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Shortcuts to Medical Progress?

WE HAVE ALL BEEN TAUGHT THAT THE SHORTEST DISTANCE BETWEEN TWO POINTS IS A straight line. But the same idea has repeatedly proven not to be true for progress in medical research. Why?

More than 80 years ago, in his great book *The Cell in Development and Heredity*, Edmund B. Wilson wrote that “the key to every biological problem must finally be sought in the cell, for every living organism is, or at sometime has been, a cell.” The striking modern advances in our understanding of cells, such as those concerning gene expression highlighted in this special section (pp. 1781–1799), make it clear that the chemistry that makes life possible is enormously complex.

I have been part of a team writing a cell biology textbook for 30 years. With each new edition, the authors are repeatedly struck by the fact that scientists still know only a small fraction of what is needed to understand even the simplest bacterial cell. The knowledge gap is of course much greater for scientists trying to come to grips with multicellularity; that is, with the workings of an organism like a fruit fly or a human, in which many billions of individual cells must cooperate to produce an individual. What does this deficit mean for the large-scale ongoing efforts across the globe to use biomedical sciences to improve human health?

The public and the Congress in the United States, including many of the most effective advocates for increased public funding of the biomedical sciences, appear largely unaware of this knowledge gap or of the need to remove it in order to intervene effectively in most human diseases.

As in many other nations, there has been a great deal of understandable pressure to increase focus on research that attempts to use what we already know about cells to cure human disease.

I certainly support a head-on assault against diseases wherever feasible. But, as has been repeatedly demonstrated, the shortest path to medical breakthroughs may not come from a direct attack against a specific disease. Critical medical insights frequently arise from attempts to understand fundamental mechanisms in organisms that are much easier to study than humans; in particular, from studies of bacteria, yeasts, insects, plants, and worms. For this reason, an overemphasis on “translational” biomedical research (which focuses on a particular disease) would be counterproductive, even for those who care only about disease prevention and cures.

This issue of *Science* illustrates how progress in basic biological research serves as a major driving force both for advancing knowledge and for spurring new technologies and therapies. Several Perspectives focus on the widespread role of different types of small RNA molecules in controlling the expression of genes. This phenomenon was discovered to be central to human biology only recently, but has already spawned the formation of numerous biotech companies that hope to use this understanding to create new types of drugs to treat humans. It is telling that the entire field developed only because of unexpected results obtained from fundamental research on gene control mechanisms in plants and worms, some of the worm work being recognized with a Nobel Prize in 2006. Without prior fundamental research on these organisms, we would probably have no understanding of the critical roles that small RNAs play in human biology today and therefore no new approach to therapies based on this knowledge.

The private sector energetically pursues translational biomedical research in many areas. But only governments (and a select group of foundations such as the Wellcome Trust and the Howard Hughes Medical Institute) provide the resources needed for pioneering work on fundamental biological mechanisms. With so many mysteries remaining about the incredibly sophisticated chemistry of life, it is certain that future medical breakthroughs will depend to a substantial extent on research on organisms that are much smaller and easier to investigate than ourselves. This counterintuitive fact may need to be much better conveyed to the public if governments are to make sound investments for improving health.

– Bruce Alberts

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