

P012 Molecular interactors influencing APP metabolism
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Amyloid peptide (A β) is derived by proteolytic processing of the amyloid precursor protein (APP). APP is subject to proteolytic cleavage by α -secretase (ADAM10), which occurs within the sequence of A β , thus precluding the peptide formation. Alternatively, APP can be cleaved by β -secretase (BACE) and γ -secretase to generate A β . These two pathways are differentially compartmentalised, therefore the molecular mechanisms regulating APP and secretase's intracellular localisation and trafficking towards neuronal membrane, may be central for Alzheimer Disease pathogenesis.

In this study, we evaluate the interaction between ADAM10 and synapse-associated protein 97 (SAP97). SAP97, a member of membrane-associated guanylate kinase protein family, is involved in the processes of targeting ionotropic glutamate receptors at postsynapse. Confocal microscopy shows that SAP97 and ADAM10 display a high co-localisation pattern in hippocampal neurons. Moreover, both SAP97 and ADAM10 are enriched at the postsynaptic density.

Co-immunoprecipitation experiments, from postsynaptic densities purified from mouse brain tissue, demonstrate that SAP97 interacts with ADAM10. Furthermore, pull down assays reveal that SAP97 interacts with ADAM10 through its SH3 domain, which recognizes proline rich motifs in ADAM10 cytoplasmic tail. These results demonstrate an interaction between ADAM10 and SAP97, which may have a functional implication for the regulation of α -secretase trafficking/activity.