MTHFR (Methylenetetrahydrofolate Reductase)

What is MTHFR?

- MTHFR is an enzyme responsible for converting 5,10-methylenetetrahydrofolate to the product 5-methyltetrahydrofolate – it is involved in the metabolism of folate and homocysteine
- The product of the reaction catalyzed by MTHFR converts homocysteine (a potentially toxic amino acid) to methionine (a useful and necessary amino acid)

Why is MTHFR Genotyping important?

- Certain mutations in the gene coding for MTHFR produce an enzyme that has reduced activity.
- Reduced activity can lead to elevated levels of homocysteine (a.k.a. hyperhomocysteinemia), especially when folate levels are low.
- High homocysteine (>13umol/L) may double the risk of developing illness or complications.
- MTHFR genotyping can provide information about potential causes of elevated homocysteine and approaches for addressing it.
- Based on MTHFR and homocysteine results, physicians can develop dietary and medical recommendations.
- Increased intake of folate alone or in combination with vitamins B6 and B12 are recommended.
- Based on results, recommendations for methotrexate dosage can be adjusted.

Risks associated with MTHFR Variants / High Homocysteine:

- Cardiovascular Disease
- Cerebral Vascular Disease (Stroke)
- Venous and Arterial Thrombosis
- Methotrexate Toxicity for Cancer Therapy

What are the Variants?

C677T

- There is a mutation from cytosine to adenine at position 677 within gene.

A1298C

- There is a mutation from adenine to cytosine at position 1298 within gene.

These variants lead to amino acid differences in the protein that reduces its ability to function.

What are the possible genotypes?

677 - CC, CT, or TT

- CC - homozygous normal
  - Approximately 45% of the population
  - No increased risk associated
- CT - one variant copy
  - Approximately 45% of the population
  - Some reduced enzyme activity, but not alone associated with increased risk.
- TT - two variant copies
  - Approximately 10% of the population
  - Increased risk for hyperhomocysteinemia and associated complications

1298 - AA, AC, CC

- AA - normal homozygous
- AC or CC - one or two variant copies
  - Approximately 30% of the population
  - Not associated with increased risk

Who should be tested?

- Those with high homocysteine levels.
- Those who have a familial history of cardiovascular disease, stroke, or thrombosis.
- Those who are candidates for long-term methotrexate therapy.