PRESIDENT'S Column

The Case for Basic Cell Biology

Accepting the gavel as incoming ASCB President is a huge honor for me. But it is also a scary responsibility. My job for the next year is to represent and promote the scientific interests and professional aspirations of our membership, which are increasingly diverse as the scope of cell biology broadens. This would be a daunting challenge even in calm times. However, 2010 will be anything but calm.

Tim Mitchison

Our science is surging forward more rapidly now than ever before, as molecular methods improve and new technologies enter the field. This is great for science. But it puts tremendous pressure on labs and institutions not to fall behind in the technology race.

Our institutions, and the ASCB, were buffeted by last year's financial meltdown. Balancing budgets remains a significant challenge. Meanwhile National Institutes of Health (NIH) extramural funding programs have seen unprecedented change, including the U.S. community-wide effort to write and review American Recovery and Reinvestment Act (ARRA) grants last year. In addition, shorter R01 applications and a new scoring system are coming into play. It is easy to feel overwhelmed by the rapid pace of change.

Commitment to Basic Research, Career-Building, Diversity, and Education

In my first editorial, I want to emphasize our safe harbor in the midst of turmoil: our single most important shared principle. That is our commitment to basic scientific research. I see this as a fixed point we can rely on to keep our resolve, and find important community, in these turbulent times. Now, more than ever, we need to communicate and explain the importance of basic research. We need to do this both as individual scientists, and using ASCB as our shared voice.

One opportunity to do that individually is easily available for those who received ARRA grants. I was lucky to be one of them. And I took advantage of the button on the ASCB website (www.ascb.org/arra) to write to President Obama and my local representatives. I recommend everyone who received an ARRA award do the same. It's critical to thank politicians, explain your work in layperson's terms, and add a note about the importance of basic research in general.

Cell biology needs to speak loudly now. ASCB is *your* Society and your voice, and I ask you to commit yourself to the profession and our future. The ASCB is thriving, with nearly 10,000 members. Our Annual Meeting, publications, and programs spotlight our exciting and broad-ranging science. With the 2009 ASCB Annual Meeting fresh in our minds, it's easy to remember "who we are" as a field.

Who are we as an organization? We are, we think, the most active society in the world representing the interests of biological researchers. We can take pride in our activities in public policy, helping young scientists build their careers, while we establish collaborations within our international community and further science education and diversity. But we cannot take future success for granted.

Adapting to Trends

The ASCB Council has identified the trend toward translational research in the NIH-funded portfolio as especially significant for our future. Increasingly, some members are prioritizing disease-specific meetings over our Annual Meeting. Students in our labs are self-identifying as cancer, stem-cell, or tissue researchers more than as cell biologists. This is the case even though they are asking fundamental questions about cells.

At the NIH, R01 grant applications to pursue pure basic cell biology, not directed to any specific disease or tissue, are decreasing in number. Increasingly, they compete against each other in a small number of study sections. For the ASCB to remain vital and important, we must adapt. In my view, we will be most successful if we pursue two paths in parallel:

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[C]uriosity-driven fundamental research has an amazing track record of contributing to progress in preventing and curing diseases.

We need to make ASCB more friendly and important for cell biologists pursuing translational research in academia and industry. This will be the subject of a future President's column. At the same time, now more than ever, we need to advocate effectively for basic biological research.

Making Our Case

Perhaps the largest challenge in promoting basic science is explaining its importance. It's easy to explain to a Representative, a neighbor, or your Dean why research into making replacement organs from stem cells is important. (If you work in the U.S. and don't know how to contact your Representative, go the ASCB's website at www.ascb.org and click on "Public Policy" under the "Committees" tab.) It may seem harder to explain why investigating the origin of an unusual organelle you have noticed in a fly embryo is important. But, if we look at the history of scientific progress, curiosity-driven fundamental research has an amazing track record of contributing to progress in preventing and curing diseases. Recent products of fundamental research include:

- RNA interference, discovered by Fire and Mello when they tracked down an unexpected side effect of RNA injection into worm embryos. Drugs that utilize the RNAi pathway may revolutionize medicine, though learning how to deliver nucleic acids to target cells remains a significant challenge.
- Green fluorescent protein (GFP), which came from Shimomura's career-long quest to understand the green glow from a jellyfish. GFP is now a critical tool for understanding how our brains work, and how we can fix damaged organs.

These momentous discoveries started with individual scientists laboring to answer basic questions in small, nonfamous labs.

Some may argue that we now know enough about how cells work that we can afford to shift the focus to curing disease. This is simply not the case. We do know a lot about conserved cellular processes. And the cytoplasm and nucleus are on the whole less mysterious than when I entered the field in 1980. In most cases, however, our understanding is still rather superficial. It's insufficient to explain differences between cell types, or between normal and diseased tissues, and therefore not at the level needed for effective drug discovery. In many cases, even basic mechanism is still unknown. All human genes may have names, but that doesn't mean we know how they work! The problem of how multiple molecules work together as systems in cells and tissues is very much a frontier, where we will need new methods from mathematics and computing to make sense of the biology.

I also think we need much more basic understanding of the science underlying therapeutics if we are to design better medicines more quickly. We still don't understand how most medicines work at the levels of cells and tissues, for example. I worry that in our current enthusiasm for human genetics and stem cells we may be promising the public too much too soon in the way of curing disease. It will take a lot of basic cellular research to get from predisposing mutations to the mechanistic understanding of disease needed to develop cures. Sustained investment in basic cell biology is required to make productive use of the insights from genomics; and we need to make sure our supporters and leaders understand that.

Showcasing Curiosity-Driven Basic Research

The power of curiosity-driven basic research was showcased at the 2009 ASCB Annual Meeting in San Diego. Keynote speaker Rudy Jaenisch provided an excellent historical perspective on the hotter-than-ever stem cell field. He emphasized the importance of the intellectual freedom provided by his scientific mentors. He also explained how experiments designed to satisfy his own curiosity opened a field. Jaenisch ended with a rousing invitation to young cell biologists to take advantage of induced pluripotent stem cell (iPS) technology, which has huge potential for basic research as well as for curing diseases.

My old University of California, San Francisco, friends Ron Vale (Keith Porter Lecturer) and Peter Walter (E.B. Wilson Medal Lecturer) gave inspiring talks on their career-long investigations into basic mechanisms underlying fundamental cell processes. These were motor-proteins in Ron's case, and stress signaling from the endoplasmic reticulum in Peter's. While neither has directly cured any diseases, their research is already making that possible for others. The biotech company Cytokinetics Inc.,

a long-term supporter of ASCB activities, is currently testing a compound that makes the human heart beat more strongly. This came from fundamental progress on motor proteins.

Stress signaling from the endoplasmic reticulum is recognized as a major factor in cancer and neurodegeneration. Proteosome inhibitors, which have revolutionized the treatment of myeloma, work by harnessing this pathway. And other medical applications are likely as our mechanistic understanding increases.

Balancing Basic and Translational Research

Another highlight of the ASCB meeting for me was meeting with Francis Collins, the new NIH director. He discussed with the ASCB Council and Public Policy Committee our concerns about how the NIH will balance support of basic and translational research. He assured us he understands the importance of small lab, curiosity-driven research. Collins emphasized that he is the PI of exactly that kind of a lab at NIH. Collins' personal warmth and political skills were evident in his discussion with ASCB leadership, as well as during his Keynote remarks. He is going to be a great person to have on our side in the upcoming negotiations for the 2011 NIH budget.

All in all, the 2009 meeting was a great start to my year in office. Please contact me (president@ascb.org) if you have ideas about how ASCB could be better at promoting basic science, in the U.S. or around the world. To get involved yourself in U.S.-focused advocacy, become an affiliate of the ASCB Public Policy Committee by joining Project 50 (www.ascb.org/project50), and/or sign up for the Congressional Liaison Committee (www.coalitionforlifesciences.org/be-an-advocate/about-the-clc/join-the-clc). 2010 and beyond will be challenging for cell biologists, but by working together through the ASCB, we can effect positive change. ■

Comments are welcome and should be sent to president@ascb.org.

Did You Know...?

March 31 is the deadline for nomination submissions for seven ASCB awards—all of which will be presented at the 2010 ASCB Annual Meeting in Philadelphia, PA, December 11–15.

For information on eligibility and submission requirements, see "Call for Nominations" on p. 21 or go to www.ascb.org and click on "Awards/Grants."

Please take the time to nominate a deserving colleague, postdoc, mentor, or student. ■

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Half-Century Society

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