Patient Info: Name: XXXXX DOB: XXX Age:XX Gender: Phone No: Collection Date: 05-19-2022 Received Date: 05-24-2022 Report Date: 06-02-2022	Body Science Tel: 305.901.5888 Fax: 305.901.2301	Client ID: XXXX Accession No: XXXXXXXX

MTHFR GENOTYPING REPORT

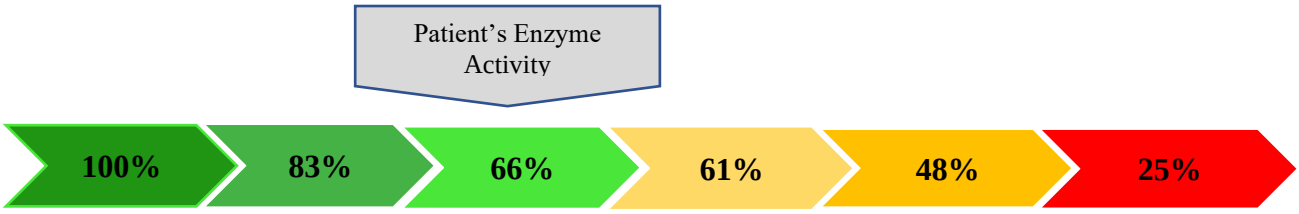
PATIENT'S TEST RESULTS AND INDICATIONS

TEST	GENOTYPE	RESULT
C677T Mutation	C/T	Positive
A1298C Mutation	A/A	Negative

This patient carries ZERO A1298C gene mutation AND ONE C677T gene mutation.

- Heterozygous C677T gene mutation involve in intermediate levels of enzyme activity.
- Heterozygous C677T gene mutation is not associated with Increased Homocysteine level.
- May have an intermediate risk level for depression.
- Increased sensitivity to Methotrexate leading to lower dosage requirements, increased side effects or intolerance of the drug.
- The patient's genotypes should be interpreted in light of clinical finding.

PATIENT'S APPROXIMATE MTHFR ENZYME ACTIVITY



MTHFR BACKGROUND INFORMATION

MTHFR gene mutation and Hyperhomocysteinemia

The MTHFR (methylenetetrahydrofolate reductase) gene produces an enzyme that helps in processing folate and regulating homocysteine levels in the body. MTHFR mutations reduces the activity of enzyme due to which folate level drops down and that contributes to the increased plasma homocysteine levels in body Folate is a critical nutrient involved in methylation, DNA synthesis and amino acid metabolism..

Homocysteine is an amino acid synthesized by the body through demethylation of methionine. In the presence of adequate B vitamins, homocysteine is either irreversibly degraded to cysteine or it is re-methylated back to methionine, an essential amino acid.4 An elevated homocysteine level is associated with an increased risk for developing atherosclerosis, which can in turn lead to coronary artery disease (CAD), heart attack, and ischemic stroke. Folate, vitamin B6 or vitamin B12 are all necessary for the proper conversion of homocysteine into methionine. A deficiency in any of these vitamins can cause homocysteine levels to rise. It has been recognized that elevated homocysteine is associated with dementia, particularly Alzheimer's disease. How homocysteine is related to dementia is not yet fully understood. It is suspected that there is a connection between homocysteine levels and blood vessel changes in the brain. Research in this area is ongoing

Two single nucleotide variants known to affect MTHFR function are C677T (a change from cytosine to thymine at position 677 within the gene) and the A1298C mutation (a change from adenine to cytosine at position 1298 within the gene). It is not uncommon for some individuals to have both MTHFR variants. Clinical relevance for hyper homocysteniemia is associated with homozygosity for C677T or A1298C variant alleles and the compound heterozygous state (presence of both heterozygous genotypes C677T/ A1298C). In general, these genotypes produce MTHFR enzyme with reduced function and activity. In addition to vascular health, defects in folate metabolism due to dietary factors or MTHFR mutations may contribute to the pathophysiology of neural tube defects and a variety of malignancies. Also, a strong association between MTHFR variants and methotrexate toxicity has been reported. Methotrexate, a drug used in treatment of cancer and autoimmune diseases, is a structural analogue of folate that interferes with folate metabolism and leads to depletion of cellular folate. MTHFR gene variants associated with reduced enzyme function and hyper homocysteinemia may affect methotrexate sensitivity and contribute to toxicity. MTHFR genotyping may support methotrexate dose adjustment and limitation / discontinuation of therapy in affected individuals.

MTHFR- BEHAVIORAL HEALTH INFORMATION

Impaired folate metabolism due to reduced MTHFR enzyme activity, or decreased folate, results in elevated plasma homocysteine which has been linked to depression, bipolar disorder, schizophrenia, attention-deficit hyperactivity disorder (ADHD), or autism. There is no evidence to suggest that the A1298C mutation alone affects plasma homocysteine levels, however, it has been demonstrated that individuals who are compound heterozygotes for both the C677T and the A1298C mutations have increased plasma homocysteine concentrations. Elevated homocysteine levels are inversely associated with memory score, and directly related to brain atrophy and depressive symptoms. Folate levels are directly related to memory scores, and inversely related to depressive symptoms in women.

MTHFR - CARDIOVASCULAR DISEASE

An MTHFR enzyme with reduced function can lead to elevated homocysteine levels has been identified as an independent risk factor for development of cardiovascular disease, ischemic stroke and venous thrombosis. Interpretation of MTHFR testing should be done in light of clinical information.