Supporting information

Title: Biochemical identification of a linear cholesterol-binding domain within Alzheimer's beta amyloid peptide

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Secondary structure predictions of APP and Aβ. Three distinct predictions methods were used: i) discrimination of secondary structure class DSC (1), ii) multivariate linear regression combiner MLRC (2), and iii) PHD (3). A consensus secondary structure prediction was then deduced from this analysis (**Figure S1**). First we studied the amino acid sequence of APP672-733, a fragment containing the whole TM domain, the extracellular part of APP corresponding to the N-terminal domain of Aβ, and a short cytoplasmic segment. Despite the fact that the TM domain adopts an α-helical structure in a membrane-like environment (15), only one of the three prediction methods (i.e. MLRC) correctly assigned an α-helix for this domain. The consensus prediction indicated that the amino acids of the TM domain have a higher propensity to form a β-strand than an α-helix. This striking property is inherent to the amino acid composition of the TM domain, as shown by the secondary structure predictions of APP700-723 (i.e. the TM domain alone without its flanking domains). Again the MLRC method predicted an α-helix, whereas the two other methods predicted a β-strand. Next we injected the amino acid sequences of Aβ1-40 and Aβ1-42. For Aβ1-40, the initial TM domain of APP (24 amino acids) is shortened to its first 12 amino acids. In this case, even MLRC failed to predict an α-helix structure for these 12-amino acids segment. All three methods converged to propose a high percentage of β-strands and no α-helix for Aβ1-40. Similar results were obtained with Aβ1-42, whose C-terminal domain corresponds to the first 14 amino acids of the TM domain of APP.

Figure S1: Secondary structure predictions of APP and Aβ.
Secondary structure predictions of the indicated fragments of APP and Aβ peptides were performed with the DSC, MLRC, and PHD methods. A consensus prediction based on these three methods is also shown. Symbols: **c**, coil; **e**, beta strand; **h**, alpha helix; **?**, uncertain.

References.

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