The Basics of Translation

The past 20 years have witnessed great advances in understanding the causes of many medical disorders, while also revealing how complex their pathogenesis can be. Hypertension, autism, and Alzheimer’s disease have each proven to be a collection of disorders with multiple causes. Although the dream of personalized treatments has been realized for a few disorders, particularly in the field of cancer, the translation of scientific discoveries into effective treatments for other diseases has been much slower than expected. There are two main reasons for this fact: the complexity of human physiology, and our limited understanding of how the vast majority of genes, proteins, and RNAs work, irrespective of whether they are disease-associated or not.

Traditionally, such fundamental knowledge has come from untargeted, discovery-driven basic research. In recent years, however, the pressure to develop treatments at an ever more rapid pace has attenuated enthusiasm for deciphering the language of life. Science, like most human endeavors, is susceptible to fads and fashions driven by money and status; and today many highly qualified basic scientists feel compelled to jump on the “translational medicine” bandwagon. For quite some time, it has been apparent that biomedical research in the United States is more likely to get funded if it is tied to a practical outcome, such as a step toward a cure for some disorder. There is no doubt that such targeted and in-depth disease-oriented research is sorely needed. But it is at least as important to support investigators dedicated to discovery-driven basic research.

Specific outcomes from discovery-driven research are hard to predict, but they often surprise and delight us with their applicability in unexpected contexts. Who, for example, would have predicted that an apparently trivial notched-wing phenotype in the fruit fly would yield a gene that is important for so many developmental processes in humans and so many ills, ranging from cancer to stroke?* Or that trying to trace how the brain develops the capacity for proprioception would suggest a potential therapy for deafness?† When basic research is made to seem silly in public discourse, and when its usefulness is questioned during key points in federal budget cycles, scientists should not yield to the bullying. We should instead educate the public about how scientific knowledge actually grows. Not everything worthwhile can be justified by its market value; what is most meaningful may have no apparent practical impact. Yet we can be sure that human imagination will find applications for knowledge, if we are allowed to develop that knowledge in the first place.

The task of translational research is not unlike the act of translating a book from one language into another. Fluency in both languages is a given; beyond that, there must be a talent, a feel, for those concepts unique to one language or culture that cannot be directly translated but must somehow still be conveyed. The challenge in translational medicine is that scientists are trying to translate a text with the sophistication and depth of Shakespeare using a first-grader’s vocabulary and experience, because our knowledge about the functions of most pathways in various cell types, during different developmental stages, and under normal physiological conditions, is still rudimentary and piecemeal.

To better translate recent discoveries into benefits for human health, we must admit the limitations of our knowledge of this language and invest in learning it in full. There is no doubt that studying human patients and the functions of disease-associated molecules will provide a rich lexicon for the language of life, but so will many molecules, organisms, and physiological processes that are not (currently) linked to any disease. The best way to promote discovery is to invest in talented researchers driven by curiosity and passion, whether for disease-oriented questions or the more obscure mysteries of nature.

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