Book Reviews

Drug Discovery Research. New Frontiers in the Post-Genomic Era. Edited by Ziwei Huang . John Wiley & Sons, Inc., Hoboken, NJ. 2007. xi + 521 pp. 16 × 24 cm. ISBN 978-0-471-67200-5. $125.00.

This book describes and exemplifies a number of computational, structural, chemical, synthetic, biological, and translational methods currently used to design, synthesize, and study potential new drug products. It includes advances made in many scientific disciplines, such as genomics, computer-aided drug design, biology, and pharmacology, and the integration of these advances to aid in the development of new medicines.

The book consists of 20 chapters written by 70 expert contributors. It is divided into three sections: Part I (Chapters 1–5) describes newer computational methods and their application in suggesting potential new ligands for receptor and enzyme targets. Aided by the sequencing of the human genome, more than 40 000 biomolecular structures are now available. Thus, the application of molecular docking simulations to suggest new ligands for protein targets has provided an increasingly important entry for the discovery of new drugs. The utility of computational methods to limit the size of chemical libraries to be screened experimentally and to predict absorption, distribution, metabolism, excretion, and toxicity is reviewed. Application of computational techniques to design novel combinatorial compound libraries for synthesis is also addressed. Part II, entitled "Chemical and Synthetic Approaches in Drug Discovery", comprises nine chapters that describe chemical strategies for discovering new drug products. Chapter 6 details synthetic research with bryostatin, a complex natural product with anticancer properties, but limited availability, to illustrate principles of rational drug design combined with synthesis in the pursuit of new therapeutic leads. In Chapter 7 small-molecule inhibitors of poly(ADP-ribose)glycohydrolase (PARG), an enzyme of critical importance in regulating cellular DNA damage, are considered for their potential in ischemic injury and cancer therapy. Second messengers, including some small molecules (e.g., cyclic adenosine diphosphate ribose (cADPR), control Ca^{2+} mobilization that is critically important for various cell functions. A proposed model of interaction of cADPR with its receptor protein is presented in Chapter 8. Neuroimmunophilin ligands in neurodegenerative diseases and nerve regeneration are the topic of Chapter 9. Chiral drugs and some asymmetric syntheses are reviewed in Chapter 10. Selected examples of recent studies with low molecular weight synthetic mimics of α-helices are described in Chapter 11. Chemokines, which are implicated in many physiological processes and a wide range of inflammatory diseases, including AIDS, as well as synthetically modified derivatives, and their application in many areas of basic research and therapeutic development are the subject of Chapter 12. Protein post-translational modification, i.e., chemical modification processes on specific amino acid residues occurring after mRNA has been translated into protein, and intervention strategies in protein therapeutics are reviewed in Chapter 13. The final chapter in Part II describes an innovative drug delivery/controlled release system in which antibodies are immobilized in silica gels. Part III focuses on the biology of drug discovery. Chapters 15–17 describe rationally designed anticancer drugs, e.g., retinoic acid and arsenic trioxide, 2-chlorodeoxyadenosine, and novel apoptosis-based entities. Development of memantine (1-amino-3,5-dimethyladamantine), a neuroprotective agent with utility in Alzheimer's disease, is the subject of Chapter 18. The use of animal models, including generic deletion (knock-out) and overexpression (knock-in) paradigms, in drug discovery is the subject of Chapter 19. The final Chapter 20 considers "Stem Cell Research and Applications for Human Therapies".

In general, the chapters are well-written, although in some instances the technical nature (e.g., in the discussion of software applications) may be demanding of those lacking specific expertise. Introductory information would aid the reader. Each chapter includes a comprehensive, up-to-date list of references, and the book concludes with a detailed subject index. Synthetic schemes, chemical structures, figures, and most tables are adequate. Many of the figures are presented in black and white in the text and in color in a separate section of the book.

In my opinion, the book achieves the objective of the Editor in providing a useful tool and reference for scientists concerned with state-of-the-art postgenomic drug discovery. As a result of its broad coverage of computational approaches to the derivation of potential new drug products, coupled with selected examples of rational new methods of drug design and their successful application in therapy, this book will be of interest to both students and practitioners of medicinal chemistry, as well as to others concerned with developing new drug products.

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