Myosin V Working Against the Clock: Participation of Myosin Vb in Aß Peptide Endocytosis and Accumulation.

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There is considerable evidence for the involvement of several classes of myosins in the endocytic uptake of extracellular "fluid phase" and ligands. Myosin V is described as essential for transporting cargos in actin-rich cortical regions, dendritic spines and axon terminals. Alzheimer's disease is the commonest neurodegenerative disorder in ageing human populations. The fundamental amyloid hypothesis suggests that the accumulation and deposition of the ß-amyloid peptide (Aß) in the brain precedes and induces the neuronal abnormalities that underlie dementia, driving AD pathogenesis. Recently intraneuronal Aß accumulation has been reported to be critical in synaptic and cognitive dysfunction and the formation of plaques in AD. In order to detect involvement of myosin Vb in that process we investigated the internalization of soluble oligomers, their distribution and their interaction with myosin Vb. Our results show that Aß is internalized in multibody vesicles of cultured retinal neurons after a brief exposure to Aß oligomers, that are soluble and in their most toxic conformational state. Under confocal microscopy the immunostained myosin Vb exhibits a strong co-localization with the vesicles containing Aß. Important findings showing that class V myosins play multiple roles in the trafficking of secretory granules are consistent with our data. We suggest that the disease process in AD result from an imbalance between Aß production and Aß clearance, with an important participation of myosin Vb in this process.

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