

Preface

Transport across the cell membrane is essential for vital processes like entry of nutrients into the intracellular compartment, delivery of cellular products to extracellular and intracellular destinations, and handling of metabolism waste products and toxic substances and is necessary to keep the intracellular milieu constant. Transport across cell membranes is mediated by a variety of different transport proteins. This book focusses on transporters for organic cations, which are not directly energy-dependent, such as organic cation transporters (OCTs), organic zwitterions/cation transporters (OCTNs), and multidrug extrusion proteins (MATEs). Because these transporters are polyspecific, they accept many different substrates of endogenous (e.g. choline, acetylcholine, histamine, and monoamine neurotransmitters) as well as of exogenous (e.g. drugs like metformin, quinine, cimetidine, and cisplatin) origin.

Since the cloning of the first transporter for organic cations (rOCT1) in 1994, profound understanding of their structure, transport properties, and regulation has been obtained. In organs expressing these transporters at high levels, such as the intestine, liver, and kidney, transporters for organic cations play a pivotal role not only in absorption and in excretion of xenobiotics but also in their accumulation and toxicity. However, their expression is not restricted to organs typically involved in the transport of xenobiotics, but is found also in other tissues, such as the brain and reproductive organs. Recent studies with genetically modified animals have helped to unveil novel physiological, pathophysiological, and pharmacological roles of transporters for organic cations. While there is no doubt about the pharmacological and toxicological implications of transporters for organic cations for the organism, their physiological functions had remained largely elusive. Moreover, gender- and species-specific differences in the expression and properties of these transporters as well as the role of single nucleotide polymorphisms on their function have become a focus of attention in physiology, pathophysiology, and medical care.

This book presents current knowledge on the expression, physiological functions (see Chap. 1 by G. Ciarimboli), and regulation (see Chap. 5 by E. Schlatter and Chap. 6 by L.M. Aleksunes) of transporters for organic cations in various organs, on

their gender and species dependencies (see Chap. 9 by I. Sabolić, D. Breljak, and T. Smital), and on their role in pathophysiological situations. This overview should be of high interest for researchers and students in various areas of integrative, organ, cell, and molecular physiology and will contribute to delineate an integrative physiological interpretation of transporter function.

Another important aspect of the book is that it conjugates integrative transporter physiology with structural and molecular biology (see Chap. 2 by H. Koepsell and T. Keller), genetics (see Chap. 4 by M.V. Tzvetkov, N. Dalila, and F. Faltraco), pharmacology, and pathophysiology (see Chap. 3 by K. Inui and H. Motohashi and Chap. 8 by K. Tieu), offering an integration of the knowledge in these fields. The different chapters of the book present the state of the art of the research in these different fields. For this reason, the book addresses both expert readers and readers with a more general interest in understanding transporter function in physiology and pathophysiology. Hence, the book should also attract people interested in adaptive mechanisms of the organism to conditions, such as salt intake, anxiety, and stress (see Chap. 7 by A. Orrico and S. Gautron).

Since up to 40 % of the prescribed drugs are organic cations, this book will provide important information on the involvement of transporters for organic cations in determining specific effects but also side effects induced by particular drugs, offering new approaches for a successful translation from physiology to clinical therapy. Finally, because of the expression of transporters for organic cations in plants, the role of these transporters for the environmental cycling of pharmaceutical residues is also presented (see Chap. 10 by T. Eggen and C. Lillo).

In conclusion, we think that a book concentrating on the latest developments of integrative, organ, cell, and molecular aspects of function of transporters for organic cations will furnish an optimal platform to integrate the knowledge on these transporters and obtain a more comprehensive physiological understanding of their function.

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