General Medical Sciences and are now managed by the National Center for Microscopy and Imaging Research under a perpetual license from ASCB.

—David Orloff
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Ribosomal proteins produced in excess are degraded by the ubiquitin–proteasome system
Min-Kyung Sung, Justin M. Reitsma, Michael J. Swerdowski, Sonja Hess, and Raymond J. Deshaies
Overexpression of ribosomal proteins in yeast is prevented by ubiquitination of unassembled ribosomal proteins in the nucleus and/or nucleolus followed by proteasome-dependent degradation. Brief inhibition of the proteasome causes strong accumulation of multiple ribosomal proteins in an insoluble fraction, suggesting that this is a general phenomenon.
Mol. Biol. Cell 27 (17), 2642–2652

AMPK activity regulates trafficking of mitochondria to the leading edge during cell migration and matrix invasion
Brian Cunniff, Andrew J. McKenzie, Nicholas H. Heintz, and Alan K. Howe
Mitochondria infiltrate leading edge lamellipodia, increasing local mitochondrial mass and relative ATP concentration. AMPK regulates infiltration of mitochondria into the leading edge of 2D lamellipodia and 3D invadopodia, coupling local metabolic sensing to subcellular targeting of mitochondria during cell movement.
Mol. Biol. Cell 27 (17), 2662–2674

Eps15 membrane-binding and -bending activity acts redundantly with Fcho1 during clathrin-mediated endocytosis
Lei Wang, Adam Johnson, Michael Hanna, and Anjon Audhya
Clathrin-mediated endocytosis involves a network of proteins that direct cargo capture while simultaneously facilitating membrane remodeling. Eps15 is a critical factor that binds and bends membranes and acts redundantly with Fcho1 to ensure clathrin lattice stability during the initial stages of plasma membrane invagination.
Mol. Biol. Cell 27 (17), 2675–2687

Cell migration involves complex coordination of localized biochemical processes, many of which are energy-expensive. Shown is a color-coded image of mitochondrial flux in an ovarian cancer cell expressing a fluorescent mitochondrial marker as the cell migrates through a three-dimensional extracellular matrix. To make the image, each frame of a time-lapse live-cell movie was assigned a different hue on the color spectrum from indigo (first time point) to red (last time point), and these images were overlaid to illustrate the infiltration of mitochondria into the invasive leading edge. Cunniff, McKenzie, et al. (Mol. Biol. Cell 27, 2662–2674) detail this mitochondrial flux and show that it is controlled by localized activation of a signaling pathway that senses subcellular changes in energy status. These observations couple localized cellular energy demand to the subcellular targeting of mitochondria during cell movement. (Image: Alan K. Howe, University of Vermont)
Detection of protein–protein interactions at the septin collar in *Saccharomyces cerevisiae* using a tripartite split-GFP system
Gregory C. Finnigan, Angela Duvalyan, Elizabeth N. Liao, Aspram Sargsyan, and Jeremy Thorner
A tripartite split-GFP system faithfully reports the order of the subunits in septin hetero-octamers (and thus can serve as a “molecular ruler”), conversely yields little or no false signal even with very highly expressed cytosolic proteins, and detects authentic interactions of other cellular proteins that are bona fide septin-binding proteins.
*Mol. Biol. Cell* 27 (17), 2708–2725

Interaction of Gcn4 with target gene chromatin is modulated by proteasome function
Gregory C. Howard and William P. Tansey
The yeast transcription factor Gcn4 requires a ubiquitin ligase and the proteasome to function. Inhibiting proteasome function prevents the interaction of Gcn4 with target gene chromatin, and this activity is suppressed by inactivation of the ubiquitin-selective chaperone Cdc48. Thus proteolysis of Gcn4 is not required for its function.
*Mol. Biol. Cell* 27 (17), 2735–2741

TSSC1 is novel component of the endosomal retrieval machinery
David C. Gershlick, Christina Schindler, Yu Chen, and Juan S. Bonifacino
A previously uncharacterized WD40 domain–containing protein named TSSC1 is shown to interact with the GARP and EARP tethering complexes, promoting retrograde transport of Shiga toxin from endosomes to the TGN, as well as recycling internalized transferrin from endosomes to the plasma membrane.
*Mol. Biol. Cell* 27 (18), 2867–2878

The internalization of macromolecules from the extracellular environment is critical for the normal growth and development of all cells. Components of the endocytic machinery direct this process and must bind and bend the relatively flat surface of the cell to generate highly curved transport carriers.

In this image, tubulation of synthetic liposomes is observed upon incubation with a new membrane binding and bending module, the EH domain of the endocytic scaffolding protein Eps15. Wang et al. (*Mol. Biol. Cell* 27, 2675–2687) demonstrate that membrane bending mediated by Eps15 functions in concert with another factor, Fcho1, to initially sculpt endocytic transport carriers. (Image: Michael Hanna and Anjon Audhya, University of Wisconsin, Madison)
**MEETINGS Calendar**

A complete list of upcoming meetings can be found at ascb.org/global-meetings-calendar.

**October 12–13, 2016. Duarte, CA**
6th International Breast Cancer Prevention Symposium.  
www.purdue.edu/breastcancer.

**November 4, 2016. Yellow Mountain, Anhui Province, China**
Yellow Mountain Conference on Single Cell Dynamics

**January 7-12, 2017. Birmingham, AL**
8th Aquatic Animal Models of Human Disease Meeting.  
www.uab.edu/aqmhd.

**ASCB Annual Meetings**

December 3–7, 2016. San Francisco
December 2–6, 2017. Philadelphia
December 8–12, 2018. San Diego

**MEMBERS in the News**

**Susan Forsburg** of the University of Southern California, an ASCB member since 1993, has been appointed the inaugural holder of the Gabilian Distinguished Professorship in Science and Engineering.

**Arthur J. Lustig** of Tulane University, an ASCB member since 2002, has been selected to join the Education Board at the American Health Council.

**ASCB Member Comments**

We welcome your comments and suggestions at ascbinfo@ascb.org

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Other ways to stay in touch: ASCBiology @ASCBiology ASCB
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Nobel laureate and ASCB member Roger Y. Tsien died August 24 in Eugene, OR, according to an official statement from the University of California, San Diego (UCSD) School of Medicine,1 where Tsien was on the faculty for 27 years. He was 64. Tsien won the 2008 Nobel Prize in Chemistry with ASCB member Marty Chalfie and with Osamu Shimomura for their work in developing green fluorescent protein (GFP) as molecular tags, transforming microscopy and setting off a revolution in cell imaging.

A professor of pharmacology, chemistry, and biochemistry at UCSD, Tsien was also a Howard Hughes Medical Institute investigator. Tsien was a continuous ASCB member since 1987. He gave the Keith Porter Lecture at the 2003 ASCB Annual Meeting and in 2008 was jointly awarded with Chalfie the E.B. Wilson Medal, the ASCB’s highest scientific honor.

“Roger was an amazing scientist who spearheaded fluorescence microscopy through his creative engineering of fluorescent proteins,” said former ASCB President Jennifer Lippincott-Schwartz. “He will be sorely missed by the cell biology community.”

ASCB member and former ASCB Treasurer Thoru Pederson remembers Tsien as outgoing, approachable, and brilliant. They first met in the early 1990s when Tsien gave an invited lecture at the University of Massachusetts Medical School in Worcester where Pederson is on the faculty. After the talk, Pederson found Tsien to be engaging and eager to field practical questions about the caged fluorescent probes that the Pederson lab was struggling to employ. “We interacted by phone and email for several years,” Pederson remembered. “And Roger was extremely generous with his time. He would even look up supply catalog numbers to make sure we were ordering the right materials.”

In the spring of 2008, Pederson served on the ASCB selection committee for the Wilson Medal. By then, GFP was in near universal use and the name of Marty Chalfie, another ASCB member closely associated with the development of GFP, “bubbled up” for the Wilson medal, Pederson recalls. “I pointed out that if we’re thinking about GFP [as the basis of a Wilson award], then we’ve got to think about Roger’s work as well.” He remembers another member of the committee pausing thoughtfully before asking, “Do you know something going on in Stockholm that we don’t?”

That October, the chemistry Nobel went to Chalfie and Tsien. The Wilson committee chair Joel Rosenbaum sent out word that ASCB had scooped the Royal Swedish Academy of Sciences, but the question remained, would Chalfie and Tsien come to San Francisco to give their ASCB lectures, only two days after the Nobel Week festivities ended in Stockholm? Both Chalfie and Tsien appeared at ASCB, a little jet lagged but otherwise ready to give their Wilson talks on GFP. Pederson recalls Tsien at the Wilson dinner afterward, answering questions about his magical week in Stockholm and volunteering to serve as a judge that night for “CellSlam,” ASCB’s stand-up science comedy contest. “That was the most informal and relaxed I’d ever seen him,” said Pederson. Eyewitnesses to Tsien’s performance as a CellSlam judge reported real concern that the Nobel winner was laughing so hard he might actually fall off his seat.
Tsien was born in New York City on February 1, 1952, the child of Chinese immigrants, into an extended family of engineers. He grew up in Livingstone, NJ, and demonstrated a flair for science at an early age, winning what was then the Westinghouse Science Talent Search in 1968 for a project demonstrating how metals bind to thiocyanate. He attended Harvard College on a National Merit Scholarship, graduating in 1972 with a degree in chemistry, and earned his doctorate in physiology in 1977 from the University of Cambridge in the UK. After postgrad work in Cambridge, he joined the faculty of the University of California, Berkeley, in 1982 before moving to UCSD in 1989.

The first green fluorescent protein was discovered in the jellyfish *Aequorea victoria* by Shimomura, who was at the Marine Biological Laboratory in Woods Hole, MA. Chalfie at Columbia University was the first to demonstrate that GFP, which glowed under ultraviolet light, could work as a molecular tag in a living organism, *Caenorhabditis elegans*. Tsien explored the biochemistry of GFP and extended the color palette so that different biological processes could be followed at the same time with differently colored GFPs. In a 2008 interview, Tsien said, “I’ve always been attracted to colors. Color helps make the work more interesting and endurable. It helps when things aren’t going well. If I had been born colorblind, I probably never would have gone into this.”

—John Fleischman

Footnote
1http://bit.ly/2bK7qmY.

In Memoriam: Ellen M. Rasch

Ellen Myrberg Rasch, an early member of ASCB who made important contributions to the histochemistry of DNA, passed away on July 31, 2016, at age 89 after a long battle with Parkinson’s disease. She leaves behind her husband Robert Rasch, son Martin, and several grandchildren and great grandchildren. Drs. Ellen and Robert Rasch were married for 66 years.

Ellen grew up in Chicago and attended the University of Chicago for her undergraduate and graduate training, obtaining her PhD in botany in 1950. A year later she returned to join the lab of Hewson Swift, first as a postdoc and later as a research associate. Watson and Crick published the structure of the DNA double helix two years after Ellen began her postdoc, but it was already evident that DNA was the hereditary material. Swift introduced Ellen to microspectrophotometry and she was off and running. Ellen developed Feulgen-DNA cytophotometry to measure the DNA content of nuclei from a wide range of organisms, especially insects. She became one of the leading experts in this methodology.

The rule of DNA constancy states that the amount of DNA is the same in all diploid cells of an organism. Ellen became especially interested in exceptions to the rule, as evidenced, for example, by DNA amplification in the “DNA puffs” of the giant polytene chromosomes of the fly *Sciara*. During her career she also studied mechanisms of meiosis, documented the first known triploid fish species, provided evidence for apomictic (asexual) reproduction in fishes, and determined the absolute haploid genome size in various organisms, especially insects. Her later work explored concepts of DNA endoduplication and
chromosome diminution during early stages of copepod development.

Because Hewson Swift was a founding member of ASCB, Program Chair of the first ASCB meeting, and ASCB’s third president, it was natural that Ellen would also become active in ASCB. She served as session chair at several ASCB Annual Meetings (1968–1971), on the editorial board of the Journal of Biophysical and Biochemical Cytology (later renamed the Journal of Cell Biology), and on the ASCB Council (1972–1976). During the same period, Ellen was also a member of the Council of the Histochemical Society, thus serving as a link between the two organizations. Ellen held other leadership positions in the Histochemical Society and later served on the editorial board of the Journal of Histochemistry and Cytochemistry. Her promise as an emerging scientist was recognized by a National Institutes of Health Research Career Development Award (1967–1972). In 1966 Ellen was elected as a Fellow of the American Association for Advancement of Science. She was also a Fellow of the Royal Microscopic Society.

It is important to put Ellen’s accomplishments and honors into the perspective of her era. At that time it was common for a woman to follow her husband to wherever his career took him. That journey took Ellen to the Medical School of Marquette University in Milwaukee, where in 1975 she was appointed the Todd C. Wehr Distinguished Professor of Biophysics, and then to East Tennessee State University, where she became a research professor in 1978. She served as interim chair of the Department of Biophysics in 1986.

Ellen was a mentor to both of us, and we recall her selflessness, her teaching expertise, her good humor, and her love of chocolate. We will miss her.

—Susan A. Gerbi, Brown University and Paul J. Monaco, East Tennessee State University

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If you have questions, contact Membership Manager Marta Chacon at 301-347-9324 or MChacon@ascb.org.

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Dear Labby,

I am a second-year graduate student and get on very well with my PI. We are very excited, as together we have made a fundamental discovery in our competitive field. In fact, I am about to start writing a major paper as the first author, and this should be a great help for my PI’s upcoming grant renewal. My rapid progress is partly because I work day and night and only took one day of vacation last year. But all that work has left me feeling really burned out, so in two months I am going on a well-deserved four-week vacation to Africa with a friend and have already bought my airline tickets! When I told my PI I would be away for a month, he seemed very upset and then muttered, “Hope you don’t get scooped in the meantime.” As I didn’t take much time off last year, I did not expect this response. This has affected our relationship and he now bugs me for progress in repeating experiments and assembling figures. Is he being reasonable?

—Burned-Out

Dear Burned-Out,

Labby is glad to hear that your project is going so well. You must be excited to be preparing such an important publication. Well done!

Your question touches on two issues. Let’s take the easiest and most important one first: open communication from both sides. You seem to have a good working relationship with your PI, so Labby wonders why you didn’t discuss the vacation plans before purchasing the tickets. Could it be that you knew your PI would be upset so you wanted to present it fait accompli? In reflecting on the situation, wouldn’t it have been better to discuss this openly and explain why you feel you deserve this vacation? And when it would be best to schedule it? It is not surprising your PI is upset, but he also seems kind enough not to make an issue of it and tell you to cancel your trip. His anxiety about assembling the paper almost certainly stems from the competitive nature of the field, and the need to get this work accepted in time for his grant renewal. However, he also needs to be open in his expectations; he should have discussed his policy about vacations.

Which brings up the second issue: How much vacation is it reasonable to take? This is very lab dependent and again needs to be discussed openly. Some PIs do not like students to take any vacation (and there is no law that says students, or even paid employees, are entitled to vacation). However, an average of two weeks’ vacation a year seems to be about the norm. Labby is a bit unusual in having a very flexible attitude toward vacations: Students should work hard and enjoy their work, but also play hard on vacation to have a full life. Labby has no firm rules but expects a reasonable balance between work and vacation and requires students to discuss plans before they book vacations. With this balance in mind, Labby has actually encouraged an occasional burned-out student to take a week of vacation to restore his or her excitement and ability to make progress.

So what would Labby advise? First apologize to your PI for not discussing your trip before you booked it, and then have an open discussion about vacations. This will clear the air and you will both feel better. You will likely find that this restores your friendship and allows for your continued shared success.

—Labby

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—Labby
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