Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | ADDRESS: | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

**TEST NAME: DetoxiGenomic® (G)**

# DetoxiGenomic™ Profile

## Detoxification & Your Health

Detoxification is the metabolic process your body uses to transform and eliminate toxins. The process can occur in two steps, called Phase I and Phase II.

- **Phase I** is our first line of defense against toxins. Enzymes in the liver act on the chemical structure of a toxin to make it easier to excrete. For some compounds, including many drugs, Phase I is all that's needed to eliminate the toxin. Other toxins are actually made more reactive after Phase I and require an additional step.

- **Phase II** is our second line of defense against toxins. Phase II further alters the chemical structure of a toxin by adding, or "conjugating," water-soluble molecules to the toxin.

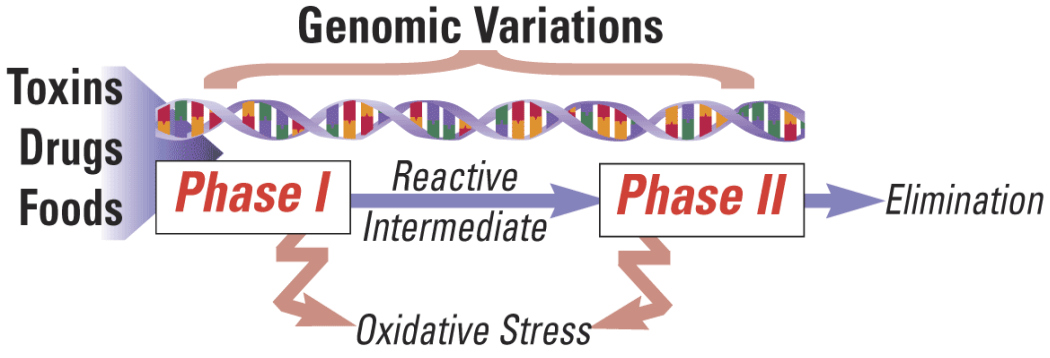
Toxic substances come from the environment, from the foods and medicines we consume, and from the body itself (natural waste products of metabolism). Examples include:

- pollution
- pesticides
- herbicides
- solvents
- pharmaceutical drugs
- charbroiled foods

**DetoxiGenomic™ Profile Personalized for**

Sample Report

Nordic Labs




Your DetoxiGenomic™ Profile identifies genetic variations that may affect your ability to detoxify specific toxins, medications, and even foods. Working with your healthcare provider, you can develop a personalized treatment plan that matches your environment to your genes in order to optimize your health.

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | ADDRESS: | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

**TEST NAME: DetoxiGenomic® (G)**

# *DetoxiGenomic™ Profile (Buccal Cells)*

*Patient's Copy*

## *PHASE I Detoxification: The First Line of Defense*

In Phase I detoxification, enzymes, known collectively as the cytochrome P-450 system, use oxygen to modify toxic compounds, drugs, or steroid hormones. Many toxins must undergo Phase II detoxification after a reactive site has been formed. Because there are many different toxic compounds the body might encounter, there are many variants of Phase I enzymes.

| *Cytochrome P-450* | |
|---|---|
| Result | Gene |
| 🔴 | CYP1A1 * |
| 🔴 | CYP1B1 * |
| ✔ | CYP2A6 |
| 🔴 | CYP2C9 * |
| ✔ | CYP2C19 * |
| ✔ | CYP2D6 |
| ✔ | CYP3A4 * |

**Your Results:** Polymorphisms (SNPs) in the genes cod ng for a particular enzyme can increase or, more commonly, decrease the activity of that enzyme. Both increased and decreased activity may be harmful. Increased Phase I clearance without increased clearance in Phase II can lead to the formation of toxic intermediates that may be more toxic than the original toxin. Decreased Phase I clearance will cause toxic accumulation in the body. Adverse reactions to drugs are often due to a decreased capacity for clearing them from the system.

## General Therapies to Improve Detoxification:

Foods that generally improve Phase I detoxification and as well improve the efficiency of Phase II conjugation are generally recommended for individuals with CYP SNPs. These include most vegetables and fruits, but especially cruciferous vegetables (broccoli, Brussels sprouts, cauliflower, watercress, and cabbage), garlic, onions, soy, grapes, berries, green and black tea, and many herbs and spices like rosemary, basil, turmeric, cumin, poppy seeds, and black pepper. Indeed, improving Phase I and Phase II detoxification helps explain why vegetables and fruits protect against many cancers.

| Key | | |
|---|---|---|
| | ✔ | Optimal genomic potential - no polymorphism detected |
| | 🔴 | Polymorphism detected in this enzyme, increasing your susceptibility to toxins, if exposed |
| | * | Multiple SNP locations were evaluated for these genes |
| | NR | See commentary if applicable |

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | ADDRESS: | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Patient's Copy*

# *PHASE II Detoxification: Conjugation of Toxins and Elimination*

In Phase II detoxification, large water-soluble molecules are added to toxins, usually at the reactive site formed by Phase I reactions. After Phase II modifications, the body is able to eliminate the transformed toxins in the urine or the feces (through the bile).

### *Methylation*

| Result | Gene | SNP Location | Affects |
|---|---|---|---|
| ++ | COMT | V158M | Liver/Gut |

**Your Results:** Catechol-O-methyl transferase is the enzyme primarily responsible for breaking down the neurotransmitters dopamine, epinephrine, and norepinephrine.

### *Acetylation (N-acetyltransferase)*

SLOW METABOLIZER POLYMORPHISM

| Result | Gene | SNP Location | Affects |
|---|---|---|---|
| −− | NAT1 | R64W | All Cells |
| −− | NAT1 | R187Q | Liver/Gut |
| −− | NAT2 | I114T | Liver/Gut |
| +− | NAT2 | R197Q | Liver/Gut |
| +− | NAT2 | G286E | Liver/Gut |
| −− | NAT2 | R64Q | Liver/Gut |

FAST METABOLIZER POLYMORPHISM

| | | | |
|---|---|---|---|
| −− | NAT2 | K268R | Liver/Gut |

**Your Results:** N-acetyl Transferase detoxifies many environmental toxins, including tobacco smoke and exhaust fumes. Polymorphisms can result in slower than normal or faster than normal addition of an acetyl group to these toxins. Slow acetylators have a build up of toxins in the system and rapid acetylators add acetyl groups so rapidly that they make mistakes in the process. Both slow and rapid acetylators are at increased risk for toxic overload if they are exposed to environmental toxins. If the toxin exposure is reduced, the risk is reduced.

### *Glutathione Conjugation (Glutathione s-transferase)*

| Result | Gene | Location | Affects |
|---|---|---|---|
| PRESENT | GSTM1 | 1p13.3 | Liver/Kidney |
| −− | GSTP1 | I105V | Brain/Skin |
| −− | GSTP1 | A114V | Brain/Skin |

**Your Results:** Glutathione-S-transferase detoxifies many water-soluble environmental toxins, including many solvents, herbicides, fungicides, lipid peroxides, and heavy metals (e.g., mercury, cadmium, and lead). The various forms of GST work together to eliminate toxins. Decreased glutathione conjugation capacity may increase toxic burden and increase oxidative stress.

### *Oxidative Protection*

| Result | Gene | SNP Location | Affects |
|---|---|---|---|
| −− | SOD1 | G93A | Cytosol |
| −− | SOD1 | A4V | Cytosol |
| +− | SOD2 | A16V | Mitochondria |

**Your Results:** Superoxide Dismutase is an enzyme that protects cells from increased oxidative stress and free radical damage to cell structures like membranes, mitochondria, DNA, and proteins.

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)*

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | ADDRESS: | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Patient's Copy*

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%.

# TEST NAME: DetoxiGenomic® (G)

*Patient's Copy*

**Phase I Detoxification** (Commentary for polymorphisms may not appear in this section unless the polymorphism has been indicated to have impaired activity.)

## CYP1A1

There are 2 SNPs measured in this gene that predict risk. In this patient, the variants MspI and I462V are both positive. The commentary below reflects these results.

**Health Implications:** Cytochrome P450 1A1 is responsible for the metabolism of estrogen and certain medications, as well as the activation of numerous environmental toxins such as polycyclic aromatic hydrocarbons (e.g., cigarette smoke, car exhaust, charbroiled meats) and chlorinated benzenes (solvents). Polymorphisms convey a higher capacity for induction with toxin exposure, thus greater activation and potential toxicity of these compounds.

**Minimizing Risk:** Do not smoke. Minimize exposure to charbroiled and well-done meats, tobacco smoke, car and diesel exhaust, industrial solvents, dioxin-contaminated meats and dairy, incineration, and PVC plastics. Excess exposure to these compounds can generate free radicals and reactive compounds that can increase your long-term risk of developing some cancers. Emphasize a diet rich in anti-oxidants (colorful fruits and vegetables). Extra protection may be afforded by cruciferous vegetables (e.g., broccoli and cauliflower) and green tea, especially in smokers.
**Physician Recommendations:**

## CYP1B1

There are 2 SNPs measured for this gene that predict risk. In this patient, the specific variants are L432V +/+ and N453S negative. The commentary below reflects these results.

**Health Implications:** Cytochrome P450 1B1 is respons ble for the 4-hydroxylation of estrogen as well as the activation of common environmental toxins such as polycyclic aromatic hydrocarbons (e.g., products from cigarette smoke, car exhaust, and charbroiled foods), polychlorinated biphenyls (e.g., PCBs), and aflatoxin B1. Polymorphisms convey a higher capacity for induction with toxin exposure, thus greater activation and potential toxicity of these compounds and greater production of 4-hydroxyestrogens.

**Minimizing Risk:** Do not smoke. Minimize exposure to xenobiotics (e.g., polycyclic aromatic hydrocarbons), also xenoestrogens (e.g., organochlorines), which tend to increase CYP1B1 activity. Eat a diet rich in antioxidants; consider supplementation. Redirect estrogen metabolism away from 4-hydroxylation with cruciferous vegetables and/or agents such as indole 3-carbinol (I3C), diindolylmethane (DIM), fish oils, or rosemary.
**Physician Recommendations:**

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | ADDRESS: | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Patient's Copy*

### CYP2C9

**Health Implications** : Cytochrome P450 2C9 is involved in the metabolism of many drugs including blood thinners like Coumadin®. Polymorphisms may prevent the normal metabolism of these drugs and side effects are possible.

**Minimizing Risks:** Your health care provider has a list of drugs cleared through CYP2C9. Consult your physician. You may still need these drugs, but your physician may opt to prescribe a smaller therapeutic dose. Should you need to be placed on a blood thinning agent in the future, make sure your physician knows you have a genetic polymorphism that impairs your ability to break down Coumadin®. If you are taking aspirin to reduce the risk of colon cancer, switch to a non-aspirin alternative.

**Physician Recommendations:**

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | ADDRESS: | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Patient's Copy*

**Phase II Detoxification** commentary is provided only for polymorphisms with known health implications.

| | | |
|---|---|---|
| + + | **COMT** | V158M |

**Health Implications:** 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. A COMT polymorphism results in a 3-4-fold reduction in COMT enzyme activity, resulting in decreased methylation. A tendency toward higher catecholamines increases the risk for nervousness/anxiety, PTSD, fibromyalgia and chronic pain syndromes. Pain threshold is reduced, which is exacerbated by one's experience of pain. Risk may also be increased for fracture (esp. in men), and for substance addiction including alcoholism. While cognitive stability (e.g., ability to focus) tends to be strong, cognitive flexibility (e.g., ability to adapt to external changes) is less.

**Minimizing Risks:** Minimize stress, since catecholamines levels may already be high. Ensure adequate intake of B6, B12, folate, magnesium, betaine, and methionine to support formation of S-adenosylmethionine and prevent elevated homocysteine; S-adenosylhomocysteine inhibits COMT.
**Physician Recommendations:**

| | | |
|---|---|---|
| + - | **NAT2** | R197Q |
| + - | **NAT2** | G286E |

**Health Implications:** N-acetyltransferase 1 is found in extra-hepatic tissues, while NAT2 is found predominantly in the liver and the gut. Both are used in the Phase II acetylation of numerous environmental toxins, including heterocyclic aromatic amines. Slow acetylators do not clear toxins well and the resulting increased total toxic burden can increase the risk of lung, colon, breast, bladder, and head and neck cancers, though results have not been consistent in all studies. Urinary bladder cancer appears to have the most consistent association with slow acetylation.

**Minimizing Risk:** If you smoke, stop. Your risk of lung cancer is substantially higher than someone with normal NAT activity. Even occasional smoking or exposure to second hand smoke is harmful. Liberal consumption of most vegetables and fruits but especially cruciferous vegetables (broccoli, Brussels sprouts, cauliflower, watercress, and cabbage), garlic, onions, soy, grapes and berries will increase Phase II efficiency, including acetylation.
**Physician Recommendations:**

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | | |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| GENDER: | Female | TESTED: | dd/mm/yyyy | ADDRESS: | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Patient's Copy*

| | | | |
|---|---|---|---|
| **PRESENT** | **GSTM1** | 1p13.3 | |
| **- -** | **GSTP1** | I105V | |

**Health Implications:** Glutathione S-transferases (GST) are responsible for detoxifying certain products of oxidative stress and a variety of electrophilic xenobiotics and carcinogens such as solvents, herbicides, pesticides, polycyclic aromatic hydrocarbons, steroids, and heavy metals. GSTM1 is located primarily in the liver, whereas GSTP1 is located primarily in the brain and lungs.

The test indicates that the GSTM1 gene is present, although it is not clear whether the gene is present on one or both chromosomes. This suggests normal GSTM1 enzyme activity and hepatic detoxification of xenobiotics and toxic metals.

GSTP1 polymorphisms are associated with either higher or lower enzyme activity, depending on the exposure. Although this I105V genotype is associated with less overall risk, it has still been associated with slightly increased risk of some cancers (especially with cigarette smoke exposure), atopy, xenobiotic-induced asthma, and COPD.

**Minimizing Risk:** Regardless of genotype, increasing the body's production of glutathione (GSH) will reduce oxidative stress and afford greater protection against a wide array of toxins. GSH precursors and cofactors include methionine, N-acetylcysteine, glutamine, glycine, magnesium, and pyridoxal-5-phosphate (B6). Allium vegetables (e.g., onions, leeks, garlic) and cruciferous vegetables (e.g., broccoli, cauliflower, and cabbage) can increase GST activity. Most importantly, minimize exposure to cigarette smoke, charred food, herbicides, fungicides, insect sprays, industrial solvents, and toxic metals.

**Physician Recommendations:**

| | | |
|---|---|---|
| **+-** | **SOD2** | A16V |

**Health Implications:** Superoxide dismutase is the primary anti-oxidant enzyme within the mitochondria of cells (where most of our energy is made). SOD2 converts reactive oxygen species into less reactive hydrogen peroxide. Polymorphisms in SOD2 (+/- and +/+) are associated with reduced SOD activity. While this may increase some risk of oxidative stress, more clinical correlations have been observed for the (-/-) genotype. This genotype has specifically been associated with increased risk of cardiomyopathy.

**Minimizing Risk:** Although this genotype is less sensitive to antioxidant status compared to the (-/-) genotype, liberal consumption of dietary antioxidants in colorful vegetables and fruits is still recommended. Broad-spectrum antioxidant supplements may also be helpful, as well as manganese, which serves as a cofactor for SOD2. Consult your health care provider to find the supplement regimen that best fits your overall health anti-oxidant needs.

**Physician Recommendations:**

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | ADDRESS: | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

# *DetoxiGenomic™ Profile (Buccal Cells)*

*Physician's Copy*

## *PHASE I Detoxification: The First Line of Defense*

In Phase I detoxification, enzymes, known collectively as the cytochrome P-450 system, use oxygen to modify toxic compounds, drugs, or steroid hormones. Many toxins must undergo Phase II detoxification after a reactive site has been formed. Because there are many different toxic compounds the body might encounter, there are many variants of Phase I enzymes.

(CYP1A1) detoxifies polycyclic aromatic hydrocarbons (PAHs) produced from the combustion of organic materials (exhaust fumes, charbroiled meats, etc.).

(CYP1B1) is involved in the 4-hydroxylation of estrogen.

(CYP2A6) detoxifies nitrosamines and nicotine

(CYP2C9) detoxifies coumadin® and sulfonylureas.

(CYP2C19) detoxifies proton-pump inhibitors (e.g. , prilosec®) and many anticonvulsants (e.g., valium®).

(CYP2D6) detoxifies ~20% of all prescription drugs including tricyclics, MAOIs, SSRIs, opiates, anti-arrhythmics, beta-blockers, Cimetidine, etc.

(CYP3A4) detoxifies over 50% of all prescription medications and most steroid hormones.

| *Cytochrome P-450* | |
|---|---|
| Result | Gene |
| ● | **CYP1A1** * |
| ● | **CYP1B1** * |
| ✔ | **CYP2A6** |
| ● | **CYP2C9** * |
| ✔ | **CYP2C19** * |
| ✔ | **CYP2D6** |
| ✔ | **CYP3A4** * |

**Your Results:** Polymorphisms (SNPs) in the genes coding for a particular enzyme can increase or, more commonly, decrease the activity of that enzyme. Both increased and decreased activity may be harmful. Increased phase I clearance without increased clearance in Phase II can lead to the formation of toxic intermediates that may be more toxic than the original toxin. Decreased Phase I clearance will cause toxic accumulation in the body. Adverse reactions to drugs are often due to a decreased capacity for clearing them from the system.

Use of H2 blockers (e.g. Cimetidine) should be avoided as these bind to the heme-containing reactive site of all CYPs inhibiting binding to toxins.

## General Therapies to Improve Detoxification:

Foods that generally improve Phase I detoxification and as well improve the efficiency of Phase II conjugation are generally recommended for individuals with CYP SNPs. These include most vegetables and fruits, but especially cruciferous vegetables (broccoli, Brussels sprouts, cauliflower, watercress, and cabbage), garlic, onions, soy, grapes, berries, green and black tea, and many herbs and spices like rosemary, basil, turmeric, cumin, poppy seeds, and black pepper. Indeed, improving Phase I and Phase II detoxification helps explain why vegetables and fruits protect against many cancers.

| Key | | |
|---|---|---|
| | ✔ | Optimal genomic potential - no polymorphism detected |
| | ● | Polymorphism detected in this enzyme, increasing your susceptibility to toxins, if exposed |
| | * | Multiple SNP locations were evaluated for these genes |
| | NR | See commentary if applicable |

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | | |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| GENDER: | Female | TESTED: | dd/mm/yyyy | ADDRESS: | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Physician's Copy*

# *PHASE II Detoxification: Conjugation of Toxins and Elimination*

In Phase II detoxification, large water-soluble molecules are added to toxins, usually at the reactive site formed by Phase I reactions. After Phase II modifications, the body is able to eliminate the transformed toxins in the urine or the feces (through the bile).

(COMT SNP) higher risk for depression, bipolar disorder, ADHD and alcoholism.

### *Methylation*

| Result | Gene | SNP Location | Affects |
|---|---|---|---|
| ++ | COMT | V158M | Liver/Gut |

**Your Results:** Catechol-O-methyl transferase is the enzyme primarily responsible for breaking down the neurotransmitters dopamine, epinephrine, and norepinephrine.

(NAT SNP) both slow and rapid acetylators are at increased risk for developing lung, colon, bladder, or head & neck cancer.

### *Acetylation (N-acetyltransferase)*

SLOW METABOLIZER POLYMORPHISM

| Result | Gene | SNP Location | Affects |
|---|---|---|---|
| −− | NAT1 | R64W | All Cells |
| −− | NAT1 | R187Q | Liver/Gut |
| −− | NAT2 | I114T | Liver/Gut |
| +− | NAT2 | R197Q | Liver/Gut |
| +− | NAT2 | G286E | Liver/Gut |
| −− | NAT2 | R64Q | Liver/Gut |

FAST METABOLIZER POLYMORPHISM

| | | | |
|---|---|---|---|
| −− | NAT2 | K268R | Liver/Gut |

**Your Results:** N-acetyl Transferase detoxifies many environmental toxins, including tobacco smoke and exhaust fumes. Polymorphisms can result in slower than normal or faster than normal addition of an acetyl group to these toxins. Slow acetylators have a build up of toxins in the system and rapid acetylators add acetyl groups so rapidly that they make mistakes in the process. Both slow and rapid acetylators are at increased risk for toxic overload if they are exposed to environmental toxins. If the toxin exposure is reduced, the risk is reduced.

(GST SNP) The GST isoforms (M1, P1, and T1) are more or less prevalent in various tissues; all catalyze the conjugation of electrophilic compounds with glutathione. Defects in GST activity can contribute to fatigue syndromes, and to various cancers throughout the body.

### *Glutathione Conjugation (Glutathione s-transferase)*

| Result | Gene | Location | Affects |
|---|---|---|---|
| PRESENT | GSTM1 | 1p13.3 | Liver/Kidney |
| −− | GSTP1 | I105V | Brain/Skin |
| −− | GSTP1 | A114V | Brain/Skin |

**Your Results:**
Glutathione-S-transferase detoxifies many water-soluble environmental toxins, including many solvents, herbicides, fungicides, lipid peroxides, and heavy metals (e.g., mercury, cadmium, and lead). The various forms of GST work together to eliminate toxins. Decreased glutathione conjugation capacity may increase toxic burden and increase oxidative stress.

(SOD SNP) SOD1 is present in the cytosol; SOD2 is present in the mitochondria . Changes in the SOD enzyme are associated with changes in risk for neurodegenerative disorders like ALS.

### *Oxidative Protection*

| Result | Gene | SNP Location | Affects |
|---|---|---|---|
| −− | SOD1 | G93A | Cytosol |
| −− | SOD1 | A4V | Cytosol |
| +− | SOD2 | A16V | Mitochondria |

**Your Results:** Superoxide Dismutase is an enzyme that protects cells from increased oxidative stress and free radical damage to cell structures like membranes, mitochondria, DNA, and proteins.

**Key**

| | | |
|---|---|---|
| −− | Neither chromosome carries the genetic variation. | Homozygous negative or wild type |
| +− | One chromosome (of two) carries the genetic variation. | Heterozygous positive |
| ++ | Both chromosomes carry the genetic variation. | Homozygous positive |

*(You inherit one chromosome from each parent)*

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | ADDRESS: | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Physician's Copy*

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.

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

## TEST NAME: DetoxiGenomic® (G)

*Physician's Copy*

**Phase I Detoxification** (Commentary for polymorphisms may not appear in this section unless the polymorphism has been indicated to have impaired activity.)

**Note:** In the following charts, substrates, inhibitors, and inducers are listed for each cytochrome P450 enzyme (Phase I) included in the DetoxiGenomic Profile.
**Substrates** are compounds that are metabolized by that enzyme. The metabolism of some of these compounds is shared by other P450 enzymes (refer to chart).
**Inhibitors** may or may not be substrates of that enzyme, but will reliably reduce that enzyme's activity if present.
**Inducers** also may or may not be substrates, but will tend to increase the enzyme's activity.

## TEST NAME: DetoxiGenomic® (G)

*Physician's Copy*

### CYP1A1

There are 2 SNPs measured in this gene that predict risk. In this patient, the specific variants for MspI and I462V are both positive. The commentary below reflects these results. Please refer to the drug pathway chart on the following page.

**Health Implications:** Cytochrome P450 1A1 is responsible for the metabolism of estrogen and certain medications, as well as the activation of numerous environmental toxins such as polycyclic aromatic hydrocarbons (e.g., cigarette smoke, car exhaust, charbroiled meats) and chlorinated benzenes (solvents). Polymorphisms convey a higher capacity for induction with toxin exposure, thus greater activation and potential toxicity of these compounds.
The 2-hydroxyestrogens produced by CYP1A1 are protective against breast cancer when further methylated, but may be carcinogenic when not. Hyperinduction of CYP1A1 also generates mutagenic metabolites, increasing the risk of cancers of the lung, ovary (in smokers), prostate, and colon (in smokers). This SNP has been associated with both decreased and increased risk (in smokers) of breast cancer. Female smokers with the SNP show higher levels of DNA damage than either non-smokers or women without the SNP. The CYP1A1 SNP is also associated with moderately increased risk of systemic lupus erythematosus and endometriosis (although studies are inconsistent).

**Minimizing Risk:** Do not smoke. Minimize exposure to charbroiled and well-done meats, tobacco smoke, car and diesel exhaust, industrial solvents, dioxin-contaminated meats and dairy, incineration, and PVC plastics. Excess exposure to these compounds can generate free radicals and reactive compounds that can increase your long-term risk of developing some cancers. Emphasize a diet rich in anti-oxidants (colorful fruits and vegetables). Extra protection may be afforded by cruciferous vegetables (e.g., broccoli and cauliflower) and green tea, especially in smokers.
DNA damage from reactive intermediates may also be minimized by rosemary, epigallocatechin gallate (EGCG), curcumin, resveratrol, genistein, hops, vitamin E, and DHEA. Support glutathione conjugation with precursors and cofactors.

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | ADDRESS: | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Physician's Copy*

| Substrates | | Inhibitors | Inducers |
|---|---|---|---|
| Chlorinated Benzenes | Ondansetron | Alpha-naphthoflavone | ***Polycyclic Aromatic Hydrocarbons:*** |
| Heterocyclic amines | Phenacetin | Amiodarone | E.g., cigarette smoke, charbroiled foods |
| Polycyclic aromatic hydrocarbons, (e.g., benzo(a)pyrene) | Propanolol | Cimetidine | ***Heterocyclic amines:*** |
| | Riluzole | Fluoroquinolones | E.g., fried meat |
| | Ropivacaine | Fluvoxamine | 3-methylcholanthrene (carcinogen) |
| Acetaminophen | Sparteine (mostly 2D6) | Furafylline | |
| Acetanilide | Tacrine | Interferon | Atorvastatin |
| Antipyrine | Tamoxifen | Mexiletine | Beta-naphthoflavone |
| Bufuralol | Testosterone | Methoxsalen | Flutamide |
| Caffeine | Theophylline | Mibefradil | Leflunomide |
| Chlorzoxazone | Verlukast | Propofol | Methyl cholanthrene |
| Coumarin activation (parts of) | Warfarin | Quinidine | Minodipine |
| Cyclobenzaprine (Flexeril) | Zoxazolamine | Safrole (e.g., root beer) | Omeprazole |
| 7-ethoxyresorufin | | Tacrine | |
| Dextromethorphan | | THC | Cruciferous vegetables (including I3C and DIM) |
| Diethylstilbestrol | | | |
| Erlotinib (minor) | | Apigenin | |
| Estradiol | | Benzoflavone | |
| Gefitinib | | Quercetin | |
| Granisetron | | Grapefruit | |
| Haloperidol | | Turmeric/Curcumin (animal & in-vitro studies) | |
| Lidocaine | | | |

**Physician Recommendations:**

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | ADDRESS: | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Physician's Copy*

### CYP1B1

There are 2 SNPs measured for this gene that predict risk. In this patient, the specific variants are L432V +/+ and N453S negative. The commentary below reflects these results.

**Health Implications:** Cytochrome P450 1B1 is responsible for the 4-hydroxylation of estrogen as well as the activation of common environmental toxins such as polycyclic aromatic hydrocarbons (e.g., products from cigarette smoke, car exhaust, and charbroiled foods), polychlorinated biphenyls (e.g., PCBs), and aflatoxin B1. Polymorphisms convey a higher capacity for induction with toxin exposure, thus greater activation and potential toxicity of these compounds and greater production of 4-hydroxyestrogens.
Hyperinduction can generate oxidative stress and the 4-hydroxyestrogens may convert to quinone compounds that can cause DNA damage in breast tissue. Polymorphisms have been associated with lower 2:16α-hydroxyestrone ratios and increased risk of breast cancer, especially if xenobiotic exposure, high body mass index, long-term HRT, or concomitant CYP1A1 polymorphism. Risk is also increased for cancers of the ovary, prostate, lung and head & neck, especially in smokers.

**Minimizing Risk:** Do not smoke. Minimize exposure to xenobiotics (e.g., polycyclic aromatic hydrocarbons), also xenoestrogens (e.g., organochlorines), which tend to increase CYP1B1 activity. Eat a diet rich in antioxidants; consider supplementation. Redirect estrogen metabolism away from 4-hydroxylation with cruciferous vegetables and/or agents such as indole 3-carbinol (I3C), diindolylmethane (DIM), fish oils or rosemary.
Use caution with long-term HRT, especially conjugated equine estrogens which are preferentially 4-hydroxylated.

| Substrates | | Inhibitors | Inducers |
|---|---|---|---|
| Polycyclic aromatic hydrocarbons, (e.g., benzo(a)pyrene)<br><br>**Antidepressants:**<br>Amitryiptyline (Elavil)<br>Clomipramine (Anafranil)<br>Imipramine (Tofranil)<br><br>Acetaminophen (NAPQI)<br>Caffeine<br>Clozapine (Clazaril)<br>Coumarin activation<br>Estradiol, Estrone (4-hydroxylation) | Heterocyclic amines<br>Naproxen<br>Propranolol (Inderal)<br>Resveratrol<br>Tacrine (Cognex)<br>Testosterone<br>Theophylline | Cimetidine<br>Ciprofloxacin (Cipro)<br>Erythromycin<br>Fluvoxamine (Luvox)<br>Pyrene<br>Ticlopidine<br><br>Grapefruit juice (naringenin)<br>Ginseng (possible) | Omeprazole (Prilosec)<br>Phenytoin (Dilantin)<br>Phenobarbital<br>Rifampin<br><br>***Polycyclic Aromatic Hydrocarbons:***<br>Cigarette smoke<br>Charbroiled foods |
| CYP1B1: Up regulator - is involved in the 4-hydroxylation of estrogen. | | | |

**Physician Recommendations:**

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | ADDRESS: | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Physician's Copy*

### CYP2C9

**Health Implications** : Cytochrome P450 2C9 is involved in the metabolism of many drugs including blood thinners like Coumadin ®. Polymorphisms may prevent the normal metabolism of these drugs and side effects are possible. Please refer to the drug pathway chart on the following page.

**Minimizing Risks:** Your health care provider has a list of drugs cleared through CYP2C9. Consult your physician. You may still need these drugs, but your physician may opt to prescribe a smaller therapeutic dose. Should you need to be placed on a blood thinning agent in the future, make sure your physician knows you have a genetic polymorphism that impairs your ability to break down Coumadin ®. If you are taking aspirin to reduce the risk of colon cancer, switch to a non-aspirin alternative.

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | ADDRESS: | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Physician's Copy*

### Substrates

**NSAIDs**
Diclofenac
Ibuprofen
Lomoxicam
Meloxicam
S-Naproxen
Piroxicam
Suprofen

**Oral Hypoglycemic Agents**
Tolbutamide
Glipizide

**Angiotensin II Blockers**
Losartan
Irbesartan

**Sulfonylureas**
Glyburide/glibenclamide
Glipizide
Glimepiride
Tolbutamide

**Miscellaneous**
Alosetron (Lotronex)
Amitriptyline (Elavil) (demethylation)
Angiotensin
Carvedilol
Celecoxib
Chloramphenicol
Clomipramine
Coumadin (Warfarin)
Desogestrel
Diazepam
Diclofenac
Dronabinol
Etravirine

**Miscellaneous Continued**
Febuxostat
Fluoxetine
Flurbiprofen
Fluvastatin
Formoterol
Glyburide
Hexobarbital
Hyzaar
Ibuprofen
Imipramine (Tofranil)
Indomethacin
Isoniazid
Nateglinide
Phenobarbital
Phenytoin (Dilantin)
Piroxicam
Retinoids
Rosiglitazone
Rosuvastatin (Crestor)
Sildenafil (Viagra)
Sulfa Drugs
Sulfaphenazole
Suprofen
Tamoxifen
THC (marijuana)
Torsemide (Demadex)
Valdecoxib
S-warfarin (active)
Zolpidem (Ambien, Edluar) (mostly CYP3A4)

### Inhibitors

**Anti-depressants**
Fluvoxamine (Luvox)
Paroxetine (Paxil)
Sertraline (Zoloft)
Fluoxetine (Prozac)

**Azole Antifungals**
Itraconazole (Sporonox)
Ketoconazole (Nizoral)
Fluconazol (Diflucan)
Miconazole (Nystatin)
Voriconazole (Vfend)

**Miscellaneous**
Amiodarone
Cimetidine (Tagamet)
Chloram-phenicol
Clopidogrel (Plavix)
Delavirdine
Disulfram
Efavirenz
Etravirine
Fenofibrate
Fluorouracil
Fluvastatin
Gemfibrozil

**Miscellaneous Continued**
Imatinib
Isoniazid
Leflunomide
Lovastatin
Metronidazole (Flagyl)
Omeprazole
Phenylbutazone
Phenytoin (Dilantin)
Probenicid
Retonavir (Norvir)
Sulfa-methoxazole-Trimethoprim (Bactrim)
Sulfaphenazole
Sulfinpyrazone
Teniposide
Ticlopidine
Valproic acid (Depakote)
Zafirlukast

Echinacea
Garlic (possible)
Kava kava
Milk thistle (in-vitro/ probably insignificant in-vivo)
Saw palmetto (in-vitro)
St. John's wort (in-vitro studies)

### Inducers

Aminoglutethimide
Aprepitant
Barbiturates
Bosentan
Carbamazepine
Ethanol
Griseovulfin
Phenobarbital
Phenytoin
Primidone
Rifabutin
Rifampin
Rifapentine
Secobarbital

Continued...

## TEST NAME: DetoxiGenomic® (G)

*Physician's Copy*

### CYP2C9

Continued...

CYP2C9: Down regulator - detoxifies coumarin and suflonylureas.
Note: Individuals with deficient CYP2C9 activity may be anti-coagulated on 0.5mg of coumadin/day, as they cannot efficiently clear S-coumadin. ARBs in these people may be ineffective because a pro-drug like losartan may be poorly activated.

**Physician Recommendations:**

## TEST NAME: DetoxiGenomic® (G)

*Physician's Copy*

**Phase II Detoxification** commentary is provided only for polymorphisms with known health implications.

**+ + COMT** V158M

**Health Implications:** 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. A COMT polymorphism results in a 3-4-fold reduction in COMT enzyme activity, resulting in decreased methylation. A tendency toward higher catecholamines increases the risk for nervousness/anxiety, PTSD, fibromyalgia and chronic pain syndromes. Pain threshold is reduced, which is exacerbated by one's experience of pain. Risk may also be increased for fracture (esp. in men), and for substance addiction including alcoholism. While cognitive stability (e.g., ability to focus) tends to be strong, cognitive flexibility (e.g., ability to adapt to external changes) is less.
Risk of anxiety appears to be higher in patients with a history of childhood trauma. Acute or chronic stress may compromise working memory, decision-making ability, or mood. Studies on breast cancer are mixed; risk may be increased in Asian women, but marginally decreased in Caucasian women.

**Minimizing Risks:** Minimize stress, since catecholamines levels may already be high. Ensure adequate intake of 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. This genotype might have a superior response to SSRI antidepressants (mixed studies). In children with ADHD, methylphenidate (Ritalin®) may be less effective (mixed studies).
**Physician Recommendations:**

**+ - NAT2** R197Q
**+ - NAT2** G286E

**Health Implications:** N-acetyltransferase 1 is found in extra-hepatic tissues, while NAT2 is found predominantly in the liver and the gut. Both are used in the Phase II acetylation of numerous environmental toxins, including heterocyclic aromatic amines. Slow acetylators do not clear toxins well and the resulting increased total toxic burden can increase the risk of lung, colon, breast, bladder, and head and neck cancers, though results have not been consistent in all studies. Urinary bladder cancer appears to have the most consistent association with slow acetylation.

**Minimizing Risk:** If you smoke, stop. Your risk of lung cancer is substantially higher than someone with normal NAT activity. Even occasional smoking or exposure to second hand smoke is harmful. Liberal consumption of most vegetables and fruits but especially cruciferous vegetables (broccoli, Brussels sprouts, cauliflower, watercress, and cabbage), garlic, onions, soy, grapes and berries will increase Phase II efficiency, including acetylation.
**Physician Recommendations:**

Nordic Laboratories

| | | | | | |
|---|---|---|---|---|---|
| PATIENT: | **Sample Report** | | | TEST REF: | **TST-##-#####** |
| TEST NUMBER: | ########## | COLLECTED: | dd/mm/yyyy | PRACTITIONER: | **Nordic Laboratories** |
| PATIENT NUMBER: | ########## | RECEIVED: | dd/mm/yyyy | | |
| GENDER: | Female | TESTED: | dd/mm/yyyy | ADDRESS: | |
| AGE: | 28 | | | | |
| DATE OF BIRTH: | dd-mm-yyyy | | | | |

## TEST NAME: DetoxiGenomic® (G)

*Physician's Copy*

| | | | |
|---|---|---|---|
| **PRESENT** | **GSTM1** | 1p13.3 | |
| **- -** | **GSTP1** | I105V | |

**Health Implications:** Glutathione S-transferases (GST) are responsible for detoxifying certain products of oxidative stress and a variety of electrophilic xenobiotics and carcinogens such as solvents, herbicides, pesticides, polycyclic aromatic hydrocarbons, steroids, and heavy metals. GSTM1 is located primarily in the liver, whereas GSTP1 is located primarily in the brain and lungs.

The test indicates that the GSTM1 gene is present, although it is not clear whether the gene is present on one or both chromosomes. This suggests normal GSTM1 enzyme activity and hepatic detoxification of xenobiotics and toxic metals.

GSTP1 polymorphisms are associated with either higher or lower enzyme activity, depending on the exposure. Although this I105V genotype is associated with less overall risk, it has still been associated with slightly increased risk of some cancers (especially with cigarette smoke exposure), atopy, xenobiotic-induced asthma, and COPD.

**Minimizing Risk:** Regardless of genotype, increasing the body's production of glutathione (GSH) will reduce oxidative stress and afford greater protection against a wide array of toxins. GSH precursors and cofactors include methionine, N-acetylcysteine, glutamine, glycine, magnesium, and pyridoxal-5-phosphate (B6). Allium vegetables (e.g., onions, leeks, garlic) and cruciferous vegetables (e.g., broccoli, cauliflower, cabbage) can increase GST activity. Most importantly, minimize exposure to cigarette smoke, charred food, herbicides, fungicides, insect sprays, industrial solvents, and toxic metals.

**Physician Recommendations:**

| | | |
|---|---|---|
| **+-** | **SOD2** | A16V |

**Health Implications:** Superoxide dismutase is the primary anti-oxidant enzyme within the mitochondria of cells (where most of our energy is made). SOD2 converts reactive oxygen species into less reactive hydrogen peroxide. Polymorphisms in SOD2 (+/- and +/+) are associated with reduced SOD activity. While this may increase some risk of oxidative stress, more clinical correlations have been observed for the (-/-) genotype. This genotype has specifically been associated with increased risk of cardiomyopathy.

**Minimizing Risk:** Although this genotype is less sensitive to antioxidant status compared to the (-/-) genotype, l beral consumption of dietary antioxidants in colorful vegetables and fruits is still recommended. Broad-spectrum antioxidant supplements may also be helpful, as well as manganese, which serves as a cofactor for SOD2. Consult your health care provider to find the supplement regimen that best fits your overall health anti-oxidant needs.

**Physician Recommendations:**