

ACE Gene

Subjects: Genetics & Heredity

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angiotensin I converting enzyme

Keywords: genes

1. Normal Function

The *ACE* gene provides instructions for making the angiotensin-converting enzyme. This enzyme is able to cut (cleave) proteins. It is part of the renin-angiotensin system, which regulates blood pressure and the balance of fluids and salts in the body. By cutting a protein called angiotensin I at a particular location, the angiotensin-converting enzyme converts this protein to angiotensin II. Angiotensin II causes blood vessels to narrow (constrict), which results in increased blood pressure. This protein also stimulates production of the hormone aldosterone, which triggers the absorption of salt and water by the kidneys. The increased amount of fluid in the body also increases blood pressure. Proper blood pressure during fetal growth, which delivers oxygen to the developing tissues, is required for normal development of the kidneys, particularly of structures called the proximal tubules, and other tissues. In addition, angiotensin II may play a more direct role in kidney development, perhaps by affecting growth factors involved in the development of kidney structures.

The angiotensin-converting enzyme can cleave other proteins, including bradykinin. Bradykinin causes blood vessels to widen (dilate), which decreases blood pressure. Cleavage by the angiotensin-converting enzyme inactivates bradykinin, helping to increase blood pressure.

2. Health Conditions Related to Genetic Changes

2.1 Renal tubular dysgenesis

Mutations in the *ACE* gene are the most common cause of a severe kidney disorder called renal tubular dysgenesis; at least 33 *ACE* gene mutations have been found in people with this disorder. Renal tubular dysgenesis is characterized by abnormal kidney development before birth, the inability to produce urine (anuria), and severe low blood pressure (hypotension). These problems result in a reduction of amniotic fluid (oligohydramnios), which leads to a set of birth defects known as the Potter sequence.

Renal tubular dysgenesis can be caused by mutations in both copies of any of the genes involved in the renin-angiotensin system. The *ACE* gene mutations that cause this disorder prevent the production of functional angiotensin-converting enzyme, which impairs the formation of angiotensin II and results in a nonfunctional renin-angiotensin system. Without this system, the kidneys cannot control blood pressure. Because of low blood pressure, the flow of blood is reduced (hypoperfusion), and the body does not get enough oxygen during fetal development. As a result, kidney development is impaired, leading to the features of renal tubular dysgenesis.

2.2 Other disorders

A certain variation in the *ACE* gene has been associated with increased risk of several conditions, including stroke and complications of diabetes. This genetic variation, called the *ACE* I/D polymorphism, involves a region of DNA that spans 287 DNA building blocks (nucleotides). One variant of the *ACE* gene includes this region; it is called the insertion, or I, allele. Another variant is missing this region of DNA and is called the deletion, or D, allele. Because people have two copies of each gene, each individual can have two I alleles (II), two D alleles (DD), or one allele of each (ID). The DD pattern is associated with higher levels of angiotensin-converting enzyme than the II pattern. The ID pattern is associated with intermediate levels.

People with the DD pattern of alleles have an increased risk of stroke. Stroke can be caused by a lack of blood flow to the brain (ischemic stroke) or bleeding in the brain (hemorrhagic stroke or intracerebral hemorrhage). Susceptibility to both types is associated with the *ACE* gene variation. However, many genetic and environmental risk factors likely contribute to this complex condition.

In people with type 1 or type 2 diabetes, the DD pattern of alleles is associated with an increased risk of developing a kidney disorder called diabetic nephropathy. Damage to the kidneys caused by this condition worsens over time and can lead to kidney failure.

3 Other Names for This Gene

- ACE1
- ACE_HUMAN
- angiotensin converting enzyme, somatic isoform
- angiotensin I converting enzyme (peptidyl-dipeptidase A) 1
- angiotensin I converting enzyme peptidyl-dipeptidase A 1 transcript
- angiotensin-converting enzyme
- CD143
- CD143 antigen
- DCP
- DCP1
- dipeptidyl carboxypeptidase 1
- dipeptidyl carboxypeptidase I
- EC 3.4.15.1
- ICH
- kininase II
- MVCD3

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