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Caveolin-1 alters the amyloidogenic processing of amyloid precursor protein to amyloid-beta

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Introduction: The 'Amyloid Hypothesis' suggests that the build-up of (Aβ) is a primary causal event in Alzheimer's disease. Aβ is cleaved from amyloid precursor protein (APP) by the β- and γ- secretases, all of which have been identified in lipid raft-regions of the plasma membrane. Caveolae are specialised forms of lipid rafts, enriched with caveolin proteins. We examined whether expression of the most ubiquitous caveolin protein, caveolin-1, could affect the processing of APP into Aβ.

Methods: Levels of caveolin-1 in astrocytoma cells were depleted by siRNA or over-expressed by delivering constructs carrying the myc-tagged caveolin-1 gene to these cells. Cells were lysed and media collected to detect intra- and extracellular protein levels of lipid raft proteins, APP and APP metabolites including Aβ.

Results: After caveolin-1 levels were reduced by siRNA APP levels were unaffected, however, expression levels of Aβ were significantly increased. Conversely, after over-expression of caveolin-1, APP levels were significantly reduced and expression levels of Aβ were unchanged.

Conclusion: These results suggest that at normal physiological levels, caveolin-1 has a regulatory effect on Aβ and may provide a novel therapeutic target for this disease.

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