

Book Reviews

Molecular Toxicology, Second Edition. By P. David Josephy and Bengt Mannervik. Oxford University Press, New York. 2006. xviii + 589 pp. 19 × 26 cm. ISBN 0-19-517620-0. \$144.50.

This book has much to offer the reader. It is an excellent blend of chemistry and biology that provides important information on how, at the molecular level, chemicals can alter biochemical and physiological processes. The book will be of immense value to students interested in toxicology and pharmacology, to postdoctoral fellows, and to practicing toxicologists who would like a “refresher” as well as an update. For this reviewer, reading the various chapters was most rewarding. It made me realize how much I did not know and how much I had forgotten over the past 30 plus years. The historical perspectives presented throughout the various chapters remind the readers of the pioneers of biochemical toxicology and how their key findings laid the foundation for molecular toxicology as we know it today. The authors have made extensive use of sidebars to ask critical questions, to provide more focused information, and to put information into perspective.

The book begins with a detailed discussion on the toxicology of oxygen. The chapter describes the reactive species of oxygen, their interactions with biological components, and the consequences of these interactions. Considerable attention is focused on the covalent binding of xenobiotics to DNA and to protein, the critical nature of DNA repair to cell survival and propagation, and the link between DNA damage and chemical mutagenesis/carcinogenesis. Chapter 5 is important because it links mutations in certain key genes (oncogenes and tumor suppressor genes) to certain cancers. This chapter also devotes some discussion to the subject of apoptosis, but it is rather focused. Clearly, this subject warrants more attention because of its role in a number of toxicities. A number of subsequent chapters is devoted to the enzymology of biotransformation. These include two chapters on cytochrome P450, which discuss the chemical and biochemical aspects of this superfamily of enzymes and the molecular mechanisms by which they are regulated (primarily the various nuclear receptors that mediate induction). Glutathione gets its fair share of coverage in three chapters.

The chapter on glutathione transferases is an excellent overview of the multiple forms of these enzymes and of their specificity for certain functional groups. The other two chapters highlight nicely why GSH and its transferases play such a key role in toxicology and also in therapeutics. The chapters on glucuronic acid conjugation, arylamine *N*-acetyltransferase, and sulfotransferase are concise discussions that provide detailed information on the chemistry, biochemistry, genetics, and molecular biology of these important biotransformation enzymes.

The book finishes with a section called Molecular Principles Applied to Specific Toxicants. These chapters made interesting reading because they integrate the important concepts in the earlier chapters with specific chemical classes. The chapter on alkylating agents expands upon DNA and protein alkylation, alkylation and cancer chemotherapy, GSTs and tumor resistance to alkylating agents, and formation of alkylating agents as a result of GSH conjugation. Oxidative stress was revisited with specific reference to the erythrocyte. The chapters on aromatic amines, polycyclic aromatic hydrocarbons, and acetaminophen are particularly appealing because they relate how observations of human toxicities associated with these particular classes of chemicals stimulated the vast amount of research that ultimately led to our advanced understanding of the molecular events that cause these toxicities.

This book represents an outstanding effort by the authors, and I can recommend it very highly. It is historical, authoritative, detailed, well-referenced, and timely. It lives up to its title in that it does strive to explain toxicological events at the molecular level. I look forward to the third edition, which should include a more detailed discussion of apoptosis, signal transduction, and the emerging role of transporters in toxicology.

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