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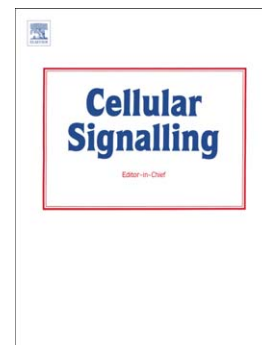
Beyond γ -secretase activity: The multifunctional nature of presenilins in cell signalling pathways

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Beyond γ -secretase activity: The multifunctional nature of presenilins in cell signalling pathways

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Abstract

The presenilins are the catalytic subunit of the membrane-embedded tetrameric γ -secretase protease complexes. More than 90 transmembrane proteins have been reported to be γ -secretase substrates, including the widely studied amyloid precursor protein (APP) and the Notch receptor, which are precursors for the generation of amyloid- β peptides and biologically active APP intracellular domain (AICD) and Notch intracellular domain (NICD). The diversity of γ -secretase substrates highlights the importance of presenilin-dependent γ -secretase protease activities as a regulatory mechanism in a range of biological systems. However, there is also a growing body of evidence that supports the existence of γ -secretase-independent functions for the presenilins in the regulation and progression of an array of cell signalling pathways. In this review, we will present an overview of current literature that proposes evolutionarily conserved presenilin functions outside of the γ -secretase complex, with a focus on the suggested role of the presenilins in the regulation of Wnt/ β -catenin signalling, protein trafficking and degradation, calcium homeostasis and apoptosis.

Keywords: Presenilin; γ -Secretase; Alzheimer's disease; Wnt Signalling; Calcium Homeostasis; Apoptosis; Protein Trafficking; Autophagy

Running Title: γ -Secretase Independent Function of Presenilins

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