CAP2, a regulator of actin filament dynamic, is a novel ADAM10 interactor

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Alzheimer's disease (AD) is a progressive and neurodegenerative disorder characterized by increased levels of amyloid β-peptides (Aβ) and their deposition as senile plaques. Aβ has been shown to play a central role in AD being responsible for synaptic dysfunction and cognitive deficits. Aβ derives from the Amyloid Precursor Protein (APP), which is sequentially cleaved by the protease vBACE1 and by the γ-secretase to produce Aβ. In the non- amyloidogenic pathway, α-secretase (ADAM10), cleaves APP within the Aβ domain, thus preventing Aβ generation. The correct spatial localization of ADAM10 in the postsynaptic membrane is pivotal for an efficient APP α- secretase cleavage, thus the mechanisms regulating the trafficking of ADAM10 to the synapse play a key role in the modulation of its activity. The results of a yeast two-hybrid screening, carried out using ADAM10 C-terminal tail as a bait, revealed CAP2 as a new ADAM10 binding partner. CAP2 is regulator of actin filament dynamics and could be involved in the modulation of ADAM10 subcellular distribution in neurons. The main aim is to analyse the role of CAP2 in the modulation of ADAM10 localization and activity towards APP in neurons.
Here we confirmed ADAM10-CAP2 interaction by biochemical approaches and we identified the domain responsible for the association. Moreover, we defined the CAP2 sequence involved in actin binding and we analysed the effect of this interaction on ADAM10 synaptic localization.
The characterization of ADAM10-CAP2 complex could favour the development of new experimental approaches to promote ADAM10 neuronal activity thus limiting Aβ generation.