KASHI CLINICAL LABORATORIES

# MTHFR Genotyping
## Healthcare Professional Information

## Methylation: Understand your Patient's Risk & Health Implications

Methylation is a ubiquitous process throughout the body. The 5,10-Methylenetetrahydrofolate reductase (MTHFR) enzyme is a central component of DNA methylation, responsible for converting folate into its active form.[1,2] This process occurs constantly as new folate is introduced, and utilized folate is recycled back into the active form. Active folate plays a role in many biological processes and interacts with many other enzymes in the methylation pathway. Inadequate amounts of active folate can lead to insufficient methylation which can contribute to many health disorders involving the cardiovascular, reproductive, and neurological systems as well as others.[2,3] Research has shown that many individuals may be at risk of methylation insufficiency due to reduced MTHFR enzyme function.[5,6]

### Associated Disorders

- Hyperhomocysteinemia[3]
- Cardiovascular Disease[3]
- Ischemic Stroke[4]
- Dementia/Alzheimer's Disease[10]
- Neural Tube Defects[3]
- Autism[10]
- Down Syndrome[10]
- Depression[10]
- Bipolar Disorder[10]
- Polycystic Ovary Syndrome[11]
- Fracture Risk[4]

### MTHFR Genotyping Can Help Make Informed Treatment Decisions

By identifying a patient's genotype and predisposition to decreased enzyme activity, you may be able to improve your patient's health and mitigate risk to disease. The MTHFR Genotyping test assesses your patient's DNA for the presence of two common single nucleotide polymorphisms (SNPs) that have been shown to impact MTHFR enzyme activity.[5-7] These SNPs differ from what we would expect to find in an individual with optimal MTHFR activity. The degree to which the enzyme function is reduced is determined by how many variant SNPs your patient may carry. The two SNPs screened are MTHFR C677T and A1298C. [5-7] C677T, as compared to A1298C, has been shown to have the greatest influence on many health disorders, but the presence of the A1298C mutation in conjunction with the C677T mutation also exerts a significant effect on the enzyme.

### MTHFR Variant Combinations and Approximated Enzyme Activity[6]

| Genotype | 677CC | 677CT Heterozygous | 677TT Homozygous |
|---|---|---|---|
| 1298AA | **100%** Enzyme activity | **66%** Enzyme activity | **25%** Enzyme activity |
| 1298AC Heterozygous | **83%** Enzyme activity | **48%** Enzyme activity | *Not analyzed* |
| 1298CC Homozygous | **61%** Enzyme activity | *Not analyzed* | *Not analyzed* |


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# COMT Genotyping
## Healthcare Professional Information

## COMT: Understand your Patient's Risk & Health Implications

**Estrogen metabolism is crucial to proper bio-identical hormone management. Whether considering estrogen dominance or breast cancer risk, COMT genotyping can help to inform your patient's treatment options.**

Bio-identical hormone therapy is a very supportive tool to help patients with various health complaints. From menopausal symptoms, to weight gain, to fatigue - many patients find the use of hormone therapy to be nothing short of a miracle to improving the quality of their everyday life. However, the use of these hormones can increase cancer risk in some patients. So how can you tailor this to be the safest treatment for your patients as possible? Personal and family history for cancer risk and well as hormone level monitoring is a very good first step. Introduction of the COMT genetic test helps to further inform your patient's risk.

The COMT (catechol-O-methyltransferase) gene codes for the essential COMT enzyme that is involved in the inactivation of the catecholestrogens.[1] Scientific research has demonstrated that a common mutation in the COMT gene resulting in the conversion of the amino acid valine to methionine at position 158 (Val158Met) causes a dramatic reduction in the enzyme's ability to metabolize these catecholestrogens.[2] Homozygous Valine (Val/Val) allele carriers have higher enzyme activity, while homozygous Methionine (Met/Met) allele carriers have lower enzyme activity, and heterozygous Val/Met allele carriers exhibit an intermediate enzyme activity.


This change in enzyme activity has been shown to play a role in estrogen metabolism through a change in the inactivation of the catecholestrogens.[3] The COMT enzyme performs this inactivation step by converting hydroxylated estrogens into methoxylated estrogens by the addition of a methyl group. This process lowers the cancer-causing potential of these metabolites, while simultaneously increasing the amount of 2-methoxyestradiol, a metabolite that has been shown to inhibit the growth of breast cancer cells.[2,4,5] Additionally, COMT polymorphisms have been shown to influence estradiol levels, the most potent of the various estrogen forms.[6] Met/Met and Met/Val allele carriers exhibit a 2-3 fold decrease in their ability to degrade catecholestrogens, resulting in higher estradiol levels than the Val/Val allele carriers.[2,7]

**TESTING YOUR PATIENT'S DNA CAN HELP TO TRULY INDIVIDUALIZE THEIR BIO-IDENTICAL HORMONE THERAPY. UNDERSTANDING YOUR PATIENT'S GENOTYPE CAN HELP TO INFORM THEIR RISK OF ACQUIRING BREAST CANCER AS WELL AS INFLUENCES ON THEIR INDIVIDUAL ESTRADIOL LEVELS.**


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