Book Reviews

Handbook of Drug Screening. Volume 114. Drugs and the Pharmaceutical Sciences. Edited by Ramakrishna Seethala and Rabhavathi B. Fernandes. Marcel Dekker, Inc., New York. 2001. xiii + 597 pp. 16 × 24 cm. ISBN 0-8247-0562-9. $195.00.

The rapid development of high-throughput screening techniques during the 1990s has led to a new revolution in drug discovery. The PUBMED database (http://www.ncbi.nlm.gov/entrez/query.fcgi) lists over 7000 references to "drug screening" or "high-throughput screening". The U.S. Patent and Trademark Office (http://www.uspto.gov) records over 2800 patents or patent applications that mention these terms in their description or specification sections. Barnes and Noble's web site (http://www.bn.com) lists 47 books that have been published on drug screening methods, most of which have come out within the past 5 years. In addition, countless conferences occur throughout the year, having as their primary focus drug discovery and high-throughput technology. The Handbook of Drug Screening provides an overview of all of the current assays, methods, strategies, and instrumentation used in drug discovery processes. The book is basic enough to allow the novice to understand the field while being sufficiently detailed to give experienced scientists critical information needed to incorporate new methods into their screening operations.

The book contains 21 chapters that have been written by 44 contributors, including the editors. Chapter 1 begins with a concise overview of drug screening that documents its wide scope and utility. The rest of the book presents chapters that are logically grouped into sections that address all of the major aspects of the technology. Chapters 2−4 provide the foundation, with a description of screening targets, developing assay strategies, and a discussion of homogeneous detection technologies. Chapters 5−10 delve into greater detail on the different types of screens, including cell-based molecular genetic designs, receptor-based assays, functional screens, enzyme assays, and transcription activation methods. This is followed by a chapter covering the screening techniques used to discover inhibitors of transcription factors.

Chapter 12 focuses on screening for natural products having therapeutic utility, using combinatorial libraries created from genomic libraries originating from "uncultivatable" microbial sources. The techniques that allow systemic searching for drugs from previously inaccessible bacterial natural products represent a fertile field for natural product discovery. Engineering these gene libraries through "shuffling" provides new unnatural products that have never before been available for drug investigation.

Chapters 13 and 14 discuss high-throughput methods to assay absorption, metabolism, and toxicity. Pharmaceutical and biotech companies want to assess ADME/toxicology data as early in the drug discovery process as possible. The techniques used to evaluate a drug candidate's potential effects in vivo using a high-throughput assay mode are important in rapidly eliminating compounds having adverse properties.

Next, chapters 15−17 explore the conversion of the vast amount of genomic information to proteomic data from which new drug targets can be gleaned. The last of these chapters addresses the large databases available in the fields of genomics, combinatorial chemistry, high-throughput screening, and clinical trials and addresses how they can be mined to help the drug discovery process.

The final five chapters address the practical aspects of setting up screening operations. The cost factors associated with high-throughput drug discovery are discussed in chapters 18 and 19. Some important parameters that affect cost are assay robustness, sensitivity, and automation. The last three chapters extend this theme into the miniaturization of screens to allow testing of more than 100 000 compounds per day. A review of the equipment and robotics necessary to accomplish this level of ultra-high-throughput is presented. Chapter 20 then discusses new assay designs that incorporate homogeneous fluorescent technology to allow one-step assays, truly providing the ultimate in rapid testing. The last chapter reviews what could be the future of screening operations: nanotechnology that presents the possibility of detecting single-molecule interactions.

The Handbook of Drug Discovery contains 1324 references extending through the year 2000, which are located at the end of their respective chapters. Most chapters are backed by recent literature citations, providing valuable detail that back up the methods reviewed in the text. The book is also liberally spattered with diagrams that illustrate the biochemical principles of each screening technique, as well as graphs and data from real-world drug discovery operations.

The index section is adequate at 14 pages of primary and nested citations, but it could have been longer to make the book more convenient for the reader to locate particular information. A technical book containing 582 pages of text probably should have an index at least one-tenth that size to reflect thoroughly the terms used within it. Overall, this book is a worthwhile addition to the chemist's bookshelf. Its practical methods are certain to make it a frequent reference for scientists involved in drug discovery.

Greg T. Hermanson

Director, Research and Development
Pierce Chemical Company
P.O. Box 117
3747 North Meridian Road
Rockford, Illinois 61105

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