

ACE gene

angiotensin I converting enzyme

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.

Health Conditions Related to Genetic Changes

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.

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 diabetes 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.

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

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ACE ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1636\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1636[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28ACE%5BTI%5D%29+OR+%28angiotensin+converting+enzyme%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D%29%29%29>)

Catalog of Genes and Diseases from OMIM

- ANGIOTENSIN I-CONVERTING ENZYME; ACE (<https://omim.org/entry/106180>)
- MICROVASCULAR COMPLICATIONS OF DIABETES, SUSCEPTIBILITY TO, 3; MVCD3 (<https://omim.org/entry/612624>)
- HEMORRHAGE, INTRACEREBRAL, SUSCEPTIBILITY TO; ICH (<https://omim.org/entry/614519>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/1636>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=ACE\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=ACE[gene]))

References

- Gribouval O, Gonzales M, Neuhaus T, Aziza J, Bieth E, Laurent N, Bouton JM, Feuillet F, Makni S, Ben Amar H, Laube G, Delezoide AL, Bouvier R, Dijoud F, Ollagnon-Roman E, Roume J, Joubert M, Antignac C, Gubler MC. Mutations in genes in the renin-angiotensin system are associated with autosomal recessive renal tubular dysgenesis. *Nat Genet.* 2005 Sep;37(9):964-8. doi: 10.1038/ng1623. Epub 2005 Aug 14. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16116425>)
- Gribouval O, Moriniere V, Pawtowski A, Arrondel C, Sallinen SL, Saloranta C, Clericuzio C, Viot G, Tantau J, Blesson S, Cloarec S, Machet MC, Chitayat D, Thauvin C, Laurent N, Sampson JR, Bernstein JA, Clemenson A, Prieur F, Daniel L, Levy-Mozziconacci A, Lachlan K, Alessandri JL, Cartault F, Riviere JP, Picard N,

Baumann C, Delezoide AL, Belar Ortega M, Chassaing N, Labrune P, Yu S, Firth H, Wellesley D, Bitzan M, Alfares A, Braverman N, Krogh L, Tolmie J, Gaspar H, Doray B, Majore S, Bonneau D, Triaou S, Loirat C, David A, Bartholdi D, Peleg A, Brackman D, Stone R, DeBerardinis R, Corvol P, Michaud A, Antignac C, Gubler MC. Spectrum of mutations in the renin-angiotensin system genes in autosomal recessive renal tubular dysgenesis. *Hum Mutat.* 2012 Feb;33(2):316-26. doi:10.1002/humu.21661. Epub 2011 Dec 22. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22095942>)

- Gubler MC, Antignac C. Renin-angiotensin system in kidney development: renal tubular dysgenesis. *Kidney Int.* 2010 Mar;77(5):400-6. doi: 10.1038/ki.2009.423. Epub 2009 Nov 18. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19924102>)
- Huang Y, Li G, Lan H, Zhao G, Huang C. Angiotensin-converting enzyme insertion/deletion gene polymorphisms and risk of intracerebral hemorrhage: a meta-analysis of epidemiologic studies. *J Renin Angiotensin Aldosterone Syst.* 2014 Mar;15(1):32-8. doi: 10.1177/1470320313481838. Epub 2013 Mar 11. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23477969>)
- Marre M, Jeunemaitre X, Gallois Y, Rodier M, Chatellier G, Sert C, Dusselier L, Kahal Z, Chaillous L, Halimi S, Muller A, Sackmann H, Bauduceau B, Bled F, Passa P, Alhenc-Gelas F. Contribution of genetic polymorphism in the renin-angiotensin system to the development of renal complications in insulin-dependent diabetes: Genetique de la Nephropathie Diabetique (GENEDIAB) study group. *J Clin Invest.* 1997 Apr 1;99(7):1585-95. doi: 10.1172/JCI119321. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9120002>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC507978/>)
- Wolf G. Angiotensin II and tubular development. *Nephrol Dial Transplant.* 2002;17 Suppl 9:48-51. doi: 10.1093/ndt/17.suppl_9.48. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12386287>)
- Wuyts B, Delanghe J, De Buyzere M. Angiotensin I-converting enzyme insertion/deletion polymorphism: clinical implications. *Acta Clin Belg.* 1997;52(6):338-49. doi: 10.1080/17843286.1997.11718599. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9489129>)
- Zhang Z, Xu G, Liu D, Fan X, Zhu W, Liu X. Angiotensin-converting enzyme insertion/deletion polymorphism contributes to ischemic stroke risk: a meta-analysis of 50 case-control studies. *PLoS One.* 2012;7(10):e46495. doi:10.1371/journal.pone.0046495. Epub 2012 Oct 1. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23049705>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3462189/>)

Genomic Location

The *ACE* gene is found on chromosome 17 (<https://medlineplus.gov/genetics/chromosome/17/>).

Last updated May 1, 2013