Editorial

Nicotinic Acetylcholine Receptors as Therapeutic Targets: Emerging Frontiers in Basic Research and Clinical Science—Editorial Perspective

In 2007, *Biochemical Pharmacology* published a special issue on nicotinic acetylcholine receptors (nAChRs) as emerging therapeutic targets covering aspects of basic research and clinical science. Many of the contributors to this special issue also participated at the Society for Neuroscience (SfN) Satellite symposium on nAChRs held in San Diego that year. The positive feedback from these events together with continued developments in the field of nAChR research clearly demonstrate the need for a biennial meeting and hence this special issue of *Biochemical Pharmacology*. The 2009 meeting and the special issue continues from the momentum in the field with focus on the physiological roles, complex pharmacology, novel modulatory mechanisms as well as further understanding the promise, challenges and lessons from ongoing clinical research.

Since the birth of the field of nAChRs some 60 years ago, tremendous advances have been made in the understanding of the biophysical, physiological and pharmacological profiles of this receptor class. Members of this family of ligand-gated ion channels have been studied for their functional roles in the nervous system including modulation of neurotransmitter release, neuronal processing during development and activation of biochemical signaling processes relevant to a wide diversity of pathophysiological conditions. More recently identified roles in non-neuronal cell function include aspects of cell growth control and modulation of immune function.

Articles in the current special issue bring together the latest concepts in basic science and clinical advances. These document breakthrough findings in the elucidation of nAChR biology in both physiological and pathological contexts and define novel approaches and targets for drug discovery and development for a range of disease indications including Alzheimer's disease, schizophrenia, pain, depression, smoking cessation and addiction. Other topics include the analysis of the role of high- and low-sensitivity heteromeric subunit combinations, pharmacological studies with novel ligands, allosteric modulation of nAChRs, and the cross talk between neurotransmitters within the various pathways that express the myriad of nAChR subtypes. Direct protein–protein interaction with other receptor subtypes, in some cases, further illustrates the complexity of receptor function.

In parallel with this enhanced insight into nAChR biology, drug discovery efforts over the past 20 years have culminated in the clinical advancement of a number of compounds that exhibit varying ranges of subtype selectivity and target interaction profiles. Beyond the $\alpha4\beta2$ partial agonist, varenicline, approved for the treatment of smoking cessation, a number of nAChR ligands are being evaluated clinically for ADHD, Alzheimer's disease, schizophrenia pain and depression. The increased number of compounds moving forward is a reflection of the therapeutic potential of nAChRs modulators. However, it is equally important to assess clinical trial results that elaborate on basic research findings and can guide ongoing research efforts.

Several of the contributors to this special issue are speakers at the Society for Neuroscience (SfN) Satellite symposium on "*Nicotinic Acetylcholine Receptors as Therapeutic Targets*", to be held in Chicago, IL, October 14–16, 2009. The Guest Editors sincerely thank the authors for their dedicated efforts in contributing state-of-the-art and timely articles to this special issue. We are also indebted to Lynn LeCount, Cindy Martin, Mike Williams and the Elsevier staff for their support for bringing this issue together.

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