Alzheimer's Disease: Unraveling the Mystery

Genetics

All living things are made up of basic units called cells, which are so tiny that you can only see them through the lens of a strong microscope. Most of the billions of cells in the human body have one nucleus containing a thread-like structure called a chromosome. Every chromosome contains genes that control the function of all the living things. Genes alone are not all-powerful. They operate in concert with other substances. Although they can use them to do things, like play the piano. They can make proteins, which are the building blocks of proteins. A gene is a thread-like structure found in the cell’s nucleus, which can carry hundreds, sometimes thousands, of genes. In humans, each of our 23 pairs of chromosomes is inherited from each parent. The genetic material on each chromosome is a strand of DNA. It is this strand of DNA that determines eye and hair color, and repair of all living things. Proteins are essential building blocks in all cells. Bones and teeth, muscle and blood, for example, are formed from different proteins. They help incorporate different materials in the body to stay healthy. Amino acids are the building blocks of proteins. A gene provides the code, or blueprint, for the type and order of amino acids needed to build a specific protein. Sometimes a genetic mutation (or defect in a gene) can occur, leading to the production of a faulty protein. Faulty proteins can cause cell malfunction and disease. Scientists are studying genes to learn more about the proteins they make and what these proteins actually do in the body. They also hope to discover what diseases are caused when there are problems with their work. The Genetics of Alzheimer’s Disease

Diseases such as cystic fibrosis, muscular dystrophy, and Huntington’s disease are single-gene disorders. If a person has a mutation in the gene that causes one of these disorders, he or she will usually get the disease. AD, on the other hand, is not caused by a single gene. More than one gene may be involved, and combinations of multiple genes are involved.

The two types of AD are early-onset and late-onset, depending on whether the disease starts before or after the age of 65. Early-onset AD (under the age of 65) is rare, and this form of the disease is associated with genes in different forms of chromosomes. Many of the genes that cause AD are genes by mutation on chromosomes 1, 19. This gene codes for a protein that helps carry cholesterol in the bloodstream. The APOE gene comes in several different forms, called alleles, but three occur most frequently: APOE ε2, ε3, and ε4. People inherit one APOE allele from each parent. Having one or two copies of the ε4 allele increases a person’s risk of getting AD. That is, the rarer the allele is a risk factor for AD, but it doesn’t work right. Diseases such as cystic fibrosis, muscular dystrophy, and Huntington’s disease are single-gene disorders. If a person has a mutation in the gene that causes one of these disorders, he or she will usually get the disease. AD, on the other hand, is not caused by a single gene. More than one gene may be involved, and combinations of multiple genes are involved.

The Genetics of Alzheimer’s Disease

Genes in Late-onset Disease

The majority of AD cases are late-onset, usually developing after age 65. Late-onset AD has no known cause and shows no obvious inherited patterns. Scientists, families, clusters of cases are seen. Although a specific gene has not been identified as the cause of late-onset AD, genetic factors appear to play a role in the development of this form of AD. One genetic factor that has been identified is the APOE ε4 allele. Researchers have identified an increased risk of developing late-onset AD related to APOE ε4 allele. APOE ε4 allele is a risk factor gene for late-onset AD. Shortly after the teens, AD is certain. Some people with two copies of the ε4 allele (the highest risk group) do not develop clinical signs of Alzheimer’s disease, while others with no ε4 do. The ε4 allele is the most common form found in the general population. The ε2 allele is associated with a lower risk of AD. The exact degree of risk of AD in a person cannot be determined based on APOE ε4 allele carriers. The APOE ε4 allele is a risk factor gene for late-onset AD. However, the relationship between the APOE ε4 allele and late-onset AD is complex.

The National Institute on Aging (NIA) has launched a major study to discover remaining genetic risk factors for AD. In a research setting, APOE testing may be used to identify individuals who may be used to identify study measures may never be able to predict AD with 100 percent accuracy. In a research setting, APOE testing may be used to identify Study measures may never be able to predict AD with 100 percent accuracy. In a research setting, APOE testing may be used to identify individuals who may be used to identify study measures may never be able to predict AD with 100 percent accuracy.
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All living things are made up of basic units called cells, which are so small they can only be seen through a microscope. All cells in the human body have one nucleus, the central control center. Genes are the basic units of the nucleus. A gene is like an instruction found in the cell's nucleus, which can carry hundreds, sometimes thousands, of genes. In humans, each of one pair of 23 chromosomes is inherited from each parent. The genetic material on each chromosome is made up of genes. Scientists believe that there are about 30,000 genes in the human genome. Genes direct almost every aspect of the construction, operation, and performance of all living things. For example, genes contain information that determines eye and hair color, and the blood type that is inherited from our parents. In addition, genes ensure that we have two hands and can use them to do things, like play a piano. Genes alone are not all-powerful. Most genes can do little or nothing on their own. But when our bodies grow, work properly, and our bodies grow, work properly, and stay healthy. Amino acids are the essential building blocks of proteins. A gene provides the code, or blueprint, for the types and order of amino acids needed to build a specific protein.

Proteins are essential building blocks in all cells. Bones and teeth, muscles and blood, and every other tissue are formed from different proteins. They help make up the shape of cells and keep the cells from falling apart. Proteins are also essential in each cell's structure. For example, the muscles that make up your body are made up of proteins. They give the muscles the ability to make muscle movements. When growth becomes slow or stops, the protein provides the cell with instructions for building a specific protein.

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The majority of AD cases are late-onset, usually developing after age 65. Late-onset AD has its known cause and shows no obvious inherit- ance pattern. Most people in families, clusters of cases are seen. Although a specific gene has not been identified as the cause of late-onset AD, genetic factors do appear to play a role in the development of this form of AD. Genetic factors, or gene mutations, have been identified as causes of early-onset AD. Genes are single-gene disorders. If a person inherits a gene that causes one of these disorders, he or she will usually get the disease. AD, on the other hand, is not caused by a single gene. More than one mutation protective gene and others with no risk. The ε4 allele is the most common form found in the general population of AD patients. It is a neutral role in AD. The rarer ε2 allele appears to be a lower risk of AD. The exact degree of risk for AD is not determined on APOE status. Therefore, the APOE ε4 allele is a risk factor gene for late-onset AD.

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Researchers have identified an increased risk of developing late-onset AD related to the APOE ε4 allele (APOE gene found on chromosome 19). APOE ε4 allele is a risk factor for late-onset AD. People inherit one APOE allele from each parent. Having one or two copies of the ε4 allele increases a person’s risk of getting AD. That is, having the ε4 allele is a risk factor for AD, but it doesn’t mean that people with the ε4 allele will get AD. Some people have two copies of the ε4 allele, but very few of these people develop AD. In fact, a person with two copies of the ε4 allele is 12 times more likely to develop AD than someone with no copies of the ε4 allele. The ε2 allele is the most common form found in the general population of AD patients. It has a neutral role in AD. The rarer ε2 allele appears to be a lower risk of AD. The exact degree of risk for AD is not determined on APOE status. Therefore, the APOE ε4 allele is a risk factor gene for late-onset AD.

The American Federation for Aging Research, the National Institute on Aging, the Alzheimer’s Association, and the Alzheimer’s Disease Education and Referral (ADEAR) Center are working to collect genetic samples from families affected by multiple cases of late-onset AD. Researchers are seeking large families with two or more living relatives with late-onset AD. Family members interested in participating in this study can contact the Alzheimer’s Disease at 1-800-536-2839. Information may also be obtained through their website, http://nctr.uic.edu.

APOE Testing in Research or Diagnosis

A blood test is available that can identify which APOE alleles a person has. However, because the APOE ε4 allele is only a risk factor for AD, this blood test cannot tell whether a person will develop AD or not.

Instead of a yes or no answer, the best information a person can get from this genetic test is that he or she may be at the risk of AD for any given person. The exact degree of risk for AD is not yet possible. In fact, some researchers believe that APOE status may be used to identify study participants. APOE status may be used to identify study participants. APOE status may be used to identify study participants. APOE status may be used to identify study participants. APOE status may be used to identify study participants. APOE status may be used to identify study participants. APOE status may be used to identify study participants.
Alzheimer's Disease

Genetics

Fact Sheet

Scientists do not yet fully understand what causes Alzheimer's disease (AD). However, the more they learn about AD, the more they know that genes play an important role in the development of this devastating disease.

Genes

All living things are made up of basic units called cells, which are so small you can only see them with a microscope. The cells in the human body have one nucleus that acts as a control center, housing the human genome. Genes are the units of information that determine our traits and behaviors. These units are basically waiting inside the cell's nucleus, and are inherited from our parents. In addition, genes ensure that we have two hands and two legs, and that we have the correct color and other traits inherited from our ancestors.

Genes alone are not all-powerful. They basically wait inside the cell's nucleus—basically like the instructions for building a specific protein. Amino acids are the building blocks of proteins. A gene provides the code, or blueprint, for the type and order of amino acids needed to build a specific protein. Proteins are essential building blocks in all cells. Bones and teeth, muscles and brain cells, are formed from different proteins. They help move our bodies and keep us healthy. Amino acids are the building blocks of proteins. A gene provides the code, or blueprint, for the type and order of amino acids needed to build a specific protein.

Sometimes a genetic mutation (or defect in a gene) can occur, leading to the production of a faulty protein. Faulty proteins can cause cell malfunctions and development of a disease.

Scientists are studying genes to learn more about the proteins they make and what these proteins actually do in the body. They also hope to discover what diseases are caused when their proteins don’t work right.

The Genetics of Alzheimer's Disease

Diseases such as cystic fibrosis, muscular dystrophy, and Huntington's disease are single-gene disorders. If a parent has the mutated gene that causes one of these disorders, he or she will usually get the disease. AD, on the other hand, is not caused by a single gene. More than one mutation probably acts together in multiple chromosomes to cause Alzheimer's disease.

The two types of AD are early onset and late onset. Determining whether the disease starts before or after the age of 65 can be a key factor. If more than 10 percent of AD is early-onset, and this form of the disease is more common in some families. Many forms of early-onset AD are caused by gene mutations on chromosomes 1, 14, or 21. Like the other diseases mentioned above, even if only one of these chromosomes is involved, the person is a parent, the person will usually develop early-onset AD. This fact alone is referred to as autosomal dominant inheritance: all children have a 50/50 chance of developing early-onset AD if one of their parents had it.

Genes in Late-onset Disease

The majority of AD cases are late-onset, usually developing after age 65. Late-onset AD has no known cause and shows no obvious inheritance pattern. People in families, clusters of cases are seen. Although a specific gene has not been identified as the cause of late-onset AD, genetic factors do appear to play a role in the development of this form of AD. One genetic factor gene has been identified as key.

Researchers have identified an increased risk of developing late-onset AD related to several factors. They think that adding additional risk factors for late-onset AD may play a role in regions of chromosomes 9, 10, and 12.

The National Institute on Aging (NIA) has launched a project to discover remaining genetic risk factors for late-onset AD. People inherit one APOE allele from each parent. Having one or two copies of the allele increases a person’s risk of getting AD. That is, the APOE ε4 allele is a risk factor for AD, but it doesn’t work right.

APOE Testing in Research or Diagnosis

A blood test is available that can identify which APOE alleles a person has. However, because the APOE ε4 allele is only a risk factor for AD, this blood test cannot tell whether a person will develop AD or not. Instead of a yes or no answer, the best information a person can get from this genetic test is their risk group. Risk group may play a role in regions of chromosomes 9, 10, and 12.

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Proteins are essential building blocks in all cells. Bones and teeth, muscles and hair, virtually all body parts, are formed from different proteins. They help move, grow, and repair; they make the body function and stay healthy. Amino acids are the building blocks of proteins. A gene provides the code, or blueprint, for the type and order of amino acids needed to build a specific protein. Sometimes a genetic mutation (or defect in a gene) can occur, leading to the production of faulty proteins. Faulty proteins can cause cell malfunction and disease.

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The two types of AD are early onset and late onset. Researchers are looking at whether the disease starts before or after the age of 65. Early-onset AD is caused by a single gene, and this form of the disease is rare. Many forms of late-onset AD are caused by gene mutations on chromosomes 1, 19. This gene codes for a protein that helps carry cholesterol in the bloodstream. The APOE gene comes in several different versions, or alleles, but three occur most frequently: APOE ε2, ε3, and ε4. People inherit one APOE allele from each parent. Having one or two copies of the ε4 allele increases a person’s risk of getting AD. That is, the ε4 allele is a risk factor for AD, but it doesn’t work right.

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volunteers who may be at a higher risk of getting AD. In this case, research- ers can find early brain changes and events. However, this process also helps researchers compare the affects of various treatment options with different APOE profiles.

Conducting research in this way is useful for studying AD in large groups of people but not for determining one person's individ- ual risk. Predictive screening in oth- erwise healthy people will be useful if an accelerable test is developed that can predict the development of AD based on the presence or treat present, and the opportunity to learn the results of APoE testing is appropriate in this setting.

A possible way for AD patients and their families to learn more about the genetics of AD is to participate in a genetic counseling session. Genetic counseling is a genetic information and counseling process for which we have few answers. Generally, confidentiality laws protect APOE information and discrimination about the appropriate use of genetic testing and counseling for AD.

For More Information

Access current, accurate information about AD and its risk factors is important to patients and their families, health professionals, and the public. The Alzheimer’s Disease Education and Referral (ADEAR) Center is a service of the National Institute on Aging (NIA) and is funded by the Federal Government. The ADEAR Center offers answers to questions about treatment, patient care, caregiver needs, information about diagnosis and staging, and AD research. Staff re- spond to telephone, e-mail, and written requests and make referrals to local and national resources. Contact:

AD and Family Support Center
1-800-438-4380
Fax: 301-495-3334
E-mail: info@alz.org
Website: www.alz.org

Additional information is available from the National Institute on Aging (NIA) and the Alzheimer’s Disease Education and Referral (ADEAR) Center at: www.alz.org or www.nia.nih.gov/alzheimers

Key Terms

Genes – DNA segments that carry specific instructions that tell a cell how to assemble one of its proteins. Proteins are essential to all life processes. They can have many functions, including the physical and chemical characteris- tics of cells and therefore organisms. Proteins determine the physical appearance and functioning of an organism.

Terminology

Familial AD: AD with a genetic basis, occurring in members of the same family who have an increased risk of getting the disease. Familial AD is also called genetic or hereditary AD.

Subjective Memory: An individual’s perception of memory loss, which may or may not be associated with memory loss determined by cognitive testing.

AD: Alzheimer’s disease is a progressive, fatal brain disorder that slowly destroys memory and cognitive function. People with AD lose the ability to think, reason, learn, communicate, and make judgments. They may also lose the ability to perform simple tasks such as dressing and cooking. In the later stages, AD causes physical impairment, such as bladder control and mobility, and the individual loses all mental functions.

Genesis – basis, units of heredity that direct

Adherence – behavior that is intended to align with a person's belief system. Adherence to treatment is a characteristic of health behavior. It is often measured in terms of the degree of compliance with prescribed treatment instructions or medications.

The National Library of Medicine’s Genetics Home Reference also maintains genetic information on the human genome. For More Information, contact:

NIH Publication No. 03-3431
August 2004

Almost every aspect of the construction, function, and regulation of organisms is controlled by the 35,000 genes. Each gene is a segment of biochemical instruc- tion that codes for a protein or produces a function that affects many different processes. Each protein has its own specific function and can be studied at the cellular, tissue, organ, or whole organism levels. The study of the human genome is essential to the understanding of the mechanisms of all disease processes.
volunteers who may be at a higher risk of getting AD. In this case, researchers can look for early brain changes indicative of AD, and neuropsychological testing also helps researchers compare the affected volunteers with control group volunteers. APOE testing may be used in combination with other diagnostic tests and treatments.

In diagnosing AD, APOE testing is not a common practice. The only situations in which APOE testing is used are those in which practitioners are looking by viewing a sample of a person’s brain tissue under a microscope to determine if a brain tissue abnormality is present. In other cases, APOE testing may be used in combination with other diagnostic tests and treatments.

Researchers are looking for ways to develop an accurate/reliable test is developed for determining one person’s individual risk of getting AD. If no other cause is identified, a diagnosis of AD is made. If a cause other than AD is found, a diagnosis of that condition is made.

Researchers are looking for ways to develop an accurate/intensive method is not recommended. APOE testing may be used in combination with other diagnostic tests and treatments.

Doctors look to diagnose AD correctly up to 90 percent of the time. Currently, there is no sure way to confirm a diagnosis of AD in a person without the symptoms of the disease. Tests, including a medical history, laboratory tests, neuropsychological tests, and a complete medical evaluation (including a tissue sample taken from a person's brain following death), help doctors create a family history. Search their records to see if other family members have the disease. The NIGMS does not provide information about specific genetic counseling services. Genetic Counseling

According to the National Society for Genetic Counseling, AD is one of the most common genetic disorders. The National Society for Genetic Counseling (NSGC) can provide a list of genetic counselors in your area. NSGC offers information about diagnosis, counseling, and treatment. People who learn through testing that they have the option of learning more about the role of genes in AD may experience emotional distress and anxiety. People with a family history of AD are at increased risk for developing the disease. Counseling through genetic counselors can help people understand the genetics of AD, the tests themselves, and potential treatment options. Due to privacy, emotional, and health care issues, the primary goal of genetic counseling is to help people explore and cope with the potential consequences of the results. Genetic Counseling

Modifying lifestyle such as through exercise, weight loss, and stopping smoking may help slow the progression of AD. Genetic counseling is to help people understand the genetics of AD, the tests themselves, and potential treatment options. Due to privacy, emotional, and health care issues, the primary goal of genetic counseling is to help people explore and cope with the potential consequences of the results.
volunteers who may be at a higher risk of getting AID. In this way, researchers can find out what early signs, if any, people who developed AD had. This research also helps researchers compare the affected individual's medical and treatment data with different APOE profiles. Many researchers believe that this is a good tool for the opportunity to learn the results of early-onset familial AD. The NIA or NINDS can provide information about the development of AD. Updated information can be found on the NIA’s website.


The National Library of Medicine's National Center for Biotechnology Information also maintains genetic information on the human genome. Additional information is available from the National Institute on Aging (NIA) and the Alzheimer's Association (NHI, NRC) at the N.I.H. Visit the Alzheimer’s Association website at www.alz.org.