MedicalXpress

Engineered mice provide insight into Alzheimer's disease

January 17 2008

One factor that determines how at risk an individual is of developing late-onset Alzheimer disease (AD) is the version of the APOE gene that they carry — those carrying the gene that enables them to make the apoE4 form of the apoE protein are at increased risk and those carrying the gene that enables them to make the apoE2 form are at decreased risk.

It has been hypothesized that increasing the amount of lipid (fat) associated with apoE by overexpressing the protein ABCA1 might decrease amyloid deposition in the brain, the hallmark of AD. Evidence to support this hypothesis has now been generated in mice by David Holtzman and colleagues at Washington University School of Medicine, St Louis.

In this study, mice that provide a model of AD (PDAPP mice) were engineered to overexpress the protein ABCA1 in the brain. These mice had characteristics almost identical to PDAPP mice lacking apoE — they had decreased amyloid deposition in the brain compared with normal PDAPP mice.

As the PDAPP mice overexpressing ABCA1 in the brain were shown to have increased amounts of lipid associated with apoE, the authors concluded the hypothesis that an ABCA1-mediated increase in the amount of lipid associated with apoE would decrease amyloid deposition in the brain was correct. Furthermore, they suggested that approaches to increase the function of ABCA1 in the brain might be of benefit to individuals with, or at risk of developing, AD.

Source: Journal of Clinical Investigation