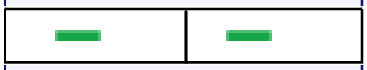
NeuroGenomic Profile (Buccal Cells)

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

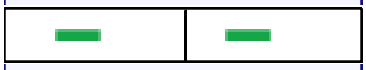
- GSTM enzyme activity is present, with normal detoxification capacity

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%.

CHECKLIST (PRIOR TO SHIPPING)

1. Cotton Swabs

❑ Swabs are returned to the original Cotton Swab Package

❑ Cotton Swabs Package is sealed in the Letter Envelope

2. Specimen Collection Label

❑ Label is filled out and adhered to the Letter Envelope

3. Test Requisition Form with Payment

❑ Test Requisition Form is complete - Test is marked, Patient's first and last name, date of birth, gender, date of collection

❑ Test requistion is placed in the collection kit envelope.

❑ Payment is included

GENOVA DIAGNOSTICS

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GENOVATIONS®

This specimen collection kit can be used for the following tests:

CardioGenomicPlus™ Profile *

DetoxiGenomic® Profile *

EstroGenomic™ Profile *

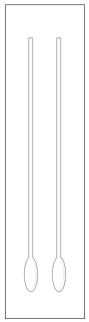
Sub Panel Estrogen Metabolism *

Sub Panel Hypercoagulation *

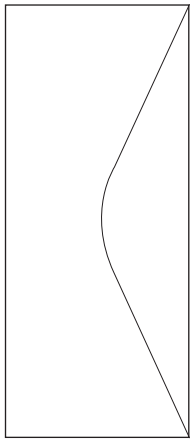
ImmunoGenomic® Profile *

NeuroGenomic™ Profile *

* Not Available in New York



Cotton Swabs and Package



Letter Envelope

SPECIMEN

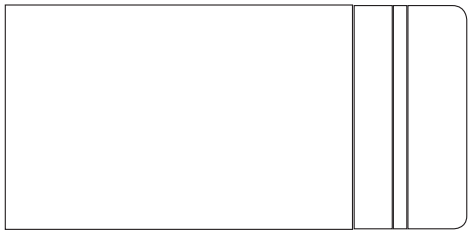
Buccal swab

COLLECTION MATERIALS

- 2 Cotton Swabs
- Returnable Cotton Swabs Package
- Letter Envelope

SHIPPING MATERIALS*

- Collection Kit Package
- Test Requisition Form
- FedEx® Billable Stamp
- Specimen Collection Label



Collection Kit Package

International shipping may vary, please see shipping instructions for more details.

IMPORTANT:

All patient specimens require two unique identifiers (***patient's name and date of birth***), as well as ***date of collection***. **Patient's first and last name, date of birth, gender,** and **date of collection** must be recorded on the **Test Requisition Form** as well as all tube(s) and/or cup(s), using a permanent marker, or the test may not be processed.

GENOVA DIAGNOSTICS

Please read all instructions carefully before beginning.

PATIENT PREPARATION

- Specimen **must be collected immediately** upon rising. **Do not practice** normal oral hygiene routine, **do not eat or drink.**
- **Prior to collection:** The night before collection, use your normal nightly routine of brushing and flossing of teeth, but **do not use mouthwash.**
- **Morning of Collection:** On the morning of collection, do not eat, brush or floss your teeth, use mouthwash, chew gum or use any tobacco, or coffee products. You may drink ONLY water before specimen collection. Just prior to collection, wash hands completely with hand soap.

SALIVA COLLECTION

1. **Write** patient's **first and last name, date of birth**, **gender** and **date of collection** on the Test Requisition Form.
   IMPORTANT: To ensure accurate test results you **MUST** provide the requested information.
2. **Peel** open the package labeled, "Sterile Cotton Tipped Applicator." *Only peel back the package far enough to remove the cotton swab applicator*. Keep the packet intact. (See Figure 1).
3. **Remove** one applicator taking care to avoid contact with the cotton tip.
4. **Open** your mouth widely and insert applicator. For at least 30 seconds, **aggressively scrape** the inside of your cheek using a back and forth, and up and down motion. Be sure to **rotate** the applicator several times to ensure the swab collects a sufficient amount of cheek cells. In addition, **swab** between the cheek and gums. (See Figure 2)
   Note: If there is not enough DNA collected on the applicator, a recollection will be required.
5. **Remove** the applicator from your mouth and allow cotton tips to air dry for 15-20 minutes (See Figure 3A) before placing it back into the original packaging, cotton swab first. (See Figure 3B)
6. **Repeat** the collection process (steps 1-3) with the second applicator on your opposite cheek.

SPECIMEN PREPARATION

1. **Place** the package containing the two collected specimen swabs into the letter envelope. Seal the letter envelope.
2. **Print name and collection date** on specimen collection label. **Place** the specimen collection label on the letter envelope.
3. **Seal** and **place** the letter envelope into the collection kit envelope.
4. **Fill** out the Test Requisition by completing all patient and billing information, including the date of collection. **Sign** the form and **place** it back inside the collection kit package.
5. **Place** FedEx billable stamp on the collection kit package and **call** 1-800-GoFedEx to schedule a pick up.

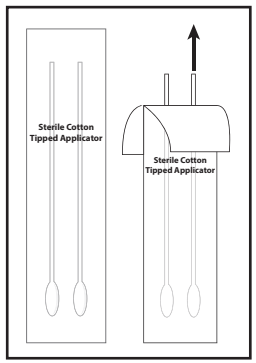


figure 1

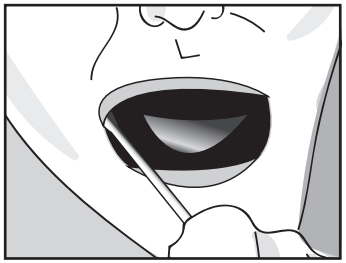


figure 2

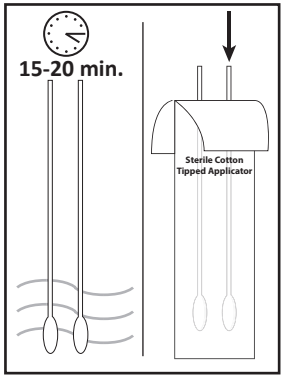
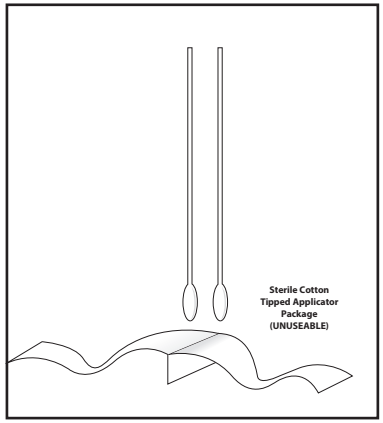


figure 3A figure 3B

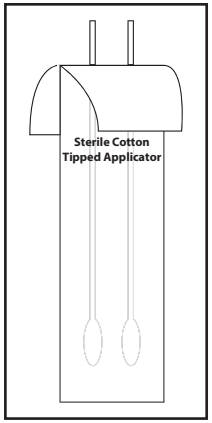
(REPEAT FIGURES 1 - 3)

NO



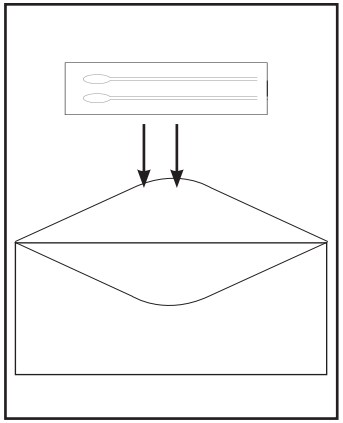
Package NOT intact
SPECIMEN UNUSABLE!!

YES



Package Intact
Specimen Usable

YES


Insert Specimens into Letter Envelope