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Alzheimer's Disease Genetics Fact Sheet

Many people wonder if Alzheimer's disease runs in the family. A person's chance of having the disease may be higher if he or she has certain genes passed down from a parent. However, having a parent with Alzheimer's does not always mean that someone will develop it.

What Are Genes?

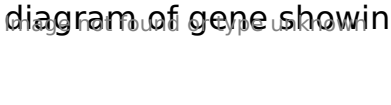

diagram of gene showing cell, chromosome, and DNA

Each human cell contains the instructions a cell needs to do its job. These instructions are made up of DNA (deoxyribonucleic acid), which is packed tightly into structures called chromosomes. Each chromosome has thousands of segments called genes.

Genes are passed down from a person's biological parents. They carry information that defines traits such as eye color and height. Genes also play a role in keeping the body's cells healthy.

Problems with genes—even small changes to a gene—can cause diseases like Alzheimer's.

Do Genes Cause Diseases?

Genetic mutations (permanent change in one or more specific genes) can cause diseases. If a person inherits a genetic mutation that causes a certain disease, then he or she will usually get the disease. Sickle cell anemia, cystic fibrosis, and some cases of early-onset Alzheimer's disease are examples of inherited genetic disorders.

Other changes or differences in genes, called **genetic variants,** may increase or decrease a person's risk of developing a particular disease. When a genetic variant increases disease risk but does not directly cause a disease, it is called a **genetic risk factor**.

Identifying genetic variants may help researchers find the most effective ways to treat or prevent diseases such as Alzheimer's in an individual. This approach, called precision medicine, takes into account individual variability in genes, environment, and lifestyle for each person.

The expression of genes—when they are “switched” on or off—can be affected, positively and negatively, by environmental and lifestyle factors, such as exercise, diet, chemicals, or smoking. The field of epigenetics is studying how such factors can alter a cell's DNA in ways that affect gene activity.

Genes and Alzheimer's Disease

There are two types of Alzheimer's—early-onset and late-onset. Both types have a genetic component.

Late-Onset Alzheimer's Disease

Alzheimer's genetics infographic

Share this infographic and help spread the word about Alzheimer's genetics.

Most people with Alzheimer's have the late-onset form of the disease, in which symptoms become apparent in their mid-60s and later.

Researchers have not found a specific gene that directly causes late-onset Alzheimer's disease. However, having a genetic variant of the apolipoprotein E *(APOE)* gene on chromosome 19 does increase a person's risk. The *APOE* gene is involved in making a protein that helps carry cholesterol and other types of fat in the bloodstream.

APOE comes in several different forms, or alleles. Each person inherits two *APOE* alleles, one from each biological parent.

- APOE ε2 is relatively rare and may provide some protection against the disease. If Alzheimer's disease occurs in a person with this allele, it usually

develops later in life than it would in someone with the APOE ε4 gene.
- APOE ε3, the most common allele, is believed to play a neutral role in the disease—neither decreasing nor increasing risk.
- APOE ε4 increases risk for Alzheimer's disease and is also associated with an earlier age of disease onset. Having one or two APOE ε4 alleles increases the risk of developing Alzheimer's. About 25 percent of people carry one copy of APOE ε4, and 2 to 3 percent carry two copies.

APOE ε4 is called a risk-factor gene because it increases a person's risk of developing the disease. However, inheriting an APOE ε4 allele does not mean that a person will definitely develop Alzheimer's. Some people with an APOE ε4 allele never get the disease, and others who develop Alzheimer's do not have any APOE ε4 alleles.

Recent research indicates that rare forms of the APOE allele may provide protection against Alzheimer’s disease. More studies are needed to determine how these variations might delay disease onset or lower a person’s risk.

Early-Onset Alzheimer's Disease

Early-onset Alzheimer’s disease is rare, representing less than 10 percent of all people with Alzheimer’s. It typically occurs between a person’s 30s and mid-60s. Some cases are caused by an inherited change in one of three genes.

The three single-gene mutations associated with early-onset Alzheimer’s disease are:

- Amyloid precursor protein (APP) on chromosome 21
- Presenilin 1 (PSEN1) on chromosome 14
- Presenilin 2 (PSEN2) on chromosome 1

Mutations in these genes result in the production of abnormal proteins that are associated with the disease. Each of these mutations plays a role in the breakdown of APP, a protein whose precise function is not yet fully understood. This breakdown is part of a process that generates harmful forms of amyloid plaques, a hallmark of Alzheimer’s disease.

A child whose biological mother or father carries a genetic mutation for one of these three genes has a 50/50 chance of inheriting that mutation. If the mutation is in fact

inherited, the child has a very strong probability of developing early-onset Alzheimer’s disease.

For other cases of early-onset Alzheimer’s, research has shown that other genetic components are involved. Studies are ongoing to identify additional genetic risk variants.

Having Down syndrome increases the risk of developing early-onset Alzheimer’s disease. Many people with Down syndrome develop Alzheimer’s as they get older, with symptoms appearing in their 50s or 60s. Researchers believe this is because people with Down syndrome are born with an extra copy of chromosome 21, which carries the APP gene.

For more information, see NIA's Early-Onset Alzheimer's Disease: A Resource List

Genetic Testing for Alzheimer's Disease

A blood test can identify which APOE alleles a person has, but results cannot predict who will or will not develop Alzheimer's disease. Currently, APOE testing is used primarily in research settings to identify study participants who may have an increased risk of developing Alzheimer's. This knowledge helps scientists look for early brain changes in participants and compare the effectiveness of possible treatments for people with different APOE profiles.

Genetic testing is also used by physicians to help diagnose early-onset Alzheimer’s disease and to test people with a strong family history of Alzheimer’s or a related brain disease.

Genetic testing for APOE or other genetic variants cannot determine an individual’s likelihood of developing Alzheimer’s disease—just which risk factor genes a person has. It is unlikely that genetic testing will ever be able to predict the disease with 100 percent accuracy, researchers believe, because too many other factors may influence its development and progression.

Some people learn their APOE status through consumer genetic testing or think about getting this kind of test. They may wish to consult a doctor or genetic counselor to better understand this type of test and their test results.

For More Information About Alzheimer's Disease Genetics

NIA Alzheimer's and related Dementias Education and Referral (ADEAR) Center

800-438-4380 (toll-free)

www.nia.nih.gov/alzheimers

The National Institute on Aging's ADEAR Center offers information and free print publications about Alzheimer's disease and related dementias for families, caregivers, and health professionals. ADEAR Center staff answer telephone, email, and written requests and make referrals to local and national resources.

National Human Genome Research Institute

www.genome.gov/health

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