IDENTIFICATION OF PROTEINS THAT INTERACT WITH HUMAN SEPTIN 5

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Septins were first identified in Saccharomyces cerevisae as proteins required for cell cycle completion. Recent works suggest they play a role in vesicle trafficking, oncogenesis, plasma membrane compartmentalization, apoptosis, and neuronal polarity. Furthermore, their presence has been observed in cytoplasmatic inclusion bodies associated with neurodegenerative disorders (Alzheimer's and Parkinson's disease). SEPT5 is predominantly expressed in the brain, where it is associated with vesicles and membranes through its interaction with the syntaxin 1 SNARE domain, and it is also known to bind the sec6/sec8 exocyst complex. Altogether, these findings suggest a regulatory role of SEPT5 in synaptic and non-synaptic exocytosis. Mutations in the parkin gene are known to cause hereditary parkinsonism. SEPT5 has shown to be a parkin substrate, for its interaction and further degradation by the latter. In this work we report the interaction profile of SEPT5 with other proteins. SEPT5 full-length was cloned into vector pBTM116 allowing its expression as a fusion protein with LexA binding domain. It was then used as the bait to screen both human leukocyte and brain fetal cDNA libraries using the yeast two-hybrid system. SEPT5 was shown to interact with: septins 2, 11, 5 itself, and mainly 6 and 8; proteins involved in intracellular trafficking; and proteins from the ubiquitin-dependent degradation system. These interactions were also already confirmed by reporter gene activation tests (ß-galactosidase assay) via yeast co-transformation with each identified gene and parental DNA-BD plasmid. Mapping of SEPT5 interaction with a representative of each group is currently being carried out by pull down.

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