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Review [Cell Mol Neurobiol.](#) 2023 Oct;43(7):3115-3136. doi: 10.1007/s10571-023-01365-1.

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Roles of ApoE₄ on the Pathogenesis in Alzheimer's Disease and the Potential Therapeutic Approaches

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Abstract

The Apolipoprotein E ϵ 4 (ApoE ϵ 4) allele, encoding ApoE4, is the strongest genetic risk factor for late-onset Alzheimer's disease (LOAD). Emerging epidemiological evidence indicated that ApoE4 contributes to AD through influencing β -amyloid (A β) deposition and clearance. However, the molecular mechanisms of ApoE4 involved in AD pathogenesis remains unclear. Here, we introduced the structure and functions of ApoE isoforms, and then we reviewed the potential mechanisms of ApoE4 in the AD pathogenesis, including the effect of ApoE4 on A β pathology, and tau phosphorylation, oxidative stress; synaptic function, cholesterol transport, and mitochondrial dysfunction; sleep disturbances and cerebrovascular integrity in the AD brains. Furthermore, we discussed the available strategies for AD treatments that target to ApoE4. In general, this review overviews the potential roles of ApoE4 in the AD development and suggests some therapeutic approaches for AD. ApoE4 is genetic risk of AD. ApoE4 is involved in the AD pathogenesis. A β deposition, NFT, oxidative stress, abnormal cholesterol, mitochondrial dysfunction and neuroinflammation could be observed in the brains with ApoE4. Targeting the interaction of ApoE4 with the AD pathology is available strategy for AD treatments.

Keywords: Alzheimer's disease (AD); Apolipoprotein E4 (ApoE4); Therapy; β -Amyloid (A β).

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Figures

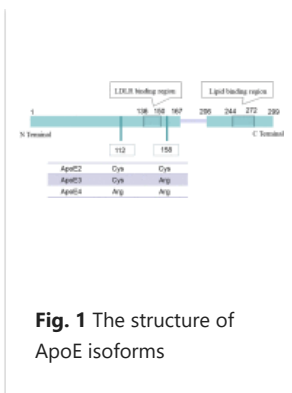


Fig. 1 The structure of ApoE isoforms

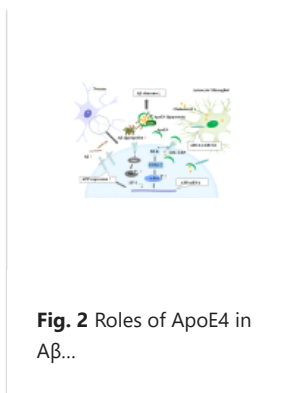


Fig. 2 Roles of ApoE4 in Aβ...



Fig. 3 Roles of ApoE4 in tau...

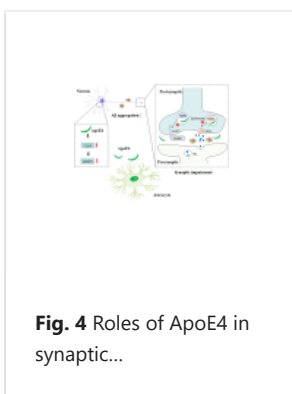


Fig. 4 Roles of ApoE4 in synaptic...



Fig. 5 Regulation of cholesterol in brain...

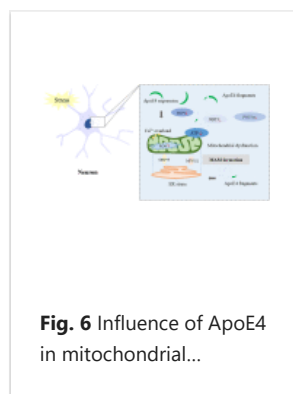


Fig. 6 Influence of ApoE4 in mitochondrial...

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