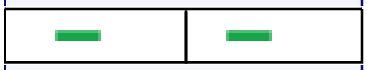
NeuroGenomic Profile (Buccal Cells)

GENOVATIONS™

63 Zillicoa Street
Asheville, NC 28801

Patient: **SAMPLE PATIENT**
DOB:
Sex:
MRN:

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 677 (-/+) results in 30-40% reduction in MTHFR enzyme activity, which may moderately limit methylation reactions in the body · High homocysteine and disease risks are primarily associated with the (+/+) genotype · Possible marginally increased risk of essential hypertension and stroke; studies are mixed · Possible slight increased risk of birth defects in the offspring, e.g., neural tube defects, cleft lip and/or palate, and Down syndrome; studies are mixed · Possible slight increased risk of gastric and esophageal cancer, the latter of which may be reversed with adequate folate intake **Clinical Management Considerations** · Ensure adequate intake of dark-green leafy vegetables and other B vitamin-rich foods · Consider supplementation with folic acid (or 5-methyltetrahydrofolate, which bypasses the MTHFR step), 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

GENOVA DIAGNOSTICS

COMT — Catechol-O-MethylTransferase : METHYLATION

Location:
Chromosome 22.11q
V158M
Your Genotype:

Catechol-O-Methyltransferase (COMT) is a key enzyme involved in the deactivation of catechol compounds, including catecholamines, catechol estrogens, catechol drugs such as L-DOPA, and catechol metabolites of various chemicals and toxins, such as aryl hydrocarbons.

Health Implications

- 3-4-fold reduction in COMT enzyme activity, resulting in decreased methylation
- Increased risk of nervousness/anxiety (esp. when history of childhood trauma) and PTSD, due to higher baseline levels of catecholamines
- Acute or chronic stress may compromise working memory, decision-making ability, or mood, by producing supraoptimal dopamine levels
- Strong cognitive stability, e.g., ability to focus (due to higher brain dopamine) but lower cognitive flexibility (e.g., ability to adapt to external changes)
- Cognitive benefit may be most apparent as dopamine levels decline with age
- Conflicting reports for breast cancer risk; possible increased risk in Asian women, but marginally decreased risk in Caucasian women
- Reduced pain threshold, which is exacerbated by one's experience of pain; increased risk of fibromyalgia and chronic pain syndromes
- Possible increased fracture risk, esp. in men, but greater BMD response to physical activity
- Possible increased risk of substance addiction, including alcoholism
- Possible increased risk of Parkinson's disease (mixed studies)

Clinical Management Considerations

- Minimize stress, since catecholamines levels may already be high
- Ensure adequate B6, B12, folate, magnesium, betaine, and methionine to support formation of S-adenosylmethionine and prevent elevated homocysteine; S-adenosylhomocysteine inhibits COMT
- Preliminary findings suggest reduced risk of cardiovascular events by taking aspirin or vitamin E
- Exercise caution using conjugated equine estrogens such as Premarin®; in-vitro studies suggest show one of its metabolites to inhibit COMT
- Individuals with this genotype may have a superior response to SSRI antidepressants (mixed studies)
- In children with ADHD, methylphenidate (Ritalin®) may be less effective (mixed studies)

GSTM1 — Glutathione S-Transferase mu-1 : DETOXIFICATION

Location:
Chromosome 1

Your Genotype:

PRESENT

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

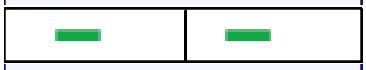
- GSTM enzyme activity is present, with normal detoxification capacity

Clinical Management Considerations

- Ensure availability of glutathione precursors, cofactors and antioxidants
- Minimize exposure to xenobiotics

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

· Polymorphisms are associated with either higher or lower enzyme activity, depending on specific environmenta exposures; therefore, the (-/-) genotype may still increase risk for some disorders. The I105V snp is the more significant of the two.

· The I105V genotype (-/-) is associated with slightly increased risk of some cancers (especially if exposed to cigarette smoke), also atopy, xenobiotic-induced asthma, and COPD

Clinical Management Considerations

· Ensure availability of glutathione precursors and cofactors, e.g., methionine-rich foods, NAC, L-glutamine, glycine, Mg, B6

· Eat a diet rich in antioxidants (colorful foods), consider supplementation

· Minimize exposure to xenobiotics, including polycyclic aromatic hydrocarbons (e.g., cigarette smoke) and toxic metals

SOD2 — *Superoxide Dismutase-2 : DETOXIFICATION*

Location:
Chromosome 6
A16V
Your Genotype:

Superoxide dismutase (SOD) is an antioxidant enzyme that converts reactive oxygen species into less reactive hydrogen peroxide (H2O2), which is then neutralized by catalase and GSH-peroxidase. SOD2 is located within cellular mitochondria and uses manganese as a cofactor.

Health Implications

· Slightly less SOD2 enzyme production compared to the homozygous-negative genotype, therefore *less* risk of H2O2 accumulation (most risk appears to be associated with the (-/-) genotype).

· Slightly increased risk of carotid atherosclerosis.

Clinical Management Considerations

· 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 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.

DNA sequencing is used to detect polymorphisms in the patient's DNA sample. The sensitivity and specificity of this assay is <100%.