

Preface

Muscarinic acetylcholine receptors have played a key role in the advancement of knowledge of pharmacology and neurotransmission since the inception of studies in these fields. Indeed, the classical work of Loewi, which led to the identification of acetylcholine as the *Vagusstoff* released by nerve stimulation, thus showing that synaptic transmission was chemical and not electrical, was based on the actions of neurotransmitter at muscarinic receptors. The physiological actions mediated by muscarinic receptors were known and exploited for both therapeutic and nontherapeutic purposes for hundreds of years before the existence of the receptors themselves was recognized. It is remarkable that the study of muscarinic receptors continues to provide new and surprising insights not just to the cholinergic system, but to the broad areas of neurobiology, cell biology, pharmacology, and therapeutics.

Like other members of the G-protein-coupled receptor superfamily, the application of molecular biological approaches to the study of the muscarinic receptors provided dramatically increased knowledge of both their biological complexity and therapeutic potential. The identification in the late 1980s of multiple genes encoding distinct muscarinic receptor subtypes provided the opportunity to develop drugs that would target discrete subsets of muscarinic receptors with decreased global side effects. The more recent demonstration that drugs can act both positively and negatively on the receptors at sites distinct from the acetylcholine binding region has provided even further promise for increasing the therapeutic specificity of muscarinic drugs.

We hope that this volume will provide a broad yet detailed review of current knowledge of muscarinic receptors that will be valuable both to long-time muscarinic investigators and to those new to the field. It describes the detailed insights that have been obtained on the structure, function, and cell biology of muscarinic receptors. This volume also describes physiological analyses of muscarinic receptors and their roles in regulating the function of the brain and of a variety of peripheral tissues. Finally, it demonstrates how the increased knowledge of the

basic biology, pharmacology, and physiology of the muscarinic receptors can be translated into improved therapeutic applications.

We also hope that this book highlights both the excitement of the study of muscarinic receptors and the amazing range of advances that have occurred in recent years. We are sure that the future will continue to yield information on facets of the muscarinic receptors that we have not yet imagined.

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