APOE Gene

Subjects: Genetics & Heredity
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Apolipoprotein E

genes

1. Normal Function

The *APOE* gene provides instructions for making a protein called apolipoprotein E. This protein combines with fats (lipids) in the body to form molecules called lipoproteins. Lipoproteins are responsible for packaging cholesterol and other fats and carrying them through the bloodstream. Maintaining normal levels of cholesterol is essential for the prevention of disorders that affect the heart and blood vessels (cardiovascular diseases), including heart attack and stroke.

There are at least three slightly different versions (alleles) of the *APOE* gene. The major alleles are called e2, e3, and e4. The most common allele is e3, which is found in more than half of the general population.

2. Health Conditions Related to Genetic Changes

2.1. Alzheimer disease

The e4 version of the *APOE* gene increases an individual's risk for developing late-onset Alzheimer disease. Alzheimer disease is a degenerative disease of the brain that causes dementia, which is a gradual loss of memory, judgment, and ability to function. The late-onset form of the condition occurs in people older than age 65. People who inherit one copy of the *APOE* e4 allele have an increased chance of developing the disease; those who inherit two copies of the allele are at even greater risk. The *APOE* e4 allele may also be associated with an earlier onset of memory loss and other symptoms compared to individuals with Alzheimer disease who do not have this allele.

It is not known how the *APOE* e4 allele is related to the risk of Alzheimer disease. However, researchers have found that this allele is associated with an increased number of protein clumps, called amyloid plaques, in the brain tissue of affected people. A buildup of amyloid plaques may lead to the death of nerve cells (neurons) and the progressive signs and symptoms of this disorder.

It is important to note that people with the *APOE* e4 allele inherit an increased risk of developing Alzheimer disease, not the disease itself. Not all people with Alzheimer disease have the *APOE* e4 allele, and not all people

who have this allele will develop the disease.

2.2. Age-related hearing loss

2.3. Age-related macular degeneration

2.4. Dementia with Lewy bodies

The e4 version of the *APOE* gene can increase the risk of developing a form of dementia called dementia with Lewy bodies; however, some people with the *APOE* e4 allele never develop this condition. Dementia with Lewy bodies is characterized by intellectual decline; visual hallucinations; sudden changes in attention and mood; and movement problems characteristic of Parkinson disease such as rigidity of limbs, tremors, and impaired balance and coordination.

People who inherit one copy of the *APOE* e4 allele have an increased chance of developing dementia with Lewy bodies. It is unclear how the *APOE* e4 allele contributes to the development of this condition. It is thought that the apolipoprotein E produced from the e4 allele of the *APOE* gene may disrupt the transport of a protein called alpha-synuclein into and out of cells. When alpha-synuclein is trapped inside or outside of cells, it accumulates in clusters, creating Lewy bodies. Accumulation of these clusters throughout the brain impairs neuron function and ultimately causes cell death. Over time, the loss of neurons increasingly impairs intellectual and motor function and the regulation of emotions, resulting in the signs and symptoms of dementia with Lewy bodies.

It is unclear why some people with the *APOE* e4 allele develop Alzheimer disease while others develop dementia with Lewy bodies.

2.5. Other disorders

Variants of apolipoprotein E have been studied extensively as risk factors for many different conditions. For example, *APOE* alleles have been shown to influence the risk of cardiovascular diseases. People who carry at least one copy of the *APOE* e4 allele have an increased chance of developing atherosclerosis, which is an accumulation of fatty deposits and scar-like tissue in the lining of the arteries. This progressive narrowing of the arteries increases the risk of heart attack and stroke.

The *APOE* e2 allele has been shown to greatly increase the risk of a rare condition called hyperlipoproteinemia type III. Most people with this disorder have two copies of the *APOE* e2 allele, leading researchers to conclude that the e2 allele plays a critical role in the development of the condition. Hyperlipoproteinemia type III is characterized by increased blood levels of cholesterol, certain fats called triglycerides, and molecules called beta-very low-density lipoproteins (beta-VLDLs), which carry cholesterol and lipoproteins in the bloodstream. A buildup of cholesterol and other fatty materials can lead to the formation of small, yellow skin growths called xanthomas and the development of atherosclerosis.

3. Other Names for This Gene

- Apo-E
- APOE_HUMAN
- Apolipoproteins E

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