Angiotensin I-Converting Enzyme

Alternative Names
ACE
ACE1
Dipeptidyl Carboxypeptidase 1
DCP1
Kininase II
Angiotensin I-Converting Enzyme, Testicular
Angiotensin I-Converting Enzyme, Plasma Level of
Angiotensin I-Converting Enzyme, Benign Serum Increase

OMIM Number
106180

Mode of Inheritance
Autosomal dominant

Gene Map Locus
17q23

Description
The angiotensins are peptides (substances smaller than proteins) that act as vasoconstricting agents (causing blood vessels to narrow) that send up the blood pressure. Angiotensin I-converting enzyme, or kininase II, is a dipeptidyl carboxypeptidase that plays an important role in blood pressure regulation and electrolyte balance by hydrolyzing angiotensin I into angiotensin II, a potent vasopressor, and aldosterone-stimulating peptide. The enzyme is also able to inactivate bradykinin, a potent vasodilator.

Although angiotensin-converting enzyme has been studied primarily in the context of its role in blood pressure regulation, this widely distributed enzyme has many other physiologic functions. The ACE gene encodes 2 isozymes. The somatic ACE isozyme is expressed in many tissues, including vascular endothelial cells, renal epithelial cells, and testicular Leydig cells, whereas the testicular or germinal ACE isozyme is expressed only in sperm.

The importance of ACE in circulatory homeostasis is well documented. Besides being present as a membrane-bound enzyme on the surface of vascular endothelial cells, ACE also circulates in plasma. The plasma enzyme may be synthesized in vascular endothelium. In normal individuals, plasma ACE levels can show as much as a 5-fold interindividual variation; on the other hand, intra-individual variation is small.

Molecular Genetics
Pedigree analyses showed that angiotensin-converting enzyme levels are influenced by a quantitative trait locus located within or close to the angiotensin-converting enzyme gene and most likely residing in the 3-prime region of this locus. A polymorphism within intron 16 of the angiotensin-converting enzyme gene has been shown to influence the activity of the renin-angiotensin system and may also have an impact on the expression of renal disorders. In addition, the absence of a 287 base pairs Alu sequence in the angiotensin-converting enzyme gene (D allele) is associated with higher angiotensin-converting enzyme levels than its presence (I allele). In addition, the D allele of the polymorphism insertion/deletion of the angiotensin-converting enzyme gene, involving the intronic deletion of 287-bp, has been linked to a higher prevalence of microalbuminuria, which is an early marker of organ damage in hypertension and a prognostic factor for cardiovascular or renal risk in hypertension. Furthermore, A huge body of conflicting reports linked angiotensin-converting enzyme insertion/deletion to hypertension, ischemic heart disease, myocardial infarction, left ventricular hypertrophy, as well as several other clinical entities.
Epidemiology in the Arab World

Laks and Passwell (1987) described an infant of Arab extraction with the Type II form of Gaucher's disease. In addition to the extensive neurological involvement and marked hepatosplenomegaly, the child’s clinical presentation also included a marked hypergammaglobulinemia and raised serum angiotensin converting enzyme levels. Frishberg et al. (1998) compared the frequency of three polymorphisms of the renin-angiotensin system, including the angiotensin converting enzyme gene insertion/deletion polymorphism in intron 16, in Arab and Jewish children with focal segmental glomerulosclerosis with that in healthy controls of matching ethnic groups. Arab patients showed a greater tendency towards progressive renal disease than their Jewish counterparts. Frishberg and colleagues concluded that homozygosity for the angiotensin converting enzyme gene insertion allele may have a protective effect in children with focal segmental glomerulosclerosis and can serve as a positive prognostic indicator at diagnosis.

Kuwait

Al-Eisa et al. (2000) studied the polymorphism within intron 16 of the angiotensin-converting enzyme in 47 Kuwaiti children with different urological abnormalities leading to variable degrees of renal impairment and in 48 healthy control subjects with a similar ethnic background. Al-Eisa et al. suggested an association of the D allele of the angiotensin-converting enzyme gene insertion/deletion polymorphism with the clinical presentation of idiopathic nephrotic syndrome in Kuwaiti children and found an association of the D-allele with the clinical manifestation of idiopathic nephrotic syndrome in Kuwaiti Arab children.

United Arab Emirates

In 1997, Frossard et al. (1997) studied an insertion/deletion dimorphism in the human angiotensin-converting enzyme (ACE) gene amongst United Arab Emirates (UAE) nationals from the Abu Dhabi Emirate. There was a lack of association between the I/D allele marker system and clinical diagnosis of essential hypertension, suggesting that variations of the angiotensin-converting enzyme gene do not play a major role in the determination of elevated blood pressure in this Arab population. This agrees with results reported on other ethnic groups. In 1998, Frossard et al. (1998) carried out a retrospective case-control study of the angiotensin-converting enzyme insertion/deletion dimorphism in relation to circulating angiotensin-converting enzyme activity, as well as to hypertension, ischemic heart disease, myocardial infarction, and left ventricular hypertrophy in a sample population of 285 United Arab Emirates nationals. The analyzed group comprised controls and patients with clinical diagnoses of hypertension, ischemic heart disease, myocardial infarction, and left ventricular hypertrophy. Frossard et al. (1998) found out that the D allele was associated with increased circulating angiotensin-converting enzyme activity, and the angiotensin-converting enzyme insertion/deletion marker accounted for 28% of the variance of the phenomenon determining angiotensin-converting enzyme levels. However, Frossard et al. (1998) did not find an association between angiotensin-converting enzyme insertion/deletion and clinical diagnoses of hypertension, ischemic heart disease, myocardial infarction, and left ventricular hypertrophy. Frossard et al. (1998) concluded that the angiotensin-converting enzyme insertion/deletion dimorphism does not constitute a predictive marker for cardiovascular diseases in the population of the United Arab Emirates.

In 2001, Obineche et al. carried out an association (case-control) study of five candidate genes, including the angiotensin converting enzyme gene, with clinical left ventricular hypertrophy in a genetically homogenous Emirati group. No significant differences in the genotype distribution of the angiotensin converting enzyme gene markers were found between the left ventricular hypertrophy and non-left ventricular hypertrophy groups.

In 2003, Saeed Mahmood and colleagues assessed the value of genotyping the ACE G2350A dimorphism in a retrospective case-control study for a putative association with essential hypertension in the UAE population. Polymerase chain reaction and restriction endonuclease analyses were used to investigate a sample population of 254 Emirati from Abu Dhabi, comprising 136 normotensive controls, and 118 patients with clinical diagnoses of essential hypertension. Detailed analysis revealed that the ACE G/G 2350 genotype was positively associated with essential hypertension. According to the literature, this...
was the first association study of the ACE G2350A dimorphism with essential hypertension. Saeed Mahmood et al. (2003) concluded that this positive result might indicate that ACE could be a quantitative trait locus for essential hypertension as originally thought.

References


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