APOE – APOLIPOPROTEIN E GENE
Healthcare Professional Information

The APOE gene and Alzheimer Disease

Alzheimer disease (AD) is a common type of dementia. The most common form of the disease, called Late-Onset Alzheimer Disease, usually starts after age 60. By 85 years old, nearly 1 in 3 adults will likely have AD.[1] Late-Onset AD is generally understood to be caused by a combination of genetic, environmental, and lifestyle factors. One well known genetic risk factor for late-onset AD is a gene called apolipoprotein E or APOE. APOE protein is involved in transporting cholesterol to neurons, which is crucial for synaptic formation, axonal growth, learning, memory, and neuronal injury repair. The APOE protein is hypothesized to affect AD pathogenesis through a variety of mechanisms, from its effects on the blood brain barrier, the innate immune system, synaptic function, to the accumulation of amyloid-β (Aβ).

The brains of AD patients frequently show abnormal clusters of a protein called amyloid-β (Aβ); these clusters are known as plaques. ApoE is a protein involved in the break-up of plaques that form in the brain.[2,3] Normal apoE protein breaks these plaques down, however when a person has a form of the apoE protein that is mutated, then it cannot remove these plaques effectively. Of the known alleles for this gene, one variant (ApoE4) increases Alzheimer's severity and risk, while the ApoE2 allele is protective.[4] In addition, the APOE genotype presents an allelic dosage effect whereby the E4/E4 allele is associated with the highest risk followed by E3/E3 and E2/E25.

- ApoE-E2 results in increased expression of ApoE which increases break down of Aβ plaques4. Studies indicate that people with this variant are at reduced risk for developing AD.
- ApoE-E3 results in normal expression of ApoE and studies indicate that people with this variant are at no additional risk for developing AD.
- ApoE-E4 results in lower expression of ApoE which decreases break down of Aβ plaques.[4] Studies indicate that people with this variant are at increased risk for developing AD.[5,6,7]

APOE does not cause AD, but is known to influence the likelihood of occurrence. However, the E4 variant may affect people differently, making it impossible to give an accurate risk assessment for AD based only on an APOE result. It is important to understand that carrying the risk allele does not mean that a person will develop AD. Genetic testing alone is not predictive of AD because there are significant health and environmental factors that overlay genetic disposition. Genetic test results should be interpreted in the light of other considerations such as environmental factors, ethnicity, nutrition, and other conditions.

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