Gene test information

MTHFR 677T AND HOMOCYSTEINE

- **Background**

  Hyperhomocysteinemia is a widely recognized risk factor for coronary artery disease, venous thrombosis, and stroke. It is also involved in the pathogenesis of neural tube defects, stillbirths, and recurrent pregnancy loss. The leading cause of hyperhomocysteinemia is folate deficiency. Other determinants include insufficient B12 intake, impaired renal function, and genetic variations including those in the MTHFR gene. Folate supplementation can correct for most causes of hyperhomocysteinemia.

  Methlyenetetrahydrofolate reductace (MTHFR) is a key enzyme in the metabolism of homocysteine. Mutations in the MTHFR gene have been reported as causes of hyperhomocysteinemia. The most common MTHFR mutation, C677T, is present in the homozygous state in 5-10% of the general Caucasian population. In homozygous individuals, this results in a thermolabile variant of the enzyme with decreased activity.

- **MTHFR 677C>T genotypes**

Genotype	Frequency	Commentary
MTHFR 677 CC	41%	Wild type genotype. No MTHFR 677-T variant detectable.
MTHFR 677 CT	47%	Heterozygous for the MTHFR 677-T variant. Moderately reduced MTHFR enzyme activity.
MTHFR 677 TT	12%	Homozygous for the FGG 10034T variant. Reduced MTHFR enzyme activity. Increased risk for hyperhomocysteinemia, particularly when deficient in folate.

- **Indications for testing**
  - Hyperhomocysteinemia
  - History of venous thromboembolism, coronary artery disease, and/or stroke
  - History of pregnancy complications including neural tube defects, stillbirths, and/or recurrent pregnancy loss

References:

Klerk M et al. MTHFR 677C->T polymorphism and risk of coronary heart disease: a meta-analysis. JAMA. 2002;288:2023-31.

Den Heijer M et al. Homocysteine, MTHFR and risk of venous thrombosis: a meta-analysis of published epidemiological studies. J Thromb Haemost. 2005:292-9.

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