

## Translational Research: From the Bench to the Bedside and Back

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Translational research attempts to “wrest from nature the secrets which have perplexed philosophers in all ages, to track to the sources the causes of disease, to correlate the vast stores of knowledge, that they may be quickly available for the prevention and cure of [human] disease” (Osler, 1902). The National Institutes of Health (NIH) Clinical Center, established in 1953, paired medical wards and scientific laboratories in the same building and affirmed bench to bedside research as a NIH priority. In 1960, the United States Congress appropriated three million dollars toward the creation of General Clinical Research Centers (GCRCs) at academic medical centers across the nation (Beitins, 1999). Since then, the concept of the GCRC has expanded to seventy-nine academic medical centers, including the Albert Einstein College of Medicine (AECOM), with over eight thousand investigators supported by more than one billion dollars in funding as of 2001 (Beitins, 1999). Clearly, translational research has altered the focus and practice of medical scientific inquiry.

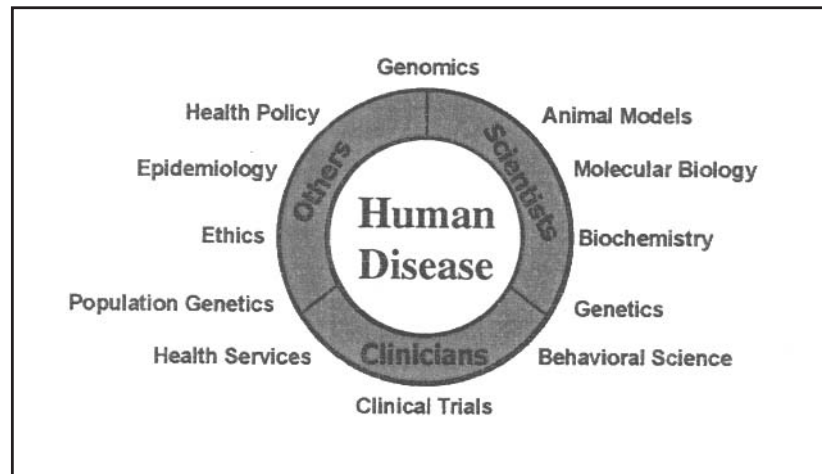
According to the Director of the AECOM Comprehensive Cancer Center, Dr. I. David Goldman (2001), the pathogenesis, diagnosis, and treatment of human disease have begun to emerge as driving forces behind biomedical research. Dr. Harry Shamoan (2001), the AECOM Associate Dean for Clinical Research and Program Director of the AECOM GCRC, acknowledged that whether research is conducted with bacteria, mice, or humans is irrelevant as long as it addresses questions that impact human health. In fact, it has been stated by Dr. Gerald Karsenty (2001) that “there is no biology without clinical validation.” It is the focus on human disease that relates translational research to clinical or patient-oriented research. Yet, it is the firm grounding in basic science that distinguishes translational research from clinical or patient-oriented research, for “there is no progress in clinical medicine without animal experimentation” (Karsenty, 2001). Therefore, the targeting of human disease is crucial to defining the purpose of a translational research program, but it is ultimately the quality of the research, be it basic, clinical, or other, that will determine the success or failure of a translational research program to elucidate the pathogenesis, diagnosis, and treatment of human disease (Goldman, 2001).

While targeting human disease is critical, it is not the tenet for which translational research is named (Shamoan, 2001). Translational research represents a broad spectrum of inquiry, involving a wide range of cli-

nicians and researchers. The melding of medicine and science creates a methodologic dichotomy, since clinicians attempt to cure first and understand second, while experimentalists attempt to understand first and rescue second (Karsenty, 2001). Yet, it creates an association of purpose, since both clinicians and experimentalists practice biology (Karsenty, 2001). It is this synergistic antagonism that stimulates the constant debate over medical scientific hypotheses, and it is this dialogue that lies at the heart of translational medicine. The poet John Donne captured this idea when he wrote, “no man is an island, entire of itself; every man is a piece of the continent, a part of the main” (Donne, 1624). In other words, one approach often does not solve clinically relevant problems. True solutions lie in the cross-pollination of disciplines where data or observations from one field drive the hypotheses of another.

The “bewilderingly rapid progress in biomedical research” has left a huge gap between the scientific knowledge base and treatments that can be applied to patients (Marwick, 2001). In addition, engineering, physics, computer science, and other non-medical disciplines have valuable information that can be incorporated into modern concepts of human disease. “The challenge is to discern which discoveries hold potential for human application and then rapidly and effectively implement them” (Beitins, 1999). Hence, the coining of the phrases “bench to bedside” or “cells to society” (Shamoan, 2001). However, translational research is a bidirectional process. Even though much needs to be done to close the gap between theory and practice, clinical observation and the segregation of patient populations remain critical to generating the hypothesis that the basic sciences attempt to address. The movement of information from the bench to the bedside and back is what defines translational research, because this dynamic is what allows the formulation of innovative solutions to complex multidisciplinary problems. Yet, it is the constant translation of information between different disciplines that presents the most difficult challenge for translational research (Baumann et al., 2000).

One might conclude that translational research should forge ahead at a rapid pace in order to close the gap between basic sciences and clinical application. However, once one considers that patients must be directly involved in the transition from theory to reality, a new level of caution needs to be observed. Institutional internal review boards turn a critical eye on proposed protocols. They rein in the zeal and passion generated by new scientific discoveries in order to ensure that experimental methods minimize patient risk and that all procedures are conducted in an ethical manner. It is important that the proper checks and balances exist to prevent



**Figure 1:** Summary of Translational Research. Integration of various disciplines by clinicians, scientists, and others contribute to the knowledge human disease and the application of diagnostic and therapeutic modalities.

abuse in the face of potential societal benefit. It is also important to recognize that the goal of the internal review board is not to slow translational research or dampen enthusiasm about new discoveries, but rather to ensure that all patient-related investigation adheres to the highest of ethical and scientific standards.

Clearly, the physician has emerged as a key player in this biomedical paradigm, because there cannot be effective, safe, and ethical research in human beings without the direct involvement of those committed to the care of patients (Shamoon, 2001). Yet, other disciplines are just as critical. Scientists conduct the molecular and cellular assays or create animal models, while statisticians illuminate population-based answers that can drive public health decisions. In fact, translational medicine and the concept of the GCRC have given impetus to the pursuit of combined degrees. The M.D.-Ph.D., M.D.-M.P.H., M.D.-J.D., and M.D.-M.B.A. lie at the boundaries of disciplines positioned to translate between the disciplines of medicine, science, statistics, policy, and even business (Figure 1). The creation of combined degree programs, like the Medical Scientist Training Program that was established by the NIH in 1964 reinforced the commitment of the NIH to sustaining translational research.

This multidisciplinary approach to biomedical research is not only reflected in educational trends but can also be seen in the efforts of the AECOM and other academic medical centers across the nation. Accordingly, AECOM has undertaken the construction of a new building that will house the Center for Genetics and Translational Research. AECOM has identified these two areas as crucial to its success as an academic research center and to the understanding of the pathogenesis, diagnosis, and

treatment of human disease (Goldman, 2001). The AECOM GCRC is funding programs ranging from the study of cancer vaccines and the prevention of diabetes to the search for longevity genes. Each of these problems requires a multifaceted team of investigators to understand every aspect of a clinical problem and apply their solution. One can see that the administration of costimulatory molecules with vaccines for malignant melanoma affords an opportunity not only to close the gap between the bench and the bedside but also an opportunity to further our understanding of the immune response to vaccination. The monitoring of patient glucose levels generates insights into the therapy as well as the pathogenesis of diabetes that can be studied in cell culture, animal models, and clinical trials. The comparison of populations, like Ashkenazi Jews, may reveal genes that regulate our lifespan. The functions of these genes and their products represent a new area of scientific inquiry that was created through clinical investigation (Shamoon, 2001). Each of these programs melds the information derived from different types of laboratories: basic, clinical, and population (Goldman, 2001). Truly, the GCRCs are moving our understanding of the basic sciences from cells to society and back. Many disciplines contribute to translational research, but the fact remains that their efforts converge on a singular goal – solving the intricate problem of human disease.

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## References

Baumann, M., Bentzen, S.M., Doerr, W., Joiner, M.C., Saunders, M., Tannock, I.F., and Thames, H.D. (2000) The Translational Research Chain: Is It Delivering the Goods? *Int. J. Radiation Oncology Biol. Phys.* **49**: 345-351.

Beitins, I.Z. (1999) Opportunities and Challenges in Pediatric Clinical Research. *J. Clin. Endocrinol. Metab.* **84**: 4302-4306.

Donne, J. (1624) No Man is an Island. *Meditation XVII, Devotions Upon Emergent Occasions.*

Goldman, I.D. (2001) personal communication.

Karsenty, G. (2001) Editorial: The Not-So-Odd Couple – The Clinician and the Experimentalist. *J. Clin. Endocrinol. Metab.* **86**: 1882-1883.

Marwick, C. (2001) Scientists Recall Progress and Promise of Translational Research. *J. Natl. Cancer Inst.* **93**: 13-15.

Osler, W. (1902) Chauvinism in Medicine. *Montr. Med. J.* **31**: 684-699.

Shamoon, H. (2001) personal communication.