

An anti-apoE4 specific monoclonal antibody counteracts the pathological effects of apoE4 in vivo

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The pathological hallmarks of Alzheimer's disease (AD), viz defective A β and tau proteins, have been the center of AD-directed therapeutic studies. Although this approach still remains valid, it has not yet produced clinically meaningful results.

This calls for the development of additional approaches and the search for new targets for AD therapy. The allele apoE4 of apolipoprotein E is the most prevalent genetic risk factor of AD. More than half of the AD patients express apoE4, which increases the risk for AD by lowering the age of onset of the disease by 7 to 9 years per allele copy. ApoE4 thus represents an important AD therapeutic target. Previous experiments with mice which express human apoE4 or which have no apoE revealed that the presence of apoE4 can be more pathological than the total absence of apoE.

This suggests that at least some of the pathological effects of apoE4 are due to a "gain of toxic function". In view of this, the present study sets out to explore the possibility that the effects of apoE4 in vivo can be counteracted by treatment with anti-apoE4 mAbs.

Initial proof of concept experiments revealed that brain related effects of apoE4 (e.g., stimulation of the accumulation of brain amyloid-?) can be counteracted by direct injection of the anti-apoE4 mAbs into the brain. Additional experiments revealed that repetitive peripheral

injection of the anti-apoE4 mAb results in the accumulation of these mAbs in the brain and in their binding to apoE4. Importantly, this resulted in reversal of key brain related pathological effects of apoE4 and of the associated cognitive deficits.

These results provide a proof-of-concept that immunotherapy based on peripheral i.p. injection of an anti-apoE4 mAb to apoE4 mice protects the mice against the cognitive and [brain](#)-related pathological effects of apoE4, and suggests that such an approach could also benefit human apoE4 carriers.

More information: Ishai Luz et al, An Anti-apoE4 Specific Monoclonal Antibody Counteracts the Pathological Effects of apoE4 In Vivo, *Current Alzheimer Research* (2016). [DOI: 10.2174/1567205013666160404120817](#)

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