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PRESIDENT'S Column

Why Basic Research in Cell Biology Is Still Critical for Human Health

Because I co-author a new edition of a cell biology textbook every few years, I am repeatedly confronted by the fact that we know only a tiny fraction of what we need to know, if we are to really understand an individual cell. The knowledge gap is, of course, much greater for those scientists trying to come to grips with multicellularity—that is, with the workings of an organism like a fruit fly—or even, more strikingly, ourselves.

The public and the Congress, including many of the most effective advocates for increased public funding of the biomedical sciences, are generally unaware of this knowledge gap. Further, they may not know why we need to fill it to intervene effectively in most human diseases. Scientists are partly to blame for not emphasizing forcefully enough that the complete sequencing of the human genome provides only a small (but very important) start to our attempt to understand human biology. But the misunderstanding is not at all surprising. After all, new discoveries that reveal the complexity of biological systems at the molecular level continue to amaze even experienced cell biologists like me. And news articles always emphasize what we have learned, rather than the vast amount that remains obscure.

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New Discoveries Impact Human Health

With each new edition of the *Molecular Biology of the Cell* textbook, we authors are forced to incorporate new discoveries that reveal a sophistication of cell chemistry not previously recognized. For example, it has only recently become clear to me that living organisms will quite generally concentrate the proteins and RNA molecules that catalyze a particular reaction in a small region of each cell. The concentrating mechanism often involves large scaffold proteins that bind the reacting partners, and both the concentrating event and its location are controlled by covalent modifications of the interacting partners. Thus, we should expect to find human diseases in which all cellular components are normal, with the only defect being in their positioning.

To take a second example, the discovery of an elaborate "histone code," and of the large set of code reader-writer and chromatin remodeling protein complexes that underlie it, reveal that eukaryotic cells make use of a remarkable array of chromatin-based epigenetic mechanisms. Defects in these epigenetic controls have recently become recognized as major contributors to a variety of human diseases, including cancer. To intervene effectively we are likely to need a much more detailed understanding of the molecular processes that occur in chromatin. Attaining this understanding will require a great deal of difficult biochemistry, much of it based on experiments with purified components in *in vitro* systems.

I could go on in this way for many pages. My point is simply that we will require a much greater understanding of these, as well as many other, fundamental mechanisms underlying the function of cells, before we can expect to deal adequately with the wide variety of diseases that plague humankind.

Can ASCB Produce Effective Case Studies of Recent Breakthroughs?

How might we best convey this message to Congress and to the many sincere and dedicated disease advocates who care deeply about funding for the National Institutes of Health, yet may view basic research into cell mechanisms with some suspicion?

As an experiment, I am suggesting that the ASCB membership email me at president@ascb.org to nominate particularly

good "case study" examples of recent breakthroughs in our understanding of cells, derived from untargeted basic research, that appear to have profound implications for the eventual prevention and treatment of human disease. In your email, please include a few references to the published work of relevance.

I hope that we can collect 20 or so outstanding examples from ASCB members. I suggest that we focus on recent discoveries, because I have seen claims that the explosion of discoveries in the past decade has brought biomedical science to the point where we should not require further advances in our understanding to cure disease—or, more modestly, to the point where the future payoffs from basic research are likely to be small. As we all know, intensive studies of yeast, *Drosophila,* and other "model organisms" very often provide a shortcut to the understanding of human biology. This fact seems strange to the public and is perhaps counterintuitive. For this reason, those examples where work with model organisms has unexpectedly illuminated human disease can be particularly useful for making our point.

At the ASCB Council's two-day meeting and retreat held in Bethesda on May 21–22, we examined a collection of previously prepared documents designed to reach Congress and the public on the payoffs from fundamental research. These had been produced by other organizations. We will use them as a starting point for selecting the format for a possible new ASCB-sponsored effort. As the next step, our Public Information Committee will work with a science writer to develop and test a few prototype brief communications—each focused on a single example from the list that we generate with your input.

My thanks for your help with this important new project. ■

—Bruce M. Alberts

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

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