Genova Diagnostics® Europe
Innovative Testing for Optimal Health

63 Zillicoa Street
Asheville, NC 28801

Patient: **SAMPLE PATIENT**
Age: 10
Sex: M
MRN:

Order Number:
Completed: February 11, 2008
Received: January 31, 2008
Collected: January 28, 2008

MTHFR — *5,10-methyltetrahydrofolate reductase : METHYLATION*

Location:
Chromosome 1

C677T
Your Genotype:

\+ ↓ | −

A1298C
Your Genotype:

\+ ↓ | −

5,10-methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism, facilitating the formation of methyltetrahydrofolate, a required cofactor in the remethylation of homocysteine (Hcy) to methionine.

Health Implications

- Heterozygosity for both 677 (-/+) and 1298 (-/+) results in 50-60% reduction in MTHFR enzyme activity, low folate status, and increased risk of elevated homocysteine (and S-adenosylhomocysteine, or SAH)
- MTHFR polymorphism-induced SAH elevations may disrupt neurotransmitter metabolism as well as synthesis of DNA, carnitine, and coenzyme Q10
- Increased risk of autism, depression, neural tube defects, cardiovascular disease, diabetic retinopathy, osteoporosis, and some cancers
- Low folate status significantly increases risk of associated disorders

Treatment Options

- Ensure adequate intake of folate-rich green vegetables
- Consider supplementation with folic acid (or folinic acid or 5-methyltetrahydrofolate), vitamins B2, B3, B6 (pyridoxal 5-phosphate), B12 (or methylcobalamin), and betaine (trimethylglycine)

Key

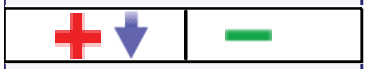
\- - Neither chromosome carries the genetic variation.
\+ - One chromosome (of two) carries the genetic variation.
\+ + Both chromosomes carry the genetic variation.
(You inherit one chromosome from each parent)

\+ ↑ Gene activity increased
\+ ↓ Gene activity decreased

GENOVATIONS™

COMT — Catechol-O-MethylTransferase : METHYLATION

Location:
Chromosome 22.11q
V158M
Your Genotype:



COMT is a key enzyme in the deactivation of catechol compounds such as catecholamines, estrogens, various chemicals, and toxins. COMT modulates the neurotransmitter functions of dopamine and norepinephrine.

Health Implications

- Moderately decreased COMT activity with increased bioavailability of catecholamines and impaired methylation of catechol estrogens
- Superior mental performance (increased brain dopamine), but increased risk of nervousness, excitability, and mood disturbances
- Reduced pain threshold and increased risk of fibromyalgia

Treatment Options

- Ensure adequate B6, B12, folate, magnesium, and methionine to support formation of S-adenosylmethionine and prevent elevated homocysteine
- Ensure adequate anti-oxidants to prevent oxidation of dopamine and pro-carcinogenic 4-hydroxyestrogens
- Exercise caution using amphetamine-based medications

GSTM1 — Glutathione S-Transferase mu-1 : DETOXIFICATION

Location:
Chromosome 1

Your Genotype:

ABSENT

The GSTM1 gene is either PRESENT or ABSENT (also called Null). If either copy is present, it is termed PRESENT. If both copies are absent, it is termed ABSENT.

GST is responsible for Phase II detoxification of xenobiotics, carcinogens, and products of oxidative stress. GSTM1 is located primarily in the liver.

Health Implications

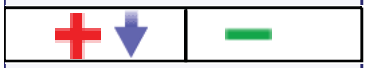
- GSTM1 enzyme activity is absent, with reduced detoxification capacity
- Increased risk of toxic burden, oxidative stress, atopic asthma, lung problems, cancer, chemical sensitivity, and coronary artery disease
- Decreased risk of cancer, only with high intake of cruciferous vegetables

Treatment Options

- Eat cruciferous vegetables and allium foods to reduce cancer risk
- Eat a diet rich in antioxidants (colorful foods), consider supplementation
- Ensure availability of glutathione precursors and cofactors
- Limit glutathione depletion with α-lipoic acid, milk thistle, or taurine
- Minimize exposure to xenobiotics, including PAHs and toxic metals

GSTP1 — Glutathione S-Transferase pi-1 : DETOXIFICATION

Location:
Chromosome 11
A114V
Your Genotype:



I105V
Your Genotype:

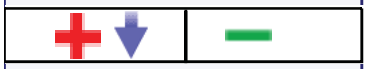
GST is responsible for Phase II detoxification of xenobiotics, carcinogens, steroids, heavy metals, and products of oxidative stress. GSTP1 is located primarily in the brain and lungs.

Health Implications

- GSTP1 polymorphisms are associated with either higher or lower enzyme activity, depending on specific environmental exposures. The I105V snp is the more significant of the two.
- Increased risk of toxic burden, oxidative stress, and various cancers, especially if "GSTM1 Absent" or exposed to cigarette smoke

Treatment Options

- Eat cruciferous vegetables and allium foods (e.g., garlic) to increase GST activity and reduce cancer risk
- Eat a diet rich in antioxidants (colorful foods), consider supplementation
- Ensure availability of GSH precursors and cofactors, e.g., methionine-rich foods, NAC, L-glutamine, glycine, Mg, B6
- Limit glutathione depletion with alpha lipoic acid, milk thistle, and taurine
- Minimize exposure to xenobiotics, including polycyclic aromatic hydrocarbons and toxic metals

SOD2	*Superoxide Dismutase-2 : DETOXIFICATION*
Location: Chromosome 6 **A16V** **Your Genotype:** 	SOD converts reactive oxygen species into less reactive H2O2. SOD2 is located within cellular mitochondria and uses manganese as a cofactor. **Health Implications** · An SOD2 polymorphism is associated with slightly lower SOD enzyme activity; however, most risk has been associated with the homozygous-negative genotype (-/-) · Slightly increased risk of cardiomyopathy, especially when associated with iron overload **Treatment Options** · Maintain a diet rich in antioxidants (colorful foods), consider antioxidant supplements · Minimize exposure to xenobiotics, including polycyclic aromatic hydrocarbons (e.g., cigarette smoke) and toxic metals

This test has been developed and its performance characteristics determined by Genova Diagnostics, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

The accuracy of genetic testing is not 100%. Results of genetic tests should be taken in the context of clinical representation and familial risk. The prevalence and significance of some allelic variations may be population specific.

Any positive findings in your patient's test indicate genetic predisposition that could affect physiologic function and risk of disease. We do not measure every possible genetic variation. Your patient may have additional risk that is not measured by this test. Negative findings do not imply that your patient is risk-free.

The Third Wave ™ Invader DNA assay is used to detect polymorphisms in the patient's DNA sample. In this assay, a solution hybridization method is used in which two oligonucleotides hybridize in tandem with the specific DNA sequences. Subsequent Cleavase® and hybridization reactions result in generation of fluorescent signal. The biplex format of the assay enables simultaneous detection of all variants in a single reaction tube. The sensitivity and specificity of this assay is 99.7%.

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