Molecular biology

Sample origin: EDTA blood

Genetic polymorphisms implicated in various pathways

Homocysteine

Result

MTHFR (C677T)	Heterozygous variant genotype CT
MTHFR (A1298C)	Homozygous wildtype AA

Interprétation

The presence of a heterozygous genotype for the [C677T] polymorphism is associated with a slightly decreased predictive enzymatic activity and slightly increased serum homocysteine levels. Presence of a weak genetic predisposition for thromboembolic diseases with regard to the two analyzed polymorphisms. The relative risk for adverse effects to a treatment with methotrexate is slightly increased.

Clinical significance of the analyzed genetic polymorphism

The enzyme methylenetetrahydrofolate reductase (MTHFR) plays an important regulatory role in the metabolism of folate. It catalyzes the irreversible reduction of 5,10-methylenetetrahydrofolate to 5-methylenetetrahydrofolate. This enzymatic reaction is necessary for the synthesis of methionine via the remethylation of homocysteine. If the enzymatic activity is reduced, the serum homocysteine is increased. This hyperhomocysteinemia is an independent risk factor for thromboembolic disease, as well as for lesions. There is also a relationship between neural tube defects in newborns and high homocysteine levels in the mother. Genetic variations of the MTHFR gene lead to the synthesis of a thermolabile enzyme that has a diminished activity, predisposing to severe side effects during treatment with methotrexate. In such cases, the detection of polymorphisms of the MTHFR gene allows an assessment of the relative risk for side effects before treatment. The two polymorphisms of clinical significance are as follows: MTHFR [C677T] and MTHFR [A1298C].
MTHFR [C677T] is defined by the substitution of a cytosine (C) to thymine (T) at position 677 in exon 3. The presence of the homozygous variant leads to a decrease of approximately 70% of the enzymatic activity. As a consequence, folic acid levels are reduced and homocysteine levels are increased. This variation has a frequency of 5 to 20% in the homozygous state and of 30 to 50% in the heterozygous state.
MTHFR [A1298C] is defined by the substitution of an adenine (A) to cytosine (C) at position 1298 in exon 7. The homozygous variant is associated with a decrease of approximately 30% of the enzymatic activity and the compound heterozygous variant is associated with a decrease of approximately 15% of the enzymatic activity. In the Caucasian population, the frequency of this variation is 4% (homozygous variant) respectively 40% (heterozygous variant).

Note

In the presence of a heterozygous or homozygous variant genotype for one or several analyzed genes, it is recommended that the same genetic analysis should also be carried out for family members of the first degree and, depending on medical recommendations, also for the spouse.

Non-accredited parameter, carried out on a sub-contractual basis and in accordance to the Additional Protocol of November 27th, 2008 to the Convention on Human Rights and Biomedicine concerning Genetic Testing for Health Purposes.

This analyses report has been validated by: Prof. Dr. med. Bernard Weber

ACCREDITATION NUMBER: 1/014 ISO 15189 OFFICE LUXEMBOURGEOIS

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