

Nicotinic Acetylcholine Receptor Signaling in Neuroprotection

Akinori Akaike • Shun Shimohama
Yoshimi Misu
Editors

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Editors

Akinori Akaike
Department of Pharmacology, Graduate
School of Pharmaceutical Sciences
Kyoto University
Kyoto, Japan

Shun Shimohama
Department of Neurology, School of
Medicine
Sapporo Medical University
Sapporo, Hokkaido, Japan

Wakayama Medical University
Wakayama, Japan

Yoshimi Misu
Graduate School of Medicine
Yokohama City University
Yokohama, Kanagawa, Japan



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Preface

Nicotinic acetylcholine receptors (nAChRs) are typical ligand-gated ion channels that evoke cation-selective currents across the plasma membrane. On exposure to agonists, nAChR exists in an active, open state, and elicits rapid depolarization of neurons. In addition to acute ionic responses, it has been widely recognized that nAChRs mediate long-term modification of cell functions. Persistent stimulation of nAChRs for a longer period occurs during habitual tobacco smoking as well as during acetylcholinesterase (AChE) inhibitor therapy for Alzheimer's disease. Long-term tobacco smoking, nicotine application, or exposure to AChE inhibitors induces upregulation of nAChRs and, in most cases, facilitates cellular responses. Such long-term nAChR stimulation contributes to the elaboration of complex intracellular signals, resulting in functional changes in cells expressing nAChRs in the central nervous system (CNS). The concept of nAChRs as ligand-gated ion channels generating rapid ionic currents is likely to be supplemented with more complex mechanisms, in which nAChRs are important elements triggering intracellular signaling toward gradual alteration of cellular functions. Neuroprotection is one of the major effects of gradual functional modification induced by nicotine and AChE inhibitors including donepezil, which is used in the treatment of Alzheimer's disease.

The goal of this book is to describe current knowledge on roles and mechanisms of signal transduction triggered by nAChR stimulation in neuroprotection against toxic effects of risk factors of neurodegenerative diseases. The major topic of this book is neuroprotection mediated by nAChRs in neurodegenerative diseases such as Alzheimer's disease. Authors of this book are members of research projects supported by the Smoking Research Foundation (SRF), Japan. The SRF project titles are "Functional changes induced by long-term stimulation of nAChRs," "Brain nicotinic acetylcholine receptors and Alzheimer's disease – for the proposal of innovative therapeutic strategies," and "Smoking and nervous system." The authors acknowledge support over many years from SRF.

In response to rapidly evolving areas in clinical and laboratory neuropharmacology and neurochemistry, we provide an in-depth coverage of nAChR-mediated neuroprotection in basic research and of future developments in clinical application of effective neuroprotective strategies in neurodegenerative diseases. We hope that our

work will result in an increased interest in the fascinating subject of nicotinic neuroprotection signaling in the CNS.

Kyoto, Japan
Sapporo, Japan
Yokohama, Japan

Akinori Akaike
Shun Shimohama
Yoshimi Misu

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