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Book reviews

"Pharmacogenomics, The Search for Individualized Therapies"

Julio Licinio, Ma-Li Wong (Editors), Wiley-VCH Verlag GmbH, Weinheim, Germany; 2002, 559 pages, 75 euros; ISBN: 3-527.30380-4

The soft bound book "Pharmacogenomics, The Search for Individualized Therapies" edited by Julio Licinio and Ma-Li Wong is a very successful approach to cover the emerging discipline of pharmacogenomics from definitions to applications including ethical issues. A multinational authorship-group of 68 experts both from industry and academia contributed to this comprehensive book containing 27 chapters. Individualized therapies have long been a dream of mankind. Pharmacogenomics, a broad introduction is given in chapter 1, is a new discipline in the frontier area between medicine and life sciences. The deciphering of the human genome (chapter 2) resulted in a wealth of genetic information which is now being applied to drug effects and therapeutic outcomes in patients. The revolutionary change in patient-oriented research is the shift from a reductionist (mostly monogenic) approach to an integrated research that tries to understand the complexity of a biological system. Each author was encouraged to contribute his definition of pharmacogenomics. Thus, the reader gets a good feeling of the scope of pharmacogenomics. All chapters (except 11) provide an abstract for brief overview, and finish with conclusions (except chapter 6) and a comprehensive list of references, research and review articles which allow the reader a more in-depth study. "Turning SNPs (single nucleotide polymorphisms) into useful markers of drug response" (chapter 3) is one of the major tasks in pharmacogenomics. Candidate gene studies, whole genome linkage disequilibrium mapping, and the design of pharmacogenomic clinical trials are explained. Examples of using SNP-maps for the identification of genetic factors influencing drug responses (association studies) and their impact for clinical studies are given in chapter 4. Cross-references between chapters 3 and 4 would have been helpful. Chapters 5–7 describe the impact of pharmacogenomics on drug target validation, drug design/discovery, and the understanding of drug action/toxicity including clinical studies from the viewpoint of pharmaceutical industrialists. Methodology (genomics, proteomics, bioinformatics), prominent examples of the variability of drug targets due to SNPs (β2-adrenoceptor, BCR-ABL, HIV-protease) and ethical and societal issues are included.

After these more general issues, chapters 8 and 9 focus on specific drug interaction sites: human P-glycoprotein (mutations contribute to variations of drug disposition, therapeutic outcome, and risk for certain diseases) and drug transporters (excellent overview on the classification and polymorphisms contributing to interindividual variations of drug disposition and effects). Unfortunately, chapter 15 ("Pharmacogenomics of the blood–brain barrier") does not follow next – where it would have best fit in (pharmacogenomics of drug interaction sites before moving to pharmacogenomics of diseases). Further, it would have been desirable to include a whole chapter on drug metabolism due to its importance even though metabolic aspects, e.g. cytochrome P450 (CYP450) or thiopurine methyltransferase (TPMT), are discussed in various chapters. Chapters 10 through 20 deal with pharmacogenomics of diseases and their pharmacotherapy (except chapter 15). An example of genetic association studies in asthma using SNP analysis of β2-adrenoceptors and 5-lipoxygenase is given in chapter 10. Chapter 11 presents therapeutic strategies in sickle cell disease (effects of hydroxyurea on gene expression in endothelial cells). After a more general introduction into pharmacogenomics, chapter 12 deals with pharmacogenomics of cardiovascular diseases (effect of polymorphic genes like angiotensin I-converting enzyme on drug effects). An analysis of the current knowledge of genetic variants of genes involved in the metabolism of plasma lipoproteins and lipid lowering drugs, e.g. statins, is given in chapter 13. An important application of pharmacogenomics is cancer chemotherapy because applied doses are often close to intoxication. Examples of genetic determinants of toxicity and the response of chemotherapeutic drugs, e.g. TPMT or thymidylate synthase gene promoter, are presented in chapter 14. Chapter 16 deals with pharmacogenomics of the neurological disease epilepsy (association studies to determine variations in antiepileptic drug response genes (ion channels) and metabolizing enzymes). Genes involved in the pathogenesis of neurodegenerative diseases (e.g. Huntington's or Parkinson's disease) and their relevance to the mode of action (and side effects) of drugs are presented in chapter 17. Psychiatric pharmacogenomics are the topics in chapters 18–20. Therapeutic outcomes and adverse effects like tardive dyskinesia or weight gain of atypical and typical antipsychotics, and approaches to the discovery of innovative, effective, and individualized treatments of major depression including ethical considerations are discussed. Gene expression studies in bipolar disorder, a disease with poorly understood pathophysiology, show an association with atrophy and loss

of neurons. The next three chapters deal with addiction, tolerance, and dependence. A detailed introduction into the problem of alcoholism including structural and kinetic features of alcohol- and acetaldehyde-dehydrogenases and their isozymes, and the correlation of various genotypes with alcoholism and consecutive disorders are given. Chapter 22 presents known polymorphic genes affecting nicotine metabolism and dopaminergic transmission and the potential benefit of future genome wide scans in tobacco addiction. Chapter 23 provides an excellent historic and pharmacologic overview on the opioid system. However, pharmacogenomics which would have included the impact of genomic variations is little discussed in this chapter. Differences between ethnic groups in drug metabolism, disposition, reasons for ethnic variations, molecular history of genetic polymorphisms, and their impact on public health (costs) and ethics are topics in chapter 24. Chapter 25 has some overlap with chapter 24 in ethnic aspects but then focuses on societal/ethical issues: pharmacogenomics will help to differentiate between human individuals based on genetic differences rather than dividing humans into different racial groups. Chapter 26 presents a "pharmacoproteomics" approach to unravel the molecular diversity of the human vasculature at the protein–protein interaction level by using a phage display random peptide library for the purpose of an individualized tissue specific targeted delivery. Finally, chapter 27 gives an extensive glossary including basic genetic terms and is a great help for newcomers in pharmacogenomics, and ends with helpful genomic resources on the World Wide Web.

In conclusion, experts describe – mostly very well and comprehensibly written – basically all facets of the exciting new discipline called pharmacogenomics. This book offers a wealth of highly actual information and can be emphatically recommended not only for those already working in pharmacogenomics but also for newcomers and life scientists who may intend to include pharmacogenomics in their research or teaching.

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"Polymeric Biomaterials" 2nd Edition

Severian Dumitriu (Editor), Marcel Dekker, New York, Basel; 2002, 1184 pages, US$ 275; ISBN 0-8247-0569-6

Searching databases for polymeric biomaterials is cumbersome. Medline and Chemical Abstracts alone provide thousands of references, a 'success' that leaves people new to the field pretty much out in the rain. The vast amount of information available on these biomaterials must be ordered not only in regards to their chemical composition and physicochemical properties, but also according to their potential applications. This has become all the more necessary as polymer biomaterials are nowadays tailored substances that are fine-tuned to the needs of specific applications. 'Polymeric Biomaterials', edited by S. Dumitriu, is an attempt to bridge this gap between the multitude of publications in the field and the need for a careful introduction. An overview over the field is also provided for the more experienced reader. Where it was deemed necessary, the editor devoted whole chapters to individual material classes such as polysaccharides, silicones and biodegradable polymers. This is certainly important as these are substances with a tremendous amount of variability and, therefore, a plethora of applications. What I found most attractive besides these material based chapters, was contributions devoted to applications of well-defined materials. Although individual chapters typically focus on specific topics, they are related to major fields such as drug delivery, tissue engineering, gene therapy, prostheses and others. These individual chapters are well written and illustrated. The book has a detailed index so that searching for materials is comfortable. The book is certainly a useful tool for all those that would like an overview of the materials, as well as their potential applications. The price of US$ 275 seems a little bit high, but is still a good investment.

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"Antimicrobial Pharmacodynamics in Theory and Clinical Practice"

C. Nightingale, T. Murakawa, P. Ambrose (Editors), Marcel Dekker, New York, Basel; 2001, 432 pages, $ 175; ISBN 0-8247-0561-0

The pharmacology of antimicrobial agents (AA) can be divided into two components: pharmacokinetic (PK) and pharmacodynamic (PD). Whereas PK parameters define the distribution of drug in serum and other compartments and elimination, PD parameters give information on the interaction between the AA and microorganism.