**HEMOSTASIS ASSESSMENT**

* MTHFR C677T GENE MUTATION IS HETEROZYGOUS POSITIVE with MTHFR A1298C gene mutation NOT detected. Single heterozygous MTHFR C677T probably is of little clinical significance. It should be noted that recent data indicate that the MTHFR mutations do not correlate well with thrombosis. Would monitor homocysteine level.

**RESULTS**

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Normal Result</th>
<th>Abnormal Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTHFR C 677T GENE MUTATION</td>
<td></td>
<td>Detected</td>
<td>Not Detected</td>
</tr>
<tr>
<td>MTHFR A 1298C GENE MUTATION</td>
<td>Not Detected</td>
<td>Heterozygous</td>
<td>Not Detected</td>
</tr>
</tbody>
</table>

* Testing for MTHFR C677T mutation has become controversial. There is a body of opinion that such testing should be reserved for patients with increased homocysteine.
* This test was evaluated and its performance characteristics determined by BioReference Laboratories. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This lab has been approved by CLIA 98, designated as a high complexity laboratory and is qualified to perform these tests.
(MTHFR) C677T GENE MUTATION

Test Name
MTHFR C 677T GENE MUTATION

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NOTES

- This patient is heterozygous for the MTHFR C677T gene mutation, i.e., this patient's DNA has the C677T mutation on one of the two MTHFR alleles.
- About half the general population carries at least one mutated allele and the frequency of the homozygous mutated genotype (C677T) ranges from 1 to 20% depending on the population.
- A heterozygous positive MTHFR C677T mutation may not have clinical significance for hyperhomocysteinemia. Patients should be assessed for homocysteine levels. Also would test for folic acid and possible B12 deficiency. We also recommend that this patient be referred for assay of a second common MTHFR mutation, A1298C.
- Individuals who are compound heterozygous for the C677T and A1298C alleles, which produces a C677T/A1298C genotype, have according to some studies 40-50% reduced MTHFR enzyme activity in vitro and a biochemical profile similar to that seen among C677T homozygotes with increased homocysteine levels and decreased folate levels.
- Milder forms of hyperhomocysteinemia are also associated with venous and arterial thrombosis. The MTHFR C677T mutation in the homozygous form is considered a risk factor for hyperhomocysteinemia, atherothrombosis and thrombotic disease. The homozygotes and heterozygotes have about a 70% and 35% reduced MTHFR enzyme activity in vitro, respectively.
- In patients with other congenital thrombophilic conditions (e.g. deficiencies of antithrombin, protein C, protein S, and DNA mutations in Factor V & factor II), the risk enhancement by the MTHFR mutation seems slight.
- The assay is highly accurate. However, rare false positive and false negative results may occur. You or your physician may request genetic counseling. Your physician should be able to provide you with access to counseling services.

METHOD:
The patient's lymphocytes are processed to extract DNA. The extracted DNA is used to perform the Invader™ assay from Third Wave Technologies Inc. for MTHFR C677T. This assay uses the Fluorescence Resonance Energy Transfer (FRET) detection format. Two different primary probes are used for each patient: one for the wild type allele and the other one for the mutant allele. The following format is used to calculate the ratio. One can then determine the genotype of the patient based on the ratio.

Ratio = Net counts from wild probe / Net counts from mutant probe.

* Testing for MTHFR C677T mutation has become controversial. There is a body of opinion that such testing should be reserved for patients with increased homocysteine.
(MTHFR) A1298C GENE MUTATION

Test Name | Normal Result | Abnormal Result | Reference Range
--- | --- | --- | ---
MTHFR A 1298C GENE MUTATION | Not Detected | Not Detected | Not Detected

**NOTES**

- The MTHFR A1298C mutation is not detected as per the described method below.
- Milder forms of hyperhomocysteinemia are also associated with venous and arterial thrombosis. The MTHFR C677T mutation in the homozygous form is considered a risk factor for hyperhomocysteinemia, atherothrombosis and thrombotic disease.
- Individuals who are compound heterozygous for the C677T and A1298C alleles, which produces a C677T/A1298C genotype, have according to some studies 40-50% reduced MTHFR enzyme activity in vitro and a biochemical profile similar to that seen among C677T homozygotes with increased homocysteine levels and decreased folate levels. The combination of both mutations is expected to occur in about 15% of the general population. So far, no one with homozygosity for both mutations has been identified.
- In patients with other congenital thrombophilic conditions (e.g. deficiencies of antithrombin, protein C, protein S, and DNA mutations in Factor V & factor II), the risk enhancement by the MTHFR mutation seems slight.
- The assay is highly accurate. However, rare false positive and false negative results may occur. You or your physician may request genetic counseling. Your physician should be able to provide you with access to counseling services.

**METHOD:**
The patient's lymphocytes are processed to extract DNA. The extracted DNA is used to perform the Invader™ assay from Third Wave Technologies Inc. for MTHFR A1298C. This assay uses the Fluorescence Resonance Energy Transfer (FRET) detection format. Two different primary probes are used for each patient: one for the wild type allele and the other one for the mutant allele. The following format is used to calculate the ratio. One can then determine the genotype of the patient based on the ratio.

Ratio = Net counts from wild probe / Net counts from mutant probe.

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