

## Polymorphisms in the ACE and angiotensinogen genes

### **Background:**

The angiotensin-converting enzyme (ACE) converts the angiotensin I protein into angiotensin II, which in turn exerts a strong prompt and long-term effect on the cardiovascular system. The plasma ACE level is typical for an individual but may vary in the population. About half of this variation is determined by an insertion/deletion polymorphism in the ACE gene, which means the presence (insertion, I) or absence (deletion, D) of a 287 base-pair fragment in intron 16, resulting three possible genotypes: II, ID, or DD. In accordance to the higher plasma ACE levels associated with the D variant, the mean plasma ACE level of individuals with the DD genotype is approximately twice as high as the ACE level of individuals carrying the II genotype, while the ID genotype represents an intermediate ACE level. The presence of the D variant has been shown to be associated with an increased risk for cardiovascular diseases. The DD genotype is significantly overrepresented among patients with myocardial infarction or stroke. The polymorphism also plays a role in the response to ACE-inhibitors used in the treatment of hypertension – patients with the II genotype tend to respond better. It is noteworthy that the II genotype is associated with higher endurance performance.

The protein encoded by the angiotensinogen gene is cleaved by renin produced when blood pressure drops to result in angiotensin I, which in turn is converted into angiotensin II by further enzymatic action. Angiotensin II is a powerful vasoconstrictor, causes salt retention by stimulating aldosterone secretion, and elevates blood pressure. A certain position in the gene (M235T) encodes for methionine at both alleles in 42%, methionine in one copy and threonine in the other copy in 46%, and threonine at both alleles in 12% of the Caucasian population, respectively. The presence of the T allele, presumably via an increased angiotensinogen production, has been shown to confer a slightly higher risk than the M allele to *hypertension*; furthermore, some authors describe a two-fold risk to develop *coronary heart disease* in the presence of the T allele.. Because of its involvement in the development of hypertension during pregnancy, the T allele is associated with an increased risk for *preeclampsia*.

### **Indications for testing:**

- increased risk for cardiovascular disease (presence of classical risk factors, positive family history)
- stroke at a young age (ACE)
- before treatment of hypertension (ACE)
- to judge development potential in endurance sports athletes (ACE)

### **Method:**

PCR and agarose gel electrophoresis (ACE), real-time PCR with hybridization probes (AGT)

### **Sample requirement:**

- buccal swab at room temperature *or*

- 2 ml blood in an EDTA (lavender top) tube, transported at +4 °C

**References:**

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