S22-1 **Conformational regulation of amyloid b-peptide by lipid membranes and metal ions**

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Conformational transition of monomeric amyloid β-peptide (Aβ) to a self-associated β-sheet structure is considered to be an initial step in the development of Alzheimer's disease. Several lines of evidence suggest that physiologically abundant lipid membranes and metal ions are involved in this step. We have demonstrated that Aβ binds to the phosphatidylcholine membrane in the lamellar gel phase but not in the liquid crystalline phase by using fluorescence and circular dichroism spectroscopy. The membrane-bound Aβ molecule takes α-helical or β-sheet structure depending on the temperature. Tightly packed phosphatidylcholine membranes appear to serve as a platform for non-electrostatic binding and self-association of Aβ. We also examined Zn(II) and Cu(II) binding modes of Aβ by Raman spectroscopy. The Raman spectra demonstrated that three histidine residues in the N-terminal region of Aβ provide primary metal binding sites. Zn(II) binds to the Nτ atom of histidine and the peptide aggregates through intermolecular His-Zn-His bridges. In contrast, Cu(II) ion is chelated by the Nπ atom of histidine and deprotonated main-chain amide nitrogens to form a soluble complex. Our findings on the conformational regulation of Aβ may help in better understanding the molecular basis for the development of Alzheimer's disease.