GENOVATIONS™

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Patient: JANE
DOE
DOB: November 02, 1990
Sex: F
MRN:

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MTHFR	*5,10-methyltetrahydrofolate reductase : METHYLATION*
Location: Chromosome 1 **C677T 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.
A1298C Your Genotype: − / −	**Health Implications** · Heterozygosity for 677 (-/+) results in 30-40% reduction in MTHFR enzyme activity · Increased risk of elevated homocysteine, esp. if low levels of B vitamins · Possible methylation impairment, including disrupted neurotransmitter metabolism and synthesis of DNA, carnitine and coenzyme Q10 · Increased risk of autism, depression, schizophrenia, neural tube defects, cardiovascular disease, essential hypertension, diabetic retinopathy, osteoporosis, and cancers of the stomach · Low levels of vitamins B2, B6, B12, and/or folate often determines the risk of these 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

GENOVA DIAGNOSTICS

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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:

- 3-4-fold reduction in COMT enzyme activity with increased bioavailability of catecholamines and impaired methylation of catechol estrogens
- Increased risk of nervousness, anxiety, or panic disorder
- Increased risk of breast cancer, esp. when coupled with cumulative estrogen exposure
- Reduced pain threshold and increased risk of fibromyalgia
- Increased risk of acute coronary events if also high homocysteine or heavy coffee consumption; increased risk of hypertension, at least among men
- Increased fracture risk, esp. in men; deficient exercise has a greater adverse effect on bone density compared to other genotypes
- In bipolar patients, more rapid switching between depressive to hypomanic episodes

Treatment Options:

- Ensure adequate B6, B12, folate, magnesium, betaine, and methionine to support formation of S-adenosylmethionine and prevent elevated homocysteine; S-adenosylhomocysteine inhibits COMT activity
- Ensure adequate anti-oxidants to prevent oxidation of dopamine and pro-carcinogenic 4-hydroxyestrogens
- Caution using amphetamine-based medications, avoid chronic stress
- Exercise caution using MAO inhibitors, tricyclics, or stimulants including Ritalin®, in bipolar disorder patients
- Inferior anti-depressant response to mirtazapine (Remeron®) or paroxetine (Paxil®)
- Parkinson's patients may respond to lower doses of levodopa and benefit from vitamin B6

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

Treatment Options

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

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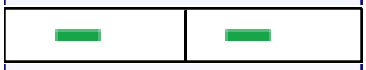
GSTP1 — Glutathione S-Transferase pi-1 : DETOXIFICATION

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

Treatment Options

- 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 (H_2O_2), 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 H_2O_2 accumulation (most risk appears to be associated with the (-/-) genotype).
- Slightly increased risk of carotid atherosclerosis.

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.

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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%.

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