INTRODUCTION

Introduction to the special Issue “functional and therapeutic aspects of the nicotinic acetylcholine receptor family”

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The special issue “Functional and therapeutic aspects of the nicotinic acetylcholine receptor family” is a comprehensive work covering some of the most important aspects of the structure and function of the nicotinic acetylcholine receptor (AChR) family in physiological and pathological conditions as well as therapeutic facets involving the functional and structural interaction of drugs with different members of this receptor family.

Since the initial discovery that the neurotransmitter acetylcholine (ACh) may activate two different cholinergic receptor families, muscarinic and nicotinic, the advancement on the structure and function of AChRs has become apparent. The first important step in this direction was the isolation of functional AChRs obtained from the Electrophorus electricus electric organ by Changeux and co-workers [1], the first characterized membrane receptor in the history, as well as the use of a snake toxin, now called α-bungarotoxin [2], that served to further determine its function, including that it has an intrinsic cation permeable to cations. Subsequently, Numa’s lab published the first complete primary sequence of α1, one of the AChR subunits [3]. Thanks to this pioneering work, we currently know that vertebrates may express several AChR subunits, including ten α (α1-α10), four β (β1-β4), one γ, one ε, and one δ subunits, whereas invertebrates express other subunits. In this regard, Dr. Orteils discusses the evolutionary aspects of the pentameric ligand-gated ion channel superfamily, including the AChR family as well as bacterial channels homologous to them.

Different AChR subtypes are expressed in the brain as well as in different organs from the human body which have important physiological functions. Among them, the α9α10 AChR is important for the modulation of the electrical activity of hair cells, topic developed by Dr. Vazquez. In addition, Dr. Damijonaitis and co-workers explain how converting the AChR into a photoreceptor by attaching a light-controlled chemical “switch” and studying its activity triggered by light instead by ACh may serve to study the precise roles of AChRs in the brain.

Neuronal AChRs are involved in many relevant ailments, including neuropsychiatric (e.g., depression, anxiety, nicotine and drug addiction), neurodegenerative (e.g., Alzheimer’s...
disease, schizophrenia, and Parkinson’s disease), and pain-related diseases. The most abundant AChRs in the brain are the α7 and α4β2 subtypes which can be differentiated by their specific pharmacological properties.

Several AChR subtypes are also expressed in non-neuronal tissues, and its malfunctioning underlies important ailments, including several chronic, inflammatory, and oncologic diseases. For instance, the role of α7 AChRs in chronic kidney diseases is reviewed by Dr. Siddiqui and co-workers, whereas the principles of how α7 AChR activation can attenuate peripheral inflammation is covered by Dr. Atzori and his collaborators. Interestingly, AChR functions have been also characterized in cellular organelles such as mitochondria, a subject developed by Dr. Skok’s team.

Since the AChR family is involved in several important diseases, in the last few decades different laboratories have been developing novel ligands to tackle these ailments. New evidence supports the idea that AChRs are also targets for the pharmacological activity of clinically relevant drugs, including antidepressants. Thus, Dr. García-Colunga and co-workers discuss the structural and functional activity of selective antidepressants on a variety of AChR subtypes.

References

