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Book Reviews

Cytochrome P450: Structure, mechanism and biochemistry, second edition, ed. Paul R. Ortiz de Montellano, Plenum Press, New York and London, 1995, x + 652 pp., price US $125.00
ISBN 0-306-45141-7

The discovery of the cytochromes P450 (CyP450) and the advances in biochemical pharmacology arising therefrom must rate as supreme events of the current half-century. The realisation that these enzymes are universally involved in the metabolism of xenobiotics in living organisms has brought together scientists with common interests across the whole spectrum of environmental science, generating over the years a 'brotherhood' dedicated to solving the many technical problems that arose, especially in early explorations of the plant and non-vertebrate animal P450s.

This book is the ten-years-on up-date of the 1st edition published in 1986 and is a mine of information on the remarkable advances achieved in the last decade. It consists of 15 chapters and two appendices written by international experts and is sub-divided into four logically arranged parts. Part I, on Model Systems, has one chapter on Models and Mechanisms of Cy P450 Action and a second on Comparison of the Peroxidase Activity of Hemoproteins and CyP450. Following this excellent, well-referenced introduction, Part II deals with Structurally defined Bacterial Enzymes, beginning with chapter 3, a fascinating account of 25 years of research on the famous $P450_{cam}$, the first microbial P450 system discovered in the laboratory of Gunsalus. Chapters 4 and 5, entitled Structural Studies on Prokaryotic CyP450s, and Bacterial P450s; Structural Similarities and Functional Differences, respectively, are richly detailed in text and illustrations and are an absorbing read.

This leads logically to Part III on Structures and Mechanisms of Membrane Bound P450s, with chapter 6 on Structures of Eukaryotic P450s, chapter 7 on NADPH CyP450-reductase, chapter 8 on Oxygen Activation and Reactivity and chapter 9 on the inhibition of CyP450s. These are all highly detailed up-dates. Chapter 9 reviews an array of inhibitory and destructive mechanisms for P450s, including some explored in the context of pesticide synergism and antagonism.

Part IV, the largest part of the book, covers Regulatory Mechanisms and Physiological Roles of CyP450, beginning with chapter 10 on enzyme induction, a phenomenon with important consequences for tolerance to xenobiotics. Chapter 11 is on Hormonal Regulation of Liver CyP450s and discusses, *inter alia*, the alteration of liver P450 expression due to hormonal perturbations arising from exposure to drugs and other foreign chemicals and pathological conditions (e.g. diabetes, liver cirrhosis). CyP450s are well known to be involved in the metabolism of endogenous substrates; their roles in the regulation of steroidogensis and in the metabolism of arachidonic acid and oxygenated eicosanoids are the subjects of chapters 12 and 13, respectively. Current knowledge of human P450s is reviewed in chapter 14, which includes a systematic presentation of individual P450-subfamilies and the oxidations they catalyse. Since there are some similarities but also many differences between human and experimental animal P450s, continued efforts in this area are vital for new drug discovery. There is a final chapter in Part IV entitled Heme-Thiolate Proteins Different from CyP450s Catalyzing Monooxygenations. This provides a useful conclusion to the body of the book by summarising the properties of the 'classical' P450 monooxygenases, then comparing these functions with other activities of P450s, such as dehydrogenation, isomerisation, dehydration, deformylation, nitric oxide reduction, etc., demonstrating the remarkable versatility of these enzymes. Some of these reactions are effected by the 'classical' P450s, others by proteins belonging to the P450 superfamily which do not even catalyse oxidation reactions.

The book is completed by Appendix A on P450 Nomenclature and Alignment of Selected Sequences and Appendix B on Substrate and Inhibitor Specificities and Functional Markers for Rat and Human Liver CyP450s. There is a large amount of tabular information in these appendices which will be appreciated by research workers in this area.

There is a good subject index. Since the book contains nearly 2900 references and much detail it would have helped quick reference if the table of contents had included the sub-heads for each chapter. This apart, the editor and all concerned are to be congratulated on an excellent product setting out the current status of basic research on CyP450. It should be welcomed by researchers as a valuable reference book and a thought-provoking read.

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