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MTHFR C677T Mutation Analysis

MTHFR point mutation C677T

Indications for Molecular Testing

- Family history of venous thrombosis
- Unprovoked thrombotic event at <45 years of age
- Women with multiple stillbirths or spontaneous abortions

Testing Methodology

The assay utilizes the Invader Plus® chemistry manufactured by Hologic for the detection of the MTHFR c.665 C>T (Ala177Val) mutation in genomic DNA (NM_005957 transcript isoform). Invader and allele-specific probes match the mutant and the wild-type alleles and have overlapping 5'-ends that are cleaved upon perfect hybridization to the amplified DNA. The cleaved 5'-end of the primary probes transiently hybridize with a corresponding fluorescence resonance energy transfer (FRET) cassettes triggering the cleavage of the fluorophore from the cassette by the cleavase enzyme and allowing signal release and detection.

Interpretation of DNA analysis

The MTHFR enzyme is essential for recycling homocysteine by catalyzing the reduction of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, which is the substrate for the re-methylation of homocysteine to methionine. The c. 665C>T polymorphism in the MTHFR gene, commonly referred to as MTHFR C677T, converts Alanine to Valine at codon 222 and renders a thermolabile enzyme with reduced MTHFR activity. This results in an elevated level of plasma homocysteine in individuals who are homozygous for the genotype.

MTHFR C677T is the most common genetic polymorphism resulting in reduced MTHFR activity. In the world population, homozygosity is identified in approximately 12% of the Caucasian, 28% of the Hispanic, and 1.2% of African population; heterozygosity is identified in 23% of the Caucasian, 55% of the Hispanic, and 2.5% of the African populations.

Because the underlying cause for symptomatic thrombosis is multifactorial, genotype alone cannot predict with certainty that thrombotic events will or will not occur in individual patients. Circumstantial factors (e.g. pregnancy, surgery, immobilization, cancer, hormonal contraceptive use) as well as possible co-inheritance with additional thrombosis-related genetic modifiers additively enhance the likelihood for the development of a venous thromboembolism (VTE).

Specimen Requirements

Peripheral blood--1 lavender-top (EDTA) tube. Invert several times to mix blood.
Do not freeze. Forward at ambient temperature to:

Molecular Diagnostic Laboratory
Barnes-Jewish Hospital, Institute of Health
Mail Stop 90-28-344
425 South Euclid Avenue, Room 5970
St. Louis, MO 63110

Current Pricing

Contact Lab Customer Service for current pricing 314 362-1470.
CPT code: 81291

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