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Topics in Medicinal Chemistry

Transporters as Targets for Drugs

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Preface to the Series

Medicinal chemistry is both science and art. The science of medicinal chemistry offers mankind one of its best hopes for improving the quality of life. The art of medicinal chemistry continues to challenge its practitioners with the need for both intuition and experience to discover new drugs. Hence sharing the experience of drug discovery is uniquely beneficial to the field of medicinal chemistry.

The series *Topics in Medicinal Chemistry* is designed to help both novice and experienced medicinal chemists share insights from the drug discovery process. For the novice, the introductory chapter to each volume provides background and valuable perspective on a field of medicinal chemistry not available elsewhere. Succeeding chapters then provide examples of successful drug discovery efforts that describe the most up-to-date work from this field.

The editors have chosen topics from both important therapeutic areas and from work that advances the discipline of medicinal chemistry. For example, cancer, metabolic syndrome and Alzheimer's disease are fields in which academia and industry are heavily invested to discover new drugs because of their considerable unmet medical need. The editors have therefore prioritized covering new developments in medicinal chemistry in these fields. In addition, important advances in the discipline, such as fragment-based drug design and other aspects of new lead-seeking approaches, are also planned for early volumes in this series. Each volume thus offers a unique opportunity to capture the most up-to-date perspective in an area of medicinal chemistry.

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Preface to Volume 4

Transporters are proteins which span the plasma membrane and regulate the traffic of small molecules in and out of the cell. Transporters play a particularly important role in chemical signalling between neurons in the CNS, where they act to control the concentration of neurotransmitters in the synapse. The majority of transporters which are actively being pursued as targets for drug discovery are CNS located and this reflects the history of the field which began with the tricyclic antidepressants (TCAs) over half a century ago. The use of transporter inhibition to regulate the synaptic concentrations of key neurotransmitters is an established approach in the discovery of psychiatric medications. This volume reviews advances in the field of transporters as targets for drug discovery in the last 10 years. The volume will be of interest to scientists engaged in drug research in the pharmaceutical industry, biotech and academia. Following an overview chapter, seven chapters written by leading experts in their area reflect a range of topics pertinent to the transporter field. General topics include recent advances in the structural biology of transporters and its impact on potential structure-based drug design and the design of ligands for Positron Emission Tomography and the importance of molecular imaging in understanding early clinical data. Medicinal chemistry approaches are described outlining the discovery of selective serotonin, noradrenaline and dopamine reuptake inhibitors, current efforts towards the discovery of mixed re-uptake inhibitors with varied "flavours" of monoamine inhibition, advances in the development of inhibitors for the glycine transporter and the discovery of subtype selective EAAT inhibitors. In addition to being an interesting read, the reader will receive a critical overview of progress made in this rapidly developing field.

January 2009

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