

Preface

Phosphodiesterases (PDEs), a superfamily of enzymes catalyzing the hydrolysis of the second messengers cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP), have been studied for half a century. This area has been developed quickly during the recent two decades, particularly since the discovery of sildenafil (Viagra®), a selective PDE5 inhibitor, for treatment of male sexual dysfunction in 1998; additional PDE5 inhibitors were approved later (tadalafil, Cialis®; vardenafil, Levitra®). Other family-selective PDE inhibitors have been developed for clinical use since then, i.e., roflumilast (Daxas®) approved by the US FDA in 2011 for treating chronic obstructive pulmonary disease (COPD) and apremilast (Otezla®; 2014) for psoriasis and psoriatic arthritis; both are selective PDE4 inhibitors. Nevertheless, while many of the 11 PDE families are involved in the mediation of intracellular signaling in the central nervous system (CNS) and could be targets for CNS diseases, PDE inhibitors are not available yet for treating neurological or psychiatric conditions. This has been due to the difficulty of overcoming significant side effects (e.g., emesis for PDE4 inhibitors), challenges encountered in synthesizing promising inhibitors (e.g., inhibitors that are selective for a subtype within a PDE family), and an incomplete understanding of the role of the various PDEs in cellular function in the brain. Therefore, it is necessary and important to understand the roles of PDEs in CNS functions, CNS diseases, and the utility of novel PDE inhibitors. To address this, we have published a special issue entitled “Targeting Phosphodiesterases (PDEs) for Treatment of CNS Diseases” in *Current Pharmaceutical Design* (Volume 21, Issue 3, 2015); the review articles have received relatively high citations since publication. We decided to publish a book focusing on the similar topic in order to have comprehensive discussions from experts with a broad expertise in PDE research. The purpose of this book is to characterize the contributions of PDEs to brain functions and identify PDEs and their isoforms as potential targets for treatment of CNS diseases, including psychiatric diseases such as depression, anxiety, and schizophrenia, and neurodegenerative diseases such as Alzheimer’s disease, Huntington’s disease, and Parkinson’s disease, as well as other CNS disorders such as stroke, alcoholism, and drug abuse.

We are very grateful to the authors, who are internationally recognized experts in the PDE research area, for their contributions of excellent chapters, which cover almost all aspects of the CNS diseases described above. We sincerely appreciate the efforts of the reviewers who made many helpful suggestions to improve the book. We gratefully acknowledge Linda Nguyen and Yongxu Huang for their assistance in editing the manuscripts. We know that, despite the hard work of the dedicated team, it is inevitable to miss some points, papers, and any issues related to the subject of this book. Any feedback from readers would be appreciated and important for improving our next edition.

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