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BS Zoology, University of Oklahoma, USA, 2007
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Current Position

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Keywords

Alzheimer's Disease – Amyloid Precursor Protein – sAPPα - Synapse Formation and Function

Science

Amyloid Precursor Protein (APP) is a type I transmembrane glycoprotein central to the pathogenesis of Alzheimer's Disease (AD). APP undergoes sequential proteolytic processing to generate, among other fragments, the amyloid-beta peptide (Aβ). In AD pathogenesis, Aβ accumulation initiates a cascade with synaptic dysfunction being one of the first events. Therapeutic strategies currently in patient trials are aimed at chronically inhibiting the proteolytic processing of APP treat AD, yet the normal physiological function of APP has not been fully elucidated.

APP and its family members, APP like protein 1 and 2 (APLP2, APLP2), have been implicated in a number of diverse functions in the development of the nervous system, including synapse formation and function. The physiological function of APP at the synapse has been attributed in part to sAPPα, which is generated by α-secretase cleavage of APP. For sAPPα, a soluble extracellular protein, to act at the synapse, an APPsα specific cell surface receptor should exist to transduce an intracellular signaling cascade and mediate its function. Yet, there currently are not any widely validated receptors known to mediate sAPPα activity. Initial findings in the laboratory indicate the presence of a yet unidentified high-affinity receptor for sAPPα on the cell surface. The aims of current studies are to (1) identify and characterize the high-affinity receptor for sAPPα at the cell surface and (2) elucidate the biological function of the sAPPα/receptor complex at the synapse. This research has the potential to further reveal the normal physiological function of APP in the brain and open up innovative drug discovery routes for AD based on the sAPPα receptor.

Selected Publications

Rice HC, Young-Pearse TL, and Selkoe DJ. (2013) Systematic evaluation of candidate ligands regulating ectodomain shedding of Amyloid Precursor Protein. Biochemistry 52 (19), pp 3264–3277

Rice HC, Townsend M, Bai J, Suth S, Cavanaugh W, Selkoe DJ, and Young-Pearse TL. (2012) Pancortins interact with the Amyloid Precursor Protein and modulate cortical cell migration. Development. Nov; 139(21):3986-96