The promise of translational physiology

“The great end in life is not knowledge but action.”
Thomas Henry Huxley

We read almost daily in the newspapers about discoveries of genes that are the “causes” of almost every human ailment imaginable, from drug addiction to obesity to heart disease. Potential new therapies are reported so frequently that one might predict a complete elimination of human disease in the next few years. Yet, most of these exciting discoveries never go beyond the laboratory bench. Obviously, some basic biomedical research is valuable even if it is not translated to therapy of human disease. However, too many important discoveries lie dormant, with little research effort directed toward their potential for understanding human physiology and pathophysiology, resulting in unrealized dividends from our investments in basic biomedical research.

What are the causes of this gap between the astonishing advances in basic research and the implementation of this knowledge to understanding and treating human disease? Two important components of translational research, integrative physiology and clinical physiology, have suffered declining activity in recent years, greatly weakening the translational research chain.

The term “translational research” is often used without much thought about what it means. The American Physiological Society (APS) has defined translational research as “the transfer of knowledge gained from basic research to new and improved methods of preventing, diagnosing, or treating disease, as well as the transfer of clinical insights into hypotheses that can be tested and validated in the basic research laboratory.” This definition implies that the process is bidirectional, from the bench to the bedside, as well as from the bedside back to the bench. Observations made in basic sciences can translate into improved patient care, and clinical and population studies can stimulate new ideas and new research approaches in basic science laboratories.

Until the 1980s, basic research and clinical studies were done side by side in most academic medical centers. However, this no longer appears to be the case. Two-track systems, with a research track and a clinical track, are now the rule rather than the exception in academic medical centers. Part of this split can be attributed to the introduction of managed care, which was intended to produce efficient, cost-effective medical practitioners. However, one of the unfortunate consequences of this approach has been the loss of the clinical researcher. This, in turn, has resulted in an almost complete absence of clinical physiology, an important link in the translational research chain.

Also contributing to the widening gap between basic research and clinical medicine has been the gradual demise of integrative physiologists working at the whole animal level who can effectively interact with molecular biologists and clinical researchers. Traditionally, the discipline of physiology has served as the bridge between the basic sciences, such as biochemistry, and clinical research. However, the technological advances in molecular biology and genomics, and the funding pressures that have pushed research in these directions, have led many of us to become very reductionist in our research, to the extent that physiologists are becoming indistinguishable from other basic scientists. In some ways, this is beneficial to the discipline of physiology. Some of the most interesting physiology takes place at the boundaries of our discipline and results from combining knowledge of various fields, such as biochemistry, genetics, engineering, pharmacology, and bioinformatics. At the same time, however, there are fewer physiologists conducting studies at the whole animal level, an area of research that is critical to the strength of the translational research chain.

Recognizing this growing gap between basic science and clinical research, the American Physiological Society recently has taken several steps to encourage translational research. One of these initiatives was to highlight translational research in APS publications, including the American Journal of Physiology (AJP). In the June issues of the APS Journals, the APS issued a special call for manuscripts in the field of translational physiology. APS has encouraged a broad definition of translational physiology in order to facilitate continuing dialog among basic scientists, clinical scientists, and population scientists. Translational physiology papers submitted to the journal may 1) transfer clinical insights into hypotheses that can be tested and validated in the basic research laboratory, 2) transfer knowledge gained from basic research to human physiology, or 3) report improved methods for diagnosing, treating, or preventing disease. The first manuscripts were accepted in July and were published in the November 2001 issue of the AJP (1, 3).

The gap between basic sciences and clinical medicine obviously cannot be closed simply by offering a forum for publication of translational research. However, the APS also has developed plans to highlight transla-
tional research at its meetings, to encourage physiologists to develop interdisciplinary research teams that bridge molecular physiology and genomics with organ system physiology and clinical research, and to promote translational research as an important career opportunity for physiologists. In the 1950s through the 1970s, physiologists often received training in medicine as well as basic research. The current training paradigm, however, usually separates clinical medicine and research. Physiology training programs often do not even provide coursework in pathophysiology, and PhD candidates usually do not engage in human research. However, translational research no longer requires that the principal investigator be a clinician. The article by Carter et al. (1) in the November 2001 issue of AJP-Cell Physiology illustrates this point. This team of researchers, including PhD scientists and clinicians, reports a new method for identifying hypertensive patients who are responsive to diuretic therapy with amiloride. Physiologists with either an MD or PhD degree obviously can play a key role in translational research and serve as leaders in this effort, if they have the appropriate training and are willing to lead multidisciplinary research teams. In this post-genomic era, integrative physiologists are especially well positioned to interact with other basic scientists, engineers, bioinformatics experts, and clinicians in translating the wealth of genetic and molecular information into a better understanding of how the human body functions in health and disease.

The APS is not alone in its efforts to highlight translational research. The importance of this effort has been recognized by many organizations, including the National Institutes of Health, the American Cancer Society, the Burroughs Wellcome Fund, the Howard Hughes Medical Institute, and others (2, 4). It is clear that new approaches are needed not only in the way we conduct our research but also in how we train basic scientists for the postgenomic era. Correcting these problems will require the concerted efforts of many organizations, including the APS, working together with government and industry. Without effective translational research, the exciting molecular discoveries that are currently being made at the research bench will not benefit the patient. Highlighting and encouraging translational research in APS journals is an important step in the right direction.

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REFERENCES