Public Abstract
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Graduation Term:SS 2007
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Degree:PhD
Title:Regulation and Function of P2Ysub2 and P2Xsub7 Nucleotide Receptors in the Central Nervous System

The central nervous system (CNS) is the major part of the nervous system, including the brain and the spinal cord. Neurodegenerative disease describes a condition in which cells in the CNS are lost such as Alzheimer's disease (AD), which is associated with neuronal cell death, glia proliferation and migration, inflammation, beta amyloid deposition and tau tangles. It is well known that ATP acts as a classic neurotransmitter in the central nervous system. It is stored in synaptic vesicles, released upon neuronal excitation, and activates both ion channel receptors (P2X) and G protein-coupled receptors (P2Y) on post-synaptic cells. In addition to its role as a neurotransmitter, ATP and other nucleotides are known to be released from injured or ischemic tissue and have been reported to affect inflammatory events in the brain and many other tissues, however, these inflammatory events as well as the subtype(s) of nucleotide receptor(s) influencing these events have not been well defined. This dissertation examines the expression patterns of P2X and P2Y nucleotide receptors in rat primary cultures of cortical neurons (rPCNs), in adult rodent brains, in cerebral ischemia and in collared rabbit carotid arteries. P2Ysub2R is up-regulated in response to cytokine stimulation in rPCNs in vitro and after collar transplantation around rabbit carotid arteries in vivo. Moreover, in vivo studies in the collared carotid artery model indicate the involvement of P2Y2Rs in the development of intimal hyperplasia. Based on these studies, particular emphasis was placed on delineating the role of the P2Ysub2 receptor subtype in neuronal inflammation and the P2Xsub7 receptor subtype in neuronal apoptosis in the central nervous system. In the rat primary cultures of cortical neurons, activation of the P2Ysub2R and P2Xsub7R caused alpha-secretase-dependent APP processing and caspase8/9/3-dependent apoptosis, respectively. These results suggest the important roles of P2 nucleotide receptors (P2Ysub2R and P2Xsub7R) and their associated signaling pathways in regulating neuronal inflammation and apoptosis in brain disorders and neurodegeneration.