Preface

Neurotransmission is a multicomponent process. Transmitters, released by neuronal activity, act on pre- and postsynaptic receptors, and many books detail advances in the receptor field. In addition, after their release from nerve endings, transmitters are removed from the neuronal vicinity by uptake into neuronal or glial cells by specific transporter proteins that have been studied intensely over the last 30 years; this information is scattered throughout numerous publishing vehicles. Therefore, the primary aim of this second edition of *Neurotransmitter Transporters: Structure, Function, and Regulation* is to offer a comprehensive picture of the characterization of neurotransmitter transporters and their biological roles. The transporter field has moved forward in stages. In the first phase, progress came from the use of substrate or blocker ligands selectively targeting transporters, the application of model systems allowing the study of transmitter transport shielded from storage, and the development of mathematical models for describing transport phenomena. In the second phase, roughly covering the last decade, advances in DNA techniques allowed the cloning of numerous genes coding for different transporter proteins. In the current, third stage, a wealth of information is being accumulated in studies relating transporter structure with function, experiments addressing regulation by posttranslational transformation, investigations into transport modulation by trafficking processes and genomic influences, characterization of channel properties of transporters by electrophysiological approaches, and the creation of transgenic animals under- or overexpressing a given transporter protein.

The first edition of *Neurotransmitter Transporters: Structure, Function, and Regulation* was published at the brink of the above 2nd and 3rd phase; the current, second edition finds the transporter field fully in the 3rd phase. This second edition of *Neurotransmitter Transporters: Structure, Function, and Regulation* has been put together with the goal of retaining most of the original material in describing for each transporter the cloning history as well as including new progress in characterizing its structure, function, regulation, and physiological relevance.

Interest in neurotransmitter transporters has increased tremendously, along with clearer understanding of their roles in the pathophysiology of schizophrenia, Tourette's syndrome, Parkinson's disease, affective disorders, attention deficit/hyperactivity disorder, neurotoxin accumulation and removal, brain ischemia, amyotropic lateral sclerosis, or in the mechanism of action of drugs of abuse, antidepressants, and antiepileptics. Thus, *Neurotransmitter Transporters: Structure, Function, and Regulation, Second Edition* will be of interest to scientists, graduate students, and advanced undergraduates who seek a comprehensive overview of this active field in neuroscience. Selected chapters will also be of interest to physicians who are carrying out imaging and postmortem measurements of neurotransmitter transporters in the human brain, or physicians who study gene linkages and polymorphisms in relation to psychiatric and other complex diseases.

Each chapter of *Neurotransmitter Transporters: Structure, Function, and Regulation* offers a critical summary and synthesis of the progress in characterizing each transporter in terms of structure–function relationships and regulation. Chapters 1–9 focus on various neurotransmitter transporters located in neuronal or glial plasma membranes and in synaptic vesicles. The Na^+, Cl^--dependent plasma membrane transporters are described for monoamines (Chapters 1–5) and for a number of compounds including amino acids (GABA, glycine, proline, betaine, taurine, and creatine (Chapters 6 and 7). The separate family of Na^+-dependent glutamate transporters is discussed (Chapters 7 and 8) as well as the family of vesicular transporters for monoamines, acetylcholine, and GABA/glycine (Chapter 9). Chapters 10–13 cover a variety of issues relevant to transporter structure and function. Chapter 10 describes posttranslational modifications with their important impact on the function of various transporters. Chapter 11 covers the various classes of blockers for the dopamine transporter with detailed discussion of structural determinants, and Chapter 12 describes the use of various in vivo imaging techniques and ligands for biogenic amine transporters, in particular the dopamine transporter in the human brain. In Chapter 13, the final chapter, the focus is on dopamine transporter changes in human brain as a result of cocaine administration, with both in vitro and in vivo imaging approaches.

A number of differences between this second edition and the original book can be highlighted. First, the more basic cloning and pharmacological information on monoamine transporters, previously in Chapter 1, can now be found in Chapters 3 and 4. The previous topic of regulation of serotonin transporters (currently Chapter 1, previ-

ously Chapter 2) has been widened to include all three biogenic amine transporters, and it now emphasizes phosphorylation and trafficking phenomena. Three new chapters on biogenic amine transporters have been added: Chapter 3 on chimera and site-directed mutagenesis studies, Chapter 4 on gene organization and the relationship of polymorphisms with psychiatric and other complex human diseases, and Chapter 5 on transgenic animals carrying altered genes for plasma membrane monoamine transporters. Current excitement about channel properties of transporters is covered in Chapters 2 and 8 regarding electrophysiological studies on cloned monoamine and amino acid transporters, respectively. The new chapter on transporter imaging, Chapter 12, entirely focuses on human results including effects of aging and brain injury, and changes in schizophrenia, phobia, drug abuse, and other complex human diseases. Chapter 13 covers changes in dopamine transporters in human brain as a result of cocaine exposure as previously, with added discussion of in vivo imaging approaches for the dopamine transporter included in this update. The previous final chapter detailing the role of biogenic amine transporters in in vivo and in vitro monoamine release studies has been omitted as more recent material on in vivo results is now presented in the new Chapter 5.

The authors of the present chapters have been instrumental in advancing our knowledge of transporters by their experimental and conceptual contributions to the field, and I feel fortunate to have been able to join all their forces together in this second edition. I thank Paul Dolgert, Tom Lanigan, Sr., Elyse O'Grady, Craig Adams, and Mark Breaugh at Humana Press for allowing the opportunity of a second edition, and I hope the book will continue to be used as a popular resource in the field.

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