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PDF文档

淀粉样蛋白Aβ的插膜作用可以抑制其形成纤维

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作为老年性痴呆（AD）患者脑中淀粉样斑块的核心蛋白，β-淀粉样蛋白(Aβ)是从淀粉样前体蛋白（APP）水解而来。该蛋白是多种长度多肽的混合物，其中Aβ40和Aβ42是主要组分。分别研究了膜中胆固醇含量及溶液pH对Aβ40和Aβ42形成纤维的影响。电镜观察发现，含有胆固醇的脂质体几乎可以完全抑制Aβ40的纤维形成，而低pH只能部分地抑制Aβ42的纤维形成。单层膜的实验证明这两种因素都有利于Aβ40和Aβ42的插膜。构象研究表明插膜会诱导Aβ40和Aβ42的二级结构发生不同的变化。结果说明， Aβ40和Aβ42的插膜作用能够在一定程度上抑制蛋白形成纤维，但两者具有不同的抑制机制。

MEMBRANE INSERTION OF Aβ WOULD INDUCE ITS FIBRIL FORMATION

β-Amyloid peptide (Aβ), the core protein of amyloid plaques in Alzheimer's disease, is a mixture of multilength peptides which are all derived from the amyloid precursor protein (APP), and Aβ40 and Aβ42 are the two major components of the mixture. The effects of membrane cholesterol and buffer pH on the fibril formation of Aβ40 and Aβ42 were investigated respectively in this paper. The observation of electronic microscopy showed that cholesterol-containing liposome could nearly completely inhibit the fibril formation of Aβ40, and low pH could partly inhibit the fibrils formation of Aβ42. Monolayer approach showed that Aβ40 and Aβ42 both were inclined to insert into membrane under the two above conditions. Further conformational measurements showed that the membrane insertion had different effects on the secondary structure of Aβ40 and Aβ42. Therefore, the results of this paper indicate that the mechanisms to inhibit the fibril formation of the two proteins are different, while the membrane insertion of Aβ40 or Aβ42 can reduce the fibril formation to a certain extent.

关键词

β淀粉样蛋白(β-Amyloid peptide); 纤维形成(Fibril formation); 脂质体(Liposome); 电镜观察(EM observation); 插膜(Membrane insertion); 圆二色光谱(CD spectra)