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Review of *Translational Medicine and Drug Discovery*

Littman BH, Krishna R, eds. *Translational Medicine and Drug Discovery.* New York, NY: Cambridge University Press; 2011. 361 pages.

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Although the term "translational research" first appeared in PubMed in 1993,[1] it was not widely used until about 2000. Attention to it has surged since then in response to the discovery of new biomarkers and, more recently, to advances in biomarkers research. As a result of this trend, this book, *Translational Medicine and Drug Discovery,* is really about the role of biomarkers in translational research.

A good biomarker can allow investigators to select patients for a targeted approach to treatment, increasing the chances that a study will have a successful outcome if the treatment is effective. A good biomarker also can shorten the time to completion of clinical (or nonclinical) studies, by permitting the early detection of safety or efficacy, or lack thereof. The need to validate biomarkers, to show their clinical relevance, is an important part of preparing to use them in clinical studies, and sometimes the validation can be incorporated in the first clinical study with the biomarker, establishing its usefulness for future studies as well.

A philosophy of using biomarkers to build a program of drug discovery is described in one chapter of the book, written by a Merck executive. Merck has used biomarkers to develop targeted therapies, to reduce the length of clinical Phases 1 and 2 (Merck claims to have reduced the time from the industry average of 3.7 years to 2.5 years), and to identify sooner those products that will not make it past Phase 2. A culture was created in which a "failed" trial or program was considered really to be a success if the failure occurred early enough to allow the advancement of better programs. Their slogan is "Fail Fast, Fail Cheap," and biomarkers have made this possible.

The core chapters of the book address translational medicine and biomarkers in each of several diseases or conditions, and these chapters make this book valuable. They cover diabetes mellitus, atherosclerosis, obesity, bone disorders, neuroscience, and oncology. There is also an extensive chapter on "imaging biomarkers."

I found the core chapter on translational medicine in diabetes mellitus to be particularly good. In studying anti-diabetic medications in normal volunteers in Phase 1, it is not possible to observe a glucose-dependant lowering of blood glucose since normal volunteer subjects are not hyperglycemic. However, biomarkers can allow one to study proof-of-mechanism in these normal subjects, to get a preliminary indication of activity of the molecule in humans at an early stage of development. This approach was used successfully in the development of DPP-4i drugs by measuring the effects of the drugs on DPP-4 activity in healthy volunteers, and validating this in later studies as a marker for the effect the drug would have on the glucose levels of hyperglycemic patients.

One unusual chapter consists of the full text of a 2004 Pfizer document on biomarker validation and use, which defines the terms that are used in biomarker studies, the processes of validation of biomarkers, and the stages of applying them. Two other interesting chapters cover the European "Innovative Medicines Initiative" and the FDA's public-private collaboration in the "Critical Path Institute" (and its Predictive Safety Testing Consortium of government, academic, and pharmaceutical company scientists working to evaluate and validate new biomarkers). Another chapter describes the Biomarkers Consortium, an organization that works under the aegis of the Foundation for the National Institutes of Health and coordinates the work of a group of government and industry organizations, as well as dozens of pharmaceutical companies and patient advocacy groups, to develop and validate new biomarkers.

One other item that I would like to mention is a fascinating figure on page 330, a flow chart illustrating the patterns of pharmaceutical industry mergers since 1993. It shows a consolidation of 23 large pharmaceutical companies, most of which were household names in 1993, into 8 consolidated mega-companies by 2009.

I only had one minor complaint about the book, and that was the excessive use of acronyms and other abbreviations in subtitles throughout the book, abbreviations such as "BIIF," "MAC," "PSTC," "M&S" etc., which slowed the pace of reading.

This is an important book in a relatively new and growing field. Anyone engaged in advanced research designed to bring new drugs and biologics to market will find it valuable.

Reference

1. Butler D. Translational research: Crossing the valley of death. *Nature.* 2008;453:840–842. Available at http://www.nature.com/news/2008/080611/full/453840a.html; last viewed December 28, 2011.