

## Therapeutic targeting of nicotinic acetylcholine receptors: From Alzheimer's to zebrafish

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Nicotinic acetylcholine receptors (nAChR) are ligand-gated ion channels permeable to Na<sup>+</sup>, K<sup>+</sup>, and Ca<sup>2+</sup>. nAChR subtypes are pentamers composed of distinct combinations of  $\alpha$  ( $\alpha 2$ - $\alpha 10$ ) and  $\beta$  ( $\beta 2$ - $\beta 4$ ) subunits. They are classically responsible for rapid excitatory neurotransmission in the nervous system as well as modulation of the release of other neurotransmitters including dopamine. The number of subtypes naturally present *in vivo* is not known, but multiple subtypes can exist in an individual cell. nAChRs are also widely expressed outside of the nervous system and multiple nAChR subtypes are expressed in non-neural tissues such as lung, skin, adipose tissue and various immune cells. Neuronal nAChRs are involved in a large number of neurological processes including pain sensation, locomotion, body temperature regulation, cognition, and reward and addiction. nAChR function is involved in several disorders including Alzheimer's disease, Parkinson's disease, schizophrenia, lung cancer, epilepsy, ADHD, Tourette's and of course nicotine addiction. Neuronal nAChRs are a rich target for drug discovery efforts.

This presentation will describe our efforts to identify and develop new compounds which specifically target nAChR subtypes. This work has involved a combination of molecular modeling of new allosteric site on the nAChR, synthesis of new drugs targeted to this site and functional analysis of these new compounds using cell lines expressing specific nAChR subtypes. These drugs could be useful in the treatment of nicotine addiction (smoking cessation). It will also describe our work in characterizing zebrafish nAChRs. The biology of zebrafish makes it ideal for use in drug discovery efforts.

### Biography

R. Thomas Boyd received a B.S in Physiology from the University of Illinois, Urbana-Champaign, an M.S. in Biology from the University of Memphis and Ph.D. in Molecular Biology from the University of Texas at Austin in 1986. He carried out postdoctoral studies at the University of California, San Diego and the Salk Institute before moving to The Ohio State University College of Medicine as Assistant Professor of Pharmacology in 1990. He is currently Associate Professor of Neuroscience in the Department of Neuroscience. He is a reviewer for numerous journals and has served on multiple NIH study sections.

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